

DISSERTATION

ANTERIOR CRUCIATE LIGAMENT INJURY AS A DRIVER OF POST-TRAUMATIC
OSTEOARTHRITIS: MECHANISMS AND OUTCOMES ELUCIDATED FROM
PRECLINICAL MODELS

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ABSTRACT

ANTERIOR CRUCIATE LIGAMENT INJURY AS A DRIVER OF POST-TRAUMATIC OSTEOARTHRITIS: MECHANISMS AND OUTCOMES ELUCIDATED FROM PRECLINICAL MODELS

Anterior cruciate ligament (ACL) injuries are among the most prevalent orthopedic injuries in active populations and are a leading cause of knee post-traumatic osteoarthritis (PTOA), a debilitating joint condition. PTOA remains a challenging clinical condition, particularly due to its multifactorial pathogenesis and lack of disease-modifying therapies. Emerging research indicates that biological sex significantly influences both the susceptibility to ACL injuries and the progression of PTOA, yet the underlying mechanisms remain poorly understood. Additionally, limitations in current surgical approaches to ACL reconstruction continue to impede long-term joint preservation. The overarching goal of this dissertation was to investigate both biological and surgical determinants of PTOA with the intent of informing improved therapeutic strategies for individuals following ACL rupture. This work is structured around three aims: 1) investigating the role of sex in PTOA progression, 2) probing estrogen signaling as a modulator of PTOA development, and 3) evaluating novel surgical reconstruction strategies in a large animal model.

In Aim 1, we used a non-surgical, mechanical mouse model of ACL rupture to explore sex-specific differences in the development of PTOA following joint trauma. Male and female C57BL/6J mice were subjected to unilateral ACL rupture and were monitored over time using functional and structural assessments to comprehensively characterize PTOA progression. These included weekly mobility analyses such as voluntary mobility, static weight-bearing, and gait analyses to track symptomatic development. In parallel, joint degeneration was evaluated

longitudinally through radiographic imaging and at terminal timepoints via histological scoring. ACL tissues from injured and control limbs were collected at multiple early timepoints for untargeted, label-free proteomic profiling, enabling characterization of dynamic molecular responses to injury. Our findings revealed that male mice demonstrated greater impairment in mobility, including reduced overall activity and altered hindlimb stance, in comparison to females. Histological analysis further confirmed more severe joint pathology in males. Interestingly, radiographic measures showed limited sex-based differences, suggesting that early structural joint changes may be more sensitively captured by histology and behavior than by imaging alone. Proteomic analysis revealed a markedly different injury response between sexes. Female mice exhibited an early, robust molecular response peaking at three days post-injury, with upregulation of pathways associated with inflammation, coagulation, and estrogen signaling. Males showed a more attenuated and prolonged proteomic response, suggesting sex-specific differences in the temporal dynamics of molecular signaling post-injury. Collectively, these findings identify significant sex-based variation in both the symptomatic and molecular trajectory of PTOA following ACL rupture, reinforcing the need for sex-specific approaches to therapeutic development and clinical management.

Aim 2 built upon these findings by exploring the role of estrogen signaling in modulating PTOA progression, with a focus on its contributions in the male mouse joint. Given the absence of early estrogenic signaling in male mice observed in Aim 1, we hypothesized that localized manipulation of estrogen pathways could influence PTOA disease trajectory. Using our established non-surgical ACL rupture model, we administered a single intra-articular (IA) injection of either 17 β -estradiol to enhance estrogen signaling or Fulvestrant, an estrogen receptor antagonist, to suppress it. Mice were evaluated over a 35-day period for symptomatic and structural indicators of PTOA development, including voluntary mobility, gait, weight-bearing, and histopathologic scoring of the injured joint. 17 β -estradiol delivery led to measurable

improvements in multiple outcome parameters, including enhanced mobility and smaller enthesophyte formation compared to saline controls. These findings suggest that estrogen may exert protective effects on PTOA development. However, interpretation of the therapeutic potential of 17 β -estradiol was complicated by the biological activity of the vehicle control, β -cyclodextrin, which independently influenced mobility outcomes, osteophyte maturity, and estrogen receptor beta (ER β) expression. Fulvestrant treatment produced an opposing phenotype characterized by decreased voluntary mobility, increased osteophyte maturity, and altered estrogen receptor dynamics. Notably, Fulvestrant led to a transient increase in estrogen receptor alpha (ER α) expression in ACL remnants at 3 days post-injury, potentially suggesting a compensatory feedback loop following initial receptor antagonism. These receptor-specific findings, combined with the distinct treatment effects on joint morphology and function, underscore the complex role of estrogen signaling in PTOA. Collectively, these data highlight both the promise and the challenge of developing hormone-based therapies for PTOA and emphasize the need for refined delivery methods and better understanding of sex-specific receptor profiles.

In Aim 3, we transitioned to a preclinical ovine model to investigate novel surgical strategies aimed at improving ACL graft healing and minimizing downstream joint degeneration. One reason for the inability of the ACL to spontaneously heal is the presence of plasmin in synovial fluid, which prevents a fibrin-platelet clot from forming between the torn ends of the ACL. Thus, we sought to determine if delivering vascular supply to ACL remnants via a graft could improve overall healing. In this pilot study, we evaluated two innovative reconstruction techniques designed to preserve native blood supply to the graft: one utilizing the lateral digital extensor tendon (LaDET) and the other employing the infrapatellar fat pad (IFP). Post-operative outcomes were evaluated through static weight-bearing, MRI, arthroscopy, macroscopic joint scoring, and histology over six months. The LaDET graft showed successful graft incorporation,

histologic continuity with native ACL remnants, minimal synovial inflammation, and restored limb function. In contrast, the IFP graft demonstrated poor structural integration, persistent inflammation, and inferior functional recovery. These results suggest that vascularized tendon grafts, such as the LaDET, may provide a biologically informed surgical strategy for enhancing graft healing in ACL reconstruction.

Overall, this dissertation advances our understanding of how biological sex, hormonal signaling, and surgical technique influence joint outcomes following ACL injury. The findings emphasize that PTOA development is driven by a combination of molecular and mechanical factors, and that effective treatment must address both. Sex-based differences in disease progression and the complex role of estrogen signaling suggest that personalized, biology-informed approaches may be potential therapeutic avenues to prevent or slow joint degeneration. Additionally, the exploration of vascularized grafts presents a promising direction for improving ACL reconstruction outcomes. Together, this work provides insight for future research aimed at integrating biological sex, molecular pathways, and surgical strategies to develop more effective, personalized interventions that improve outcomes and reduce the long-term impact of ACL injury.

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CHAPTER 1: INTRODUCTION

1.1 ACL Structure and Function

The anterior cruciate ligament (ACL) is a dense band of connective tissue in the knee that connects the femur to the tibia. It originates from the posterior aspect of the medial surface of the lateral femoral condyle, and descends distally through the intercondylar fossa to insert on the tibia, anterior and lateral to the medial intercondylar tubercle.^{1,2} Due to its anatomical position, the ACL functions as the primary restraint to anterior tibial translation and a secondary restraint to internal rotational movement between the femur and tibia.¹

In humans, the ACL is composed of two distinct bundles: the anteromedial (AM) and posterolateral (PL) bundles. These bundles differ in their biomechanical roles due to their unique origin and insertion points. During knee flexion, the AM bundle lengthens and tightens while the PL bundle shortens and becomes lax. In contrast, during knee extension, the PL bundle tightens and lengthens while the AM bundle remains taut, but to a lesser degree.²

At the microstructural level, the ACL primarily consists of an extracellular matrix (ECM) rich in collagen types I, II, III, and V, elastin, and proteoglycans.³ Type I collagen dominates, accounting for approximately 60% of the ligament's dry weight and largely determining its tensile strength.³ The cellular composition of the ACL is predominantly fibroblast subtypes.⁴ Vascular supply for the ACL is limited, with small branches stemming from the middle, lateral inferior, and medial inferior genicular arteries, along with contributions from the infrapatellar fat pad and surrounding synovium.⁵ These vessels penetrate the ACL sparsely, resulting in regions of relative avascularity.¹ Innervation is provided by the posterior articular branches of the tibial nerve.¹ This neural supply includes specialized mechanoreceptors that serve a critical proprioceptive function, detecting changes in tension, speed, acceleration, and movement to provide essential feedback for joint stability and neuromuscular control.⁶

1.2 Epidemiology and Treatment of ACL Injuries

The ACL is the most frequently injured ligament in the knee, with an estimated 120,000 ACL tears occurring annually in the United States.^{7,8} This equates to approximately 3 to 40 ACL tears per hour in the United States.⁹ Notably, ACL injuries have increasing incidence, particularly among high school and college aged athletes.^{9,10} This trend is partially attributed to increased athletic participation among adolescents, improved recognition of ACL injuries, and more competitive play at younger ages.¹⁰

1.2.1 Sex Differences in ACL Injury

Females are significantly more susceptible to ACL injuries than males, particularly among adolescent and young adult athletes. Epidemiological studies report that females are two to ten times more likely to sustain an ACL tear than their male counterparts participating in the same sport.^{11–15} This disparity is especially evident in high-risk contact sports involving rapid cutting, pivoting, and landing, such as soccer and basketball.¹⁶ However, this increased risk of ACL injury among females also persists in non-contact sports like alpine skiing and gymnastics.^{15,16} A growing body of evidence has identified a range of intrinsic sex-based factors that contribute to this increased risk in females.

The increased susceptibility to ACL injury in females likely stems from a multi-factorial interplay of anatomical, biomechanical, and hormonal factors. From an anatomical perspective, several features in females increase the risk of ACL injury. These include a steeper posterior tibial slope (especially in the lateral compartment), a narrower intercondylar femoral notch, and a larger quadriceps angle, which affects the alignment of the knee joint.^{17–19} These structural variations influence overall knee geometry and joint loading, ultimately increasing the risk of ACL injury.

Biomechanical and neuromuscular differences further contribute to the elevated risk of ACL injuries in females.¹⁹ Female athletes often demonstrate greater extension in their knees and hips during landing, greater dynamic knee valgus, and increased quadriceps activation with less hamstring activity.²⁰ These factors may lead to greater ACL loading during athletic tasks.^{19,21} In addition, slower hamstring torque development and reduced core and hip stability can impair neuromuscular control, further predisposing females to injury.²²

Hormonal influences, particularly those related to estrogen, are also thought to play a significant role in ACL injuries. Estrogen is a steroid hormone that fluctuates with the estrous cycle in females and is present at lower, stable levels in males.^{23,24} It is well established that increased knee laxity elevates the risk of ACL injury.²⁵ Females experience cyclical changes in knee laxity, with the greatest laxity occurring prior to ovulation when estrogen levels typically peak.²⁶ Notably, the risk of ACL injury is higher during the preovulatory phase of the cycle when estrogen levels are rising.^{27,28} These observations have led to the hypothesis that estrogen increases ACL injury risk in females by promoting joint laxity. However, the precise mechanisms by which estrogen modulates knee laxity remain unclear. Current evidence suggests that estrogen may impair ACL function by reducing fibroblast proliferation and type I collagen synthesis, decreasing the activity of the lysyl oxidase (LOX) enzyme, which is essential for collagen and elastin crosslinking in the ECM, and acting synergistically with relaxin, a peptide hormone with collagenolytic effects on the ACL.^{29–34} Together, these factors may contribute to estrogen-related changes in joint laxity observed throughout the cycle. As sports participation continues to grow among females, addressing these sex-specific risk factors is essential for reducing injury rates and minimizing long-term consequences such as post-traumatic osteoarthritis (PTOA).

1.2.2 Diagnosis and Treatment

Complete ACL tears are typically accompanied by pain, swelling, and hemarthrosis.³⁵ Diagnosis of an ACL tear can be reliably achieved through physical examination, with a sensitivity of 82% and specificity of 94%.³⁶ Three tests are commonly used during a physical exam to evaluate joint stability for diagnosis of an ACL tear: the Lachman test, the anterior drawer test, and the pivot shift test.³⁵ While arthroscopic evaluation is the most accurate tool for diagnosis of an ACL tear, it is invasive and costly.³⁷ Magnetic resonance imaging (MRI) offers a non-invasive alternative, with a sensitivity of 95% and specificity of 92%.³⁷ MRI also facilitates the identification of concomitant injuries such as meniscal tears, bone contusions, or collateral ligament tears.³⁷

Following a complete ACL tear, the ligament is unable to heal spontaneously. Several theories have been proposed to explain this, with one leading hypothesis attributing failure to heal to the intra-articular (IA) environment of the knee.^{38,39} Specifically, it is believed that synovial fluid, rich in the fibrinolytic enzyme plasmin, prevents the formation of a stable fibrin-platelet clot between the torn ligament ends.⁴⁰ In typical tissue repair, this clot serves as an essential scaffold for collagen deposition and tissue regeneration.^{41,42} In the ACL, however, plasmin-mediated degradation of fibrin appears to inhibit clot formation, thereby disrupting the early stages of the healing process.³⁹

Due to the limited healing capacity of the ACL, surgical intervention is typically required to restore knee function.⁴³ This is particularly critical for athletes, as ACL deficiency leads to joint instability, impaired dynamic movements such as pivoting or cutting, and recurrent episodes of knee buckling.⁴⁴ Surgical approaches have evolved significantly over the past century.⁴³ Early techniques focused on primary repairs, such as Mayo Robson's 1895 method of suturing the torn ligament ends.⁴⁵ Later, more advanced reconstruction techniques were developed by surgeons like Ernest Groves, who explored preserving the graft's vascular supply to enhance healing.⁴⁶ Currently, arthroscopic reconstruction using bone-patellar tendon-bone autografts is considered the gold standard, offering favorable mechanical properties, minimal joint laxity, and

consistent outcomes.^{47,48} However, bone-patellar tendon-bone grafts are associated with notable risks, including the development of PTOA, contralateral joint injuries, and graft failure or reinjury, highlighting the ongoing need for improved therapeutic strategies.^{49–51}

1.3 Epidemiology and Burden of PTOA

Following ACL injury, up to 87% of individuals develop knee PTOA, even after successful reconstructive ACL surgery.⁵¹ PTOA is a form of secondary osteoarthritis (OA) that arises due to joint trauma.⁵² Other forms of OA include primary OA, a degenerative joint disease typically associated with aging but has no known inciting cause, and rheumatoid arthritis, an autoimmune disease which targets the joints.^{53,54} While this dissertation focuses on PTOA in the knee, relevant insights may also be drawn from broader OA literature.

OA affects approximately 600 million people worldwide, making it the most common joint disease.⁵⁵ PTOA, a subset of OA, represents about 12% of symptomatic OA cases and often emerges in younger, more active individuals due to injury.^{56,57} In 2006, the economic burden of PTOA in the United States was over \$3 billion annually.⁵⁶ Although this accounted for 0.15% of total direct healthcare costs in the United States, PTOA-focused research received only 0.067% of total National Institutes of Health grant awards.⁵⁶ This discrepancy highlights a significant mismatch between the burden of PTOA and the resources allocated for its study, underscoring a critical need for increased research and therapeutic development.^{56,58} PTOA differs from primary OA in both etiology and demographic profile. It typically arises earlier in life, following injuries such as ACL rupture, which are increasing in incidence, suggesting that PTOA incidence is also rising.^{9,10,57–59}

1.3.1 Sex Differences in PTOA

In humans, the epidemiology of primary OA demonstrates well-established sex differences. Primary OA is significantly more prevalent, and often more severe, in women,

particularly after the age of 50.^{60–62} This age range aligns with menopause, after which women experience a drastic rise in PTOA incidence, frequently presenting with multi-joint involvement.^{63,64} These patterns suggest a protective role of sex hormones in women before menopause and highlight the complex hormonal regulation involved in OA susceptibility.

The influence of sex on PTOA is less clear, as studies analyzing disease progression following surgical ACL reconstruction have reported inconsistent findings regarding sex-based differences in prevalence and severity. Males exhibit significantly worse radiographic signs of PTOA 7 – 12 years following ACL reconstruction compared to females.^{65,66} However, this finding has been reported in only two studies, while others have observed no significant sex-based differences in PTOA severity, underscoring the need for further research to clarify the role of sex in PTOA development.^{67,68}

In preclinical animal models of PTOA, sex-based differences in disease severity have been observed, though the magnitude of these effects seem to vary by species and model. In mouse models, males frequently exhibit more severe PTOA features than females, including greater cartilage degeneration, osteophyte formation, synovitis, and elevated MMP activity.^{64,69} Male mice also demonstrated heightened pain-related behaviors and a persistent inflammatory synovial transcriptome, whereas females show greater resolution of inflammation.⁶⁹ Hormonal influences have been implicated, as ovariectomized females develop more severe disease than intact females, suggesting a protective role for estrogen.^{64,70} However, in a porcine surgical model of ACL injury, females exhibited significantly worse macroscopic cartilage damage compared to males.⁷¹ Together, these findings underscore the complexity of sex as a biological variable in PTOA and highlight the need for further research to uncover the mechanisms driving these variations.

1.3.2 Diagnosis and Clinical Management of PTOA

Diagnosis of knee PTOA generally occurs only after symptom onset, with pain being the primary reason patients seek medical care.⁷² Diagnosis includes physical examination and imaging modalities such as radiographs, ultrasound, computed tomography, or magnetic resonance imaging.⁷³ Given the high functional demands of the typically younger PTOA population, earlier and more frequent treatments are often necessary compared to those with primary OA.⁵⁷

Current treatments for knee PTOA are largely limited to symptomatic modification including non-steroidal anti-inflammatory drugs, corticosteroid injections, and physical therapy.⁷⁴ Lifestyle modifications such as weight loss and low-impact exercise such as Tai Chi are also beneficial for managing symptoms.^{57,74} However, once PTOA progression is too severe for symptomatic management, surgical intervention may be required, most commonly total knee replacement (TKR).⁷⁵ While TKR significantly improves quality of life by reducing pain, it does not restore full joint function and imposes limitations on dynamic movements such as squatting, moving laterally, turning and cutting, and carrying loads.^{75,76} Additionally, about 20% of TKRs fail within 25 years, posing a significant concern for the younger population affected by PTOA as many patients could require revision surgeries.⁷⁷ Thus, there is a clear clinical need for improved treatment options for PTOA, with an expanded interest in early therapeutic intervention, prior to symptomatic development to delay the need for TKR.

1.3.3 Research Trends

Interest in PTOA research is growing as a recent bibliometric analysis of PTOA literature revealed a steady increase in PTOA-related publications over the past decade.⁵⁷ Emerging therapies include modulation of inflammation and cartilage repair through intra-articular injections of anti-cytokine drugs, improved surgical treatments to preserve joint integrity, and regenerative strategies like autologous chondrocyte implantation.⁵⁷ Thus, despite the significant healthcare burden of PTOA and the currently limited treatment options, the field shows promise

with many novel therapies emerging. While progress is being made, a definitive therapeutic option has yet to be identified, highlighting the need for continued investigation. Although PTOA represents only a subset of all OA cases, it shares many characteristics with primary OA, particularly in the later stages. Framing PTOA within the broader context of OA research underscores its interdisciplinary relevance, as insights from PTOA can inform the entire OA field.⁵⁷

1.4 Pathogenesis of PTOA

Understanding the pathogenesis of PTOA is critical for developing targeted therapeutic interventions and improving patient outcomes following ACL injury. Unlike primary OA, which develops gradually over decades with idiopathic origins, PTOA follows a distinct trajectory initiated by joint trauma that triggers a cascade of inflammatory and degenerative processes.^{53,78} The transition from initial injury to progressive joint disease involves complex interactions between mechanical, biological, and molecular factors that ultimately lead to irreversible cartilage damage and joint dysfunction.^{78,79}

The pathogenesis of PTOA can be conceptualized as a progression through distinct but overlapping phases, each characterized by specific cellular and molecular events that drive disease advancement (Figure 1.1). OA progression is generally categorized into early and late stages, with each stage exhibiting characteristic histopathological features and underlying mechanisms.⁸⁰ Central to this pathogenic process is inflammation, which serves as both an initiating factor and a perpetuating force that drives the transition from acute injury to chronic joint degeneration.⁷⁹

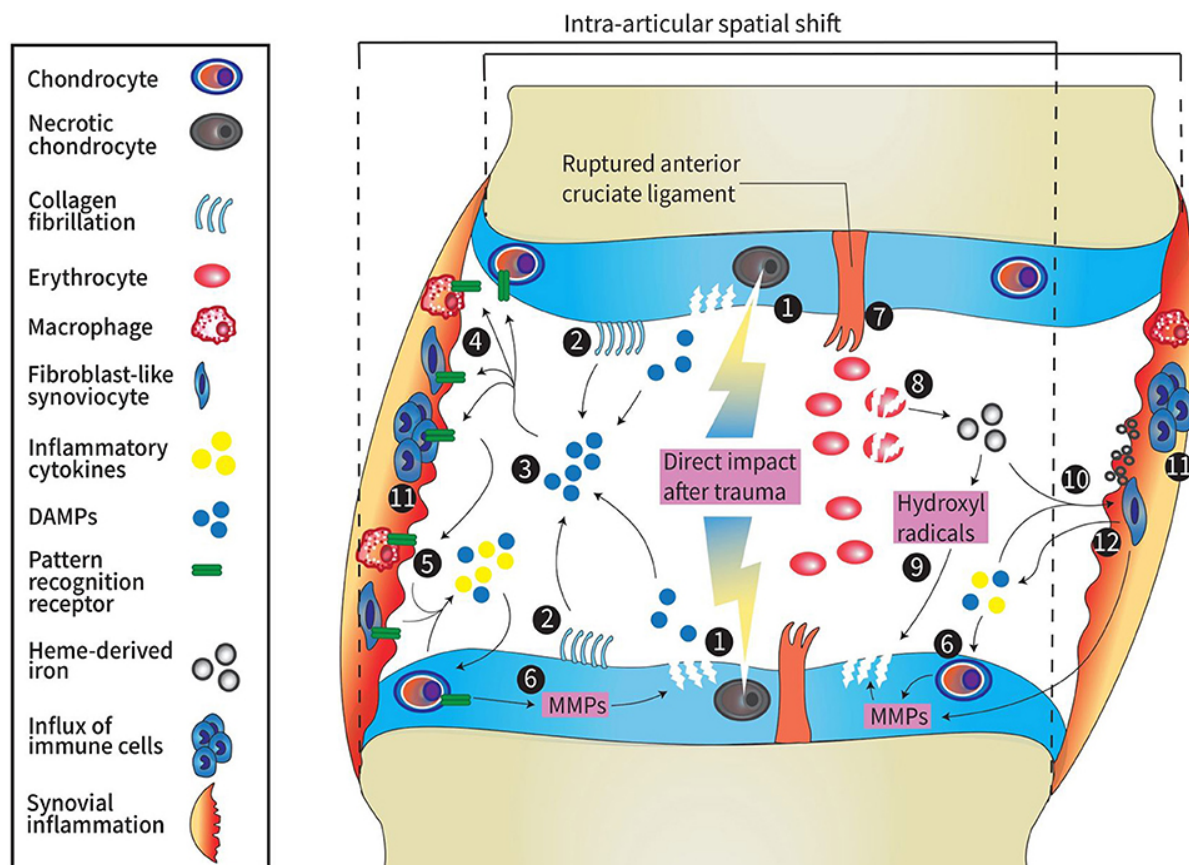


Figure 1.1. Schematic overview of pathophysiology of PTOA progression after ACL injury. **1:** Joint trauma results in necrotic cell death of chondrocytes and damage to the ECM of the cartilage. **2:** Increased joint laxity after ligament rupture causes a spatial shift in the joint resulting in changes to the load bearing contact area. This leads to fibrillation of the collagen network and when fractured, these fibrils act as DAMPs. **3:** DAMPs (glycoproteins and proteoglycans) are released into the articular cavity as result of acute traumatic cartilage damage. **4:** DAMPs bind to pattern recognition receptors (TLRs, NLRs, and RAGE) on the surface of immune cells, chondrocytes, osteoblasts (not shown), macrophages and fibroblasts. **5:** Activated cells release inflammatory cytokines such as IL-1, IL-4, IL-6, IL-8, IL-10, IL-17, TNF- α , chemokines, cathepsins, complement cascade factors, and DAMPs (S-100 proteins, high-mobility group box protein 1 (HMGB1), or uric acid). **6:** Inflammatory factors promote release of MMPs and ADAMTS by synoviocytes and chondrocytes which leads to cartilage degradation. **7:** ACL rupture causes hemarthrosis. Degradation of erythrocytes causes the release of heme-derived iron molecules. **8:** Heme-derived iron molecules react with oxygen metabolites generated by monocytes and macrophages forming hydroxyl radicals. **9:** Hydroxyl radicals induce chondrocyte apoptosis and therefore promote cartilage damage. **10:** Synovial inflammation is induced by DAMPs, pro-inflammatory factors and hemosiderin deposits in the synovium formed by the accumulation of iron molecules. **11:** Synovial inflammation is characterized by influx of immune cells. **12:** Cells in the inflamed synovium release cytokines, DAMPs and promote release of MMPs leading to cartilage breakdown which again promotes the release of DAMPs into the joint cavity. Reprinted from Evers et al. (2022), "Post-traumatic knee osteoarthritis; the role of inflammation and hemarthrosis on disease progression".⁷⁹

1.4.1 Inflammatory Phases in PTOA Development

Inflammation is a key driver of PTOA and can be divided into three phases after ACL injury: immediate, acute, and chronic.^{78,79} The immediate phase occurs directly following injury and is marked by abnormal mechanical loading and joint instability.⁷⁹ Direct impact to the cartilage and bone resulting from the initiating injury can lead to chondrocyte necrosis and extracellular matrix (ECM) disruption.^{74,81} Additionally, knee joint kinematics are altered in ACL-deficient knees, resulting in abnormal force distributions that can further damage the articulating surfaces, perpetuating chondrocyte stress and death.⁸² This cellular stress drives the upregulation of catabolic factors such as matrix metalloproteinases (MMPs) and inflammatory cytokines, creating a volatile inflammatory environment that primes the joint for ongoing degeneration and progression of PTOA.^{79,83}

The acute inflammatory phase follows the immediate post-injury response and is characterized by sustained inflammation, fragmentation of the ECM, continued cell death, and hemarthrosis.⁷⁹ During this phase, damage-associated molecular patterns (DAMPs), including ECM fragments (glycoproteins and proteoglycans) and factors released from dying chondrocytes (S100 proteins, high mobility group box 1 proteins, and uric acid), are present at high levels in the joint space. DAMPs bind to pattern recognition receptors (toll-like receptors, NOD-like receptors, and the receptor for advanced glycation end-products) on joint cells, including chondrocytes, osteoblasts, fibroblasts, and immune cells, and trigger an immense downstream release of inflammatory cytokines such as IL-1, IL-6, IL-8, IL-17, and TNF- α .^{78,79,84,85} These factors activate chondrocytes and synoviocytes to produce MMPs and other degradative enzymes that promote further cartilage breakdown and stimulate synovial inflammation.⁸⁶ As a result, the joint can enter a non-stop cycle of degradation and inflammation that perpetuates tissue damage.⁷⁹ Importantly, the timeline for the acute phase has not been strictly defined in humans, as the response varies depending on the individual nature of the

inciting injury. Instead, the acute phase is characterized by the presence and progression of these underlying cellular and molecular processes.⁷⁹

Hemarthrosis, or bleeding into the joint, frequently occurs following ACL injury and contributes to the acute inflammatory response.⁷⁹ In addition to causing pain, swelling, and decreased range of motion, hemarthrosis perpetuates inflammation through the breakdown of erythrocytes which releases heme, an iron-containing complex that reacts with oxygen metabolites to form hydroxyl radicals capable of inducing chondrocyte apoptosis and cartilage damage.^{79,87–89} Accumulated heme-derived iron can also form synovial hemosiderin deposits, which further stimulate synovial inflammation and promote the production of pro-inflammatory cytokines.⁹⁰ If unresolved, the combined effects of tissue degradation, inflammation, and hemarthrosis during the acute injury phase can drive the joint into a persistent, chronic inflammatory state.^{78,79}

The chronic inflammatory phase of PTOA is marked by persistent synovitis, joint pain, swelling, and stiffness.⁷⁹ Chronic synovitis is characterized by synovial hyperplasia, increased vascularity, and infiltration of inflammatory cells such as fibroblast-like synoviocytes and macrophages, which continue to release pro-inflammatory mediators and degradative enzymes, contributing to sustained cartilage degeneration.^{79,91,92} This chronic state of inflammation and synovitis has been shown to occur in both early and late-stage PTOA.⁷⁹

1.4.2 Histological Progression and Classification of OA

The result of persistent inflammation and degradation in the joint is the development of classic histopathologic features of OA. Although OA is now understood as a complex, multi-tissue disease, the Osteoarthritis Research Society International (OARSI) has established a widely adopted histologic grading system to characterize cartilage pathology across the OA spectrum.⁸⁰ A key goal of this system was to distinguish between early and late-stage OA, identifying subsets of disease that may occur regardless of etiology, including PTOA.⁸⁰ The

OARSI grading scale ranges from 0 – 6 and is based on the depth and extent of cartilage lesions. Grades 1 – 3 define early or mild OA and include features such as superficial fibrillation with intact articular surface and matrix alterations (Grade 1), surface discontinuity through the superficial zone (Grade 2), and vertical fissures extending into the mid-zone cartilage (Grade 3).⁸⁰ Late-stage OA, defined by Grades 4 – 6, reflects more advanced cartilage damage. This includes extensive matrix loss through delamination (Grade 4), complete erosion of hyaline cartilage to the subchondral bone (Grade 5), and bone remodeling with articular surface deformation and possible osteophyte formation (Grade 6).⁸⁰ While focused primarily on cartilage, this grading system was developed to be broadly applicable across clinical samples and experimental OA models. Importantly, the OARSI grading system has been expanded and modified to capture features specific to PTOA, as well as to accommodate distinct adaptations for various animal models, including mouse models (Chapters 2 & 3) and sheep models (Chapter 4).^{93,94}

1.5 Animal Models of ACL Injury and PTOA

ACL injuries and the development of PTOA remain major clinical challenges resulting in the need for improved treatment options. Comprehensive study of these conditions in humans presents significant limitations. *In vivo* assessments are typically restricted to imaging and functional evaluations, and tissue samples for biochemical, histological, or molecular analyses are limited to end-stage disease as they are taken at the time of joint replacement surgery.⁹⁵ Therefore, translational animal models are critical to better understand disease mechanisms and evaluate new therapies.

The primary advantages of animal models for studying ACL injury and PTOA can be broadly categorized into two domains: comprehensive characterization of disease progression and therapeutic testing. Compared to *in vitro* testing, animal models preserve the complex, dynamic interactions among joint tissues, enabling investigation of how ACL injury initiates and

drives PTOA within a physiologically relevant environment. Animal models also allow for the temporal profiling of disease progression through longitudinal analyses and tissue collection at multiple timepoints. Furthermore, animal models are essential for evaluating the safety and efficacy of emerging therapeutics, including biologics and surgical techniques, before they are used in human clinical trials.

1.5.1 Terminology and Anatomical Considerations

In humans, the anatomical term for the joint formed by the femur, tibia, and patella is the knee. In quadrupeds, this analogous structure is referred to as the stifle. Throughout this dissertation, “knee” will generally refer to the human joint, while “stifle” will refer to animal models. However, for simplicity and consistency with broader usage, “knee” may occasionally be used as a general term. Additionally, the cranial cruciate ligament (CrCL) in animals functions analogously to the human ACL. To maintain consistency with the human-focused literature and for clarity, the CrCL will be referred to as the ACL throughout this dissertation, even in animal studies.

It is important to recognize anatomic and biomechanical differences between species that may impact the translational relevance of findings. Importantly, the difference between a bipedal gait in humans and a quadrupedal gait in animals results in differences to the joint structure and load distribution that must be considered. Posterior tibial slope (PTS), the angle of the tibial plateau from the anterior to posterior relative to the longitudinal axis of the tibia, is one such difference with important implications. Differences in PTS greatly alter joint mechanics and, in humans, steeper PTS can lead to increased risk of ACL injury.⁹⁶ In humans, the average PTS is around 10.7°, though the range can be anywhere from 5° to 15.5°.⁹⁷ In standard C57BL6/J mice, the PTS is around 25 ± 1°.⁹⁸ In sheep, the PTS is approximately 20 ± 3°.⁹⁹ In large breed dogs, a normal PTS ranges from 23.5° to 28°.¹⁰⁰ In dogs, a steeper PTS is thought

to increase risk for cranial cruciate ligament disease (CCLD), or degeneration of the CrCL.^{101,102} These interspecies differences in PTS have important implications for modeling ACL injury and PTOA, as they influence the mechanical environment of the knee. Understanding and accounting for these variations is essential when interpreting results from preclinical animal models and translating findings to humans. A visual depiction of the differences in joint structure for mice, dogs, sheep, and humans is shown in Figure 1.2.

1.5.2 Mouse Models

Mice are considered advantageous small animal models for initial investigations into post-traumatic osteoarthritis (PTOA) for several reasons. They are relatively inexpensive, require minimal housing space, are easy to handle, and enable rapid testing due to their fast maturation rates and disease progression timelines.¹⁰³ One of their key advantages is the availability of extensive genetic tools, including a wide variety of transgenic lines, which make them highly versatile for studying molecular signaling pathways, mechanisms of therapeutic action, and the roles of specific genes or proteins involved in osteoarthritis, bone remodeling, inflammation, and pain.^{104–106} The genetic uniformity of inbred laboratory mice also aids in the isolation of the impact of specific genes on observed phenotypes.^{106,107} Mouse models are also particularly well suited for investigating sex-based differences in disease susceptibility, progression, pain, and treatment response, as both male and female mice can be studied in parallel under controlled genetic and environmental conditions.¹⁰⁸ Notably, female mice have an estrous cycle length of 3 – 5 days, resulting in frequent hormone fluctuations.¹⁰⁹ For these reasons, mice are often the model of choice for early-stage, mechanistic research and preclinical therapeutic screening. Commonly used mouse models of PTOA include surgical approaches such as ACL transection and destabilization of the medial meniscus, non-surgical

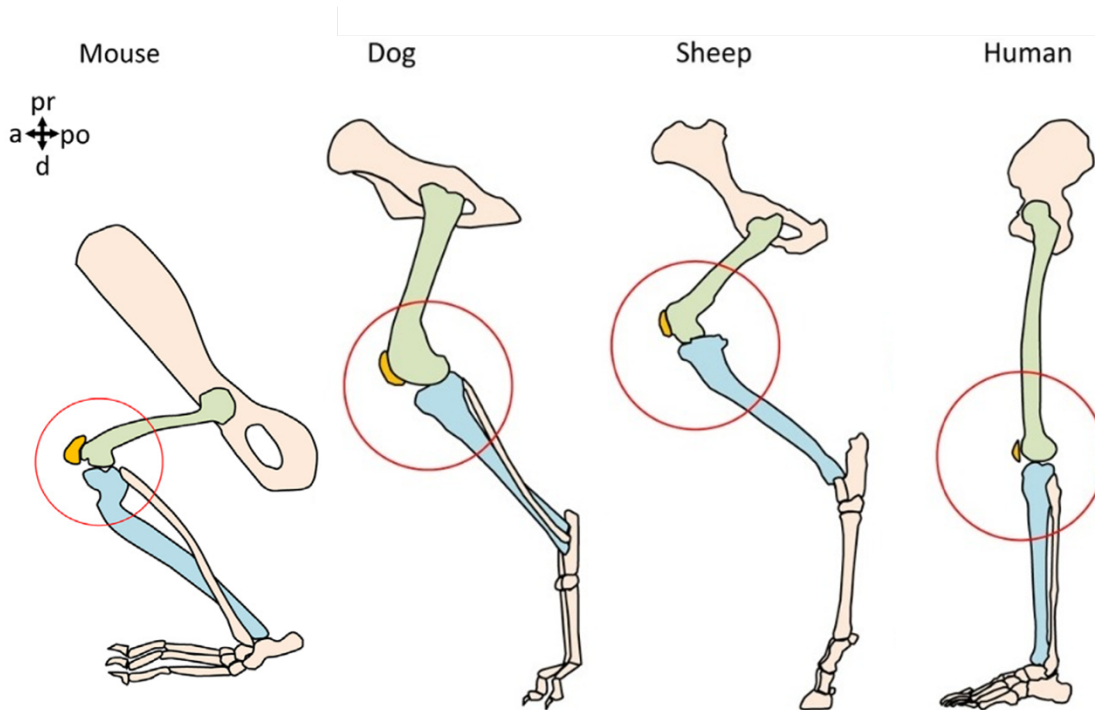


Figure 1.2. Idealized (not to scale) comparison of the gross skeletal anatomy of the hind limbs in mice, dogs, sheep, and humans. Red circles indicate the knee/stifle joints. The femur is shown in green, the tibia blue, and the patella orange. a = anterior, d = distal, po = posterior, pr = proximal. Adapted from Oláh et al. (2021), “Comparative anatomy and morphology of the knee in translational models for articular cartilage disorders. Part I: Large animals & Part II: Small animals.”^{106,110}

mechanical models like tibial compression-induced ACL rupture (used in these dissertation studies), and chemically induced models.^{95,107}

Despite these advantages, several important limitations affect the translational relevance of mouse models to human ACL injury and PTOA. Mouse stifles remain in a flexed position throughout gait and do not achieve full extension as human knees do, resulting in distinct biomechanical loading patterns.¹⁰⁶ In addition, mice possess a greater intrinsic capacity for cartilage repair than humans, which may limit the applicability of mouse findings to chronic, non-healing conditions seen clinically.¹¹¹ The small size of mouse joints also presents a technical barrier to surgical ACL reconstruction. Although some groups have successfully developed surgical reconstruction models in mice, most studies rely on inducing PTOA through ACL injury without reconstruction.^{112,113} This approach does not fully replicate the human clinical scenario, where most patients with ACL injuries undergo surgical repair. As a result, PTOA progression in mouse models may be more heavily influenced by mechanical instability than in reconstructed human knees.

1.5.3 Sheep Models

Sheep are widely used and well-validated for preclinical orthopedic research, particularly in studies of OA, osteoporosis, and the evaluation of novel surgical techniques, medical devices, and biologics.^{110,114–116} Their similar body weight, joint size, and anatomical structure compared to humans make them ideal for applying clinically relevant outcome measures such as imaging, kinematics, arthroscopy, and biomarker analysis.^{110,114} Sheep are also relatively easy to handle compared to other large animal models, and while more expensive to maintain than rodents, female sheep (ewes) can be group housed, helping reduce costs.^{115,117} Male sheep (rams), if left sexually intact, are more aggressive and difficult to manage, so most ovine studies are conducted exclusively in ewes.¹¹⁵ This presents a limitation, as both sexes are not typically represented. Additionally, ewes are seasonally polyestrous, with their reproductive

cycle influenced by factors such as photoperiod, temperature, and nutritional status.¹¹⁸ During the breeding season, primarily in the fall, the estrous cycle of an ewe typically lasts around 17 days.^{118,119} These seasonal and species-specific reproductive patterns pose challenges for translating findings directly to humans, particularly in studies involving hormonal influences, where continuous or monthly cycling, as seen in humans, may play a critical role. Another notable drawback of using sheep is their ruminant physiology, which complicates studies involving oral drug administration unless specific interventions such as an abomasal fistula are implemented.¹¹⁵

Sheep are among the most commonly used large animal models for ACL and PTOA research.^{116,117,120} While no model perfectly replicates human ACL anatomy, sheep are particularly valuable for translational studies due to having a posterior tibial slope (PTS) most similar to that of humans.¹¹⁷ Sheep also replicate important aspects of human PTOA progression, such as cartilage degeneration, osteophyte formation, and synovitis.^{94,121} However, PTOA develops more slowly in sheep, possibly due to anatomical differences like the presence of the long digital extensor tendon, which may provide additional joint stability not found in humans, though these implications are not fully understood.^{94,122,123} Despite these limitations, the sheep model remains a robust platform for testing surgical reconstruction techniques and evaluating disease-modifying therapies in a preclinical setting.

1.5.4 Other Animal Models

In addition to mice and sheep, canine models are commonly used in orthopedic research due to their relatively large joint size and general anatomical similarities between the canine stifle and the human knee.¹¹⁰ They are also compatible with a wide range of diagnostic and monitoring tools, including advanced imaging and molecular assessments, and are relatively easy to train for functional and mobility testing.¹¹⁰ Importantly, dogs frequently develop spontaneous OA that closely mirrors the degenerative changes observed in humans.¹¹⁰

However, their utility as models for ACL injury is more limited. In humans, ACL rupture typically results from an acute traumatic event, often involving pivoting or cutting motions during sports.¹⁶ In contrast, CrCL rupture in dogs typically occurs as the result of a chronic, degenerative process characterized by progressive collagen fiber deterioration, synovitis, and eventual ligament failure.^{102,124} Epidemiologically, CCLD, is one of the most common causes of lameness in dogs, particularly in certain breeds predisposed by age, conformation, genetic factors, and reproductive status.^{102,124,125} This supports the canine model's strength in studying naturally occurring OA rather than acute ligament trauma. While this fundamental difference in injury mechanism limits the value of the canine model for investigating ACL injury pathogenesis, dogs remain valuable for studying OA progression due to their genetic diversity, shared risk factors such as obesity and hormonal influences, and environmental exposures similar to humans.¹¹⁰ However, their use is constrained by significant ethical considerations, public perception, and husbandry requirements.¹¹⁰

Several other animal species are also utilized for preclinical study of ACL injuries and PTOA, each offering distinct advantages. Pigs, particularly minipigs, have stifle joints similar in anatomy and cartilage thickness to humans and exhibit bone remodeling patterns analogous to human bone, though they do not typically develop spontaneous OA and require specialized care.^{110,126} Goats, similar to sheep, possess stifle joints and meniscal anatomy highly comparable to humans, but their cartilage is thicker and significantly stiffer, with a greater elastic modulus than human knee cartilage.^{110,127} Horses provide the largest joint models and frequently develop naturally occurring cartilage lesions, yet their use is limited by cost, husbandry demands, and ethical concerns.^{110,128} Among small animals, rabbits are widely used for cartilage defect studies but have thinner cartilage and vastly different joint loading mechanics than humans.^{106,127} Dunkin Hartley guinea pigs are useful for studying spontaneous, age-related OA with a pathogenesis similar to that seen in humans.^{129,130} Rats, like mice, are economical and genetically accessible, and also have slightly larger joints that can accommodate some

surgical manipulations.¹⁰⁶ Together, these species provide a diverse toolkit for modeling ACL injury and PTOA across a range of experimental needs.

1.5.5 Appropriate Animal Model Selection

No single animal model completely recapitulates the human condition, and the choice of model must align with the specific goals of the study. Common factors that may influence model selection include the need for genetic tools, high-throughput screening, or commercially-available antibodies which favors rodents, compared to the need for surgical simulation or implant testing, favoring large animals such as sheep. There are also considerations of cost, housing, handling, regulatory, and ethical factors that must be analyzed for each study. Altogether, animal model selection should be intentional and evidence-based, as it critically impacts the relevance and applicability of study findings as well as the ethical use of animals by ensuring that the chosen model maximizes scientific value while minimizing harm and unnecessary use. While each model has its own strengths and limitations, carefully designed preclinical animal studies remain a powerful tool to bridge the gap between bench research and clinical care. In this study, a mouse model is used in Chapters 2 and 3 to study symptomatic, structural, and molecular responses in PTOA development, while a large animal sheep model is used in Chapter 4 to assess surgical ACL reconstruction outcomes.

1.6 Study Purpose

1.6.1 Overall Study Purpose

This work of this dissertation aimed to identify strategies to improve patient outcomes following ACL injury. We focused on two broad areas with high potential for clinical impact: delaying the onset and progression of PTOA and enhancing surgical ACL reconstruction techniques. First, we investigated PTOA development and identified biological sex, specifically the hormone estrogen, as a potential protective factor (Chapter 2). We then explored the role of

estrogen in modulating PTOA progression (Chapter 3). Finally, we evaluated novel surgical reconstruction approaches designed to improve graft healing and reduce long-term joint degeneration (Chapter 4). Together, these investigations provide critical insight into both the biological and surgical determinants of knee health following ACL injury, informing future therapeutic development and clinical strategies.

1.6.2 Study Aim 1

The overall goal of this aim was to explore the role of sex on PTOA progression following ACL rupture, with the end goal of identifying novel avenues for future mechanistic-based studies and potential therapeutic development. To do so, we induced PTOA using our previously published mechanical, non-surgical mouse model of ACL rupture.¹³¹ We then comprehensively characterized injury progression following mechanical ACL rupture using symptom, disease, and proteomic analyses in male and female mice. We first delineated variations in the structural and functional responses of male and female mouse knees following mechanical ACL rupture. Next, we investigated proteomic pathway differences between the ACL in male and female mice following injury.

Hypothesis: We hypothesized that male mice would display increased severity of joint disease and differential regulation of PTOA-associated proteins compared to females following ACL injury.

1.6.3 Study Aim 2

We next aimed to elucidate the role of estrogen in PTOA progression. We used a mouse model of PTOA development induced via mechanical ACL rupture to induce PTOA in male mice. To do so, we assessed the ability of exogenous intra-articular 17 β -estradiol to delay the onset and progression of PTOA. Next, we aimed to demonstrate a direct relationship between estrogen receptor reduction and PTOA development through the administration of intra-articular

Fulvestrant (ICI 182,780), an estrogen receptor antagonist. To investigate the relationship between estrogen and PTOA, we evaluated symptomatic and structural progression of PTOA. We also profiled the estrogen receptor expression on the ACL remnants.

Hypothesis: We hypothesized that local enhancement of estrogen signaling via 17 β -estradiol would delay onset and progression of PTOA, while inhibition of signaling through Fulvestrant would exacerbate joint degeneration, evidenced by alterations in mobility, histologic, and radiographic outcomes.

1.6.4 Study Aim 3

In this aim, we sought to investigate novel approaches for ACL repair that improve graft healing and reduce the development of PTOA. In this aim, we evaluated two novel techniques for ACL reconstruction using an ovine model of surgically induced ACL injury. The primary objective was to assess the feasibility of preserving vascular supply in an ACL graft and to explore its potential impact on graft healing. To achieve this, we developed two surgical approaches in an ovine model, utilizing either the lateral digital extensor tendon (LaDET) or the infrapatellar fat pad (IFP) as graft material. In both techniques, the grafts' native blood supply remained intact. This aim was a pilot study in which our primary goal was to determine if either of our developed reconstruction methods warranted further investigation.

Hypothesis: We hypothesized that the LaDET graft, which is more structurally comparable to the native ACL, would demonstrate superior healing compared to the IFP graft, based on assessments of limb function, joint integrity, and graft viability.

References

1. Zantop T, Petersen W, Fu FH. Anatomy of the anterior cruciate ligament. Oper Tech Orthop. 2005;15(1):20-28. doi:10.1053/j.oto.2004.11.011

2. Dienst M, Burks RT, Greis PE. Anatomy and Biomechanics of the Anterior Cruciate Ligament.
3. Yoo H, Raghavendra ;, Affiliations MG. Anatomy, Bony Pelvis and Lower Limb, Knee Anterior Cruciate Ligament.
<https://www.ncbi.nlm.nih.gov/books/NBK559233/?report=printable>
4. Yang R, Xu T, Zhang L, Ge M, Yan L, Li J, et al. A single-cell atlas depicting the cellular and molecular features in human anterior cruciate ligament degeneration: A single cell combined spatial transcriptomics study. *Elife*. 2023;12. doi:10.7554/eLife.85700
5. Toy BJ, Yeasting RA, Morse DE, McCann P, Morse are professors in the DE. Arterial Supply to the Human Anterior Cruciate Ligament.
6. Zimny ML, Schutte M, Dabezies E. Mechanoreceptors in the Human Anterior Cruciate Ligament.; 1986.
7. Bollen S. Epidemiology of knee injuries: diagnosis and triage. *Br J Sports Med*. 2000;34(3):227.2-228. doi:10.1136/bjsm.34.3.227-a
8. Kaeding CC, Léger-St-Jean B, Magnussen RA. Epidemiology and Diagnosis of Anterior Cruciate Ligament Injuries. *Clin Sports Med*. 2017;36(1):1-8. doi:10.1016/j.csm.2016.08.001
9. Murray MM, Vavken P, Fleming BC. The ACL Handbook. 1st ed. (Murray MM, Vavken P, Fleming B, eds.). Springer New York; 2013. doi:10.1007/978-1-4614-0760-7
10. Gornitzky AL, Lott A, Yellin JL, Fabricant PD, Lawrence JT, Ganley TJ. Sport-Specific Yearly Risk and Incidence of Anterior Cruciate Ligament Tears in High School Athletes: A Systematic Review and Meta-analysis. *American Journal of Sports Medicine*. 2016;44(10):2716-2723. doi:10.1177/0363546515617742
11. Hutchinson MR, Ireland ML. Knee Injuries in Female Athletes. Vol 19.; 1995.
12. Arendt EA, Agel J, Dick R. Anterior Cruciate Ligament Injury Patterns Among Collegiate Men and Women. Vol 34.; 1999. www.nata.org/jat

13. Kiapour AM, Shalvoy MR, Murray MM, Fleming BC. Validation of Porcine Knee as a Sex-specific Model to Study Human Anterior Cruciate Ligament Disorders. *Clin Orthop Relat Res.* 2015;473(2):639-650. doi:10.1007/s11999-014-3974-2
14. Gwinn DE, Wilckens JH, Mcdevitt ER, Ross G, Kao TC. The Relative Incidence of Anterior Cruciate Ligament Injury in Men and Women at the United States Naval Academy*. Vol 28.; 2000.
15. Montalvo AM, Schneider DK, Webster KE, Yut L, Galloway MT, Heidt RS, et al. Anterior cruciate ligament injury risk in sport: A systematic review and meta-analysis of injury incidence by sex and sport classification. *J Athl Train.* 2019;54(5):472-482. doi:10.4085/1062-6050-407-16
16. Ireland ML. The female ACL: why is it more prone to injury? Published online 2002.
17. Sturnick DR, Vacek PM, Desarno MJ, Gardner-Morse MG, Tourville TW, Slaughterbeck JR, et al. Combined anatomic factors predicting risk of anterior cruciate ligament injury for males and females. *American Journal of Sports Medicine.* 2015;43(4):839-847. doi:10.1177/0363546514563277
18. Gant H, Ghimire N, Min K, Musa I, Ashraf M, Lawan A. Impact of the Quadriceps Angle on Health and Injury Risk in Female Athletes. *Int J Environ Res Public Health.* 2024;21(12). doi:10.3390/ijerph21121547
19. Sutton KM, Bullock JM. Anterior cruciate ligament rupture: Differences between males and females. *Journal of the American Academy of Orthopaedic Surgeons.* 2013;21(1):41-50. doi:10.5435/JAAOS-21-01-41
20. Pappas E, Shiyko MP, Ford KR, Myer GD, Hewett TE. Biomechanical deficit profiles associated with acl injury risk in female athletes. *Med Sci Sports Exerc.* 2016;48(1):107-113. doi:10.1249/MSS.0000000000000750
21. Editorial. The female ACL: Why is it more prone to injury? *J Orthop.* 2016;13(2):A1-A4. doi:10.1016/S0972-978X(16)00023-4

22. Lephart SM, Abt JP, Ferris CM. Neuromuscular contributions to anterior cruciate ligament injuries in females. Published online 2002.
23. Sherman BM, Korenman SG. Hormonal Characteristics of the Human Menstrual Cycle Throughout Reproductive Life.
24. Hess RA, Cooke PS. Estrogen in the male: A historical perspective. *Biol Reprod.* 2018;99(1):27-44. doi:10.1093/biolre/iy043
25. Ramesh R, Arx O Von, Azzopardi T, Schranz PJ, Azzopardi " T Ed. The risk of anterior cruciate ligament rupture with generalised joint laxity. 2005;87:800-803. doi:10.1302/0301-620X.87B6
26. Shultz SJ, Sander TC, Kirk SE, Perrin DH. Sex Differences in Knee Joint Laxity Change across the Female Menstrual Cycle. Vol 45.; 2005.
27. Hewett TE, Zazulak BT, Myer GD. Effects of the menstrual cycle on anterior cruciate ligament injury risk: A systematic review. *American Journal of Sports Medicine.* 2007;35(4):659-668. doi:10.1177/0363546506295699
28. Shultz SJ. The effect of sex hormones on ligament structure, joint stability and ACL injury risk. In: *Sex Hormones, Exercise and Women: Scientific and Clinical Aspects.* Springer International Publishing; 2016:113-138. doi:10.1007/978-3-319-44558-8_7
29. Katherine M. B, Helen E. M. The Effect of Estrogen on Anterior Cruciate Ligament Structure and Function: A Systematic Review. *J Musculoskelet Disord Treat.* 2023;9(3). doi:10.23937/2572-3243.1510127
30. Parker EA, Duchman KR, Meyer AM, Wolf BR, Westermann RW. Menstrual Cycle Hormone Relaxin and ACL Injuries in Female Athletes: A Systematic Review. *Iowa Orthop J.* 2024;44(1):113-123.
31. Lee CA, Lee-Barthel A, Marquino L, Sandoval N, Marcotte GR, Baar K. Estrogen inhibits lysyl oxidase and decreases mechanical function in engineered ligaments. *J Appl Physiol.* 2015;118(10):1250-1257. doi:10.1152/japplphysiol.00823.2014

32. Yu WD, Panossian V, Hatch JD, Liu SH, Finerman GAM. Combined Effects of Estrogen and Progesterone on the Anterior Cruciate Ligament. Vol 383.; 2001.
33. Shultz SJ, Wideman L, Montgomery MM, Beasley KN, Nindl BC. Changes in serum collagen markers, IGF-I, and Knee joint laxity across the menstrual cycle. *Journal of Orthopaedic Research*. 2012;30(9):1405-1412. doi:10.1002/jor.22093
34. Yoshida A, Morihara T, Kajikawa Y, Arai Y, Oshima Y, Kubo T, et al. In vivo effects of ovarian steroid hormones on the expressions of estrogen receptors and the composition of extracellular matrix in the anterior cruciate ligament in rats. *Connect Tissue Res*. 2009;50(2):121-131. doi:10.1080/03008200802531287
35. Cimino F, Naval Hospital U, Bradford Scott Volk J, Setter D. Anterior Cruciate Ligament Injury: Diagnosis, Management, and Prevention. Vol 82.; 2010. www.aafp.org/afp.
36. Solomon DH, Simel DL, Bates DW, Katz JN, Schaffer JL. Does This Patient Have a Torn Meniscus or Ligament of the Knee? Value of the Physical Examination. <http://jama.jamanetwork.com/>
37. Zhao M, Zhou Y, Chang J, Hu J, Liu H, Wang S, et al. The accuracy of MRI in the diagnosis of anterior cruciate ligament injury. *Ann Transl Med*. 2020;8(24):1657-1657. doi:10.21037/atm-20-7391
38. Senftl M, Petek D, Jacobi M, Schallberger A, Spycher J, Stock A, et al. Occurrence of inadequate ACL healing after Dynamic Intraligamentary Stabilization and functional outcome—a multicentre case series. *European Journal of Orthopaedic Surgery and Traumatology*. 2022;32(7):1265-1274. doi:10.1007/s00590-021-03096-9
39. Murray MM. Current Status and Potential of Primary ACL Repair. *Clin Sports Med*. 2009;28(1):51-61. doi:10.1016/j.csm.2008.08.005

40. Wang Q, Shao G, Zhao X, Wong HH, Chin K, Zhao M, et al. Dysregulated fibrinolysis and plasmin activation promote the pathogenesis of osteoarthritis. *JCI Insight*. 2024;9(8). doi:10.1172/jci.insight.173603
41. Enoch S, Leaper DJ. *Basic Science of Wound Healing*.; 2007.
42. Nurden AT, Nurden P, Sanchez M, Andia I, Anitua E. *Platelets and Wound Healing*. Vol 13.; 2008.
43. Mahapatra P, Horriat S, Anand BS. Anterior cruciate ligament repair – past, present and future. *J Exp Orthop*. 2018;5(1). doi:10.1186/s40634-018-0136-6
44. Bogunovic L, Matava MJ. Operative and nonoperative treatment options for ACL tears in the adult patient: a conceptual review. *Phys Sportsmed*. 2013;41(4):33-40. doi:10.3810/psm.2013.11.2034
45. Mayo Robson AW. RUPTURED CRUCIAL LIGAMENTS AND THEIR REPAIR BY OPERATION.1 Consulting Surgeon to the General Infirmary at Leeds.
46. W ME, Ernest Whey Groves B, Eng F. OPERATION FOR THE REPAIR OF THE CRUCIAL LIGAMENTS.
47. Kraeutler MJ, Bravman JT, McCarty EC. Bone-patellar tendon-bone autograft versus allograft in outcomes of anterior cruciate ligament reconstruction: A meta-analysis of 5182 patients. *American Journal of Sports Medicine*. 2013;41(10):2439-2448. doi:10.1177/0363546513484127
48. Morrey BF. Why bone–patella tendon–bone grafts should still be considered the gold standard for anterior cruciate ligament reconstruction. *Yearbook of Orthopedics*. 2010;2010:164. doi:10.1016/s0276-1092(09)79651-8
49. Webster KE, Feller JA, Leigh WB, Richmond AK. Younger patients are at increased risk for graft rupture and contralateral injury after anterior cruciate ligament reconstruction. *American Journal of Sports Medicine*. 2014;42(3):641-647. doi:10.1177/0363546513517540

50. Barber-Westin SD, Noyes FR. Objective criteria for return to athletics after anterior cruciate ligament reconstruction and subsequent reinjury rates: a systematic review. *Phys Sportsmed*. 2011;39(3):100-110. doi:10.3810/psm.2011.09.1926
51. Friel NA, Chu CR. The Role of ACL Injury in the Development of Posttraumatic Knee Osteoarthritis. *Clin Sports Med*. 2013;32(1):1-12. doi:10.1016/j.csm.2012.08.017
52. Buckwalter JA, Brown TD. Joint injury, repair, and remodelling: Roles in post-traumatic osteoarthritis. In: *Clinical Orthopaedics and Related Research*. Vol 423. Lippincott Williams and Wilkins; 2004:7-16. doi:10.1097/01.blo.0000131638.81519.de
53. Glyn-Jones S, Palmer AJR, Agricola R, Price AJ, Vincent TL, Weinans H, et al. Osteoarthritis. In: *The Lancet*. Vol 386. Lancet Publishing Group; 2015:376-387. doi:10.1016/S0140-6736(14)60802-3
54. Firestein GS. Evolving concepts of rheumatoid arthritis. *Nature*. 2003;423(6937):356-361. doi:10.1038/nature01661
55. Institute for Health Metrics and Evaluation (IHME). Global Burden of Disease Collaborative Network. Global Burden of Disease Study. Published online 2021.
56. Brown TD, Johnston RC, Saltzman CL, Marsh JL, Buckwalter JA. Posttraumatic Osteoarthritis: A First Estimate of Incidence, Prevalence, and Burden of Disease. *J Orthop Trauma*. 2006;20(10).
57. Gao S, Zhang Y, Ge Y, Lu H, Li M. Global trends and current research in post-traumatic osteoarthritis A bibliometric and visualization analysis from 2010 to 2024. *Medicine (United States)*. 2024;103(47):e40604. doi:10.1097/MD.00000000000040604
58. Olson SA, Guilak F. Post-Traumatic Arthritis: Pathogenesis, Diagnosis and Management. Springer; 2015. doi:10.1007/978-1-4899-7606-2
59. Thomas AC, Hubbard-Turner T, Wikstrom EA, Palmieri-Smith RM. Epidemiology of posttraumatic osteoarthritis. *J Athl Train*. 2017;52(6):491-496. doi:10.4085/1062-6050-51.5.08

60. Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis Cartilage*. 2005;13(9):769-781. doi:10.1016/j.joca.2005.04.014
61. Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. *EClinicalMedicine*. 2020;29-30. doi:10.1016/j.eclinm.2020.100587
62. Silverwood V, Blagojevic-Bucknall M, Jinks C, Jordan JL, Protheroe J, Jordan KP. Current evidence on risk factors for knee osteoarthritis in older adults: A systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2015;23(4):507-515. doi:10.1016/j.joca.2014.11.019
63. Sowers M. Epidemiology of Risk Factors for Osteoarthritis: Systemic Factors. Vol 13.; 2001.
64. Ma HL, Blanchet TJ, Peluso D, Hopkins B, Morris EA, Glasson SS. Osteoarthritis severity is sex dependent in a surgical mouse model. *Osteoarthritis Cartilage*. 2007;15(6):695-700. doi:10.1016/j.joca.2006.11.005
65. Costa MQ, Badger GJ, Chrostek CA, Carvalho OD, Faiola SL, Fadale PD, et al. Effects of Initial Graft Tension and Patient Sex on Knee Osteoarthritis Outcomes After ACL Reconstruction: A Randomized Controlled Clinical Trial With 10- to 12-Year Follow-up. *American Journal of Sports Medicine*. 2022;50(13):3510-3521. doi:10.1177/03635465221124917
66. Salmon LJ, Refshauge KM, Russell VJ, Roe JP, Linklater J, Pinczewski LA. Gender differences in outcome after anterior cruciate ligament reconstruction with hamstring tendon autograft. *American Journal of Sports Medicine*. 2006;34(4):621-629. doi:10.1177/0363546505281806
67. Jones MH, Oak SR, Andrish JT, Brophy RH, Cox CL, Dunn WR, et al. Predictors of Radiographic Osteoarthritis 2 to 3 Years After Anterior Cruciate Ligament

- Reconstruction: Data From the MOON On-site Nested Cohort. *Orthop J Sports Med.* 2019;7(8). doi:10.1177/2325967119867085
68. Jones MH, Spindler KP. Risk factors for radiographic joint space narrowing and patient reported outcomes of post-traumatic osteoarthritis after ACL reconstruction: Data from the MOON cohort. *Journal of Orthopaedic Research.* 2017;35(7):1366-1374. doi:10.1002/jor.23557
 69. Bergman RF, Lammlin L, Junginger L, Farrell E, Goldman S, Darcy R, et al. Sexual dimorphism of the synovial transcriptome underpins greater PTOA disease severity in male mice following joint injury. *Osteoarthritis Cartilage.* Published online 2023. doi:10.1016/j.joca.2023.07.012
 70. Hwang HS, Park IY, Hong JI, Kim JR, Kim HA. Comparison of joint degeneration and pain in male and female mice in DMM model of osteoarthritis. *Osteoarthritis Cartilage.* Published online May 1, 2021. doi:10.1016/j.joca.2021.02.007
 71. Pinette MP, Molino J, Proffen BL, Murray MM, Fleming BC. Effects of Male and Female Sex on the Development of Posttraumatic Osteoarthritis in the Porcine Knee After Anterior Cruciate Ligament Surgery. *American Journal of Sports Medicine.* 2022;50(9):2417-2423. doi:10.1177/03635465221102118
 72. Pietrosimone B, Blackburn JT, Golightly YM, Harkey MS, Luc BA, Defreese JD, et al. Certified Athletic Trainers' knowledge and perceptions of posttraumatic osteoarthritis after knee injury. *J Athl Train.* 2017;52(6):541-549. doi:10.4085/1062-6050-51.2.13
 73. Fogarty AE, Chiang MC, Douglas S, Yaeger LH, Ambrosio F, Lattermann C, et al. Posttraumatic osteoarthritis after athletic knee injury: A narrative review of diagnostic imaging strategies. *PM and R.* Published online January 1, 2024. doi:10.1002/pmrj.13217

74. Punzi L, Galozzi P, Luisetto R, Favero M, Ramonda R, Oliviero F, et al. Post-traumatic arthritis: overview on pathogenic mechanisms and role of inflammation. *RMD Open*. 2016;2:279. doi:10.1136/rmdopen-2016
75. Liddle AD, Pegg EC, Pandit H. Knee replacement for osteoarthritis. *Maturitas*. 2013;75(2):131-136. doi:10.1016/j.maturitas.2013.03.005
76. Noble PC, Gordon MJ, Weiss JM, Reddix RN, Conditt MA, Mathis KB. Does total knee replacement restore normal knee function? *Clin Orthop Relat Res*. 2005;431:157-165. doi:10.1097/01.blo.0000150130.03519.fb
77. Evans JT, Walker RW, Evans JP, Blom AW, Sayers A, Whitehouse MR. How long does a knee replacement last? A systematic review and meta-analysis of case series and national registry reports with more than 15 years of follow-up. *The Lancet*. 2019;393(10172):655-663. doi:10.1016/s0140-6736(18)32531-5
78. Lieberthal J, Sambamurthy N, Scanzello CR. Inflammation in joint injury and post-traumatic osteoarthritis. *Osteoarthritis Cartilage*. 2015;23(11):1825-1834. doi:10.1016/j.joca.2015.08.015
79. Evers BJ, Van Den Bosch MHJ, Blom AB, van der Kraan PM, Koëter S, Thurlings RM. Post-traumatic knee osteoarthritis; the role of inflammation and hemarthrosis on disease progression. *Front Med (Lausanne)*. 2022;9. doi:10.3389/fmed.2022.973870
80. Pritzker KPH, Gay S, Jimenez SA, Ostergaard K, Pelletier JP, Revell K, et al. Osteoarthritis cartilage histopathology: Grading and staging. *Osteoarthritis Cartilage*. 2006;14(1):13-29. doi:10.1016/j.joca.2005.07.014
81. Torzilli PA, Grigienė R, Borrelli J, Helfet DL. Effect of Impact Load on Articular Cartilage: Cell Metabolism and Viability, and Matrix Water Content.; 1999. <http://www.asme.org/abou>
82. Heijink A, Gomoll AH, Madry H, Drobnič M, Filardo G, Espregueira-Mendes J, et al. Biomechanical considerations in the pathogenesis of osteoarthritis of the knee. *Knee*

- Surgery, Sports Traumatology, Arthroscopy. 2012;20(3):423-435.
doi:10.1007/s00167-011-1818-0
83. Andriacchi TP, Undermann AM, Lane Smith R, Alexander EJ, Dyrby CO, Koo S. A Framework for the in Vivo Pathomechanics of Osteoarthritis at the Knee. Vol 32.; 2004.
 84. Homandberg GA, Hui F. Association of Proteoglycan Degradation with Catabolic Cytokine and Stromelysin Release from Cartilage Cultured with Fibronectin Fragments. Vol 334.; 1996.
 85. Khella CM, Asgarian R, Horvath JM, Rolauffs B, Hart ML. An evidence-based systematic review of human knee post-traumatic osteoarthritis (Ptoa): Timeline of clinical presentation and disease markers, comparison of knee joint ptoa models and early disease implications. *Int J Mol Sci.* 2021;22(4):1-48. doi:10.3390/ijms22041996
 86. Lambert C, Zappia J, Sanchez C, Florin A, Dubuc JE, Henrotin Y. The Damage-Associated Molecular Patterns (DAMPs) as Potential Targets to Treat Osteoarthritis: Perspectives From a Review of the Literature. *Front Med (Lausanne).* 2021;7. doi:10.3389/fmed.2020.607186
 87. Roosendaal G, Vianen ME, van den Berg HM, Lafeber FP, Bijlsma JW. Cartilage damage as a result of hemarthrosis in a human in vitro model. *J Rheumatol.* 1997;24(7):1350-1354.
 88. Hooiveld MJJ, Roosendaal G, van den Berg HM, Bijlsma JWJ, Lafeber FPJG. Haemoglobin-derived iron-dependent hydroxyl radical formation in blood-induced joint damage: an in vitro study. *Rheumatology (Oxford).* 2003;42(6):784-790. doi:10.1093/rheumatology/keg220
 89. Swärd P, Frobell R, Englund M, Roos H, Struglics A. Cartilage and bone markers and inflammatory cytokines are increased in synovial fluid in the acute phase of knee injury (hemarthrosis) - a cross-sectional analysis. *Osteoarthritis Cartilage.* 2012;20(11):1302-1308. doi:10.1016/j.joca.2012.07.021

90. Pulles AE, Mastbergen SC, Schutgens REG, Lafeber FPJG, van Vulpen LFD. Pathophysiology of hemophilic arthropathy and potential targets for therapy. *Pharmacol Res.* 2017;115:192-199. doi:10.1016/j.phrs.2016.11.032
91. Loeuille D, Chary-Valckenaere I, Champigneulle J, Rat AC, Toussaint F, Pinzano-Watrin A, et al. Macroscopic and microscopic features of synovial membrane inflammation in the osteoarthritic knee: Correlating magnetic resonance imaging findings with disease severity. *Arthritis Rheum.* 2005;52(11):3492-3501. doi:10.1002/art.21373
92. Maglaviceanu A, Wu B, Kapoor M. Fibroblast-like synoviocytes: Role in synovial fibrosis associated with osteoarthritis. *Wound Repair and Regeneration.* 2021;29(4):642-649. doi:10.1111/wrr.12939
93. Haubruck P, Heller R, Blaker CL, Clarke EC, Smith SM, Burkhardt D, et al. Streamlining quantitative joint-wide medial femoro-tibial histopathological scoring of mouse post-traumatic knee osteoarthritis models. *Osteoarthritis Cartilage.* 2023;31(12):1602-1611. doi:10.1016/j.joca.2023.07.013
94. Little CB, Smith MM, Cake MA, Read RA, Murphy MJ, Barry FP. The OARSI histopathology initiative - recommendations for histological assessments of osteoarthritis in sheep and goats. *Osteoarthritis Cartilage.* 2010;18(SUPPL. 3). doi:10.1016/j.joca.2010.04.016
95. Little CB, Hunter DJ. Post-traumatic osteoarthritis: From mouse models to clinical trials. *Nat Rev Rheumatol.* 2013;9(8):485-497. doi:10.1038/nrrheum.2013.72
96. Giffin JR, Vogrin TM, Zantop T, Woo SLY, Harner CD. Effects of Increasing Tibial Slope on the Biomechanics of the Knee. *American Journal of Sports Medicine.* 2004;32(2):376-382. doi:10.1177/0363546503258880
97. Matsuda S, Miura H, Nagamine R, Urabe K, Ikenoue T, Okazaki K, et al. Posterior tibial slope in the normal and varus knee. *Am J Knee Surg.* 1999;12(3):165-168.

98. Ochocki DN, Loflin BE, Ahn T, Colglazier KA, Young AR, Snider AA, et al. Endurance running during late murine adolescence results in a stronger anterior cruciate ligament and flatter posterior tibial slopes compared to controls. *J Exp Orthop*. 2022;9(1). doi:10.1186/s40634-021-00439-7
99. Allen MJ, Houlton JEF, Ecv's D, Adams SB, Acv's D, Rushton N. The Surgical Anatomy of the Stifle Joint in Sheep. *Veterinary Surgery*. 1998;(27):596-605.
100. Su L, Townsend KL, Au J, Wittum TE. Article Comparison of Tibial Plateau Angles in Small and Large Breed Dogs. Vol 56.; 2015.
101. Duerr FM, Duncan CG, Savicky RS, Park RD, Egger EL, Palmer RH. Risk factors for excessive tibial plateau angle in large-breed dogs with cranial cruciate ligament disease. *J Am Vet Med Assoc*. 2007;231(11):1688-1691. doi:10.2460/javma.231.11.1688
102. Rafla M, Yang P, Mostafa A. Canine Cranial Cruciate Ligament Disease (CCLD): A Concise Review of the Recent Literature. *Animals*. 2025;15(7). doi:10.3390/ani15071030
103. Oláh T, Cai X, Michaelis JC, Madry H. Comparative anatomy and morphology of the knee in translational models for articular cartilage disorders. Part I: Large animals. *Annals of Anatomy - Anatomischer Anzeiger*. 2021;235:151680. doi:10.1016/j.aanat.2021.151680
104. Oláh T, Michaelis JC, Cai X, Cucchiari M, Madry H. Comparative anatomy and morphology of the knee in translational models for articular cartilage disorders. Part II: Small animals. *Annals of Anatomy*. 2021;234. doi:10.1016/j.aanat.2020.151630
105. Thysen S, Luyten FP, Lories RJU. Targets, models and challenges in osteoarthritis research. *DMM Disease Models and Mechanisms*. 2015;8(1):17-30. doi:10.1242/dmm.016881

106. Malfait AM, Little CB, McDougall JJ. A commentary on modelling osteoarthritis pain in small animals. *Osteoarthritis Cartilage*. 2013;21(9):1316-1326. doi:10.1016/j.joca.2013.06.003
107. Cope PJ, Ourradi K, Li Y, Sharif M. Models of osteoarthritis: the good, the bad and the promising. *Osteoarthritis Cartilage*. 2019;27(2):230-239. doi:10.1016/j.joca.2018.09.016
108. Christiansen BA, Guilak F, Lockwood KA, Olson SA, Pitsillides AA, Sandell LJ, et al. Non-invasive mouse models of post-traumatic osteoarthritis. *Osteoarthritis Cartilage*. 2015;23(10):1627-1638. doi:10.1016/j.joca.2015.05.009
109. Alves-Simões M. Rodent models of knee osteoarthritis for pain research. *Osteoarthritis Cartilage*. 2022;30(6):802-814. doi:10.1016/j.joca.2022.01.010
110. Ajayi AF, Akhigbe RE. Staging of the estrous cycle and induction of estrus in experimental rodents: an update. *Fertil Res Pract*. 2020;6(1). doi:10.1186/s40738-020-00074-3
111. Cook JL, Hung CT, Kuroki K, Stoker AM, Cook CR, Pfeiffer FM, et al. Animal models of cartilage repair. *Bone Joint Res*. 2014;3(4):89-94. doi:10.1302/2046-3758.34.2000238
112. Yu H, Fu F, Yao S, Luo H, Xu T, Jin H, et al. Biomechanical, histologic, and molecular characteristics of graft-tunnel healing in a murine modified ACL reconstruction model. *J Orthop Translat*. 2020;24:103-111. doi:10.1016/j.jot.2020.05.004
113. Kamalidinov TB, Fujino K, Shetye SS, Jiang X, Ye Y, Rodriguez AB, et al. Amplifying Bone Marrow Progenitors Expressing α -Smooth Muscle Actin Produce Zonal Insertion Sites During Tendon-to-Bone Repair. *Journal of Orthopaedic Research*. 2020;38(1):105-116. doi:10.1002/jor.24395

114. Lussier B, Behr L, Borenstein N, Brants I, Garabedian C, Ghesquiere L, et al. Sheep models in translational surgery. *European Surgical Research*. Published online April 26, 2025;1-9. doi:10.1159/000546157
115. Turner AS. Animal models of osteoporosis - Necessity and limitations. *Eur Cell Mater*. 2001;1:66-81. doi:10.22203/ecm.v001a08
116. Potes JC, Da Costa Reis J, Capela E Silva F, Relvas C, Cabrita AS, Simões JA. *The Sheep as an Animal Model in Orthopaedic Research.*; 2008.
117. Bascuñán AL, Biedrzycki A, Banks SA, Lewis DD, Kim SE. Large Animal Models for Anterior Cruciate Ligament Research. *Front Vet Sci*. 2019;6. doi:10.3389/fvets.2019.00292
118. Bartlewski PM, Baby TE, Giffin JL. Reproductive cycles in sheep. *Anim Reprod Sci*. 2011;124(3-4):259-268. doi:10.1016/j.anireprosci.2011.02.024
119. Christenson RK. Estrous activity in different breeds and breed crosses of sheep. *Theriogenology*. 1983;20(6):707-713. doi:10.1016/0093-691X(83)90191-7
120. Proffen BL, McElfresh M, Fleming BC, Murray MM. A comparative anatomical study of the human knee and six animal species. *Knee*. 2012;19(4):493-499. doi:10.1016/j.knee.2011.07.005
121. Heard BJ, Solbak NM, Achari Y, Chung M, Hart DA, Shrive NG, et al. Changes of early post-traumatic osteoarthritis in an ovine model of simulated ACL reconstruction are associated with transient acute post-injury synovial inflammation and tissue catabolism. *Osteoarthritis Cartilage*. 2013;21(12):1942-1949. doi:10.1016/j.joca.2013.08.019
122. Katie J. Sikes, Johnson JW, Michalko B, Brekhus C, Montoya T, Easley J, et al. Biomechanical Contributions of the LDE and ACL in the Ovine Stifle: Implications for a Novel Model of Post-Traumatic Osteoarthritis . In: *Orthopaedic Research Society Annual Meeting*. ; 2023.

123. Elliott CRB, Vasey JR, Russell TM. Transection of the lateral and long digital extensor tendons in racehorses. *Aust Vet J.* 2012;90(1-2):20-23. doi:10.1111/j.1751-0813.2011.00871.x
124. Niebauer GW, Restucci B. Etiopathogenesis of Canine Cruciate Ligament Disease: A Scoping Review. *Animals.* 2023;13(2). doi:10.3390/ani13020187
125. Spinella G, Arcamone G, Valentini S. Cranial cruciate ligament rupture in dogs: Review on biomechanics, etiopathogenetic factors and rehabilitation. *Vet Sci.* 2021;8(9). doi:10.3390/vetsci8090186
126. Sun C, Chang K, Fleming BC, Owens BD, Beveridge JE, Gage A, et al. A novel large animal model of posttraumatic osteoarthritis induced by inflammation with mechanical stability. *Am J Transl Res.* 2023;15(7):4573-4586. <http://www.ncbi.nlm.nih.gov/pubmed/37560216>
127. Frisbie DD, Cross MW, McIlwraith CW. A comparative study of articular cartilage thickness in the stifle of animal species used in human pre-clinical studies compared to articular cartilage thickness in the human knee. *Vet Comp Orthop Traumatol.* 2006;19(3):142-146. <http://www.ncbi.nlm.nih.gov/pubmed/16971996>
128. McIlwraith CW, Frisbie DD, Kawcak CE, Fuller CJ, Hurtig M, Cruz A. The OARSI histopathology initiative - recommendations for histological assessments of osteoarthritis in the horse. *Osteoarthritis Cartilage.* 2010;18(SUPPL. 3). doi:10.1016/j.joca.2010.05.031
129. Jimenez PA, Glasson SS, Trubetskoy O V, Haimes HB. Spontaneous osteoarthritis in Dunkin Hartley guinea pigs: histologic, radiologic, and biochemical changes. *Lab Anim Sci.* 1997;47(6):598-601.
130. Musci R V., Walsh MA, Konopka AR, Wolff CA, Peelor FF, Reiser RF, et al. The Dunkin Hartley Guinea Pig Is a Model of Primary Osteoarthritis That Also Exhibits Early Onset

- Myofiber Remodeling That Resembles Human Musculoskeletal Aging. *Front Physiol.* 2020;11. doi:10.3389/fphys.2020.571372
131. Timkovich AE, Sikes KJ, Andrie KM, Afzali MF, Sanford J, Fernandez K, et al. Full and Partial Mid-substance ACL Rupture Using Mechanical Tibial Displacement in Male and Female Mice. *Ann Biomed Eng.* 2023;51(3):579-593. doi:10.1007/s10439-022-03065-

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CHAPTER 2: STRUCTURAL, FUNCTIONAL, AND PROTEOMIC BASED SEX DIFFERENCES IN MURINE POST-TRAUMATIC OSTEOARTHRITIS DEVELOPMENT FOLLOWING MECHANICAL ANTERIOR CRUCIATE LIGAMENT INJURY¹

2.1 Introduction

Over 120,000 anterior cruciate ligament (ACL) injuries occur each year in the United States.¹ Following ACL injury, up to 87% of individuals develop post-traumatic osteoarthritis (PTOA) in their knee joint.² Knee PTOA is a debilitating condition that, in its later stages, requires patients to undergo invasive total knee arthroplasty to restore mobility and alleviate pain, accounting for nearly \$1 billion in reconstructive surgery costs per year.^{1,3} The increasing annual incidence of ACL injuries and subsequent rise in PTOA, emphasizes the need for expanded prevention and treatment options.^{4,5} Since PTOA is a known risk after ACL injury, preventing its development more closely to the time of the initiating injury presents a promising opportunity to develop therapeutic targets.

Sex differences play a pivotal role in ACL injury induction, with female athletes two to ten times more likely to sustain an ACL rupture compared to males.⁶⁻⁸ Various factors, including anatomical differences and hormone fluctuations, likely contribute to this heightened risk among females.^{9,10} Notably, estrogen, a steroid hormone with greater concentrations in females, contributes to increased joint laxity, which is associated with a greater risk for ACL injury.^{11,12}

Sexual dimorphism may also influence PTOA development following ACL injury, though current data provides an incomplete picture. In humans, males and females do not show a significant difference in patient-reported outcomes following ACL reconstruction.^{13,14} Specifically, humans have not shown consistent differences in functional outcomes such as anterior-posterior

¹ This chapter includes the complete published manuscript: Van Zeeland EM, Kassel B, Montoya T, Saviola AJ, Burton LH, Easley JT, Nelson BB, Santangelo KS, Sikes KJ. Structural, functional, and proteomic based sex differences in murine post-traumatic osteoarthritis development following mechanical anterior cruciate ligament injury. *Osteoarthritis Cartilage*. 2025 May, doi:10.1016/j.joca.2025.05.004.

laxity or hop deficit testing.¹⁴ Imaging assessments, such as magnetic resonance imaging (MRI)- and radiograph-based PTOA scoring, have also yielded conflicting results regarding sex differences in knee joint pathology.^{14,15} These discrepancies in human studies demonstrate the need for translatable animal models to comprehensively investigate PTOA development following ACL rupture.

Similar confounding results are also seen with PTOA development following ACL injury in animal models. In a porcine model of ACL reconstruction, females showed greater cartilage damage than males.¹⁶ However, in murine models of PTOA, males have consistently demonstrated more severe PTOA development than females through worsened joint pathology, increased pain-related behaviors, and decreased injured limb loading.^{17–21} Hormonal fluctuations between males and females, which may vary by species, could contribute to these discrepancies, though further research is warranted to elucidate these mechanisms. Exogenous estrogen administration in both male and female mice following destabilization of the medial meniscus (DMM) has been shown to have a protective role in preventing PTOA development.^{18,22} This is consistent with findings that postmenopausal women (decreased estrogen levels) are more likely to develop osteoarthritis (OA).²³

Many of these pre-clinical studies were performed in surgical models, such as DMM or ACL transection, and lack correlations between different OA outcomes (such as mobility and pathology) in the same animal, limiting the clinical impact of their findings. Thus, a significant need exists to study the sexual differences of PTOA development in a more clinically relevant model. The groundbreaking recent work by Bergman et al., utilizing a non-surgical ACL rupture model to induce PTOA in mice, made significant progress in addressing this gap.¹⁷ Here, we aim to expand upon that research by exploring disease progression over longer time periods, while employing diverse outcome parameters.

The overall goal of this work was to explore the role of sex on PTOA progression following ACL rupture, with the end goal of identifying novel avenues for potential therapeutic development.

To do so, we induced PTOA using our previously published mechanical, non-surgical mouse model of ACL rupture.²⁴ We then comprehensively characterized PTOA progression in male and female mice utilizing longitudinal mobility assessments, radiographic imaging, histologic scoring, and untargeted proteomics.

2.2 Methods

2.2.1 Experimental Animals

All procedures were approved by the Colorado State University Institutional Animal Care and Use Committee (#2137). Seventy female and seventy male C57BL/6J (NCI 556) wild-type mice were purchased from Charles River Laboratories at approximately 70 days of age and were acclimated to the vivarium for 14 days before experimentation. Animals were housed by sex in groups of 3 – 5 in solid bottom cages with corncob bedding, ad libitum water, and standard rodent chow, and were maintained at 22 – 24 °C on a 12-hour light/dark cycle. Animals were assessed daily with body weights monitored weekly (Appendix I.1A, C) and were randomly assigned to the outcome groups outlined in Figure 2.1 using the Excel RAND function, with randomization stratified by sex.

At study endpoints, mice were anesthetized with 2% isoflurane inhalation and euthanized via cardiac blood draw and confirmatory cervical dislocation. Five animals were excluded from all analyses due to lack of complete ACL rupture or severe extraneous injury (Figure 2.1, Appendix I.2).

2.2.2 Mouse Anterior Cruciate Ligament Rupture Model

Animals were anesthetized via 2% isoflurane inhalation and placed in the custom bioreactor. The right hindlimb of each animal underwent our ACL rupture protocol.²⁴ Output loading data were recorded for each animal (Figure 2.2, Appendix I.3). Analgesia was administered at the time of injury via subcutaneous injection of slow-release buprenorphine

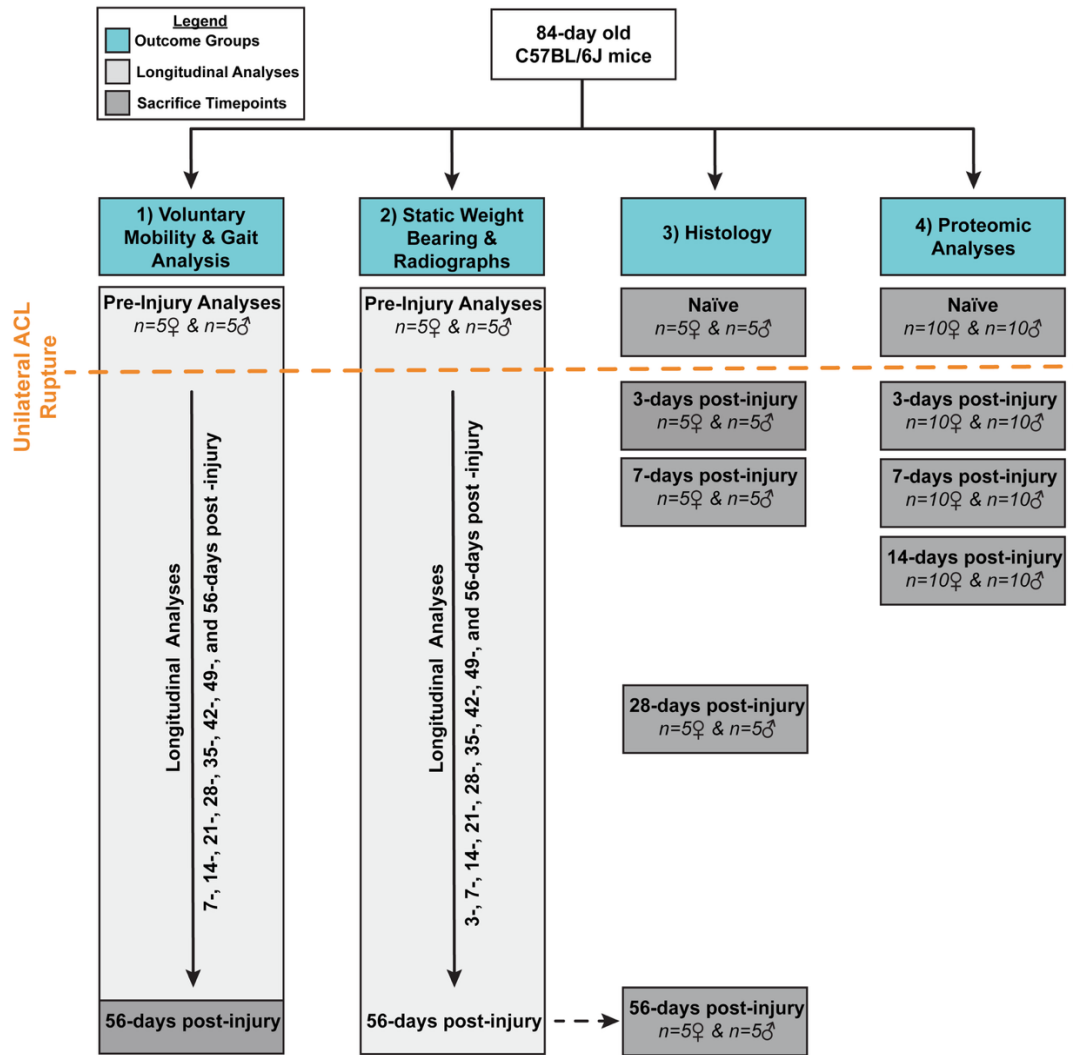


Figure 2.1. Overview of experimental design. Animals were randomly assigned to the following outcome groups: 1) Longitudinal Voluntary Mobility (ANY-maze) and Gait Analysis (Digigait), 2) Longitudinal Static Weight Bearing (Bioseb) and Radiographs, 3) Histology at timepoints of pre-injury and 3-, 7-, 28-, and 56-days post-injury, and 4) Proteomic Analyses at timepoints of pre-injury and 3-, 7-, and 14-days post-injury. Longitudinal analyses were conducted prior to injury and weekly for 56-days post-injury. The 56-day post-injury animals from the Longitudinal Static Weight Bearing and Radiograph group were used for the histology timepoint (indicated by black dashed line). Pre-injury animals for histology and proteomics were age-matched to the time of ACL rupture for all other groups, approximately 84-days old. At the endpoints for each outcome, mice were anesthetized with 2% isoflurane inhalation and euthanized via cardiac blood draw, followed by cervical dislocation. Five animals were excluded from all analyses in the study. Four were due to believed partial ACL ruptures identified during histologic analyses ($n=1$ 7d♂, $n=1$ 28d♂, $n=1$ 28d♀, $n=1$ 56d♂). One animal was excluded due to extreme severity of injury that could not be attributed to the ACL rupture itself ($=1$ 56d♀). It is suspected that an injury to the MCL occurred at some point between 14- and 28-days post-injury, based on evidence from longitudinal radiographic imaging of this animal. Since compromise to the MCL is not seen with the ACL rupture model, it is suspected that an extraneous injury beyond ACL rupture occurred and hastened the damage (Appendix I.2).

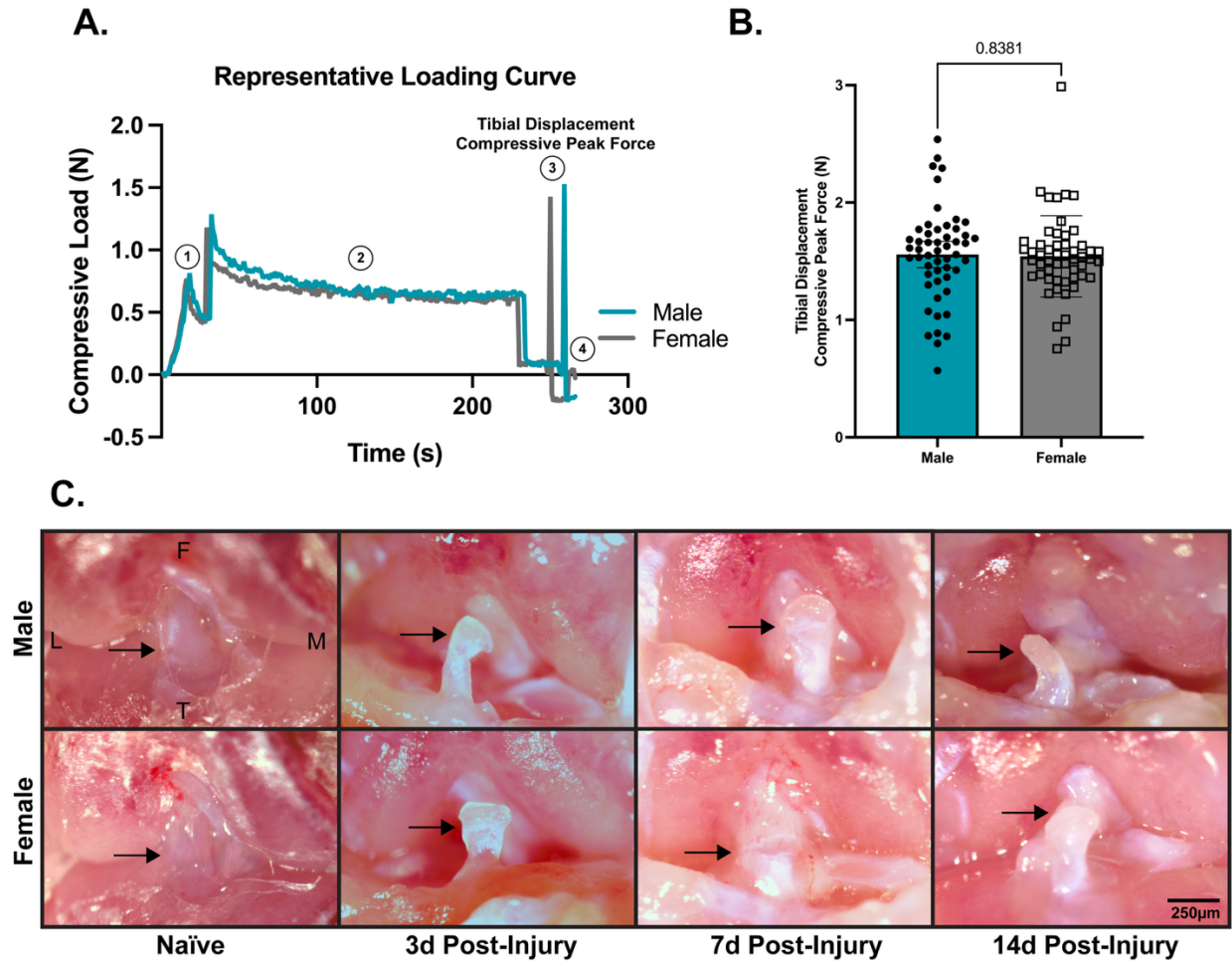


Figure 2.2. Confirmation of ACL rupture. **(A)** Output loading data was obtained for each animal during ACL rupture. The following steps of the previously developed ACL rupture protocol can be seen in Figure 2,2A: 1) manual preload, 2) preconditioning, 3) tibial displacement instantaneous loading, and 4) post-injury displacement test. **(B)** No difference between male and female mice was observed in the force (tibial displacement compressive peak force) required to achieve ACL rupture (bars represent mean $\pm$ 95% confidence interval with individual animals represented by each datapoint). Two-tailed unpaired t-test, $n=52$ males and $n=53$ females (see exclusion statement in Figure 2.1 and Appendix I.2). **(C)** Anterior macroscopic imaging at the time of necropsy confirmed consistent mid-substance ACL rupture. Arrows denote ACLs from naïve groups and ACL remnants, F = Femur, T = Tibia, L = Lateral, M = Medial.

(1mg/kg), which provides 48 – 72 hours of analgesia without modulating anti-inflammatory activity.²⁵

2.2.3 Mobility and Behavioral Assessments

Longitudinal mobility analyses were conducted prior to injury and weekly for eight weeks (56 days) post-injury to assess symptoms of PTOA development by three methods: individual cage monitoring, gait analysis, and static weight bearing. For all outcomes, mice were acclimated over one week, and two pre-injury measurements were collected on separate days and averaged to establish a pre-injury baseline for each animal. Handlers were not blinded to the sex of the animal. For all measurements, testing occurred during the same time of day and was performed by the same handlers (EMV, BK)

To determine general behavior and activity levels, each mouse was placed individually in its home cage with security hut for 10 min. The video analysis software (ANY-maze, IL) automatically collected mobility parameters.

Gait abnormalities were monitored using the treadmill-based Digigait analysis system (Mouse Specifics, MA). Three runs per animal were taken while jogging (40 cm/sec) at each of the following grades: flat, 10° incline, and 10° decline. The three runs for each setting were averaged for each animal. Paw statistics were calculated using the Digigait analysis software (Version 16).

To assess postural equilibrium, mice were minimally restrained, and static weight bearing assessed (Bioseb, FL) on both hindlimbs. Three measurements, 10 s each, were taken per animal per day and averaged. Animals were weighed at the time of testing, and loading of each hindlimb was normalized to each animal's bodyweight. Hindlimb weight distribution was calculated as Right/Left hindlimb.

For all mobility and behavioral tests, parameters of interest were assessed between male and female mice prior to injury, and longitudinally between groups over time with values normalized to pre-injury baseline values.

2.2.4 Radiograph Imaging and Scoring

Before injury and weekly for eight weeks (56 days) post-injury, animals were anesthetized via 2% isoflurane inhalation and placed in a XPERT 80-L X-Ray System (Kubtec, CT). Animals were placed in dorsal recumbency, and both craniocaudal and mediolateral views of the stifles were obtained. For the craniocaudal view, tape was used to achieve consistent stifle extension and internal rotation of the femur. For the mediolateral view, the hindlimbs were allowed to naturally abduct (Appendix I.4A).

To quantify evidence of joint-wide manifestations of PTOA development, the canine stifle OA scoring system by Hurley et al. was modified (Appendix I.4B).²⁶ Radiographs were scored by a blinded board-certified veterinary surgeon (BBN).

2.2.5 Histology and Scoring

Following euthanasia, hindlimbs were fixed in 10% neutral buffered formalin for 48 – 72 hours, decalcified in 5% ethylenediaminetetraacetic acid (EDTA)/ phosphate-buffered saline (PBS) for at least six weeks, then processed, paraffin-embedded, and microtome sectioned coronally (5 µm). Slides were dual-stained using an adapted protocol for toluidine blue and fast green (Appendix I.5). To quantify joint pathology, the murine PTOA scoring system developed by Haubruck et al. was modified for coronal sections (Appendix I.5).²⁷ Slides were scored by a blinded board-certified veterinary pathologist (KSS).

2.2.6 Proteomic Sample Preparation and Analyses

At endpoints of 3, 7, and 14 days post-injury, ACL remnants from ten mice per sex per timepoint were assessed for untargeted label-free protein quantification. Intact ACLs from naïve mice were analyzed under the same conditions to establish baseline sex differences.

Immediately following euthanasia, a #11 blade was used to transect the patellar tendon, collateral ligaments, and remove the infrapatellar fat pad under a dissecting microscope. With the stifle joint fully flexed, ACL rupture was confirmed. The native ACL or ACL remnants were removed, flash-frozen in liquid nitrogen, and stored at -80°C . Ligament samples were normalized by peptide weight during digestion. Full proteomic preparation details are available in Appendix I.6.

After alignment, 2415 proteins were identified. 19 of these proteins were identified as having multiple isoforms or fragments. Combining redundant entries yielded 2396 unique proteins. Data was log2-transformed using NormalyzerDE.²⁸ Filtering, imputation, and global comparisons were performed with Metaboanalyst 5.0.²⁹ Features with > 67% missing values were removed, and remaining missing values were imputed with 1/5 of the minimum positive value per variable. After processing, 493 proteins remained for analysis. Quality control figures are available in Appendix I.7.

2.2.7 Statistical Analysis

Statistical comparisons, excluding proteomics, were conducted in Graphpad Prism 10 (San Diego, CA). For histologic scores, each mouse contributed to a single timepoint (no repeated measures). Two-way models were fit separately for each histology parameter. These models included sex (male, female), time (categorical: naïve and 3, 7, 28, 56 days post-injury) and sex*time interaction. Tukey's multiple comparison post-hoc testing was performed to compare all possible pairs of group means.

For mobility analyses, behavioral tests, and radiographic scoring, repeat observations were conducted on the same mice over time. Two-sample t-tests were used to compare

between male and female at the pre-injury timepoint, separately for each response.

Normalization to pre-injury values was performed by calculating the difference between later timepoints and pre-injury values for each mouse and each response. Repeated measures mixed models were fit separately for each outcome using the difference as the response variable. Fixed effects included sex (male, female), time (categorical: 3, 7, 14, 21, 28, 42, 49, 56 days post-injury) and sex*time interaction. Mouse was included as a random effect to account for the repeated measures design. Tukey's multiple comparison post-hoc testing was performed to compare all possible pairs of group means.

Simple linear regressions were performed to assess the association between tibial displacement compressive peak force (dependent variable) and both mouse weight and tibial length (independent variables) (Appendix I.3).

For all models, assumptions were checked using residual diagnostic plots in Graphpad, ensuring equal variance through residual vs. predicted plots and assessing normality with QQ plots. Significance for all comparisons was set to $p\text{-values} < 0.05$. Output data from statistical comparisons, including p-values and 95% confidence intervals, can be found in the corresponding Supplemental for each outcome measure.

For proteomics, statistical analyses and group comparisons were conducted using Amica v3.0.1.³⁰ Significance for all comparisons was set to $p\text{-values} < 0.05$ and $\log_2(\text{fold-change})$ threshold of 1.5. Groups were analyzed using a pair-wise two-way model (no repeated measures). These models included sex (male, female), time (categorical: naïve and 3, 7, 14 days post-injury) and sex*time interaction. Kyoto Encyclopedia of Genes and Genomes (KEGG) and gene ontology pathway analyses assessed sex differences and the impact of injury in the ACL proteome using ShinyGO 0.77.³¹ Analyses compared significantly different proteins between sexes at each timepoint (Figure 2.8C) and, separately for each sex, proteins differing at 3, 7, or 14 days post-injury relative to naïve (Appendix I.8C).

A priori sample size calculations were conducted in GPower v3.1.1. For mobility and behavioral assessments, radiographs, and histology, calculations were based on data from previous ANY-maze experiments comparing male and female mice 14 days post-ACL rupture.²⁴ The outcome variable was number of Top of Hut Exits, assuming a within-group standard deviation of 5 and a between-group difference of 12.2 exits (effect size=2.44). Power calculations were performed using a two-sample t-test, with alpha=0.05 and power>90%, yielding a sample size of 5 animals per sex per timepoint. For proteomic analyses, calculations were based on pilot ACL proteomic data (unpublished), using COL1a1 intensity levels with an assumed standard deviation of 8063369.279 and a between-group difference of 12628553.3 (effect size=1.57). Using the same statistical parameters, the required sample size was 10 animals per sex per timepoint.

2.3 Results

2.3.1 Sex-Based Evaluation of a Mouse Model of Non-Surgical ACL Rupture

Examination of output loading data (Figure 2.2A) from our mid-substance ACL rupture model revealed no differences in the force required for ACL rupture between male and female mice (Figure 2.2B). Further, tibial displacement compressive peak force was not correlated with body weight or tibia length (Appendix I.3A-B, E). Additional analyses of ACL injury induction parameters, such as percent stress relaxation during preconditioning, were not different between male and female mice (Appendix I.3C, E), although female mice exhibited reduced loading in the post-injury displacement test compared to males (Appendix I.3D, E).

Complete rupture of the ACL was found to occur in 95% (105/110) of mice. Macroscopic imaging confirmed uniform mid-substance ruptures of the ACL, with no evident damage to other intra- or extra-articular structures (Figure 2.2C).

2.3.2 Influence of Sex on Symptomatic and Functional Progression of PTOA

Voluntary mobility of mice using the ANY-maze cage monitoring system (Figure 2.3A) revealed no significant differences in pre-injury head distance traveled (Figure 2.3B) or top of hut entries (Figure 2.3C) between male and female mice. Notably, before injury, male mice exhibited a higher number of body rotations (Figure 2.3D) and average speed traveled (Figure 2.3E) compared to females. However, post-injury, female mice displayed increased overall head distance traveled (Figure 2.3F, mean difference 56d: -3.81 [95% CI: -7.45 to -0.18]), top of hut entries (Figure 2.3G, mean difference 42d: -28.4 [95% CI: -45.97 to -10.83]), body rotations (Figure 2.3H, mean difference 56d: -9.4 [95% CI: -15.70 to -3.10]), and average speed traveled (Figure 2.3I, mean difference 42d: -0.0059 [95% CI: -0.0110 to -0.0008]) compared to male mice. Analysis of all ANY-maze parameters can be found in Appendix I.9.

The functional gait of mice evaluated using the Digigait treadmill system (Figure 2.4A) revealed that pre-injury values of stance width (Figure 2.4B) and stance time (Figure 2.4C) did not differ significantly between male and female mice. Following injury, male mice demonstrated increased hindlimb stance width (Figure 2.4D, mean difference 56d: 0.28 [95% CI: 0.01 to 0.56]) and decreased stance time (Figure 2.4E, mean difference 56d: -0.0122 [95% CI: -0.0236 to -0.0009]) compared to female mice. Furthermore, female mice exhibited increased internal rotation of their injured paw post-injury, despite having greater natural external rotation than male mice prior to injury (Appendix I.10). Analysis of all Digigait parameters can be found in Appendix I.10.

Postural equilibrium of mice evaluated using Bioseb static weight bearing (Figure 2.5A) revealed no sex differences in hindlimb weight bearing before injury (Figure 2.5B) and no disparities in loading between the right and left limbs (Appendix I.11). Following injury, both male and female mice showed an initial imbalanced hindlimb weight distribution. However, female mice exhibited a gradual return to pre-injury loading values while male mice continued to offload their injured limb (Figure 2.5C, mean difference 56d: 0.30 [95% CI: 0.08 to 0.52]).

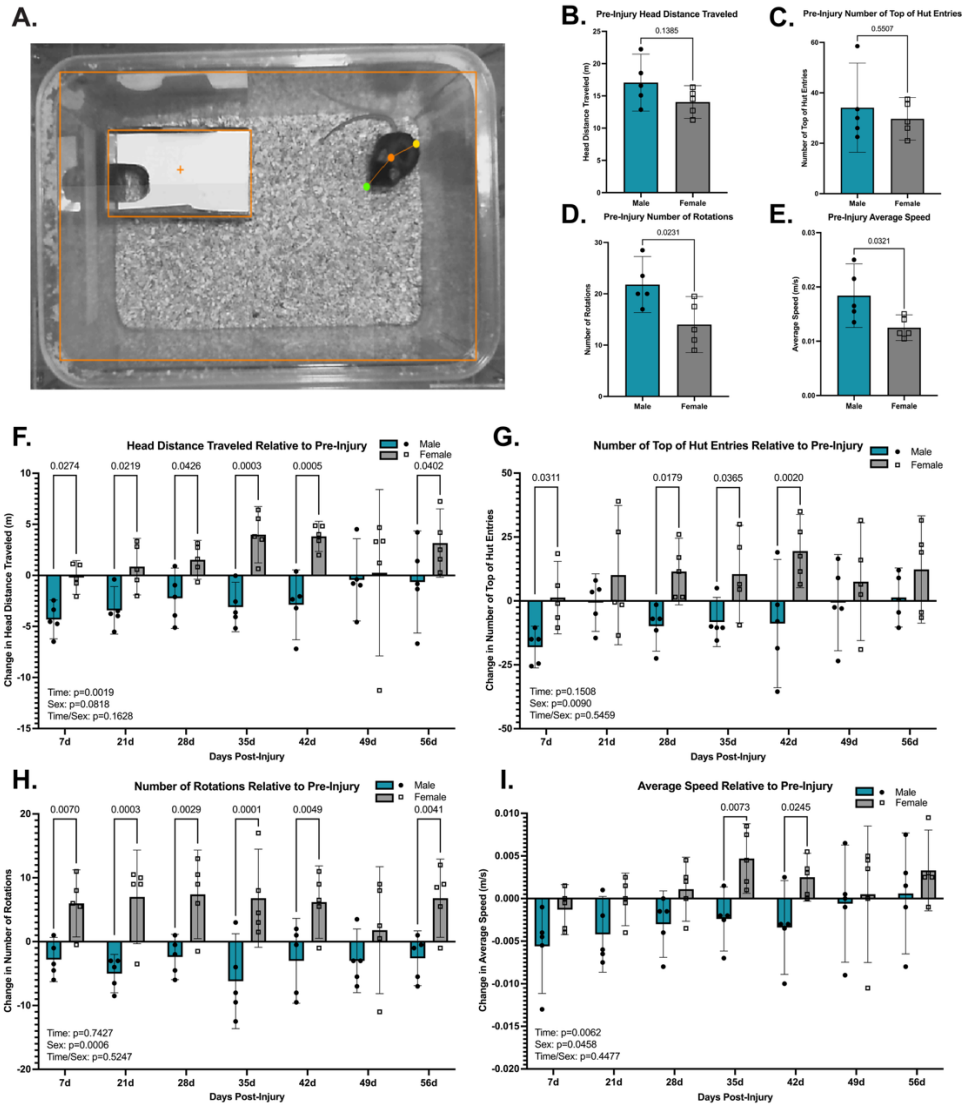


Figure 2.3. Analysis of longitudinal voluntary mobility following ACL rupture. **(A)** Mice were placed in their home cage for ten minutes and subjected to ANY-maze overhead cage monitoring. Male and female mice showed no differences in pre-injury **(B)** head distance traveled or **(C)** number of top of hut entries. However, compared to female mice, males exhibited increased **(D)** number of body rotations and **(E)** average speed traveled prior to injury. A two-tailed unpaired t-test with $n=5$ males and $n=5$ females was used to investigate pre-injury differences. For post-ACL rupture timepoints, all parameters measured were normalized to each individual animal's pre-injury values. Compared to male mice, females demonstrated an increase in **(F)** head distance traveled at 7-, 21-, 28-, 35-, 42-, and 56-days post-injury, **(G)** number of top of hut entries at 7-, 28-, 35-, and 42-days post-injury, **(H)** number of body rotations at 7-, 21-, 28-, 35-, 42-, and 56-days post-injury, and **(I)** average speed at 35- and 42-days post-injury. A repeated measures mixed model with multiple comparisons was utilized and p -values calculated for sex, time, and sex/time interaction factors. **F-I** depict multiple comparisons between male and female mice at each timepoint with p -values less than 0.05 shown. Bars represent mean $\pm$ 95% confidence interval with individual animals marked. Additional outcome parameters measured and statistical analyses, including 95% confidence intervals and changes seen over time, can be found in Appendix I. 9.

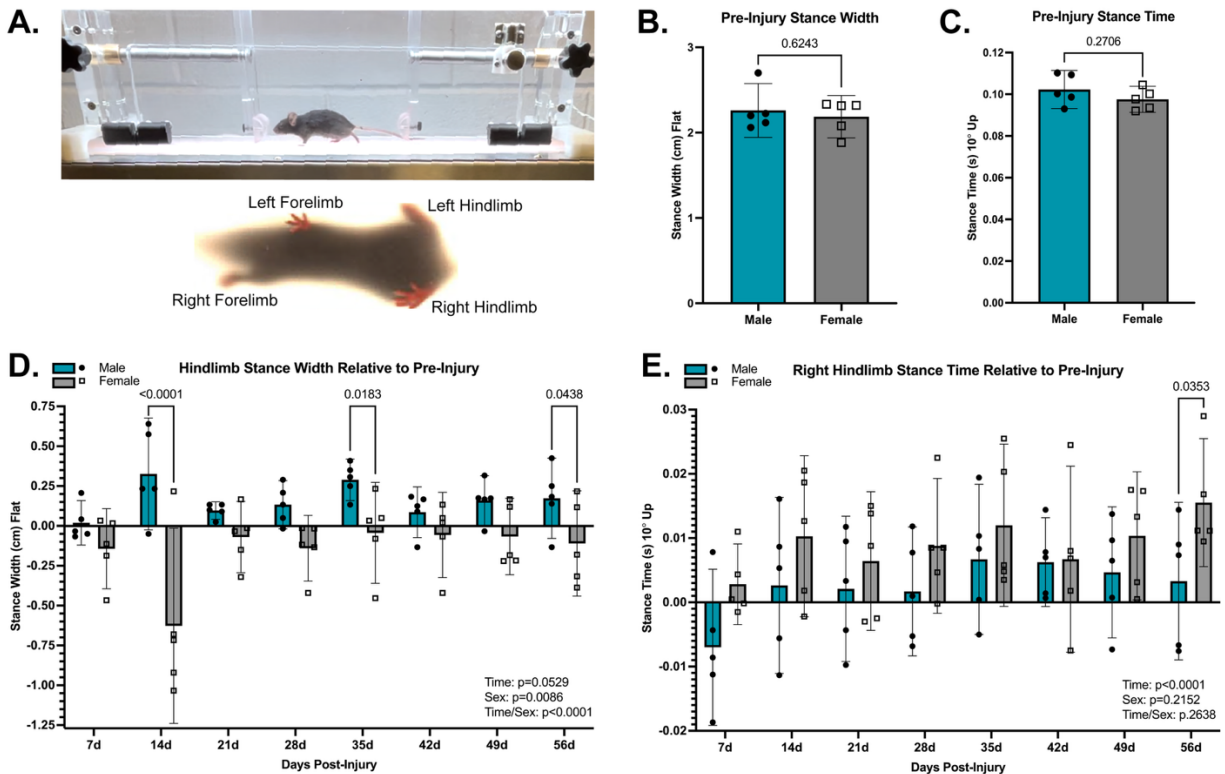


Figure 2.4. Longitudinal gait analyses of male and female mice following ACL rupture. (A) Mice were placed in the treadmill based Digigait analysis system, shown from the side (upper panel) and underneath/ventrally (lower panel) camera view. Values were tracked for each limb at 40 cm/sec on a flat treadmill, 10° inclined treadmill, and 10° declined treadmill. Three runs per animal were taken and averaged. Male and female mice showed no differences in pre-injury (B) hindlimb stance width or (C) right hindlimb stance time. Stance width represents the perpendicular distance between the centroids of each hindlimb during peak stance. Stance time is the duration in which the paw of the mouse is in contact with the treadmill belt. Detailed definitions for all DigiGait parameters are provided in Appendix I.10. A two-tailed unpaired t-test with $n=5$ males and $n=5$ females was used to investigate pre-injury differences. After normalization to pre-injury values, males demonstrated increases in (D) hindlimb stance width at 14-, 35-, and 56-days post-injury and (E) decreases in stance time at 56-days post-injury compared to female mice. A repeated measures mixed model with multiple comparisons was utilized and p-values calculated for sex, time, and sex/time interaction factors. D and E depict multiple comparisons between male and female mice at each timepoint with p-values less than 0.05 shown. Bars represent mean $\pm$ 95% confidence interval with individual animals marked. Additional outcome parameters measured and statistical analyses, including 95% confidence intervals and changes seen over time, can be found in Appendix I.10.

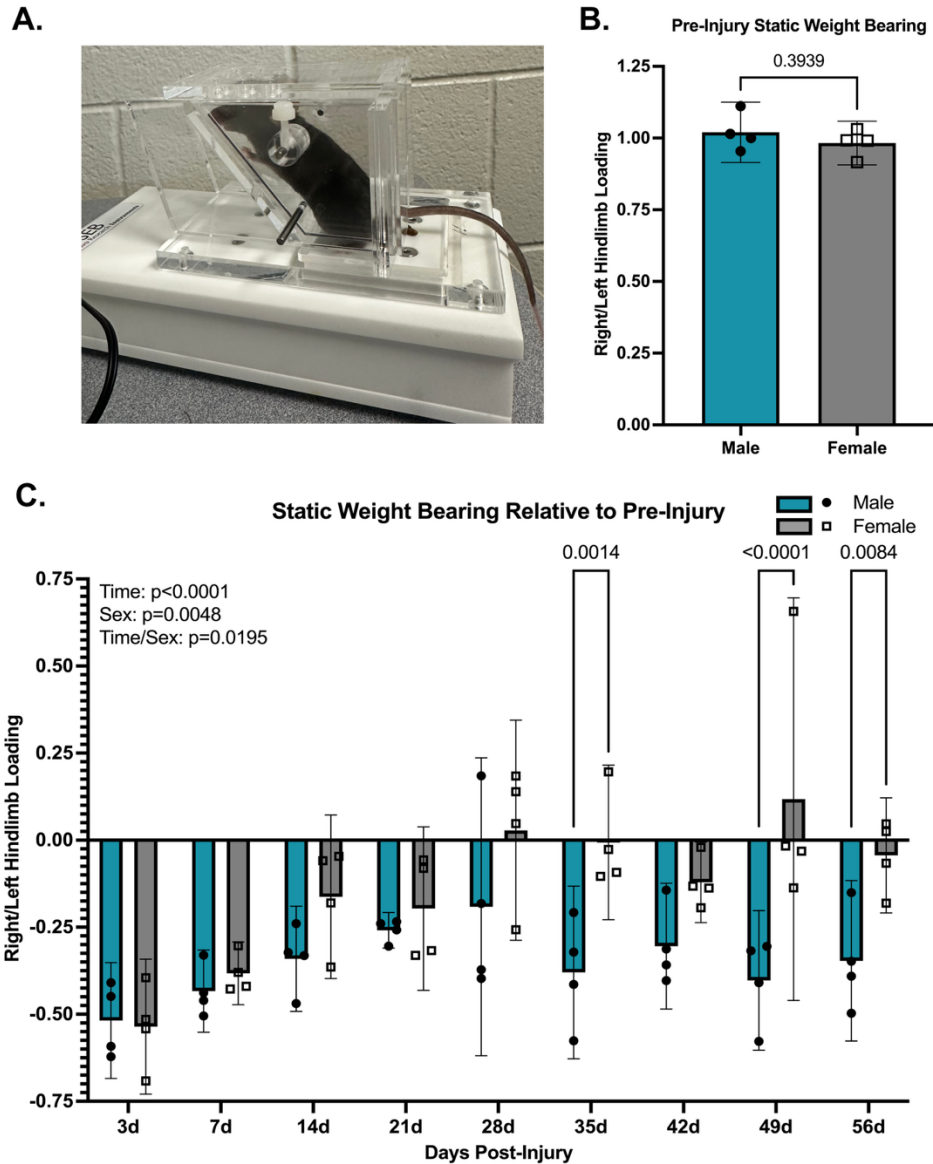


Figure 2.5. Longitudinal assessment of hindlimb static weight bearing. Mice were placed in the (A) Bioseb testing chamber with each hindlimb on a separate load cell. All output loads were normalized to each animal's bodyweight measured at the time of testing. (B) Pre-injury measurements showed no differences in hindlimb weight distribution (Right hindlimb/Left hindlimb) between male and female mice, with values observed representing the anticipated postural equilibrium (close to 1). A two-tailed unpaired t-test with $n=4$ males and $n=4$ females (see exclusion statement in Figure 2.1 and Appendix I.2) was used to investigate pre-injury differences. When post-injury values were normalized to pre-injury measurements, male mice demonstrated (C) increased offloading of their injured right hindlimb compared to female mice at 35-, 49-, and 56-days post-injury. A repeated measures mixed model with multiple comparisons was utilized and p -values calculated for sex, time, and sex/time interaction factors. (C) Multiple comparisons between male and female mice at each timepoint with p -values less than 0.05 shown. Bars represent mean $\pm$ 95% confidence interval with individual animals marked. Additional statistical analyses, including 95% confidence intervals and changes seen over time, can be found in Appendix I.11.

2.3.3 Analysis of Structural Differences in PTOA Development Between Male and Female Mice

Longitudinal radiograph scoring demonstrated no discernible sex-based differences before ACL injury or at any of the post-injury timepoints (Figure 2.6A, B). PTOA development became apparent starting 21 days post-injury relative to 14 days post-injury and progressively worsened throughout the study duration (Appendix I.12). Manifestations of PTOA included features such as osteophyte development and meniscal mineralization (Figure 2.6C, Appendix I.13).

Histological sections of mouse stifles at 56 days post-injury revealed that male mice exhibited a more severe joint pathology compared to females (Figure 2.7A, mean difference 56d: 49.97 [95% CI: 5.78 to 94.15]). This differential pathology predominantly stemmed from alterations in the cartilage, bone, and cruciate ligament domains (Figure 2.7B, Appendix I.14, Appendix I.15). Temporal factors also influenced PTOA progression, as indicated by an initial increase in scores at 3 days post-injury compared to naïve, followed by a trend toward resolution by day 7. Pathology worsened at later timepoints, particularly at 28- and 56-days post-injury. Representative histological sections illustrating these changes are depicted in Figure 2.7C.

2.3.4 Proteomics

Clustering analysis of group averages from naïve and injured ACL remnant tissue revealed distinct segregation by timepoint (Figure 2.8A, Appendix I.16A). The ACL proteome response followed a dynamic, sex-specific pattern across timepoints. Before injury, only 2 of 22 significantly different proteins were higher in males. At 3 days post-injury, none of the 41 differed proteins were higher in males, and at 7 days, only 1 of 14 was elevated. By 14 days, however, 6 of 8 significantly different proteins were higher in males. This suggests that while females had a stronger naïve and early proteome response, sex differences shifted over time,

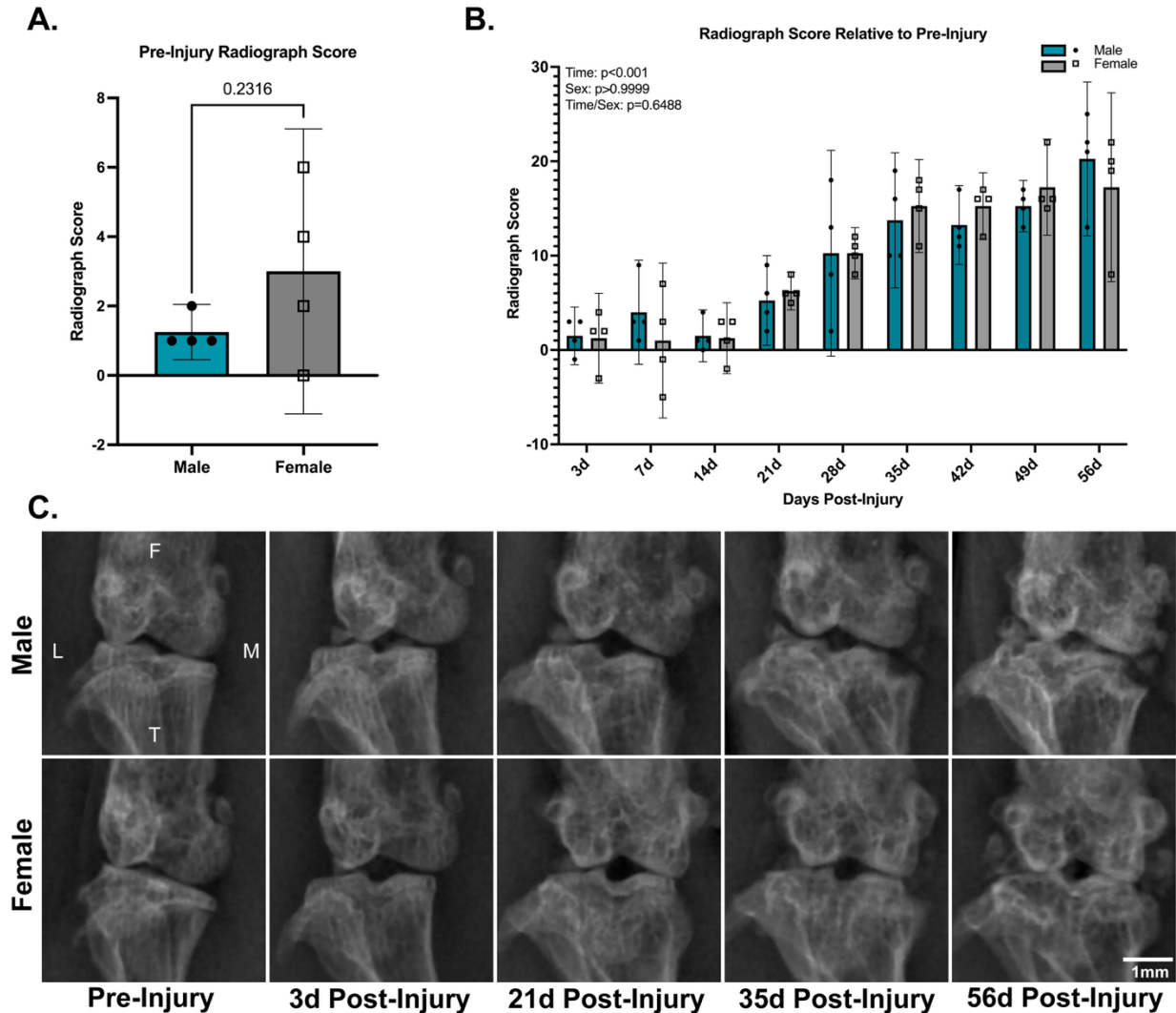


Figure 2.6. Longitudinal stifle radiographic images following ACL rupture. **(A)** Male and female mice did not show a difference in pre-injury radiograph score. A two-tailed unpaired t-test with $n=4$ males and $n=4$ females (see exclusion statement in Figure 2.1 and Appendix I.2) was used to investigate pre-injury differences. **(B)** When post-injury scores were normalized to pre-injury measurements, no differences were seen between male and female mice in overall radiograph scores at each timepoint. A repeated measures mixed model with multiple comparisons was utilized and p -values calculated for sex, time, and sex/time interaction factors. Multiple comparisons between male and female mice at each timepoint with p -values less than 0.05 shown (none). Bars represent mean $\pm$ 95% confidence interval with individual animals marked. Additional statistical analyses, including 95% confidence intervals and changes seen over time, can be found in Appendix I.12. Radiographic evidence of PTOA progression was observed by 21-days post-injury with radiographic score increasing significantly at 35-days post-injury. After 35-days post-injury, radiographic scores continued to trend higher until study completion at 56-days post-injury. **(C)** Representative craniocaudal views of select timepoints for the same male and female animal throughout the study timeline are shown. F = Femur, T = Tibia, L = Lateral, M = Medial. Representative radiographs for all timepoints can be found in Appendix I.1

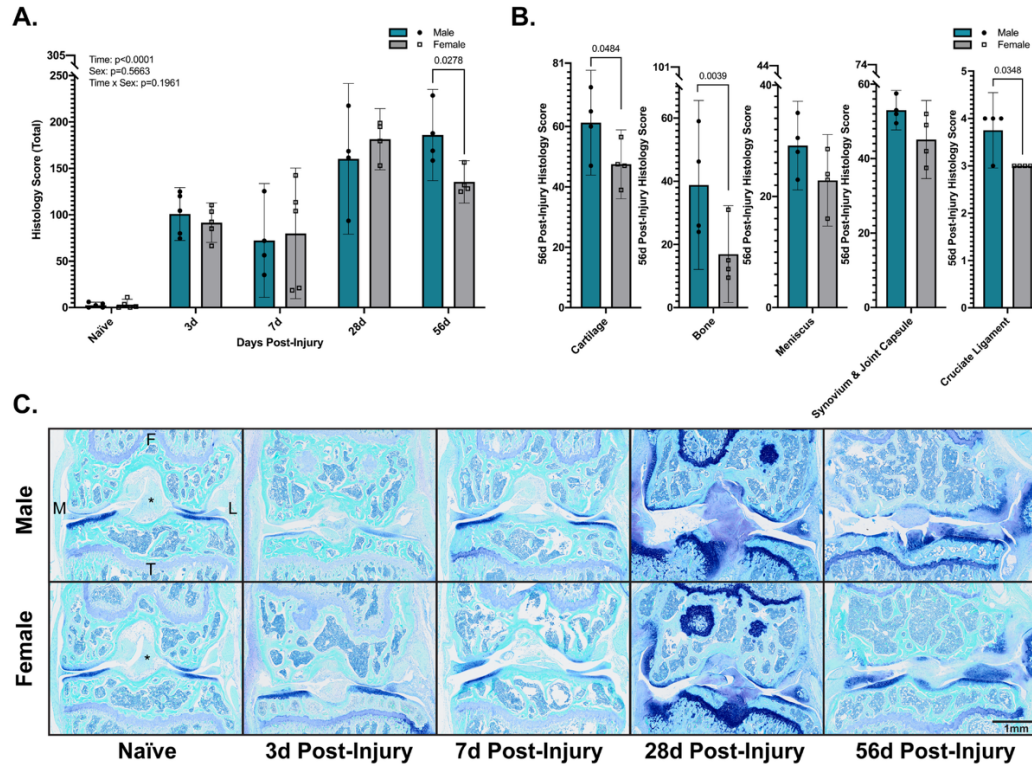


Figure 2.7. Histologic characterization of male and female mouse stifle joints following non-surgical ACL injury. **(A)** 56-days following injury, male mice displayed an overall higher histology score than female mice. Two-way models were fit for each histology parameter and p-values calculated for sex, time, and sex/time interaction factors for $n=4$ males and $n=4$ females (see exclusion statement in Figure 2.1 and Appendix I.2). Due to unequal animal numbers across groups, a mixed-effects model with multiple comparisons was utilized (no repeated measures). **(B)** Cartilage, bone, and cruciate ligament scores were greater in male mice compared to female mice at 56-days post-injury, with no differences observed between male and female mice for meniscus and synovium and joint capsule scores. Multiple comparisons between male and female mice at each timepoint with p-values less than 0.05 shown. The maximum y-axes values represent the highest possible histology score, with axis breaks included for improved data visualization. Bars represent mean $\pm$ 95% confidence interval with individual animals marked. Additional statistical analyses, including changes seen over time and 95% confidence intervals can be found in Appendix I.14 and Appendix I.15. **(C)** Representative coronal sections at 20X magnification of male and female stifle joints prior to ACL rupture and 3-, 7-, 28-, and 56-days following injury. Sections are stained with toluidine blue and fast green. ACL = *, F = Femur, T = Tibia, L = Lateral, M = Medial.

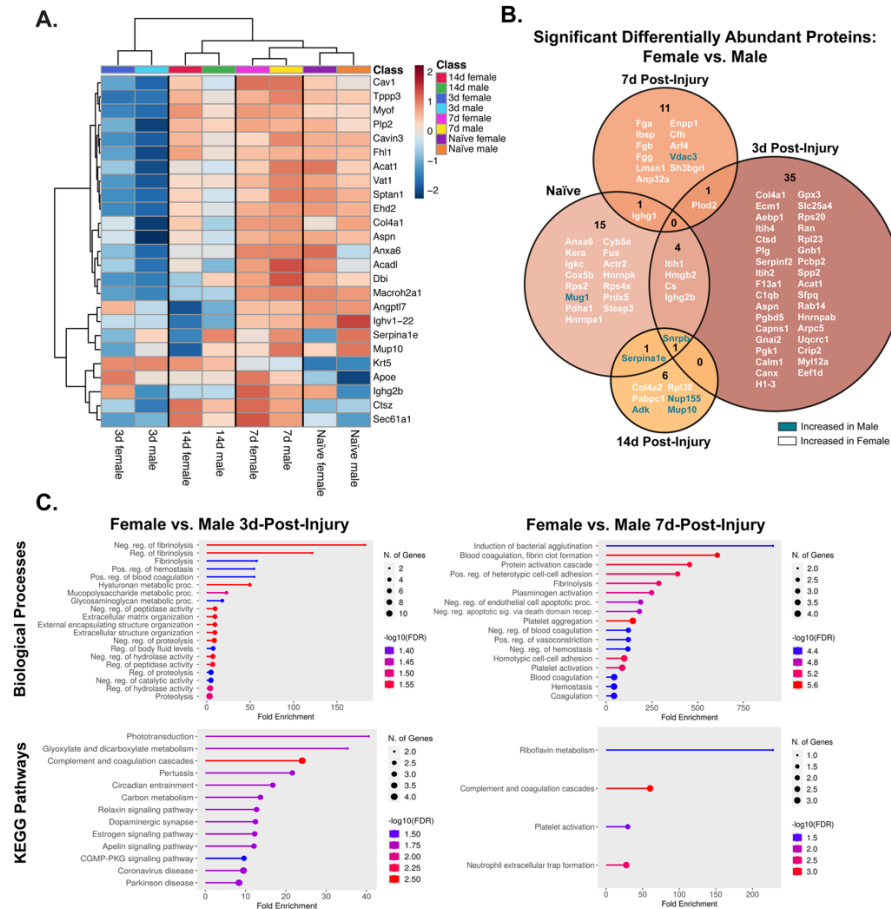


Figure 2.8. Untargeted proteomic analyses of naïve and injured ACL tissue in male and female mice. Complete rupture of the ACL in mice utilized for proteomics was confirmed via macroscopic imaging during ACL remnant collection (**Figure 2.2C**). (**A**) Heatmap clustering analysis demonstrated global sex and time dependent ACL proteome profiles following injury. Each row represents a distinct protein, with the top 25 most divergent proteins displayed. These proteins were selected based on the greatest change (most significant p-values) across all groups and comparisons. Each column denotes an average of the n=10 mouse samples for that group. (**B**) Differentially abundant proteins were identified between male and female mice at each timepoint. Proteins upregulated in males are shown in blue, while those upregulated in females are shown in white. Three days following ACL injury, all identified proteins were increased in female mice compared to male mice (list of all proteins can be found in **Appendix I.17**). Significant differentially abundant proteins were defined as having a p-value of less than 0.05 and a log2(fold-change) threshold of 1.5. To explore the robust early injury response of females compared to males, pathway analyses was performed. (**C**) In response to injury, females were found to have increased activation of pathways related to the coagulation cascade, extracellular matrix organization, and hormone signaling. Shown are the top upregulated Biological Processes and KEGG pathways, sorted by Fold Enrichment, in ACL remnants between female and male mice at 3- and 7-days post-injury. The figure displays the top 20 pathways with the highest Fold Enrichment, or all pathways identified if fewer than 20. Circle size indicates the number of genes associated with a pathway and color represents the False Discovery Rate (FDR). No significant KEGG or Biological Processes pathway differences were seen between male and female mice at 14d post-injury.

with males showing a greater number of elevated proteins at the later timepoint (Figure 2.8B, Appendix I.8A, B). Following ACL injury, females demonstrated increased signaling associated with fibrinolysis, blood coagulation, extracellular matrix changes, relaxin, estrogen receptors, and platelet activity compared to males (Figure 2.8C, Appendix I.8C). Importantly, naïve males and females did not show differences in these pathways, although naïve females did display enriched signaling relating to DNA repair, RNA processing, metabolic energy cycles, and protein synthesis relative to naïve males (Appendix I.16B).

2.4 Discussion

In this study, we investigated the progression of PTOA and its potential sexual dimorphism using a mechanical, non-surgical model of ACL rupture in mice. Through longitudinal mobility assessments, radiographic imaging, histologic scoring, and untargeted proteomics, we characterized the functional, structural, and molecular changes associated with PTOA development in male and female mice. Our findings provide valuable insights into the differential effects of sex on PTOA progression, highlighting potential therapeutic targets for future interventions.

Pain is the primary reason patients seek OA treatment.³² However, rodent studies investigating OA often focus on histological evaluations of joint changes, as early OA models were designed to study structural rather than symptomatic aspects of the disease.^{32,33} Since OA-related pain does not always correlate with structural changes, incorporating comprehensive pain-based outcomes in preclinical models is essential.³⁴ This study employed three distinct behavior and mobility assessments as a proxy for pain response during PTOA progression. Utilizing multiple outcome measures helped mitigate variability in reproducibility and individual differences among animals in any single mobility-based assessment. Collectively, our findings suggest that male mice exhibited more pronounced alterations in mobility compared to females

following ACL rupture, including reduced voluntary movement, gait irregularities, and increased injured limb offloading.

Observed gait alterations in male mice, such as a widened hindlimb stance, may reflect a response to pain or an adjustment to improve stability by expanding their base of support.³⁵ Additionally, decreased stance time in the injured hindlimb suggests males spent less time in contact with the ground, likely as a response to joint pain.³⁴ These findings align with previous PTOA studies in rodents which reported alterations in voluntary movement, increased hindlimb stance width, decreased stance time, and weight bearing imbalance.^{24,34,36–38} Human OA studies have demonstrated similar changes to walking speed, stance phase, and postural equilibrium.^{39–}⁴² While direct gait comparisons between quadrupedal and bipedal species are challenging, these similarities suggest that changes in stance time and weight distribution may be fundamental biomechanical adaptations to joint injury and OA progression. Sex-based alterations in functional PTOA measures remain less explored. However, previous studies have identified increased pain in male mice with PTOA compared to females.¹⁷ Similarly, human studies have found sex-specific gait changes, including decreased gait regularity and increased knee adduction in males.^{43,44} Future research is warranted to elucidate the mechanisms behind these sex differences in functional outcomes, which could inform tailored treatment strategies for PTOA.

To characterize PTOA development, we utilized radiographic and histologic scoring. Throughout this study, significant progression of both radiographic and histologic PTOA was observed over time in both sexes. Corroborating our mobility data, histologic scoring revealed worsened PTOA in male mice compared to female mice at 56 days post-injury, a finding consistent with previous research indicating worsened histologic PTOA in male mice.¹⁷ Radiographic scoring did not show sex-based differences in PTOA progression. Interestingly, this finding aligns with human studies where sex-based discrepancies in radiographic PTOA remain unclear. Some studies report worse knee joint pathology in males, while others find no

association between sex and worsened radiographic PTOA following ACL reconstruction.^{14,15}

This discrepancy highlights the need for clinically relevant preclinical models. The lack of alignment between radiograph and histologic scores in this study may be attributed to the significant histologic differences between male and female mice in cartilage and cruciate ligament scores, which are not captured in radiographic scoring.

Given the significant histologic differences in cruciate ligament scores, we investigated sex-specific ACL proteome mechanisms associated with PTOA progression. Before injury, ACLs from naïve female mice exhibited increased signaling relating to DNA repair, RNA processing, metabolic energy cycles, and protein synthesis compared to males. These processes are essential for maintaining cellular function and genetic integrity. Since female sex is a known risk factor for ACL injury in humans, further evaluation of these pathways as potential contributors is warranted.

After ACL injury, both sexes exhibited increased fibrinolysis and coagulation-related pathway signaling, with females showing greater activation at injury timepoints relative to males. Disruptions in these pathways, linked to elevated joint plasmin levels, contribute to PTOA development through processes including cartilage degeneration and inflammation.⁴⁵ Interestingly, these pathways have been implicated in the inability of the ACL to spontaneously heal.⁴⁶ At 3 and 7 days post-injury, female mice also displayed a stronger early injury response, characterized by increased inflammation, coagulation cascade activity, and sex-hormone signaling, indicative of an increased initial inflammatory response compared to male mice. These findings suggest that early differences in injury response may lead to divergent disease progression between males and females.

Previous transcriptomic analyses of male and female mouse synovial fluid following ACL injury revealed that, at 28 days post-injury, males tend to maintain transcriptional programs promoting chronic inflammation and fibrosis, thought to contribute to worsened PTOA development.¹⁷ Since our data showed no significant pathway differences between sexes at 14

days post-injury, males and females may regulate acute and chronic inflammation differently or follow distinct injury timelines. Future studies are needed to determine if the early inflammatory response in females helps attenuate PTOA development.

Additionally, female mice exhibited heightened relaxin and estrogen receptor signaling 3 days post-injury compared to males. Sex hormone signaling, specifically estrogen, has been shown to have a protective effect against PTOA development by modulating inflammation, enhancing collagen synthesis, and regulating bone remodeling.^{18,22,47} Reduced estrogen signaling through deletion of both ER α and ER β has been linked to greater cartilage damage and osteophyte formation.⁴⁸ Our findings, coupled with existing literature, indicate that the coagulation cascade and estrogen signaling are two potential avenues that require further exploration as potential therapeutic targets for PTOA.

While the non-surgical ACL rupture model employed in this study better mimics human PTOA induction compared to surgical transection, it has reproducibility limitations. Complete, isolated ACL ruptures occurred in 95% of mice, consistent with our previous model validation.²⁴ However, this necessitated the exclusion of 5 of 110 animals due to either incomplete ACL rupture or damage to stifle structures beyond the ACL. Future studies will adjust sample sizes to account for injury variability. This model also lacks ACL reconstruction, a common procedure performed in humans after ACL injury. However, omitting ACL reconstruction accelerates PTOA development, reducing study duration and animal use. Another limitation was that naïve mice were age-matched to the time of ACL injury (not age-matched per study endpoint), potentially introducing confounding age-related changes to the stifle joint. However, it is noteworthy that C57Bl/6J mice do not develop spontaneous OA until nine months of age, while our study ended at four and a half months.⁴⁹ Additionally, male mice weighed more than females, and all mice experienced weight gain throughout the study. While static weight-bearing results were normalized to each animal's bodyweight, inherent weight differences may have influenced behavioral and mobility test outcomes. Lastly, spatial verification of proteomic changes was not

performed. Future research will use immunohistochemistry to confirm key protein changes and examine additional joint tissues.

In conclusion, our findings revealed more severe progression of PTOA in male mice compared to female mice. This was evidenced by pronounced mobility impairments, exacerbated histologic scores, and distinct proteome responses with decreased signaling of pathways related to extracellular matrix remodeling, the coagulation cascade, and estrogen signaling. Similarities between the mouse data herein and human clinical data further emphasize the reliability and translatability of our non-surgical ACL rupture model for investigating PTOA. Importantly, these results furnish pivotal insights for advancing future research endeavors focused on therapeutic strategies for PTOA prevention.

References

1. Kaeding CC, Léger-St-Jean B, Magnussen RA. Epidemiology and Diagnosis of Anterior Cruciate Ligament Injuries. *Clin Sports Med.* 2017;36(1):1-8. doi:10.1016/j.csm.2016.08.001
2. Wang LJ, Zeng N, Yan ZP, Li JT, Ni GX. Post-traumatic osteoarthritis following ACL injury. *Arthritis Res Ther.* 2020;22(1). doi:10.1186/s13075-020-02156-5
3. Murtha AS, Johnson AE, Buckwalter JA, Rivera JC. Total knee arthroplasty for posttraumatic osteoarthritis in military personnel under age 50. *Journal of Orthopaedic Research.* 2017;35(3):677-681. doi:10.1002/jor.23290
4. Beck NA, Lawrence JTR, Nordin JD, DeFor TA, Tompkins M. ACL tears in school-aged children and adolescents over 20 years. *Pediatrics.* 2017;139(3). doi:10.1542/peds.2016-1877
5. Sanders TL, Maradit Kremers H, Bryan AJ, Larson DR, Dahm DL, Levy BA, et al. Incidence of anterior cruciate ligament tears and reconstruction: A 21-year

- population-based study. *American Journal of Sports Medicine*. 2016;44(6):1502-1507. doi:10.1177/0363546516629944
6. Arendt EA, Agel J, Dick R. Anterior Cruciate Ligament Injury Patterns Among Collegiate Men and Women. *J Athl Train*. 1999;34(2). www.nata.org/jat
 7. Kiapour AM, Shalvoy MR, Murray MM, Fleming BC. Validation of Porcine Knee as a Sex-specific Model to Study Human Anterior Cruciate Ligament Disorders. *Clin Orthop Relat Res*. 2015;473(2):639-650. doi:10.1007/s11999-014-3974-2
 8. Gwinn DE, Wilckens JH, Mcdevitt ER, Ross G, Kao TC. The Relative Incidence of Anterior Cruciate Ligament Injury in Men and Women at the United States Naval Academy. *Am J Sports Med*. 2000;28(1). doi:10.1177/03635465000280012901
 9. Sutton KM, Bullock JM. Anterior cruciate ligament rupture: Differences between males and females. *Journal of the American Academy of Orthopaedic Surgeons*. 2013;21(1):41-50. doi:10.5435/JAAOS-21-01-41
 10. Ireland ML. The female ACL: why is it more prone to injury? *J Orthop*. 2016;13:A1-A4. doi:10.1016/S0972-978X(16)00023-4
 11. Shultz SJ, Sander TC, Kirk SE, Perrin DH. Sex differences in knee joint laxity change across the female menstrual cycle. *J Sports Med Phys Fitness*. 2005;45(4):594-603.
 12. Ramesh R, Arx O Von, Azzopardi T, Schranz PJ, Azzopardi " T Ed. The risk of anterior cruciate ligament rupture with generalised joint laxity. 2005;87:800-803. doi:10.1302/0301-620X.87B6
 13. Ryan J, Magnussen R, Cox C, Hurbanek J, Flanigan D, Kaeding C. ACL reconstruction: do outcomes differ by sex? A systematic review. *J Bone Joint Surg Am*. 2014;96(6):507-5012. doi:10.2106/JBJS.M.00299
 14. Costa MQ, Badger GJ, Chrostek CA, Carvalho OD, Faiola SL, Fadale PD, et al. Effects of Initial Graft Tension and Patient Sex on Knee Osteoarthritis Outcomes After ACL Reconstruction: A Randomized Controlled Clinical Trial With 10- to 12-

- Year Follow-up. American Journal of Sports Medicine. 2022;50(13):3510-3521.
doi:10.1177/03635465221124917
15. Jones MH, Oak SR, Andrish JT, Brophy RH, Cox CL, Dunn WR, et al. Predictors of Radiographic Osteoarthritis 2 to 3 Years After Anterior Cruciate Ligament Reconstruction: Data From the MOON On-site Nested Cohort. Orthop J Sports Med. 2019;7(8). doi:10.1177/2325967119867085
 16. Pinette MP, Molino J, Proffen BL, Murray MM, Fleming BC. Effects of Male and Female Sex on the Development of Posttraumatic Osteoarthritis in the Porcine Knee After Anterior Cruciate Ligament Surgery. American Journal of Sports Medicine. 2022;50(9):2417-2423. doi:10.1177/03635465221102118
 17. Bergman RF, Lammlin L, Junginger L, Farrell E, Goldman S, Darcy R, et al. Sexual dimorphism of the synovial transcriptome underpins greater PTOA disease severity in male mice following joint injury. Osteoarthritis Cartilage. Published online 2023. doi:10.1016/j.joca.2023.07.012
 18. Ma HL, Blanchet TJ, Peluso D, Hopkins B, Morris EA, Glasson SS. Osteoarthritis severity is sex dependent in a surgical mouse model. Osteoarthritis Cartilage. 2007;15(6):695-700. doi:10.1016/j.joca.2006.11.005
 19. van Osch G, van der Kraan P, Vitters E, Blankevoort L, van den Berg W. Induction of osteoarthritis by intra-articular injection of collagenase in mice. Strain and sex related differences. Osteoarthritis Cartilage. 1993;1(3):171-177. doi:10.1016/s1063-4584(05)80088-3
 20. Hwang HS, Park IY, Hong JI, Kim JR, Kim HA. Comparison of joint degeneration and pain in male and female mice in DMM model of osteoarthritis. Osteoarthritis Cartilage. Published online 2021. doi:10.1016/j.joca.2021.02.007

21. Temp J, Labuz D, Negrete R, Sunkara V, Machelska H. Pain and knee damage in male and female mice in the medial meniscal transection-induced osteoarthritis. *Osteoarthritis Cartilage*. 2020;28(4):475-485. doi:10.1016/j.joca.2019.11.003
22. Lu Z, Zhang A, Wang J, Han K, Gao H. Estrogen alleviates post-traumatic osteoarthritis progression and decreases p-EGFR levels in female mouse cartilage. *BMC Musculoskelet Disord*. 2022;23(1). doi:10.1186/s12891-022-05608-y
23. Sowers M. Epidemiology of risk factors for osteoarthritis: systemic factors. *Curr Opin Rheumatol*. 2001;13:447-451. doi:10.1097/00002281-200109000-00018
24. Timkovich AE, Sikes KJ, Andrie KM, Afzali MF, Sanford J, Fernandez K, et al. Full and Partial Mid-substance ACL Rupture Using Mechanical Tibial Displacement in Male and Female Mice. *Ann Biomed Eng*. 2023;51(3):579-593. doi:10.1007/s10439-022-03065-1
25. Foley P, Liang H, Crichlow A. Evaluation of a Sustained-Release Formulation of Buprenorphine for Analgesia in Rats. *J Am Assoc Lab Anim Sci*. 2011;50(2):198-204.
26. Hurley CR, Hammer DL, Shott S. Progression of radiographic evidence of osteoarthritis following tibial plateau leveling osteotomy in dogs with cranial cruciate ligament rupture: 295 cases (2001–2005). *Journal of the American Veterinary Medical Association*. 2007;230(11). doi:10.2460/javma.230.11.1674
27. Haubruck P, Heller R, Blaker CL, Clarke EC, Smith SM, Burkhardt D, et al. Streamlining quantitative joint-wide medial femoro-tibial histopathological scoring of mouse post-traumatic knee osteoarthritis models. *Osteoarthritis Cartilage*. 2023;31(12):1602-1611. doi:10.1016/j.joca.2023.07.013
28. Willforss J, Chawade A, Levander F. NormalizerDE: Online Tool for Improved Normalization of Omics Expression Data and High-Sensitivity Differential Expression Analysis. *J Proteome Res*. 2019;18(2):732-740. doi:10.1021/acs.jproteome.8b00523

29. Xia J, Psychogios N, Young N, Wishart DS. MetaboAnalyst: A web server for metabolomic data analysis and interpretation. *Nucleic Acids Res.* 2009;37(SUPPL. 2). doi:10.1093/nar/gkp356
30. Didusch S, Madern M, Hartl M, Baccarini M. amica: an interactive and user-friendly web-platform for the analysis of proteomics data. *BMC Genomics.* 2022;23(1). doi:10.1186/s12864-022-09058-7
31. Xijin Ge S, Jung D, Yao R. ShinyGO: a graphical gene-set enrichment tool for animals and plants. doi:10.5281/zenodo.1451847
32. Creamer P. Osteoarthritis pain and its treatment. *Curr Opin Rheumatol.* 2000;12(5):450-455. doi:10.1097/00002281-200009000-00019
33. Bendele AM. *Animal Models of Osteoarthritis.* Vol 1.; 2001.
34. Jacobs BY, Kloefkorn HE, Allen KD. Gait Analysis Methods for Rodent Models of Osteoarthritis. *Curr Pain Headache Rep.* 2014;18(10). doi:10.1007/s11916-014-0456-x
35. Henry SM, Fung J, Horak FB, Dow RS. Effect of Stance Width on Multidirectional Postural Responses. *J Neurophysiol.* 2001;85(2):559-570. doi:10.1152/jn.2001.85.2.559
36. Kaiser JM, Bernard FC, Pucha K, Raval SK, Eng T, Fulton T, et al. Mild exercise expedites joint clearance and slows joint degradation in a joint instability model of osteoarthritis in male rats. *Osteoarthritis Cartilage.* Published online April 2024. doi:10.1016/j.joca.2024.03.120
37. Hamilton CB, Pest MA, Pitelka V, Ratneswaran A, Beier F, Chesworth BM. Weight-bearing asymmetry and vertical activity differences in a rat model of post-traumatic knee osteoarthritis. *Osteoarthritis Cartilage.* 2015;23(7):1178-1185. doi:10.1016/j.joca.2015.03.001

38. Croen BJ, Carballo CB, Green SJ, Sevvick JL, Piacentini AN, Chen T, et al. Markers of Pain in 3 Different Murine Models of Posttraumatic Osteoarthritis: A Comparison Using Gait Analysis, Imaging, Histology, and Gene Expression. *American Journal of Sports Medicine*. 2023;51(10):2711-2722. doi:10.1177/03635465231183088
39. Duffell LD, Southgate DFL, Gulati V, McGregor AH. Balance and gait adaptations in patients with early knee osteoarthritis. *Gait Posture*. 2014;39(4):1057-1061. doi:10.1016/j.gaitpost.2014.01.005
40. Kumar D, Manal KT, Rudolph KS. Knee joint loading during gait in healthy controls and individuals with knee osteoarthritis. *Osteoarthritis Cartilage*. 2013;21(2):298-305. doi:10.1016/j.joca.2012.11.008
41. Mills K, Hunt MA, Ferber R. Biomechanical deviations during level walking associated with knee osteoarthritis: A systematic review and meta-analysis. *Arthritis Care Res (Hoboken)*. 2013;65(10):1643-1665. doi:10.1002/acr.22015
42. Fu S, Duan T, Hou M, Yang F, Chai Y, Chen Y, et al. Postural Balance in Individuals With Knee Osteoarthritis During Stand-to-Sit Task. *Front Hum Neurosci*. 2021;15. doi:10.3389/fnhum.2021.760960
43. Kobsar D, Barden JM, Clermont C, Wilson JLA, Ferber R. Sex differences in the regularity and symmetry of gait in older adults with and without knee osteoarthritis. *Gait Posture*. 2022;95:192-197. doi:10.1016/j.gaitpost.2022.04.023
44. Hart HF, Birmingham TB, Sritharan P, Primeau C, King MG, Fischer LK. Sex-related differences in gait characteristics and their associations with symptoms in individuals with patellofemoral osteoarthritis. *Gait Posture*. 2023;107:35-41. doi:10.1016/j.gaitpost.2023.09.009
45. Wang Q, Shao G, Zhao X, Wong HH, Chin K, Zhao M, et al. Dysregulated fibrinolysis and plasmin activation promote the pathogenesis of osteoarthritis. *JCI Insight*. 2024;(9). doi:doi:10.1172/jci.insight.173603

46. Murray MM. Current Status and Potential of Primary ACL Repair. Clin Sports Med. 2009;28(1):51-61. doi:10.1016/j.csm.2008.08.005
47. Martín-Millán M, Castañeda S. Estrogens, osteoarthritis and inflammation. Joint Bone Spine. 2013;80(4):368-373.
48. Sniekers YH, van Osch GJVM, Ederveen AGH, Inzunza J, Gustafsson JÅ, van Leeuwen JPTM, et al. Development of osteoarthritic features in estrogen receptor knockout mice. Osteoarthritis Cartilage. 2009;17(10):1356-1361. doi:10.1016/j.joca.2009.04.008
49. Yamamoto K, Shishido T, Masaoka T, Imakiire A. Morphological studies on the ageing and osteoarthritis of the articular cartilage in C57 black mice. Journal of Orthopaedic Surgery. 2005;13(1):8-18. doi:10.1177/230949900501300103

CHAPTER 3: INVESTIGATION OF ESTROGEN SIGNALING ON POST-TRAUMATIC OSTEOARTHRITIS DEVELOPMENT IN MALE MICE

3.1 Introduction

Osteoarthritis (OA) is the most prevalent joint disease, affecting an estimated 600 million individuals worldwide.¹ Although commonly associated with age-related degeneration, joint trauma is a major contributor to OA in younger populations.² Traumatic knee injuries, particularly to the anterior cruciate ligament (ACL), lead to the development of post-traumatic osteoarthritis (PTOA) in up to 87% of individuals.³ Current treatment options for OA are limited to symptom management, and total knee replacement (TKR) remains the primary solution for advanced disease.⁴ This presents a significant challenge for younger patients with PTOA, as approximately 20% of TKRs fail within 25 years, often resulting in the need for revision surgeries.⁵ Therefore, there is a critical need for therapeutic strategies that prevent PTOA progression and delay the subsequent need for TKR, especially in younger individuals at high risk of long-term joint complications.

Sex-based differences in OA susceptibility have become a growing area of interest. Women are disproportionately affected, accounting for approximately 60% of OA cases.¹ This disparity has largely been attributed to hormonal changes associated with menopause, but anatomic and metabolic factors also play important roles.⁶⁻⁸ Specific to PTOA, the influence of sex on joint degeneration is less well characterized, although emerging evidence suggests that males may experience more severe PTOA following ACL injury compared to females. Imaging studies in humans have demonstrated greater structural joint deterioration in males following ACL reconstruction surgery, though these findings are often limited by subjective assessments and the lack of direct tissue evaluation.⁹

To overcome these challenges, preclinical animal models have been used to study sex-based differences in PTOA. In mouse models using non-surgical mechanical ACL rupture, male

mice have shown more severe PTOA than females, as evidenced by worsened pain-based outcomes, more severe histologic evidence of PTOA, and molecular evidence of chronic synovitis and impaired extracellular matrix remodeling.^{10,11} One mechanism that has been identified as a potential contributor to the varied PTOA progression in males and females is estrogen signaling.^{11–13}

Estrogen is a steroid hormone that fluctuates with the estrous cycle in females and is present at lower, stable levels in males.^{14–17} Previous work from our group has demonstrated that female mice exhibit increased activation of estrogen-related pathways compared to males during the acute injury response following joint trauma.¹¹ Other groups have found that exogenous administration of 17 β -estradiol, the primary form of circulating estrogen, lessens PTOA development in mice following destabilization of the medial meniscus.^{12,13} This is consistent with human clinical data linking lower estrogen levels in postmenopausal women to increased susceptibility for primary OA.^{8,18} However, most prior studies in preclinical models have used invasive surgical techniques to induce joint degeneration, such as destabilization of the medial meniscus or surgical ACL transection. In addition, systemic hormone modulation, typically via gonadectomy or slow-release subcutaneous estrogen implants, has been the predominant method for studying estrogen's role in PTOA. While these approaches have advanced our understanding, they limit the ability to trace hormone delivery to the joint and may introduce confounding variables such as pain, systemic inflammation, or infection, making it difficult to isolate the local effects of estrogen signaling.¹⁸

Recent studies have started to directly investigate the role of intra-articular estrogen signaling in arthritis by targeting estrogen receptors (ERs), particularly ER α and ER β . Much of this work, however, has focused on rheumatoid arthritis (RA), an autoimmune disease in which immune-mediated joint degeneration occurs. Although RA and PTOA have distinct etiologies, they share several end-stage histological features, such as cartilage degeneration, osteophyte

formation, and synovitis.¹⁹ As such, findings from RA research may offer valuable insights into estrogen signaling relevant to PTOA, particularly as the field begins to explore this area. For example, in a mouse model of RA, systemic 17 β -estradiol treatment reduced joint destruction through ER α signaling.²⁰ Similar findings in mice and rats have shown that ER α (but not ER β) acts as a key inflammatory modulator in suppressing RA.^{21,22} More broadly, a mouse model of primary OA has shown that mice lacking both ER α and ER β exhibit increased osteophyte formation in the stifle joint.²³ In humans, polymorphisms in the ER α gene (ESR1) are associated with radiographically distinct patterns of primary OA progression.²⁴ Collectively, these findings suggest that ER modulation can influence joint integrity and the development of arthritis. However, most prior studies have not examined ER signaling specifically in the context of PTOA and have rarely assessed both joint pathology and pain-related behavior within the same animal. This gap limits the translational impact of existing findings and underscores the need for a clinically relevant model capable of evaluating tissue-specific estrogen signaling.

To address this gap, we investigated the role of intra-articular (IA) estrogen signaling in PTOA development using a previously validated non-surgical model of ACL rupture in mice.^{11,25} Following injury, male mice received IA injections of either 1) 17 β -estradiol to enhance local estrogen signaling or 2) Fulvestrant (ICI 182,780) to inhibit it. Fulvestrant is a selective estrogen receptor degrader that functions as a pure ER antagonist, promoting receptor degradation by preventing nuclear localization of the ligand-receptor complex and enhancing proteolytic receptor breakdown.^{26,27} This localized, joint-specific approach enables targeted modulation of estrogen signaling without the systemic side effects or variability associated with whole-body hormonal changes. Only male mice were used to eliminate estrous cycle variability in females and to better isolate the impact of estrogen signaling in the joint microenvironment. To control for potential effects of the injection procedure and vehicle, additional groups received either 3) β -cyclodextrin (vehicle control for 17 β -estradiol) or 4) saline (injection control). We

comprehensively assessed PTOA development using longitudinal mobility assessments, radiographic imaging, and histologic evaluation. Estrogen receptor expression was also profiled via fluorescent immunohistochemistry (IHC) to evaluate receptor modulation within the joint.

We hypothesized that local enhancement of estrogen signaling via 17 β -estradiol would delay onset and progression of PTOA, while inhibition of signaling through Fulvestrant would exacerbate joint degeneration. This multifaceted approach allowed us to directly examine how modulation of joint-specific estrogen signaling influences functional outcomes and tissue pathology in PTOA, setting the stage for future therapeutic interventions that address the underlying mechanisms of PTOA development.

3.2 Methods

3.2.1 Animals and Experimental Design

All procedures were approved by the Colorado State University Institutional Animal Care and Use Committee (Protocol #4577). Seventy male C57BL/6J (NCI 556) wild-type mice were obtained from Charles River Laboratories at approximately 70 days of age. Mice were acclimated to the vivarium for approximately 14 days before experimentation. Animals were group-housed (1 – 5 per cage) in solid bottom cages with corncob bedding, ad libitum water, and standard rodent chow. The vivarium was maintained at 22 – 24 °C on a 12-hour light/dark cycle. Animals were assessed daily with body weights monitored weekly. Mice were randomly assigned to the outcome groups outlined in Figure 3.1. At study endpoints, mice were anesthetized with 2% isoflurane inhalation and euthanized by cardiac blood draw followed by confirmatory cervical dislocation. Five animals were excluded from this study based on previously established criteria described in Chapter 2, with one excluded for partial ACL rupture (n=1, 7d 17 β -estradiol) and four excluded due to extreme severity of injury that could not be attributed to the ACL rupture itself (n=1 each, 3d 17 β -estradiol, 7d saline, 7d Fulvestrant, and

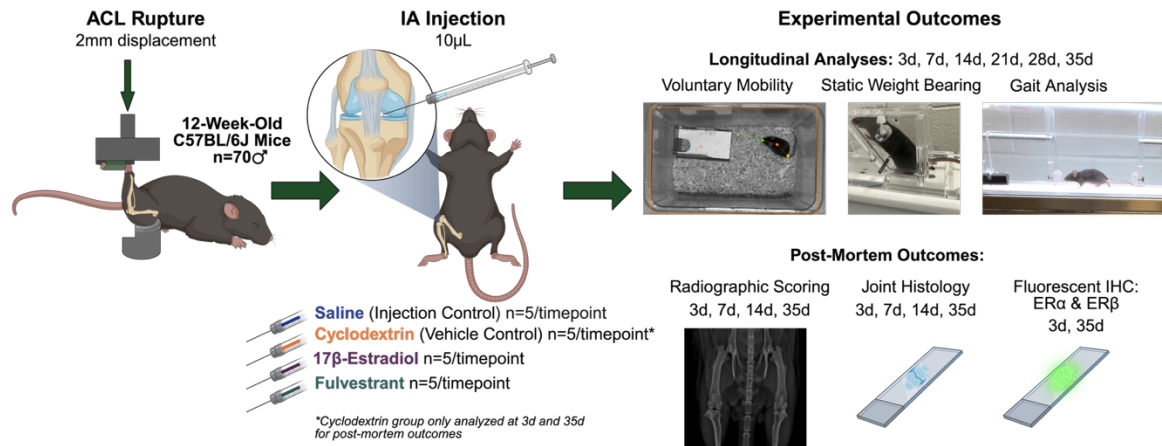


Figure 3.1. Overview of experimental design. Male mice underwent unilateral ACL rupture immediately followed by intra-articular injection of either 1) 17 β -estradiol, 2) Fulvestrant, 3) β -cyclodextrin (vehicle control), or 4) saline (injection control). Mice were sacrificed at 3, 7, 14, or 35 days post-injury. The 3, 7, and 14 day groups were used solely for post-mortem analyses, while the mice in the 35 day group underwent longitudinal assessments prior to sacrifice for post-mortem outcomes.

14d 17 β -estradiol).¹¹

3.2.2 Induction of Osteoarthritis

Unilateral ACL rupture was induced in the right hindlimb as described previously (Chapter 2).^{11,25} Analgesia was provided via subcutaneous injection of sustained-release buprenorphine (1 mg/kg), offering 48 – 72 hours of pain relief without modulating anti-inflammatory activity.²⁸ This model consistently induces signs of early PTOA development within two weeks following injury.^{11,25}

3.2.3 Intra-articular Injection

IA injections were administered immediately following ACL rupture, under the same anesthetic event. The right hindlimb was shaved and cleansed with 70% isopropyl alcohol. The right stifle was flexed to a 90° angle, and 10 μ L of either 1) 17 β -estradiol, 2) Fulvestrant, 3) (2-Hydroxypropyl)- β -cyclodextrin (vehicle control), or 4) saline (injection control) was injected into the joint using a 27G needle attached to a Hamilton syringe. The needle was inserted medial to the patellar tendon and directed laterally into the joint space. Accurate joint space delivery was confirmed by joint capsule swelling and low injection resistance.

17 β -estradiol (Millipore Sigma E4389) was dissolved at 0.01 mg/kg in saline. The dosing protocol of 17 β -estradiol was developed based upon previously published data demonstrating alterations to OA development and safety of dose.^{29–32} This formulation of 17 β -estradiol used contains β -cyclodextrin to improve water-solubility. Thus, the vehicle control group received 2.17 mg/kg β -cyclodextrin (Millipore Sigma, C0926) in saline, matching the concentration used in the 17 β -estradiol solution. Fulvestrant (Millipore Sigma, I4409) was first dissolved in dimethyl sulfoxide (DMSO) and diluted in saline to a final concentration of 10 nM of Fulvestrant with 0.00003% DMSO. This DMSO concentration has been previously reported to have no adverse

effects on mouse joints.^{33,34} The concentration of Fulvestrant used was determined using literature demonstrating safety and efficacy at this dose.^{35–38} 0.9% sodium chloride sterile saline was used for all dilutions and for the injection control. All solutions were freshly prepared on the day of injection under aseptic conditions and filtered through a 0.22 µm sterile filter. Mice recovered from anesthesia on a heating pad.

3.2.4 Mobility and Behavioral Assessments

All mobility and behavior assessments were conducted as previously described (Chapter 2).¹¹ Three forms of longitudinal assessments were used: individual cage monitoring, static weight bearing, and gait analysis. For all outcomes, mice were acclimated over one week, and two pre-injury measurements were collected on separate days and averaged to establish a pre-injury baseline for each animal. Handlers were not blinded to the sex of the animal. For all measurements, testing occurred during the same time of day. Values for mobility and behavioral assessments were normalized to pre-injury baseline values.

Individual cage monitoring (ANY-maze, IL) was used to determine general behavior and activity levels. Each testing period lasted for 10 minutes, and mobility parameters were automatically collected by the video analysis software.

Static weight bearing was assessed (Bioseb, FL) on both hindlimbs. Three measurements, 10 seconds each, were taken per animal per day and averaged. Animals were weighed at the time of testing, and loading of each hindlimb was normalized to each animal's bodyweight. Hindlimb weight distribution was calculated as Right/Left hindlimb.

The treadmill-based Digigait analysis system (Mouse Specifics, MA) was used to observe gait abnormalities. Three runs per animal were taken while jogging (40 cm/sec) at each of the following grades: flat, 10° incline, and 10° decline. The three runs for each setting were averaged for each animal. Gait values were calculated using the Digigait analysis software (Version 16).

3.2.5 Radiograph Imaging and Scoring

Radiographs were collected post-mortem at each timepoint using an XPERT 80L X-Ray System (Kubtec, CT) as previously described (Chapter 2).¹¹ Animals were placed in dorsal recumbency to obtain craniocaudal and mediolateral views of the stifles. Radiographs were scored by a blinded board-certified veterinary surgeon (BBN) using a validated published system.^{11,39}

3.2.6 Histology and Scoring

Stifle joints were harvested, fixed, decalcified, paraffin-embedded, and microtome sectioned coronally as previously described (Chapter 2).¹¹ Slides were dual stained using toluidine blue and fast green. A blinded board-certified veterinary pathologist (KSS) scored the anterior portion of the joint using a modified OARSI scoring system.^{11,40}

3.2.7 Fluorescent Immunohistochemistry

Dual fluorescent IHC was performed to detect expression of ER α and ER β . From each experimental group, three of five animals were randomly selected for IHC analysis using the Excel RAND function. Tissue sections containing ACL remnants were chosen for analysis. Experiments were performed in three batches, each containing one slide per group to minimize batch effects. Each batch contained a positive control, isotype control, and negative control. Positive control slides used sections from female mouse ovary, a tissue known to contain high expression of ER α and ER β .^{41,42} The isotype and negative controls utilized sections of mouse stifles from the experimental groups.

Slides were deparaffinized, rehydrated, and underwent heat-induced epitope retrieval in citrate buffer at 55 °C. Slides were permeabilized (0.2% Tween20/1.5% goat serum in

phosphate-buffered saline (PBS)) and blocked (10% goat serum in PBS with 0.1% Tween20 (PBST)). Endogenous mouse IgG was blocked using Goat anti-Mouse IgG (H+L) Secondary Antibody (ThermoFisher, 31160) at 50ug/mL in PBST. For primary antibodies, Estrogen Receptor alpha Monoclonal Antibody (ThermoFisher, MA1-27107) was used at 1:75 in permeabilization buffer and Estrogen Receptor beta Polyclonal Antibody (ThermoFisher, PA1-311) was used at 1:150 in permeabilization buffer. Mouse IgG1 kappa Isotype Control (ThermoFisher, 14-4714-81) and Rabbit IgG Isotype Control (ThermoFisher, #31235) were used as isotype controls for ER α and ER β , respectively, at the same concentrations as the primary antibodies. Negative control slides did not receive primary antibodies. Slides were incubated overnight with the primary antibodies at 4 °C. Secondary antibodies used were Goat anti-Mouse IgG AlexaFluor488 (ThermoFisher, A32723) and Goat anti-Rabbit IgG AlexaFluor647 (ThermoFisher, A32733), both at 1:200 in permeabilization buffer. Slides were incubated with the secondary antibodies for 1 hour at room temperature. Slides were mounted with Vectashield Antifade Mounting Media (Vector Laboratories, H-1800) which contains DAPI as a nuclear counterstain. A complete IHC protocol can be found in Appendix II.1.

For each slide, a brightfield image was taken at 2.5X to identify the ACL remnants. Z-stack images were captured using a Zeis LSM 980 confocal microscope with a 40X oil immersion objective. Using ImageJ (Fiji v 2.16.0), Z-stacks were split by color channel and compressed using “Sum Slices”. On the DAPI channel, three cells in the ACL midsubstance were randomly selected and outlined. These ROIs were transferred to the green (ER α) and red (ER β) channels to measure florescence intensity. For each slide, the mean intensity of the three cells was averaged, and background fluorescence (determined with negative controls) was subtracted.

3.2.8 Statistical Analysis

Statistical analyses were performed in Graphpad Prism 10 (San Diego, CA). For radiographic scores, histologic scores, and IHC data, each mouse contributed to a single timepoint (no repeated measures). Two-way models were fit separately for each parameter. These models included group, time (categorical), and group*time interaction. Tukey's multiple comparison post-hoc testing was performed to compare all possible pairs of group means.

For longitudinal mobility and behavioral analyses, repeat observations were conducted on the same mice over time. One-way ANOVA tests were used to compare parameters between groups at the pre-injury timepoint, separately for each response. Post-injury outcomes were normalized to pre-injury baselines by calculating the difference between later timepoints and pre-injury values for each mouse and each response. Repeated measures mixed models were used for each parameter, with group, time (categorical), and group*time interaction as fixed effects and mouse included as a random effect. Tukey's multiple comparison post-hoc testing was performed to compare all possible pairs of group means.

Model assumptions were checked in Graphpad using residual vs. predicted plots (homoscedasticity) and QQ plots (normality). Significance for all comparisons was set to p -values < 0.05.

A priori sample size calculations were conducted in GPower v3.1.1. Calculations were based on data from previous experiments comparing histologic evidence of PTOA between male and female mice 56 days post-ACL rupture.¹¹ The outcome variable was Total Histology Score, assuming a within-group standard deviation of 20 and a between-group difference of 50.5 (effect size=2.50). Power calculations were performed using a two-sample t-test, with α =0.05 and power>90%, yielding a sample size of four animals per group per timepoint. Five animals were included per group based on findings from previous studies, which showed that approximately 5% of animals needed to be excluded due to partial ACL rupture or excessively severe injuries (Chapter 2).¹¹

3.3 Results

3.3.1 Symptomatic Progression of PTOA

Pre-injury assessments revealed no significant group differences in voluntary mobility measures, including distance traveled and body rotations (Figure 3.2A, B). At 3 days post-injury, mice treated with saline traveled significantly greater distances compared to all other groups (Figure 3.2C). However, this pattern reversed by 35 days, with 17 β -estradiol-treated mice traveling further than saline-treated controls (Figure 3.2C). Fulvestrant-treated mice demonstrated consistently fewer body rotations than saline-treated mice at 3, 28, and 35 days post-injury (Figure 3.2D).

Static weight bearing analysis revealed no significant pre-injury group differences in hindlimb loading (Figure 3.3A). At 35 days post-injury, mice treated with 17 β -estradiol showed reduced offloading of the injured limb relative to saline-treated controls (Figure 3.3B).

Gait analysis using the Digigait treadmill system identified pre-injury group differences in stance width and stance time (Figure 3.4B, C). At 28 days post-injury, β -cyclodextrin-treated mice exhibited increased stance time on an inclined treadmill relative to saline controls (Figure 3.4F). At 35 days post-injury, stride length during decline running and hindlimb stance width during incline running were significantly increased in β -cyclodextrin-treated mice compared to saline (Figure 3.4D, E).

3.3.2 Structural Analysis of PTOA Development

Radiographic evaluation revealed no significant differences in total joint scores between treatment groups at any individual timepoint (Figure 3.5A). Notably, scores worsened by 35 days post-injury across all groups, indicating progressive PTOA development (Figure 3.5A). At

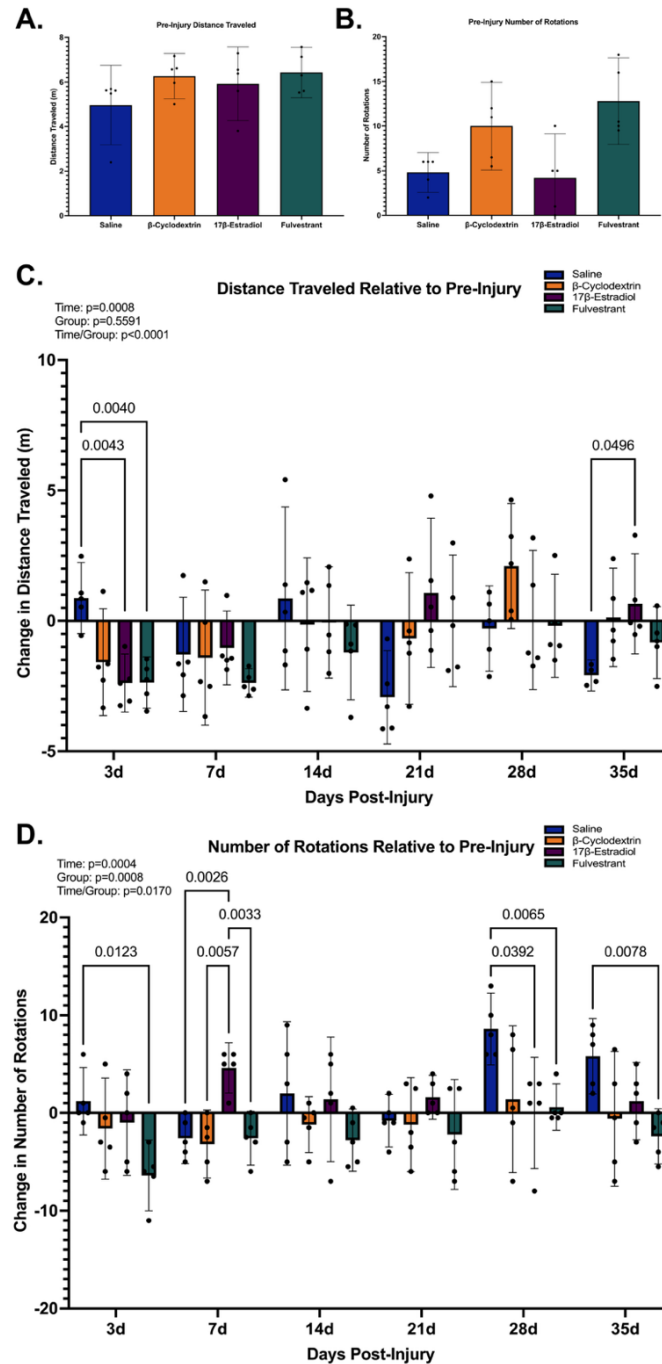
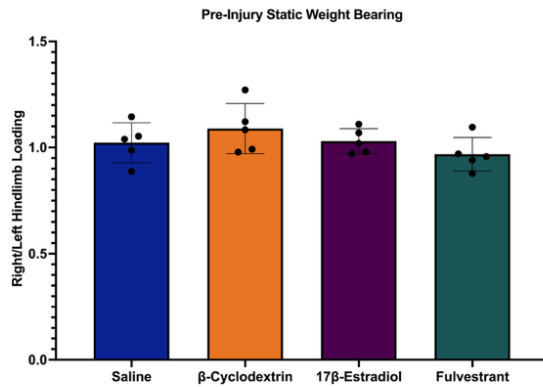


Figure 3.2. Longitudinal voluntary mobility analysis (ANY-maze). No group differences were observed prior to injury for either (A) distance traveled or (B) number of rotations. (C) 3 days after injury, mice that received saline traveled a greater distance than those that received 17 β -estradiol or Fulvestrant. By 35 days post-injury, mice treated with 17 β -estradiol traveled farther than those treated with saline. (D) Mice treated with Fulvestrant exhibited fewer body rotations than saline-treated mice at 3, 7, 28, and 35 days post-injury. Panels (C) and (D) show group comparisons with p -values < 0.05 . Differences over time within groups are not shown. Bars represent mean 95% confidence interval; individual animals are indicated.

A.



B.

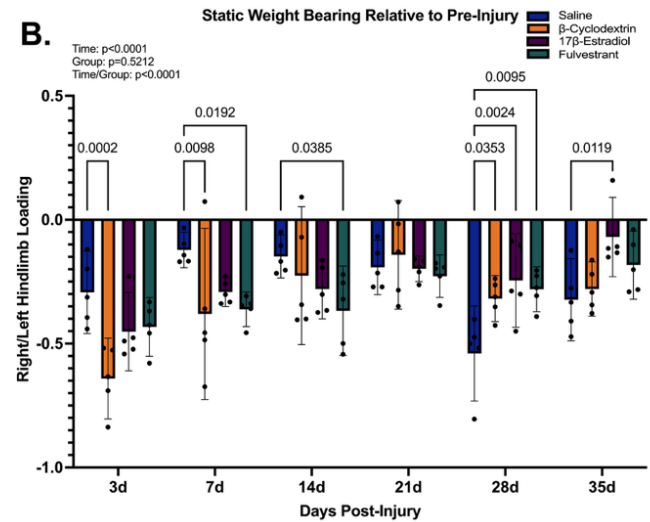


Figure 3.3. Longitudinal static weight bearing assessment (Bioseb). All output loads were normalized to each animal's body weight at the time of testing and are represented as the ratio of right (injured) to left (uninjured) hindlimb. **(A)** No group differences were observed prior to injury, with values near 1.0, reflecting the expected postural equilibrium. **(B)** Following injury, compared to saline, β-cyclodextrin-treated mice showed reduced injured limb loading at 3 and 7 days, Fulvestrant-treated mice showed reduced loading at 7 and 14 days; and 17β-estradiol-treated mice demonstrated improved loading at 35 days. At 28 days, saline-treated mice exhibited worse loading than all other groups. Group comparisons with p -values < 0.05 are shown. Timepoint comparisons within groups are not displayed. Bars represent mean $\pm$ 95% confidence interval, with individual animals indicated.

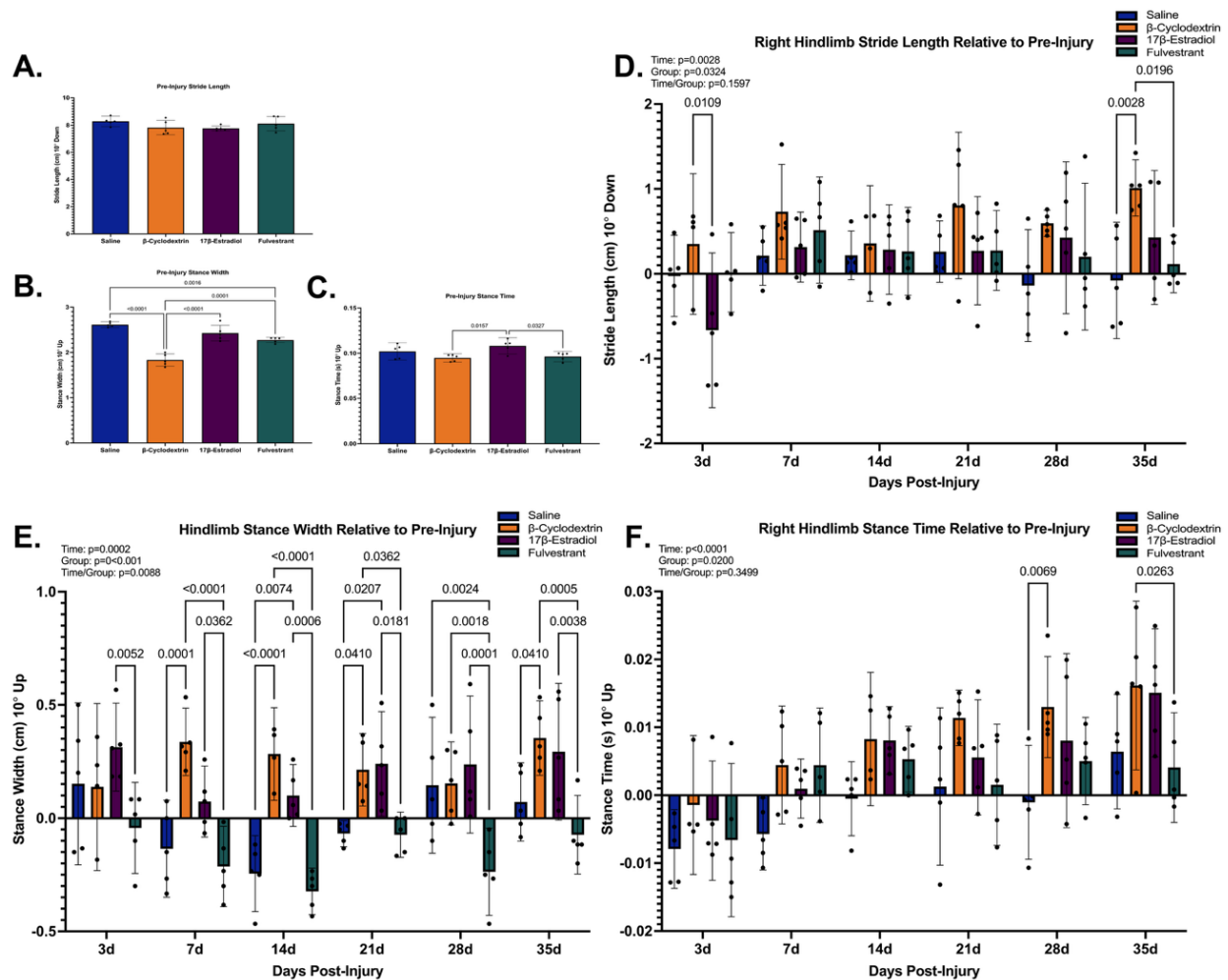


Figure 3.4. Longitudinal gait analysis (Digigait). Prior to injury, no differences between groups were observed in (A) stride length. However, (B) mice in the β -cyclodextrin group exhibited decreased hindlimb stance width compared to all other groups and mice in the saline group showed greater stance width than those in the Fulvestrant group. (C) Mice in the 17 β -estradiol group also demonstrated a greater proportion of time spent in the stance phase compared to mice in the β -cyclodextrin and Fulvestrant groups. Following injury, (D) β -cyclodextrin-treated mice showed greater stride length than the 17 β -estradiol group at 3 days, and greater than both the saline and Fulvestrant groups at 35 days. (E) β -cyclodextrin-treated mice had a wider stance than all other groups at 7, 14, 21, and 35 days, and at 28 days, both β -cyclodextrin- and saline-treated mice exhibited wider stance than the Fulvestrant group. (F) Mice treated with β -cyclodextrin also spent more time in the stance phase than the saline group at 28 days and the Fulvestrant group at 35 days. Panels D – F depict group comparisons at each timepoint with p -values < 0.05. Differences over time within groups are not shown. Bars represent mean $\pm$ 95% confidence interval, with individual animals indicated.

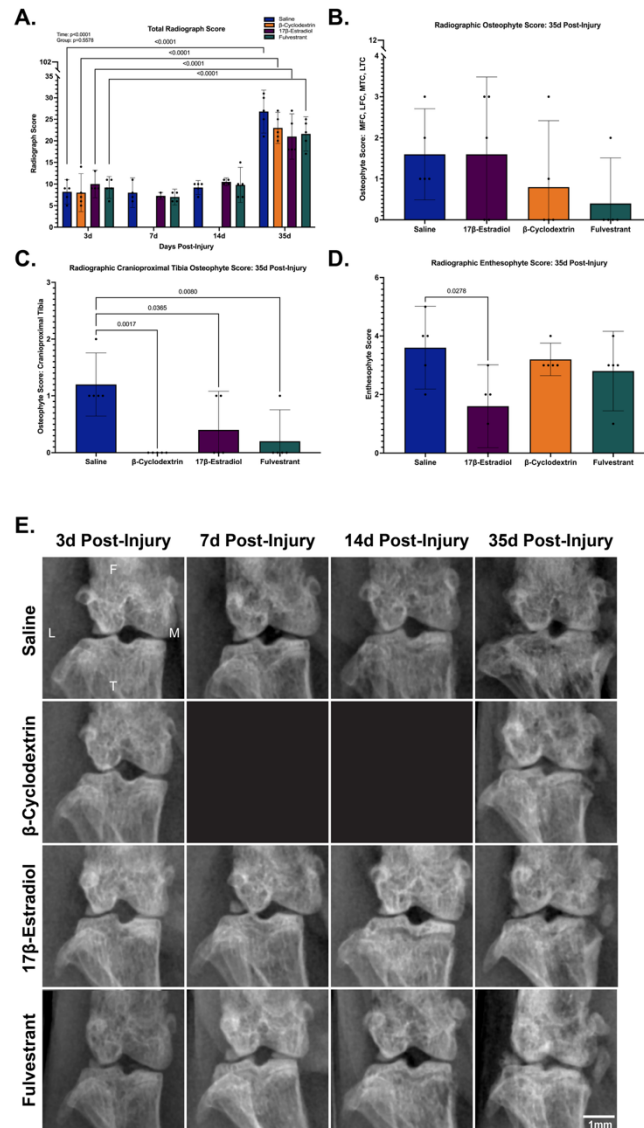


Figure 3.5. Radiographic analysis of PTOA development. (A) No significant differences were observed between groups in overall radiographic scores at any timepoint. However, radiographic evidence of PTOA progression was present in all groups at 35 days compared to their respective 3-day scores. Additional time-based differences within groups relative to the 35-day timepoint were observed but are not shown for simplicity. (B) At 35 days, there were no between-group differences in summed osteophyte scores encompassing the medial femoral condyle, lateral femoral condyle, medial tibial condyle, and lateral tibial condyle. (C) However, the saline group exhibited higher osteophyte scores on the cranioproximal tibia compared to all other groups, and (D) also demonstrated greater enthesophyte formation than the 17β-estradiol-treated group. Enthesophyte scores were derived from a sum of medial and lateral collateral ligament enthesopathy. Additional analyses, including further time-based comparisons and evaluation of additional parameters, are available in Appendix II.2. *p*-values < 0.05 are indicated. Bars represent mean $\pm$ 95% confidence interval, with individual animals marked. (E) Representative craniocaudal radiographic images of the right stifle are shown. The β-cyclodextrin group was only evaluated at 3 and 35 days, which accounts for the absence of 7- and 14-day timepoints for this group. F = Femur, T = Tibia, L = Lateral, M = Medial.

35 days, no significant group differences were detected in a summed osteophyte score, encompassing the medial femoral condyle, lateral femoral condyle, medial tibial condyle, and lateral tibial condyle (Figure 3.5B). Notably, osteophyte formation on the cranioproximal tibia was reduced in all experimental groups compared to saline controls at 35 days post-injury (Figure 3.5C). Additionally, 17 β -estradiol-treated mice exhibited reduced enthesophyte development at 35 days relative to saline controls (Figure 3.5D), based on a composite score that included both medial and lateral collateral ligament enthesopathy. Isolated analysis of lateral collateral ligament enthesophytes revealed increased formation in Fulvestrant and β -cyclodextrin-treated mice relative to saline controls at 35 days. (Appendix II.2.). Representative craniocaudal radiographic images are provided in Figure 3.5E.

Histological analysis also revealed no significant group differences in total joint pathology scores at any timepoint (Figure 3.6A). Notably, scores increased over time, indicating temporal progression of PTOA (Figure 3.6A, Appendix II.3A.). At 3 days post-injury, 17 β -estradiol-treated mice exhibited greater fibrotic coverage of the lateral joint capsule relative to saline-treated mice (Figure 3.6B). At 35 days, both β -cyclodextrin and Fulvestrant-treated mice showed more mature osteophytes than saline controls (Figure 3.6C), while 17 β -estradiol-treated mice demonstrated smaller enthesophytes (Figure 3.6D). This reduction appeared to be driven by lateral tibial enthesophyte size, which was greater in the saline group compared to all other treatments (Appendix II.3B.). No group differences were observed in overall osteophyte size or enthesophyte maturity at 35 days (Appendix II.3D, E). Composite scores for osteophyte and enthesophyte formation included all major joint regions: medial femoral condyle, lateral femoral condyle, medial tibial condyle, and lateral tibial condyle. Representative coronal histologic sections are shown in Figure 3.6E.

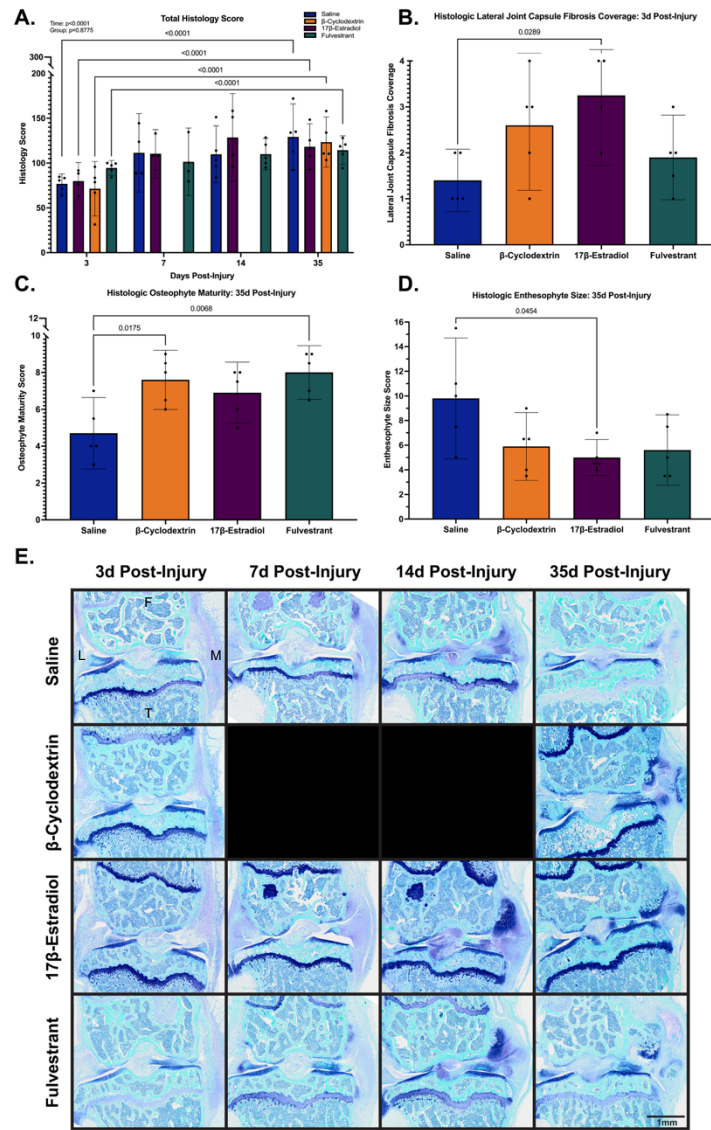


Figure 3.6. Histologic evaluation of PTOA development. (A) No significant differences were observed between groups in total histology scores at any timepoint. However, all groups exhibited histologic evidence of PTOA progression by 35 days compared to their respective 3-day scores. Additional time-based differences within groups relative to the 35-day timepoint were observed but are not shown for simplicity. (B) At 3 days post-injury, the 17 β -estradiol-treated group showed increased fibrosis coverage of the lateral joint capsule compared to the saline group. (C) At 35 days, the β -cyclodextrin and Fulvestrant groups exhibited more mature osteophyte development than the saline group, while (D) the 17 β -estradiol group displayed smaller enthesophytes compared to saline-treated mice. Osteophyte and enthesophyte scores included evaluations of the medial and lateral femoral condyles and tibial condyles. Additional analyses, including further time-based comparisons and evaluation of other parameters, are provided in Appendix II.3. p -values < 0.05 are indicated. Bars represent mean $\pm$ 95% confidence interval, with individual animals shown. (E) Representative coronal sections of the right stifle joint at 20X magnification are shown at 3, 7, 14, and 35 days post-injury. Sections were stained with toluidine blue and fast green. The β -cyclodextrin group was only assessed at 3 and 35 days, accounting for the absence of the 7 and 14 day timepoints for this group. F = Femur, T = Tibia, L = Lateral, M = Medial.

3.3.3. Estrogen Receptor Expression

Estrogen receptor profiling in mouse ACL tissue was performed using fluorescent IHC to detect the presence of ER α and ER β . In naïve male mice, both ER α and ER β were expressed within the ACL (Figure 3.7A – D). The expression of these receptors in ACL remnants was not significantly altered by ACL rupture alone, either in the acute injury response at 3 days post-injury or at 56 days following the onset of PTOA (Figure 3.7A – D; slides from Chapter 2).

To evaluate the impact of the experimental treatments on ER expression, ER α and ER β levels were assessed across treatment groups at multiple timepoints. No significant changes in ER expression were observed in mice treated with 17 β -estradiol or saline across all timepoints (Figure 3.8 A, B). Notably, Fulvestrant injection led to a transient elevation in ER α fluorescent intensity relative to all other groups at 3 days post-injury (Figure 3.8A). However, by 35 days, ER α expression in Fulvestrant-treated mice was no longer elevated, showing no difference compared to other groups and a significant reduction relative to Fulvestrant-treated mice at 3 days (Figure 3.8A). Additionally, ER β expression in β -cyclodextrin-treated mice significantly increased from 3 to 35 days post-injury, indicating a progressive upregulation over time in this group (Figure 3.8B). Representative IHC images for each group are shown in Figure 3.8C. Additional statistical comparisons and IHC controls are provided in Appendix II.4.

3.4 Discussion

3.4.1 Overview

PTOA is a common consequence of joint trauma, notably following ACL injury, and currently lacks effective disease and symptom modifying treatments. Given the established but complex role of estrogens in modulating inflammation and pain, this study aimed to investigate how IA injection of 17 β -estradiol (increased estrogen signaling) and Fulvestrant (decreased estrogen signaling via ER antagonism) affects PTOA progression in a male mouse model. Our

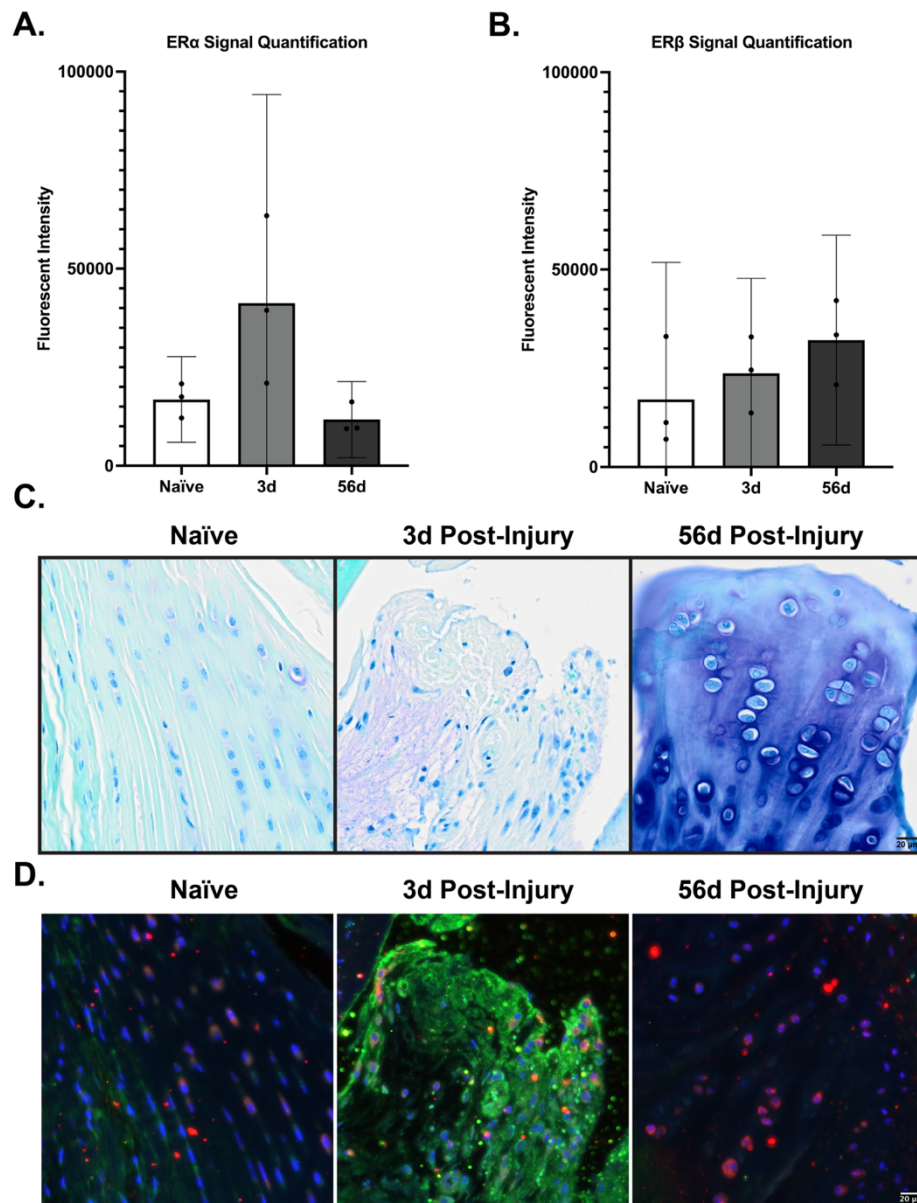


Figure 3.7. *ERα* and *ERβ* expression levels in response to ACL rupture. Male mouse ACL cells showed no significant differences in *ERα* (A) or *ERβ* (B) signal intensity. ER expression was measured using fluorescent IHC in the naïve state and at 3 and 56 days following injury. *p*-values < 0.05 are indicated (none shown). Bars represent mean $\pm$ 95% confidence interval, with individual animals shown. (C) Representative histologic sections stained with toluidine blue and fast green illustrate the ACL structure and were imaged at 20X and zoomed to match the corresponding 40X fluorescent images. These sections are serial to those used for ER fluorescent profiling and provide anatomical context for identifying individual ACL cells. (D) Representative 40X dual-stained fluorescent IHC images from naïve, 3-day, and 56-day post-injury ACLs/ACL remnants show DAPI (blue), *ERα* (green), and *ERβ* (red). These tissue sections were collected from animals used in previous studies (Chapter 2) that underwent ACL rupture without IA injection.

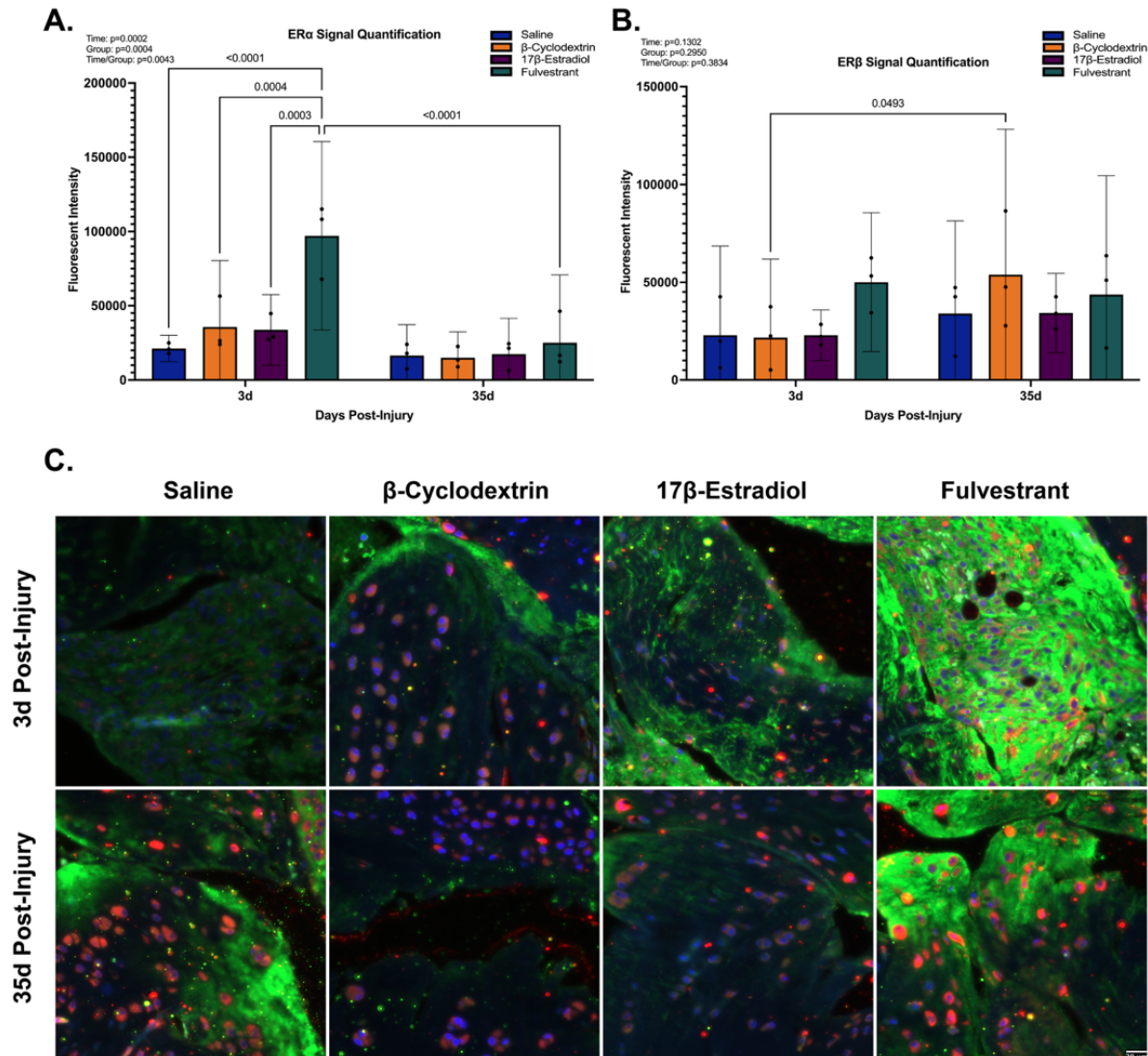


Figure 3.8. Effect of IA injection and ACL injury on $ER\alpha$ and $ER\beta$ expression at 3 and 35 days, assessed using fluorescent immunohistochemistry. **(A)** Mice that received Fulvestrant showed increased $ER\alpha$ signal intensity in ACL tissue at 3 days post-injury compared to all other groups. This difference did not persist at 35 days. **(B)** Mice treated with β -cyclodextrin exhibited increased $ER\beta$ signal intensity at 35 days post-injury compared to β -cyclodextrin-injected mice at 3 days. However, no between-group differences in $ER\beta$ expression were observed at either timepoint. Comparisons are shown both between groups at each timepoint and across time within each group. Full statistical results are provided in Appendix II.4. p -values < 0.05 are indicated. Bars represent mean $\pm$ 95% confidence interval, with individual animals shown. **(C)** Representative 40X dual-stained fluorescent IHC images of mouse ACL remnants at 3 and 35 days post-injury. Mice received intra-articular injection of either 1) 17 β -estradiol, 2) Fulvestrant, 3) β -cyclodextrin (vehicle control), or 4) saline (injection control). Fluorescent channels show DAPI (blue), $ER\alpha$ (green), and $ER\beta$ (red). Images and signal quantification for positive controls, isotype controls, and negative controls are included in Appendix II.4.

results indicate time-dependent and treatment-specific effects on joint structure, mobility, and ER expression, with implications for understanding the interplay between estrogen signaling, pain, inflammation, and joint degeneration.

In the progression of PTOA, the injury response can be broadly categorized into two phases, early-stage and late-stage. In our model, early-stage PTOA spans from the time of injury to approximately 7 days post-injury and is primarily characterized by synovial inflammation and painful behaviors such as offloading of the injured joint.¹¹ Based on findings from the broader literature, this phase is also typically associated with joint swelling and increased levels of reactive oxygen species, pro-inflammatory cytokines (such as IL-1, IL-6, and TNF- α), and infiltration of inflammatory cells including macrophages and lymphocytes.⁴³ The later-stage of PTOA progression, occurring after 35 days post-injury in our model, is marked by structural joint changes including cartilage degeneration, focal loss of proteoglycans, the formation of osteophytes and enthesophytes, and further alterations to mobility and behavior.^{11,43}

At 3 days following injury, mice treated with either 17 β -estradiol or Fulvestrant had decreased voluntary distance traveled compared to saline controls. Fulvestrant treatment also resulted in reduced body rotations, and β -cyclodextrin led to decreased injured limb-weight bearing. These functional deficits, paired with histologic evidence of increased joint capsule fibrosis in the 17 β -estradiol group, suggest that injection of our treatments may be amplifying acute, early-stage inflammation and pain in the joint relative to saline. When broadly compared to our prior data from male mice that received ACL rupture without IA injection (Chapter 2), saline-injected mice did not exhibit substantial differences 3 days following injury in average static weight-bearing (-0.52 no injection vs. -0.29 injection), total radiograph score (2.8 no injection vs. 8.2 injection), or total histology score (100.85 no injection vs. 76.75 injection). These findings indicate that the IA injection itself has limited impact on early-stage joint

pathology, and that the observed changes are more likely driven by treatment-specific effects. Therefore, the early-stage functional and histological alterations following treatment injection likely reflect the bioactivity of the compounds. Unlike inert saline, these treatments may transiently disrupt joint homeostasis, leading to enhanced early inflammatory responses.

At 35 days post-injury, in a later-stage of disease progression, comparisons to historical data (Chapter 2) again showed that saline injection alone does not appear to significantly alter PTOA outcomes. Specifically, mice that received saline did not greatly differ in average static weight bearing (-0.32 no injection vs. -0.38 injection), total radiograph score (15 no injection vs. 26.8 injection), or total histology score (160.25 at 28d no injection vs. 129.25 injection) compared to mice that had not received an IA injection. This observation contrasts with recent literature reporting mild benefits of saline in human OA studies, although those studies may involve placebo effects that are not present in preclinical models.⁴⁴

Broadly, the results at 35 days post-injury were somewhat confusing. Thus, we have created a summary table of the most relevant results for each group at 35 days relative to saline (Table 3.1). Due to some unexpected results in the β -cyclodextrin group, this group is included in the table as well. Overall, we observed differences in symptomatic progression of PTOA in each treatment group as well as differences in structural quantification of PTOA, namely alterations in enthesophyte and osteophyte formation.

3.4.2 β -Cyclodextrin (Vehicle Control)

At 35 days following injury, we observed that the vehicle control, β -cyclodextrin, caused impacts on PTOA development relative to the saline control group, including altered gait parameters and increased osteophyte maturity. Specifically, β -cyclodextrin-treated mice demonstrated both increased stride length and decreased stance width on treadmill-based gait

Table 3.1. Summary of outcome parameters that differed significantly from saline-treated controls at 35 days post-injury in the experimental treatment groups (17 β -estradiol and Fulvestrant). The β -cyclodextrin vehicle control group is also included due to observed treatment-related effects. Upward ($\uparrow$) or downward arrows ($\downarrow$) indicate the direction of change for each parameter relative to saline. Arrow color denotes the interpreted impact on PTOA: green arrows denote changes generally associated with less severe PTOA features, while red arrows indicate changes typically associated with greater PTOA severity.

	Symptomatic Progression of PTOA					Structural Quantification of PTOA					
	ANY-maze		Static Weight Bearing	Digigait		Radiographic Scoring*		Histologic Scoring*			
	Distance Traveled	Rotations		Stride Length	Stance Width	Osteophytes [‡]	Enthesophytes	Osteophyte Maturity	Osteophyte Size	Enthesophyte Maturity	Enthesophyte Size
β-cyclodextrin	-	-	-	$\uparrow$	$\uparrow$	-	-	$\uparrow$	-	-	-
17β-estradiol	$\uparrow$	-	$\uparrow$	-	-	-	$\downarrow$	-	-	-	$\downarrow$
Fulvestrant	-	$\downarrow$	-	-	-	-	-	$\uparrow$	-	-	-

*Composite osteophyte and enthesophyte scores for radiographs and histology include the medial femoral condyle, lateral femoral condyle, medial tibial condyle, and lateral tibial condyle

[‡]Although no differences were seen in the radiographic composite osteophyte score, differences were observed in osteophyte development on the cranioproximal tibia (Figure 3.5C)

evaluation, presenting an interesting paradox, as classic PTOA development is typically characterized by increased hindlimb stance width coupled with decreased stride length.^{45–47} However, osteophyte development can act to stabilize joints, particularly in the stance phase.^{48,49} It is plausible that at 35 days, the β -cyclodextrin group had developed sufficient osteophytes to help stabilize the joint without aggressive cartilage or bone degeneration severe enough to cause significant pain, resulting in the observed increase in stride length.

While β -cyclodextrin has traditionally been considered an inert drug delivery vehicle, emerging evidence suggests it can exert both anti-inflammatory and pro-inflammatory effects, which may help explain the paradoxical outcomes we observed in symptomatic and structural PTOA development.^{50,51} Studies in atherosclerosis models have demonstrated that cyclodextrin reduces pro-inflammatory cytokines (IL-1 α , TNF- α , IL-6) and modulates macrophage metabolism, indicating potential anti-inflammatory mechanisms that could influence the improved gait parameters in our study.⁵⁰ Conversely, studies investigating metabolic inflammation have revealed a pro-inflammatory profile following β -cyclodextrin administration, including hepatic inflammation and increased expression of inflammatory genes (IL-1 β , CCL2, IL-18, SAA1).⁵¹ These effects may have contributed to the indicators of worsened PTOA observed in our model, including increased osteophyte maturity and widened hindlimb stance width. Collectively these findings highlight the complexity of β -cyclodextrin's role in modulating inflammation and PTOA progression. Our results align with growing evidence that β -cyclodextrin is not biologically inert and underscores the need for further studies to elucidate its mechanistic effects on PTOA development.^{50,51}

Another notable finding was the increased ER β expression observed 35 days after β -cyclodextrin injection compared to 3 days. While the mechanism remains unclear, this may relate to β -cyclodextrin's reported ability to reduce TNF- α levels, potentially dampening NF- κ B activity, a known suppressor of ER expression.^{50,52–56} The absence of this effect when 17 β -

estradiol was co-delivered suggests a potential counteractive effect with each component targeting distinct inflammatory compared to direct hormonal pathways. However, the precise mechanisms remain speculative, and further studies are needed to clarify how β -cyclodextrin influences ER β regulation in the joint.

These findings highlight the importance of appropriate vehicle controls in estrogen research, as many studies have utilized cyclodextrin-encapsulated formulations without accounting for potential independent effects of the cyclodextrin carrier.^{57–60} The lack of significant difference between β -cyclodextrin and 17 β -estradiol groups in multiple outcome measures suggests that some effects previously attributed solely to estrogen may involve contributions from cyclodextrin itself, emphasizing the necessity for rigorous experimental design in future estrogen-based therapeutic investigations. Although we did not observe group-based differences between β -cyclodextrin and 17 β -estradiol, the differences between the groups relative to saline were distinct, indicating that different mechanisms may be at play. For the purposes of this study, we will examine the impact of 17 β -estradiol relative to saline with the understanding that some of these changes are likely confounded by the ambiguous pro- and anti-inflammatory effects of β -cyclodextrin.

3.4.3 Estrogen Administration

Interestingly, we did not observe changes to ER expression levels at 3 or 35 days post-injury with 17 β -estradiol administration. However, other studies have revealed complex dynamics between estradiol supplementation and ER expression. For example, primary cultures of mesenchymal stem cells from female ovariectomized mice showed increased ER α expression and decreased ER β expression following estradiol treatment.⁶¹ In another study utilizing mouse hippocampal cells, exposure to estradiol triggered localization of ER β to the plasma membrane, but did not affect ER α .⁶² These findings underscore the complexity of the

relationship between estradiol and ER dynamics, and suggest that estradiol may influence receptor localization or activity rather than just total expression. Moreover, it is likely that different dosing regimens, timepoints, or joint-specific microenvironments may influence ER dynamics. Thus, although no expression differences were detected here, this does not preclude more nuanced effects, and further studies are warranted to capture transient or cell-specific changes.

Despite no observed changes in ER expression, 17 β -estradiol-treated mice showed improved voluntary mobility and static weight-bearing at 35 days post-injury compared to saline controls. These outcomes, which are closely associated with symptomatic relief and pain modulation, suggest that 17 β -estradiol may reduce joint pain. The connection between estrogen and pain is well established, though the underlying mechanisms are highly complex and vary across different physiological systems.⁶³ When examining primary OA pain, estrogen replacement therapy has been shown to reduce joint pain and improve subjective pain scores in clinical studies.^{64,65} The pain-modulating effects of estrogen appear to work through multiple mechanisms, including reduction of inflammatory neuropeptides in synovial tissue, and direct analgesia effects mediated by ERs.^{66,67} Research to date indicates that ER α and ER β each contribute to pain modulation through distinct but overlapping mechanisms.⁶⁸ Both receptors inhibit TNF- α , while ER α additionally suppresses IL-1 β , prevents chondrocyte senescence via the PI3K/Akt/mTOR and MAPK pathways, and modulates spinal enkephalin and NMDA/P2X3 receptor activity.⁶⁵ ER β appears to be more strongly associated with anti-inflammatory effects, such as reducing edema and neutrophil recruitment, and enhances nervous system inhibition through 5-HT pathways and P2X3 attenuation via cAMP/PKA/ERK signaling.^{65,67–69} Taken together, these mechanisms, alongside our observed functional outcomes, indicate that mice that received 17 β -estradiol may be experiencing less pain than mice that received saline.

Radiographic and histologic findings revealed that estradiol-treated mice developed smaller enthesophytes compared to saline-treated controls. Although a direct connection between estrogen signaling and enthesophyte formation has not been established, enthesophytes commonly arise from inflammation related to repetitive mechanical stress.⁷⁰ The observed reduction in enthesophyte development may reflect estrogen's anti-inflammatory influence. Additionally, because estrogen is known to protect against bone loss and cartilage degradation, primarily by inhibiting osteoclasts and supporting osteoblast survival, it was surprising that we did not observe significant improvements in cartilage or bone histopathology.^{64,71–74} These outcomes may reflect the complexity of estrogen's context-dependent effects on bone, which vary by anatomical site, estrogen dose, and mechanical environment.^{72,73} Further studies are necessary to optimize injection parameters to better assess potential protective effects on joint structure.

3.4.4 Fulvestrant (Estrogen Receptor Antagonism)

Administration of Fulvestrant led to notable differences compared to saline 35 days after injury, including alterations to voluntary mobility (decreased rotations) and increased osteophyte maturity histologically, although this was not mirrored radiographically. The lack of correlation between histologic and radiographic scoring may be due to differences in what each method captures. Radiographs primarily assess osteophyte size, while histologic analysis provides separate evaluations of both size and maturity for osteophytes. In our study, increased osteophyte maturity in the β -cyclodextrin and Fulvestrant groups may not have produced radiographically detectable changes in overall osteophyte size. The observed increased osteophytes align with prior research in a female mouse model of ER α and ER β knockout, where increased osteophyte formation was noted relative to wild-type controls.²³

Interestingly, in this study, administration of Fulvestrant led to a transient increase in ER α expression 3 days following injury relative to all other groups. Although Fulvestrant is known to function as an ER antagonist and degrader, its pharmacokinetics and the timing of administration may have influenced the observed outcomes. Given that the half-life of Fulvestrant is approximately 13.5 – 18.5 hours when administered intravenously, and that ER turnover is relatively rapid (3 – 5 hours in human breast cancer cells), the single intra-articular dose used in this study may have resulted in transient ER α degradation, followed by compensatory upregulation once the drug effect diminished.^{75,76} This increase in ER α expression may reflect a feedback response to initial receptor inhibition, as suppression of active ER α signaling can lead to increased transcription of ESR1, the gene encoding ER α .⁷⁷ Fulvestrant inhibits ER function by preventing receptor dimerization and promoting degradation via the ubiquitin-proteasome pathway.^{78,79} However, while Fulvestrant is considered a full ER antagonist, some studies suggest it may preferentially affect ER α over ER β , particularly in male tissues.^{62,80} It is also important to note that most mechanistic insights into Fulvestrant come from studies in female breast cancer models, and its actions in male joint tissue may differ. This transient suppression followed by receptor upregulation could have contributed to downstream changes in joint pathology, including osteophyte development.

Ultimately, without clear evidence of sustained ER degradation, it is difficult to delineate a cause for the observed functional impairments and osteophyte development. However, it is possible that decreased estrogen signaling immediately following injection, even if temporary, could have diminished the protective, anti-inflammatory effects of estrogen, thereby contributing to the later-stage outcomes. These results indicate that Fulvestrant can influence ER α dynamics in male mouse joints and may be involved in the progression of both symptomatic and structural features of PTOA.

3.4.5 Limitations and Future Directions

This study had multiple limitations. Most important, only male mice were utilized. While this was important for delineating the impact of estrogen on the localized joint environment without the influence of systemic hormone fluctuations, the lack of females results in a significant gap in understanding of these responses. Future work is ongoing to examine the responses of β -cyclodextrin, 17 β -estradiol, and Fulvestrant in female mice. Another limitation is that the dosing strategy of our treatments may not be optimal. While timing our injection immediately after ACL rupture allowed for only one anesthetic event for the mice, it also meant that the injection occurred in a very volatile and dynamic joint environment. This timeline is also not the most translationally relevant, as in humans there would be a delay between ACL rupture and therapeutic intervention. The response observed in our Fulvestrant group also indicates that multiple injections may be needed. Future studies will work to optimize our dosing timeline. Additionally, the systemic response to the treatments in this study is being examined in both male and female mice through serum analysis for sex hormones and gonad histology. This study is also limited by the lack of molecular outcomes that could delineate specific mechanisms for the observed alterations in mobility, pathology, and ER expression.

Much work is still needed in the field focused on determining the specific mechanisms at work in our study and optimizing dosing regimens, timing of intervention, and treatment combinations for the development of novel therapeutics to delay onset and progression of PTOA. Future investigations should include female subjects, multiple dosing strategies, and mechanistic studies to advance our understanding in this area.

3.4.6 Summary

Cumulatively, this work highlights the exceedingly complex and dynamic relationships between estrogen signaling, pain, inflammation, and OA. Altogether, in our model, we demonstrated that IA injection of 17 β -estradiol provided some protective effects against PTOA

progression in male mice, particularly in terms of pain-related mobility parameters and enthesophyte formation, though these benefits were confounded by unexpected effects of the β -cyclodextrin vehicle. Mice treated with β -cyclodextrin alone showed paradoxical anti- and pro-inflammatory properties that influenced joint pathology and ER expression, challenging the traditional view of β -cyclodextrin as an inert vehicle. Fulvestrant treatment showed detrimental effects on some PTOA outcomes and resulted in increases in ER α expression, highlighting the complex dose- and receptor-dependent relationships in estrogen signaling that demand more sophisticated approaches to hormone-based therapeutic development in PTOA. Together, these findings demonstrate that estrogen signaling likely plays a nuanced role in PTOA progression, with therapeutic effects influenced not only by hormone type and receptor specificity but also by the delivery vehicle, underscoring the need for precise, mechanism-informed strategies in future investigations.

References

1. Institute for Health Metrics and Evaluation (IHME). Global Burden of Disease Collaborative Network. Global Burden of Disease Study. Published online 2021.
2. Khella CM, Asgarian R, Horvath JM, Rolaufts B, Hart ML. An evidence-based systematic review of human knee post-traumatic osteoarthritis (Ptoa): Timeline of clinical presentation and disease markers, comparison of knee joint ptoa models and early disease implications. *Int J Mol Sci.* 2021;22(4):1-48. doi:10.3390/ijms22041996
3. Friel NA, Chu CR. The Role of ACL Injury in the Development of Posttraumatic Knee Osteoarthritis. *Clin Sports Med.* 2013;32(1):1-12. doi:10.1016/j.csm.2012.08.017
4. Liddle AD, Pegg EC, Pandit H. Knee replacement for osteoarthritis. *Maturitas.* 2013;75(2):131-136. doi:10.1016/j.maturitas.2013.03.005

5. Evans JT, Walker RW, Evans JP, Blom AW, Sayers A, Whitehouse MR. How long does a knee replacement last? A systematic review and meta-analysis of case series and national registry reports with more than 15 years of follow-up. *The Lancet*. 2019;393(10172):655-663. doi:10.1016/s0140-6736(18)32531-5
6. Mahajan A, Patni R. Menopause and Osteoarthritis: Any Association ? *J Midlife Health*. 2018;9(4):171-172. doi:10.4103/jmh.JMH_157_18
7. Hernandez PA, Bradford JC, Brahmachary P, Ulman S, Robinson JL, June RK, et al. Unraveling sex-specific risks of knee osteoarthritis before menopause: Do sex differences start early in life? *Osteoarthritis Cartilage*. 2024;32(9):1032-1044. doi:10.1016/j.joca.2024.04.015
8. Sowers M. Epidemiology of Risk Factors for Osteoarthritis: Systemic Factors. Vol 13.; 2001.
9. Costa MQ, Badger GJ, Chrostek CA, Carvalho OD, Faiola SL, Fadale PD, et al. Effects of Initial Graft Tension and Patient Sex on Knee Osteoarthritis Outcomes After ACL Reconstruction: A Randomized Controlled Clinical Trial With 10- to 12-Year Follow-up. *American Journal of Sports Medicine*. 2022;50(13):3510-3521. doi:10.1177/03635465221124917
10. Bergman RF, Lammlin L, Junginger L, Farrell E, Goldman S, Darcy R, et al. Sexual dimorphism of the synovial transcriptome underpins greater PTOA disease severity in male mice following joint injury. *Osteoarthritis Cartilage*. Published online 2023. doi:10.1016/j.joca.2023.07.012
11. Van Zeeland EM, Kassel B, Montoya T, Saviola AJ, Burton LH, Easley JT, et al. Structural, functional, and proteomic based sex differences in murine post-traumatic osteoarthritis development following mechanical anterior cruciate ligament injury. *Osteoarthritis Cartilage*. Published online May 2025. doi:10.1016/j.joca.2025.05.004

12. Ma HL, Blanchet TJ, Peluso D, Hopkins B, Morris EA, Glasson SS. Osteoarthritis severity is sex dependent in a surgical mouse model. *Osteoarthritis Cartilage*. 2007;15(6):695-700. doi:10.1016/j.joca.2006.11.005
13. Lu Z, Zhang A, Wang J, Han K, Gao H. Estrogen alleviates post-traumatic osteoarthritis progression and decreases p-EGFR levels in female mouse cartilage. *BMC Musculoskelet Disord*. 2022;23(1). doi:10.1186/s12891-022-05608-y
14. Nelson JF, Feliciot LS, Osterburg HH, Finch CE. Differential Contributions of Ovarian and Extraovarian Factors to Age-Related Reductions in Plasma Estradiol and Progesterone during the Estrous Cycle of C57BL/6J Mice*.
15. Ajayi AF, Akhigbe RE. Staging of the estrous cycle and induction of estrus in experimental rodents: an update. *Fertil Res Pract*. 2020;6(1). doi:10.1186/s40738-020-00074-3
16. Sherman BM, Korenman SG. Hormonal Characteristics of the Human Menstrual Cycle throughout Reproductive Life.
17. Hess RA, Cooke PS. Estrogen in the male: A historical perspective. *Biol Reprod*. 2018;99(1):27-44. doi:10.1093/biolre/iroy043
18. Bapat S, Hubbard D, Munjal A, Hunter M, Fulzele S. Pros and cons of mouse models for studying osteoarthritis. *Clin Transl Med*. 2018;7(1). doi:10.1186/s40169-018-0215-4
19. Pritzker KPH, Gay S, Jimenez SA, Ostergaard K, Pelletier JP, Revell K, et al. Osteoarthritis cartilage histopathology: Grading and staging. *Osteoarthritis Cartilage*. 2006;14(1):13-29. doi:10.1016/j.joca.2005.07.014
20. Engdahl C, Börjesson AE, Forsman HF, Andersson A, Stubelius A, Krust A, et al. The role of total and cartilage-specific estrogen receptor alpha expression for the ameliorating effect of estrogen treatment on arthritis. *Arthritis Res Ther*. 2014;16(4). doi:10.1186/ar4612

21. Yang YH, Ngo D, Jones M, Simpson E, Fritzemeier KH, Morand EF. Endogenous estrogen regulation of inflammatory arthritis and cytokine expression in male mice, predominantly via estrogen receptor α . *Arthritis Rheum.* 2010;62(4):1017-1025.
doi:10.1002/art.27330
22. Dulos J, Vijn P, van Doorn C, Hofstra CL, Veening-Griffioen D, de Graaf J, et al. Suppression of the inflammatory response in experimental arthritis is mediated via estrogen receptor α but not estrogen receptor β . *Arthritis Res Ther.* 2010;12(3).
doi:10.1186/ar3032
23. Sniekers YH, van Osch GJVM, Ederveen AGH, Inzunza J, Gustafsson JÅ, van Leeuwen JPTM, et al. Development of osteoarthritic features in estrogen receptor knockout mice. *Osteoarthritis Cartilage.* 2009;17(10):1356-1361.
doi:10.1016/j.joca.2009.04.008
24. Bergink AP, Van Meurs JB, Loughlin J, Arp PP, Fang Y, Hofman A, et al. Estrogen receptor α gene haplotype is associated with radiographic osteoarthritis of the knee in elderly men and women. *Arthritis Rheum.* 2003;48(7):1913-1922.
doi:10.1002/art.11046
25. Timkovich AE, Sikes KJ, Andrie KM, Afzali MF, Sanford J, Fernandez K, et al. Full and Partial Mid-substance ACL Rupture Using Mechanical Tibial Displacement in Male and Female Mice. *Ann Biomed Eng.* 2023;51(3):579-593. doi:10.1007/s10439-022-03065-1
26. Howell A, Osborne CK, Morris C, Wakeling AE. ICI 182,780 (Faslodex(TM)): Development of a novel, "pure" antiestrogen. *Cancer.* 2000;89(4):817-825.
doi:10.1002/1097-0142(20000815)89:4<817::AID-CNCR14>3.0.CO;2-6

27. Robertson JFR. ICI 182,780 (FulvestrantTM) - The first oestrogen receptor down-regulator - Current clinical data. *Br J Cancer*. 2001;85(3332):11-14.
doi:10.1054/bjoc.2001.1982
28. Foley P, Liang H, Crichlow A. Evaluation of a Sustained-Release Formulation of Buprenorphine for Analgesia in Rats. *J Am Assoc Lab Anim Sci*. 2011;50(2):198-204.
29. Tsai CL, Liu TK. Estradiol-Induced Knee Osteoarthritis in Ovariectomized Rabbits. *Clinical Orthopaedics and Related Research*. 1993;(291):295-392.
30. Schneider AH, Kanashiro A, Dutra SGV, de Souza R do N, Veras FP, Cunha F de Q, et al. Estradiol replacement therapy regulates innate immune response in ovariectomized arthritic mice. *Int Immunopharmacol*. 2019;72:504-510.
doi:10.1016/j.intimp.2019.04.048
31. Chapman JC, Min SH, Freeh SM, Michael SD. The estrogen-injected female mouse: New insight into the etiology of PCOS. *Reproductive Biology and Endocrinology*. 2009;7. doi:10.1186/1477-7827-7-47
32. Roman-Blas JA, Castañeda S, Largo R, Herrero-Beaumont G. Osteoarthritis associated with estrogen deficiency. *Arthritis Res Ther*. 2009;11(5).
doi:10.1186/ar2791
33. Rodrigues JFS, E Silva CS, Muniz TF, De Aquino AF, Da Silva Nina LN, Sousa NCF, et al. Sulforaphane modulates joint inflammation in a murine model of complete freund's adjuvant-induced mono-arthritis. *Molecules*. 2018;23(5).
doi:10.3390/molecules23050988
34. Gelse K, Pfander D, Obier S, Knaup KX, Wiesener M, Hennig FF, et al. Role of hypoxia-inducible factor 1 alpha in the integrity of articular cartilage in murine knee joints. *Arthritis Res Ther*. 2008;10(5). doi:10.1186/ar2508

35. Hoffmann J, Bohlmann R, Heinrich N, Hofmeister H, Kroll J, Künzer H, et al. Characterization of new estrogen receptor destabilizing compounds: Effects on estrogen-sensitive and tamoxifen-resistant breast cancer. *J Natl Cancer Inst.* 2004;96(3):210-218. doi:10.1093/jnci/djh022
36. Imgenberg J, Rolauffs B, Grodzinsky AJ, Schünke M, Kurz B. Estrogen reduces mechanical injury-related cell death and proteoglycan degradation in mature articular cartilage independent of the presence of the superficial zone tissue. *Osteoarthritis Cartilage.* 2013;21(11):1738-1745. doi:10.1016/j.joca.2013.07.007
37. Li W, Tang L, Xiong Y, Zhou X, Wu L. The chondroprotective effects of dehydroepiandrosterone probably exerted by its conversion to estradiol. *Journal of Steroid Biochemistry and Molecular Biology.* 2013;134(1):15-22. doi:10.1016/j.jsbmb.2012.10.001
38. Fda, Cder. Faslodex (Fulvestrant) Injection Label. www.fda.gov/medwatch
39. Hurley CR, Hammer DL, Shott S. Progression of radiographic evidence of osteoarthritis following tibial plateau leveling osteotomy in dogs with cranial cruciate ligament rupture: 295 cases (2001–2005). *Journal of the American Veterinary Medical Association.* 2007;230(11). doi:10.2460/javma.230.11.1674
40. Haubruck P, Heller R, Blaker CL, Clarke EC, Smith SM, Burkhardt D, et al. Streamlining quantitative joint-wide medial femoro-tibial histopathological scoring of mouse post-traumatic knee osteoarthritis models. *Osteoarthritis Cartilage.* 2023;31(12):1602-1611. doi:10.1016/j.joca.2023.07.013
41. Sar M, Welsch F. Differential Expression of Estrogen Receptor-and Estrogen Receptor-in the Rat Ovary.; 1999.
42. Hishikawa Y, Damavandi · E, Izumi · S, Koji · T. Molecular histochemical analysis of estrogen receptor α and β expressions in the mouse ovary: in situ hybridization and

- Southwestern histochemistry. *Med Electron Microsc.* 2003;36:67-73.
doi:10.1007/s00795-002-0193-9
43. Punzi L, Galozzi P, Luisetto R, Favero M, Ramonda R, Oliviero F, et al. Post-traumatic arthritis: overview on pathogenic mechanisms and role of inflammation. *RMD Open.* 2016;2:279. doi:10.1136/rmdopen-2016
 44. Altman RD, Devji T, Bhandari M, Fierlinger A, Niazi F, Christensen R. Clinical benefit of intra-articular saline as a comparator in clinical trials of knee osteoarthritis treatments: A systematic review and meta-analysis of randomized trials. *Semin Arthritis Rheum.* 2016;46(2):151-159. doi:10.1016/j.semarthrit.2016.04.003
 45. Jacobs BY, Kloefkorn HE, Allen KD. Gait Analysis Methods for Rodent Models of Osteoarthritis. *Curr Pain Headache Rep.* 2014;18(10). doi:10.1007/s11916-014-0456-x
 46. Taş S, Güneri S, Baki A, Yildirim T, Kaymak B, Erden Z. Effects of severity of osteoarthritis on the temporospatial gait parameters in patients with knee osteoarthritis. *Acta Orthop Traumatol Turc.* 2014;48(6):635-641.
doi:10.3944/AOTT.2014.13.0071
 47. Lakes EH, Allen KD. Gait analysis methods for rodent models of arthritic disorders: reviews and recommendations. *Osteoarthritis Cartilage.* 2016;24(11):1837-1849.
doi:10.1016/j.joca.2016.03.008
 48. van der Kraan PM, van den Berg WB. Osteophytes: relevance and biology. *Osteoarthritis Cartilage.* 2007;15(3):237-244. doi:10.1016/j.joca.2006.11.006
 49. Steele A, Gonzalez R, Garbalosa JC, Steigbigel K, Grgurich T, Parisi EJ, et al. Osteoarthritis, osteophytes, and enthesophytes affect biomechanical function in adults with X-linked hypophosphatemia. *Journal of Clinical Endocrinology and Metabolism.* 2020;105(4):E1798-E1814. doi:10.1210/clinem/dgaa064

50. Appleton SL, Navarro-Orcajada S, Martínez-Navarro FJ, Caldera F, López-Nicolás JM, Trotta F, et al. Cyclodextrins as anti-inflammatory agents: Basis, drugs and perspectives. *Biomolecules*. 2021;11(9). doi:10.3390/biom11091384
51. Houben T, Yadati T, de Kruijf R, Gijbels MJJ, Luiken JJFP, van Zandvoort M, et al. Pro-Inflammatory Implications of 2-Hydroxypropyl- β -cyclodextrin Treatment. *Front Immunol*. 2021;12. doi:10.3389/fimmu.2021.716357
52. Guo Q, Jin Y, Chen X, Ye X, Shen X, Lin M, et al. NF- κ B in biology and targeted therapy: new insights and translational implications. *Signal Transduct Target Ther*. 2024;9(1). doi:10.1038/s41392-024-01757-9
53. Liu T, Zhang L, Joo D, Sun SC. NF- κ B signaling in inflammation. *Signal Transduct Target Ther*. 2017;2. doi:10.1038/sigtrans.2017.23
54. Kalaitzidis D, Gilmore TD. Transcription factor cross-talk: The estrogen receptor and NF- κ B. *Trends in Endocrinology and Metabolism*. 2005;16(2):46-52. doi:10.1016/j.tem.2005.01.004
55. Frasor J, El-Shennawy L, Stender JD, Kastrati I. NF κ B affects estrogen receptor expression and activity in breast cancer through multiple mechanisms. *Mol Cell Endocrinol*. 2015;418:235-239. doi:10.1016/j.mce.2014.09.013
56. Xing D, Oparil S, Yu H, Gong K, Feng W, Black J, et al. Estrogen modulates NF κ B signaling by enhancing I κ B α levels and blocking p65 binding at the promoters of inflammatory genes via estrogen receptor- β . *PLoS One*. 2012;7(6). doi:10.1371/journal.pone.0036890
57. Saraceno GE, Bellini MJ, Garcia-Segura LM, Capani F. Estradiol activates PI3K/Akt/GSK3 pathway under chronic neurodegenerative conditions triggered by perinatal asphyxia. *Front Pharmacol*. 2018;9(APR). doi:10.3389/fphar.2018.00335

58. Song CH, Kim N, Kim DH, Lee HN, Surh YJ. 17- β estradiol exerts anti-inflammatory effects through activation of Nrf2 in mouse embryonic fibroblasts. *PLoS One*. 2019;14(8). doi:10.1371/journal.pone.0221650
59. Sander AM, Connizzo BK. Estrogen and progesterone exhibit distinct yet coordinated roles in the regulation of tendon extracellular matrix remodeling. Published online March 10, 2025. doi:10.1101/2025.03.05.641754
60. Son HJ, Kim N, Song CH, Lee SM, Lee HN, Surh YJ. 17 β -estradiol reduces inflammation and modulates antioxidant enzymes in colonic epithelial cells. *Korean Journal of Internal Medicine*. 2020;35(2):310-319. doi:10.3904/kjim.2018.098
61. Zhou S, Zilberman Y, Wassermann K, Bain SD, Sadovsky Y, Gazit D. Estrogen Modulates Estrogen Receptor α and β Expression, Osteogenic Activity, and Apoptosis in Mesenchymal Stem Cells (MSCs) of Osteoporotic Mice. Vol 36.; 2001.
62. Sheldahl LC, Shapiro RA, Bryant DN, Koerner IP, Dorsa DM. Estrogen induces rapid translocation of estrogen receptor β , but not estrogen receptor α , to the neuronal plasma membrane. *Neuroscience*. 2008;153(3):751-761. doi:10.1016/j.neuroscience.2008.02.035
63. Craft RM. Modulation of pain by estrogens. *Pain*. 2007;132(SUPPL. 1):S3. doi:10.1016/j.pain.2007.09.028
64. Yang X, Yan K, Zhang Q, Yusufu A, Ran J. Meta-Analysis of Estrogen in Osteoarthritis: Clinical Status and Protective Effects. *Altern Ther Health Med*. 2023;29(1):224-230.
65. Zhao H, Yu F, Wu W. The Mechanism by Which Estrogen Level Affects Knee Osteoarthritis Pain in Perimenopause and Non-Pharmacological Measures. *Int J Mol Sci*. 2025;26(6). doi:10.3390/ijms26062391
66. Yoshida A, Morihara T, Matsuda KI, Sakamoto H, Arai Y, Kida Y, et al. Immunohistochemical analysis of the effects of estrogen on intraarticular neurogenic

- inflammation in a rat anterior cruciate ligament transection model of osteoarthritis. *Connect Tissue Res.* 2012;53(3):197-206. doi:10.3109/03008207.2011.628059
67. Lu Y, Jiang Q, Yu L, Lu ZY, Meng SP, Su D, et al. 17 β -estradiol rapidly attenuates P2X3 receptor-mediated peripheral pain signal transduction via ER α and GPR30. *Endocrinology.* 2013;154(7):2421-2433. doi:10.1210/en.2012-2119
 68. Chen Q, Zhang W, Sadana N, Chen X. Estrogen receptors in pain modulation: cellular signaling. *Biol Sex Differ.* 2021;12(1). doi:10.1186/s13293-021-00364-5
 69. Schneider AH, Kanashiro A, Dutra SGV, de Souza R do N, Veras FP, Cunha F de Q, et al. Estradiol replacement therapy regulates innate immune response in ovariectomized arthritic mice. *Int Immunopharmacol.* 2019;72:504-510. doi:10.1016/j.intimp.2019.04.048
 70. Sudoł-Szopińska I, Kwiatkowska B, Prochorec-Sobieszek M, Maśliński W. Enthesopathies and enthesitis. Part 1. Etiopathogenesis. *J Ultrason.* 2015;15(60):72-84. doi:10.15557/JoU.2015.0006
 71. Bertoldo E, Adami G, Rossini M, Giollo A, Orsolini G, Viapiana O, et al. The Emerging Roles of Endocrine Hormones in Different Arthritic Disorders. *Front Endocrinol (Lausanne).* 2021;12. doi:10.3389/fendo.2021.620920
 72. Manolagas SC, O'Brien CA, Almeida M. The role of estrogen and androgen receptors in bone health and disease. *Nat Rev Endocrinol.* 2013;9(12):699-712. doi:10.1038/nrendo.2013.179
 73. Emmanuelle NE, Marie-Cécile V, Florence T, Jean-François A, Françoise L, Coralie F, et al. Critical role of estrogens on bone homeostasis in both male and female: From physiology to medical implications. *Int J Mol Sci.* 2021;22(4):1-18. doi:10.3390/ijms22041568
 74. Ji M, Yu Q. Primary osteoporosis in postmenopausal women. *Chronic Dis Transl Med.* 2015;1(1):9-13. doi:10.1016/j.cdtm.2015.02.006

75. Robertson JFR, Harrison M. Fulvestrant: Pharmacokinetics and pharmacology. *Br J Cancer*. 2004;90:S7-S10. doi:10.1038/sj.bjc.6601630
76. Eckert RL, Mullick A, Rorke EA, Katzenellenbogen BS, Katzenellenbogen S. Estrogen Receptor Synthesis and Turnover in MCF-7 Breast Cancer Cells Measured by a Density Shift Technique*. Vol 114.; 1984.
77. Ellison-Zelski SJ, Solodin NM, Alarid ET. Repression of ESR1 through Actions of Estrogen Receptor Alpha and Sin3A at the Proximal Promoter . *Mol Cell Biol*. 2009;29(18):4949-4958. doi:10.1128/mcb.00383-09
78. Carlson RW. The history and mechanism of action of fulvestrant. *Clin Breast Cancer*. 2005;6(SUPPL. 1):S5. doi:10.3816/CBC.2005.s.008
79. Long X, Nephew KP. Fulvestrant (ICI 182,780)-dependent interacting proteins mediate immobilization and degradation of estrogen receptor- α . *Journal of Biological Chemistry*. 2006;281(14):9607-9615. doi:10.1074/jbc.M510809200
80. Oliveira CA, Nie R, Carnes K, Franca LR, Prins GS, Saunders PT, et al. The Antiestrogen ICI 182,780 Decreases the Expression of Estrogen Receptor-Alpha but Has No Effect on Estrogen Receptor-Beta and Androgen Receptor in Rat Efferent Ductules.; 2003. <http://www.RBEj.com/content/1/1/75>

CHAPTER 4: PILOT STUDY OF NOVEL ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

4.1 Introduction

The anterior cruciate ligament (ACL) is the most commonly injured knee ligament, with an estimated 120,000 ACL tears occurring each year in the United States.^{1,2} A ruptured ACL does not heal on its own and typically requires surgical intervention.³ Surgical repair or reconstruction is necessary to restore knee function, prevent meniscal injury, and minimize development of post-traumatic osteoarthritis (PTOA).³

ACL repair (also called primary repair) involves suturing the torn ligament ends together, whereas reconstruction (secondary reconstruction) entails replacing the damaged ligament with a graft.⁴ The first successful primary ACL repair was performed in 1895 by A. W. Mayo Robson, who attached the distal ACL remnant to the lateral femoral condyle with catgut ligatures.⁵ Since then, the field of orthopedic medicine has sought to improve surgical approaches to ACL injuries.

By the 1920s, ACL reconstruction gained favor over primary repair, which was limited to proximal tears and often yielded unpredictable outcomes.⁴ Ernest William Hey Groves pioneered early ACL reconstruction by detaching the iliotibial band from its tibial insertion, reflecting it proximally, and passing it through bone tunnels in the femur and tibia to replicate the path of the native ACL.⁶ Groves believed that maintaining the tendon's connection to its proximal muscle belly would enhance graft survival by providing a blood supply.⁴ However, his approach required extensive joint exposure and was technically demanding, limiting its widespread adoption.⁴ Although other reconstruction techniques followed, none gained substantial traction, and conservative, non-surgical management remained the most popular treatment for ACL injuries until the rise of arthroscopic surgery in the 1980s.^{3,4}

Today, the gold standard for ACL reconstruction is arthroscopic placement of a bone-patellar tendon-bone autograft due to its appropriate size, minimal laxity, high durability, and reproducibility in patient outcomes.^{7,8} While this method restores mechanical knee function, it remains associated with several complications, including a high incidence of PTOA, reinjury, and contralateral ACL rupture.^{9–11} These limitations emphasize the ongoing need for improved surgical techniques.

Over a century after Groves introduced his ACL reconstruction technique, we revisited his hypothesis that maintaining vascular supply to the graft could enhance healing. Modern research suggests that one reason the ACL fails to heal spontaneously is that the intra-articular environment may impede clot formation between the torn remnants. In normal wound healing, a fibrin-platelet clot serves as the initial scaffold for collagen deposition between wound edges, in this case the ACL remnants.^{12,13} However, synovial fluid within the joint contains the fibrinolytic enzyme plasmin.¹⁴ In response to inflammation following ACL injury, the concentrations of plasmin in synovial fluid increase, likely as a result of increased urokinase plasminogen activator.^{15,16} Plasmin degrades fibrin clots, preventing the formation of a fibrin-platelet clot between the ACL remnants, thereby inhibiting the wound healing process.¹⁷

This hypothesis is supported by our previous findings and work from others. Using a mouse model of mechanical ACL rupture, we observed upregulation of proteomic pathways related to coagulation at 3 and 7 days post-injury compared to naïve controls.¹⁸ Specifically, the injury state was associated with increased expression of key proteins involved in the fibrin-platelet clot formation, including FGA (fibrinogen alpha chain), FGB (fibrinogen beta chain), PLG (plasminogen), F2 (thrombin), and SERPINF2 (plasmin inhibitor).¹⁸ Additional support for this concept comes from studies of the medial and lateral collateral ligaments, which are extra-synovial and capable of spontaneous healing, likely due to their ability to form and maintain a fibrin-platelet clot.^{19,20}

The idea that lack of blood flow within the joint space and the presence of plasmin prevent a fibrin-platelet clot from forming between ACL remnants was most notably articulated by Martha Murray in 2009.¹⁷ Building on this theory, she developed the Bridge-Enhanced ACL Restoration (BEAR) technique, which uses a blood-seeded scaffold to facilitate healing of the torn ACL.²¹ Clinical trials have shown that the BEAR technique is not inferior to reconstruction with a hamstring tendon graft in short- and mid-term outcomes.²² However, 15% of patients experienced retears within two years, typically resulting from pivoting or jumping injuries.²² Histologic evaluation of these re-tear patients revealed that the BEAR-repaired tissue resembled native ACL, indicating that providing blood to the area may have facilitated the formation of healed ACL tissue.²³ Despite these promising outcomes, BEAR has limitations. It requires a midsubstance tear and good quality remnant tissue, restricting its use to a small subset of patients.^{21,22} Furthermore, the relatively high re-tear rate and unknowns regarding PTOA development remain a concern.

Inspired by the work of Robson, Groves, Murray, and many others, we sought to develop a new approach to ACL reconstruction that enhances vascularity to support healing between ACL remnants. The objective of this study was to evaluate a novel reconstruction strategy in a preclinical ovine model aimed at improving graft healing and reducing PTOA development. We selected two anatomical structures as potential graft candidates for this pilot study: the lateral digital extensor tendon (LaDET) and the infrapatellar fat pad (IFP).

The LaDET originates from the lateral digital extensor muscle on the lateral tibial condyle, fibula, and lateral collateral ligament of the ovine stifle. It inserts on the dorsolateral aspect of the distal phalanx of digit IV and functions to extend the digits and the tarsus.^{24,25} We selected the LaDET because it has a diameter comparable to the ovine ACL, shares the mechanical properties of tendon and ligament, its function can be compensated by the long digital extensor tendon, and it can be used as a graft while preserving its muscle-tendon origin and muscle belly to provide vascular support.^{24,26}

The IFP, located within the anterior compartment of the stifle, is intra-capsular but extra-synovial, with its posterior surface lined by synovium.²⁷ We chose the IFP for its rich vascularity and because it is frequently partially resected during ACL reconstruction to improve surgical visualization, indicating that it is both accessible and, to some extent, expendable.^{28,29} Furthermore, IFP resection is not associated with donor site morbidity and does not significantly impair joint mechanics.^{29,30}

As this was a pilot study, our primary goal was to determine whether either reconstruction method (LaDET or IFP) warranted further investigation. We hypothesized that the LaDET graft, which is more structurally comparable to the native ACL, would demonstrate superior healing compared to the IFP graft, based on assessments of limb function, joint integrity, and graft viability.

4.2 Materials and Methods

4.2.1 Animals and Experimental Design

All procedures were approved by the Colorado State University Institutional Animal Care and Use Committee (Protocol #4642) and conducted in an AAALAC-accredited facility. Two healthy, skeletally mature, conventionally-raised Rambouillet-cross ewes, aged at least 4 years old, were enrolled in this pilot study, selected based on incisor presentation. Due to the exploratory nature of the study, a power analysis was not performed. Animals received either a LaDET or IFP graft. All surgical procedures were performed by a board-certified veterinary surgeon. Outcome measures occurred at matched intervals relative to surgery but conducted separately, as the procedures were performed approximately 8 months apart, with the LaDET graft procedure occurring first.

Throughout the 6-month study, outcome measures included mobility assessments, arthroscopic joint evaluation, MRI, and histology, among others (Figure 4.1). Animals received a standard diet of alfalfa and grass hay supplemented with grain as needed. Commercial, human-

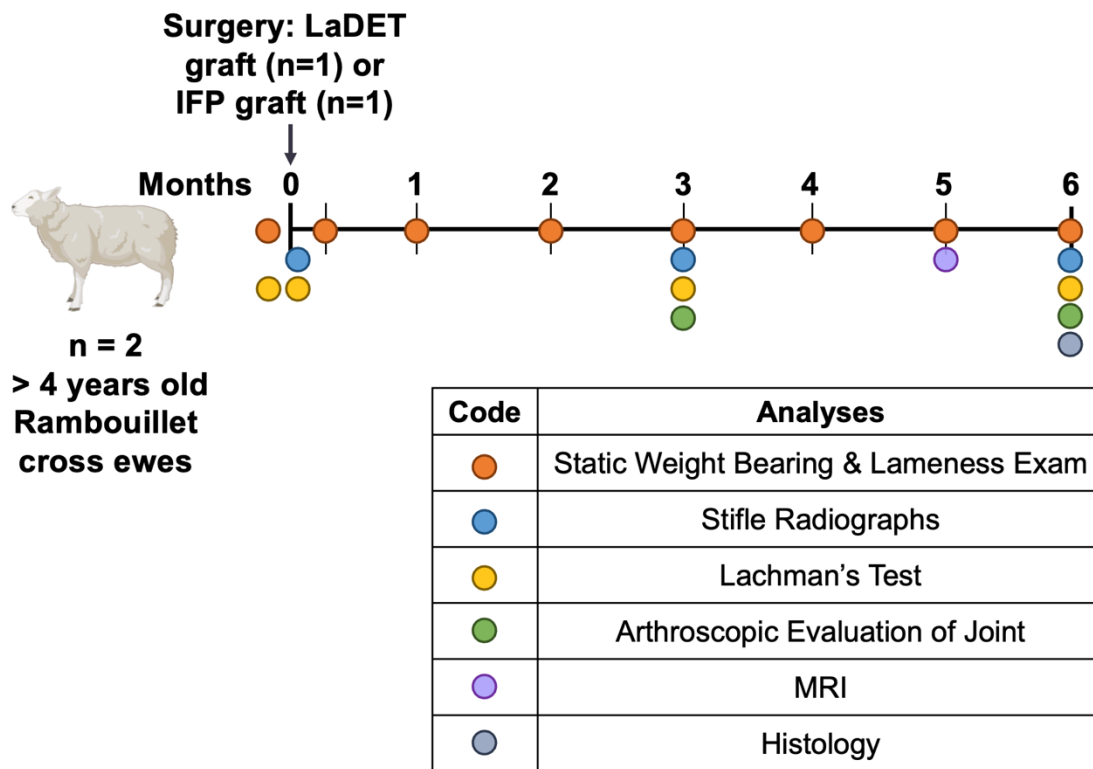


Figure 4.1. Overview of experimental design. Each animal received either a LaDET or IFP graft. A variety of outcome measures were assessed throughout the 6-month study period.

grade animal crackers were used as positive reinforcement during static weight-bearing trials and comprised less than 5% of daily caloric intake. Feed was withheld for 24 hours prior to surgery, arthroscopy, and MRI to prevent anesthesia-related bloat.

Following surgical ACL reconstruction, animals were cohoused in a standard indoor box pen for 4 months, followed by 1 month in an indoor/outdoor pen, and finally turned out to pasture for the last month of the study. Animal care staff monitored general health, neurologic status, lameness, and incision healing daily.

4.2.2 Anesthesia and Perioperative Care

For all surgical procedures, animals were anesthetized with intravenous Midazolam (0.1mg/kg) and Ketamine (4mg/kg). Animals were maintained under anesthesia with Isoflurane (1-3% in 100% oxygen). Analgesia was provided using transdermal Fentanyl patches (15mg, applied one day prior to surgery and maintained for 6 days), oral Phenylbutazone (1g, daily for 6 days, starting one day prior to surgery), subcutaneous Morphine (0.5mg/kg, during surgery), and a continuous rate infusion of Ketamine (10 µg/kg/min) and Lidocaine (25 mcg/kg/min). Antimicrobial prophylaxis included subcutaneous Penicillin G (3 million units daily for 6 days, beginning one day prior to surgery) and intravenous Cefazolin (1g) administered intraoperatively.

4.2.3 LaDET Graft Surgical Procedure

The sheep receiving the LaDET graft was positioned in lateral recumbency on the surgical table and the right hindlimb shaved and aseptically prepared. A longitudinal incision was made on the dorsolateral aspect of the distal third of the tibia, approximately 6cm proximal to the tarsus. The LaDET was identified, isolated, and transected (Figure 4.2A). A tendon stripper was used to free the LaDET from its fascial attachments proximal to the site of the

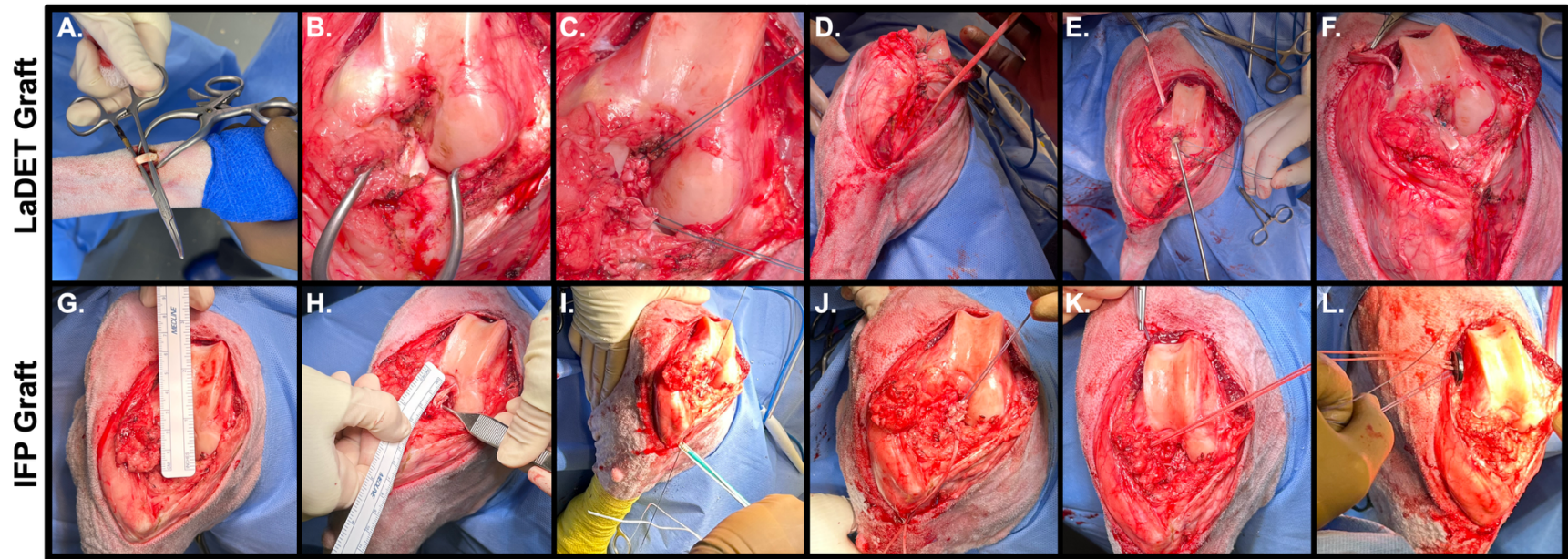


Figure 4.2. Surgical procedure for ACL reconstruction using either the (A – F) LaDET or (G – L) IFP graft.

transaction, up to the stifle. A second longitudinal incision was made on the lateral aspect of the tibia, approximately 10cm distal to the cranial ridge. The LaDET was reflected subcutaneously from the initial distal incision and pulled out of the second incision. It was then passed subcutaneously over the tibial tuberosity to rest on the medial side of the stifle. The graft remained in this position under the skin until reconstruction.

The animal was then repositioned in dorsal recumbency. A medial parapatellar arthrotomy was performed to expose the ACL (Figure 4.2B). A 5mm tibial bone tunnel was drilled originating slightly cranial to the native tibial footprint of the ACL. Next, a 5mm femoral bone tunnel was created just cranial to the ACL origin. The native ACL was transected in the mid-substance using a #11 scalpel blade and suture holds placed in the distal and proximal ACL remnants (Figure 4.2C). A passing pin was used to guide the LaDET graft through the tibial and femoral bone tunnels (Figure 4.2D). The graft was tensioned with the stifle in extension and secured in the femoral tunnel using a 7x23mm PEEK interference screw (Arthrex AR-1370P) (Figure 2E). The ACL remnants were then anchored to the LaDET graft using 2-0 PDO Quill barbed suture (Figure 4.2F). The ACL remnants were not sutured to each other. The excess graft emerging from the femoral tunnel was trimmed. The joint capsule and surround muscle were closed with 2-0 absorbable suture, and the skin incisions were closed with 2-0 nylon suture.

4.2.4 IFP Graft Surgical Procedure

For the IFP graft procedure, the sheep was positioned in dorsal recumbency. The right hindlimb was shaved and aseptically prepared. A parapatellar arthrotomy was performed to expose the joint. The IFP was released from its distal and medial attachments (Figure 4.2G). The native ACL was transected at its femoral origin, leaving a distal remnant attached to the tibia (Figure 4.2H). A 2.4mm tibial bone tunnel was drilled slightly cranial to the ACL tibial footprint, followed by a 2.4mm femoral bone tunnel cranial to the femoral ACL origin. A pilot hole

was created slightly medial and distal to the tibial tuberosity for the suture anchor placement. FiberWire (Arthrex AR-7200) and LabralTape (Arthrex AR-7276) were secured to the tibia using a 4.75mm DX Knotless SwiveLock anchor (Arthrex AR-8980BC) (Figure 4.2I). The FiberWire and LabralTape were passed through the tibial tunnel and then through the distal ACL remnant. A portion of the IFP, still attached to the main body, was dissected and used as the graft tissue. A Scorpion Suture Passer was used to attach the FiberWire to both bundles of the distal ACL remnant (Figure 4.2J). The Suture Passer was also used to secure the LabralTape to the IFP graft (Figure 2K). The FiberWire and LabralTape were passed through the femoral tunnel and secured to the lateral femoral condyle using a button fixation (Figure 4.2L). The joint capsule and surrounding muscle were closed with 1-0 absorbable suture. The skin incision was closed with 2-0 absorbable suture.

4.2.5 Static Weight Bearing

Weight distribution across limbs was evaluated at multiple timepoints using a custom-built device.³¹ Baseline measurements were collected approximately 1 week pre-surgery. The device was calibrated using a range of six standard weights (0-100lbs) prior to each testing session. Animals were guided to stand on the platform, with each limb on a separate loading platform. Data was recorded by an Arduino circuit board at 1Hz for a 60-second testing period. Testing was repeated if the animal moved. Average limb load was calculated and normalized to total bodyweight, which was measured immediately following the weight bearing test. Individual animal bodyweights at each timepoint can be found in Appendix III.1. Static weight bearing control data were obtained from a previous study involving ACL transection without reconstruction (unpublished).

4.2.6 Lameness Assessments

Animals were evaluated for lameness at a walk and trot (only walk at 1-week post-surgery) by herding them down the barn aisle. Animals were observed from behind and from the side. A single observer (EMV) scored lameness of the operated limb on a 0-4 scale with half-points permitted. Scoring criteria are detailed in Appendix III.2.

4.2.7 Lachman's Test

Joint laxity was assessed via Lachman's test at five time points: pre-operatively, post-ACL transection, post-ACL reconstruction, and at 3- and 6-months post-operatively. All assessments were conducted under anesthesia by a board-certified veterinary surgeon. Scoring details for Lachman's Test are provided in Appendix III.3.

4.2.8 Arthroscopic Evaluation of the Joint

At 3- and 6-months post-ACL reconstruction (with the 6-month evaluation performed post-euthanasia), arthroscopy was used to assess graft status. After aseptic preparation of the right stifle, a 0.5cm incision was made adjacent to the patellar tendon, and the arthroscope inserted. A second portal was created using a 20-gauge needle followed by a #11 scalpel blade. Conservative dissection of the synovium was performed to allow for graft visualization using an Arthrex Dissector (AR-8400DS). Images and video recordings were obtained of the joint space and graft. The joint capsule was closed with 2-0 absorbable suture and skin incisions were closed with 2-0 nylon suture.

4.2.9 Radiographic Imaging

Radiographs of the stifle (lateromedial and caudocranial views) were taken under anesthesia immediately following surgery and at timepoints of 3- and 6-months. 6-month radiographs were taken following euthanasia.

4.2.10 Magnetic Resonance Imaging (MRI)

5-months post-ACL reconstruction, MRI was performed to evaluate graft viability and joint structure. With animals in dorsal recumbency, right stifles were imaged in sagittal, coronal, and transverse planes. Sequences included proton density fat saturation (PDFS), T1-weighted (T1W), and T2-weighted (T2W). A full imaging protocol is included in Appendix III.4.

4.2.11 Macroscopic Joint Scoring

Post-euthanasia, the right and left stifles were dissected to expose the ACL grafts or native ACLs and surrounding joint structures. A board-certified veterinary surgeon assessed articular cartilage, osteophytes, and synovium using the OARSI macroscopic scoring system for sheep and goats.³²

4.2.12 Histology

Following macroscopic joint scoring, an oscillating necropsy saw was used to excise a tissue block from the right and left stifles that included the lateral femoral condyle, the ACL graft or native ACL, and the medial tibial condyle. Additional tissues samples, including cartilage, meniscus, IFP, bone, were also collected for future analysis. All samples were fixed in 10% neutral buffered formalin for approximately 7 days.

Samples containing bone were decalcified using a combination of 10% EDTA in PBS and 20% formic acid in PBS. Decalcification of LaDET graft samples was performed in 10% EDTA for approximately 8 months, with the EDTA solution refreshed weekly. These samples were then transferred to 20% formic acid for an additional 3 weeks. Bone samples from the IFP graft animal were decalcified in 10% EDTA for 5 weeks, followed by treatment with 20% formic acid for 6 weeks. Continuous agitation was maintained throughout the decalcification process to enhance efficiency.

Complete decalcification was confirmed radiographically using an XPERT 80-L Cabinet X-Ray System (Kubtec, Stratford, CT). Following decalcification, samples were processed, embedded in paraffin, and sectioned sagittally at 6 μm through the entire tissue block. Slides were stained with hematoxylin and eosin in a single batch to ensure consistency. Histological evaluation was conducted by a board-certified veterinary pathologist, focusing on graft viability and overall cellular composition.

4.2.13 Statistics

As this was a pilot study with a sample size of $n=1$ per group, statistical comparisons were not performed. All findings presented are descriptive observations based on individual animals. Future studies will increase sample size to allow for statistical analysis.

4.3 Results

4.3.1 Functional Limb Assessments

Weight distribution on each limb was measured using the static weight bearing system (Figure 4.3A). Prior to surgery, the LaDET graft animal exhibited ideal right hindlimb weight distribution of approximately 20% bodyweight (Figure 4.3B).³³ One week postoperatively, the animal offloaded the right hindlimb (17% bodyweight) with compensatory loading on the left hindlimb (25% bodyweight). By 2 months following surgery, the right hindlimb returned to ideal loading, and by 3 months, exceeded baseline loading values (23% bodyweight). Arthroscopy after the 3-month timepoint temporarily caused an offloading of the right hindlimb at 4 months (17% bodyweight). However, by 5-6 months following surgery, all limbs achieved an ideal weight distribution.

The IFP graft animal began with ideal weight distribution with 30% bodyweight on each forelimb and 20% on each hindlimb (Figure 4.3C). One week post-surgery, the animal was

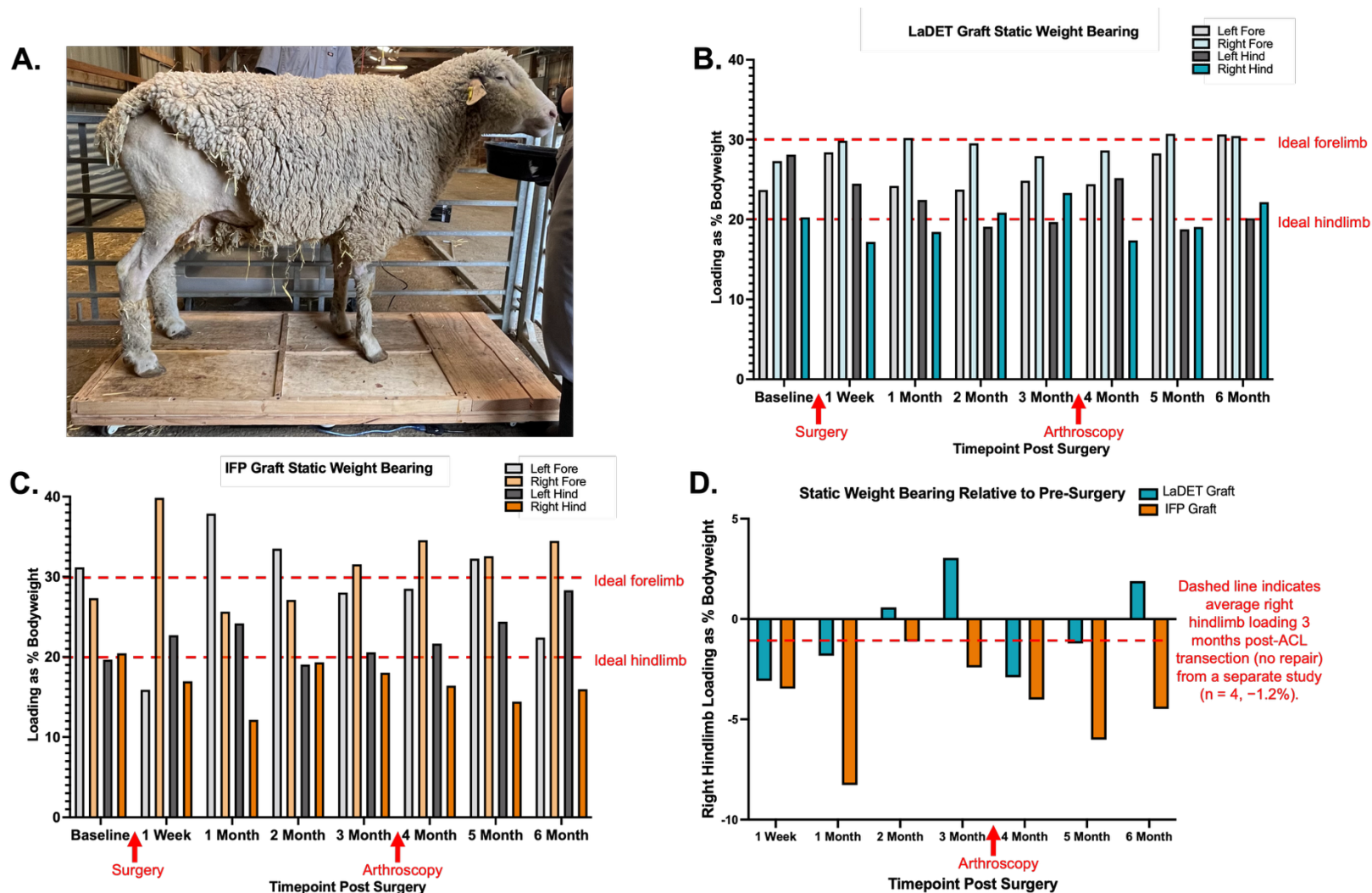


Figure 4.3. Longitudinal static weight bearing. **(A)** Animals were led onto a custom weight bearing device and minimally restrained. Limb loading as a percentage of total body weight is shown for the **(B)** LaDET graft animal and the **(C)** IFP graft animal. Red dashed lines indicate ideal forelimb (30% bodyweight) and hindlimb (20% bodyweight) loading. Red arrows indicate relative surgery and arthroscopy timepoints. **(D)** Loading of the right (surgical) hindlimb as a percent of bodyweight relative to each animal's pre-surgery values. The red dashed line indicates average loading of animals that underwent ACL transection only in a separate study.

offloading the right hindlimb (17% bodyweight) and left forelimb (16% bodyweight), shifting weight to the right forelimb (40% bodyweight) and left hindlimb (23% bodyweight). At 1 month, right hindlimb loading was further reduced (12% bodyweight). By 2-3 months, weight distribution on the right hindlimb trended toward baseline (19% bodyweight), although this limb never fully recovered to 20% bodyweight. Post-arthroscopy, loading on the right hindlimb declined further and did not recover by the study endpoint (16% bodyweight).

Normalized to pre-surgery baseline values, both animals showed initial right hindlimb offloading postoperatively, followed by a gradual return toward baseline (Figure 4.3D). After arthroscopy at 3 months, the LaDET animal recovered and exceeded baseline loading, while the IFP animal continued to offload the right hindlimb. At 3 months post-surgery, the LaDET animal outperformed ACL transection only controls from a separate study, whereas the IFP animal performed worse (LaDET: 3.0%, IFP: -2.4%, ACL-transection: -1.2%).

Pre-operatively, neither animal demonstrated lameness on the right hindlimb (Table 4.1). At 1-week post-surgery, both animals displayed slight to moderate lameness on the operated limb. By 3 months (LaDET) and 2 months (IFP), normal ambulation resumed. Arthroscopy did not result in an observable lameness.

Joint laxity was assessed with Lachman's testing (Table 4.2). Both animals had a negative, normal test at baseline, indicating an intact ACL. Post-ACL transection, scores increased (LaDET:2, IFP: 1), but returned to normal after reconstruction. At 3 months, the IFP animal had a score of 0.5. By 6 months, both animals again had normal tests.

4.3.2 Graft and Joint Integrity Evaluation

Arthroscopy at 3 months in the LaDET graft animal revealed an intact, tensioned graft indistinguishable from the ACL remnants (Figure 4.4A). Macroscopically, the graft structure was encased in vascularized soft tissue. At 6 months, the graft remained intact and under tension

Table 4.1. Lameness Scoring

Timepoint	LaDET Graft Right Hind	IFP Graft Right Hind
Baseline	0	0
1 Week	1.5	2
1 Month	1	1
2 Month	0.5	0
3 Month	0	0
4 Month	0	0
5 Month	0	0
6 Month	0	0

Table 4.2. Lachman's Test

Timepoint	LaDET Graft Right Hind	IFP Graft Right Hind
Baseline	0	0
Post-ACL Transection	2	1
Post-ACL Reconstruction	0	0
3 Month	0	0.5
6 Month	0	0

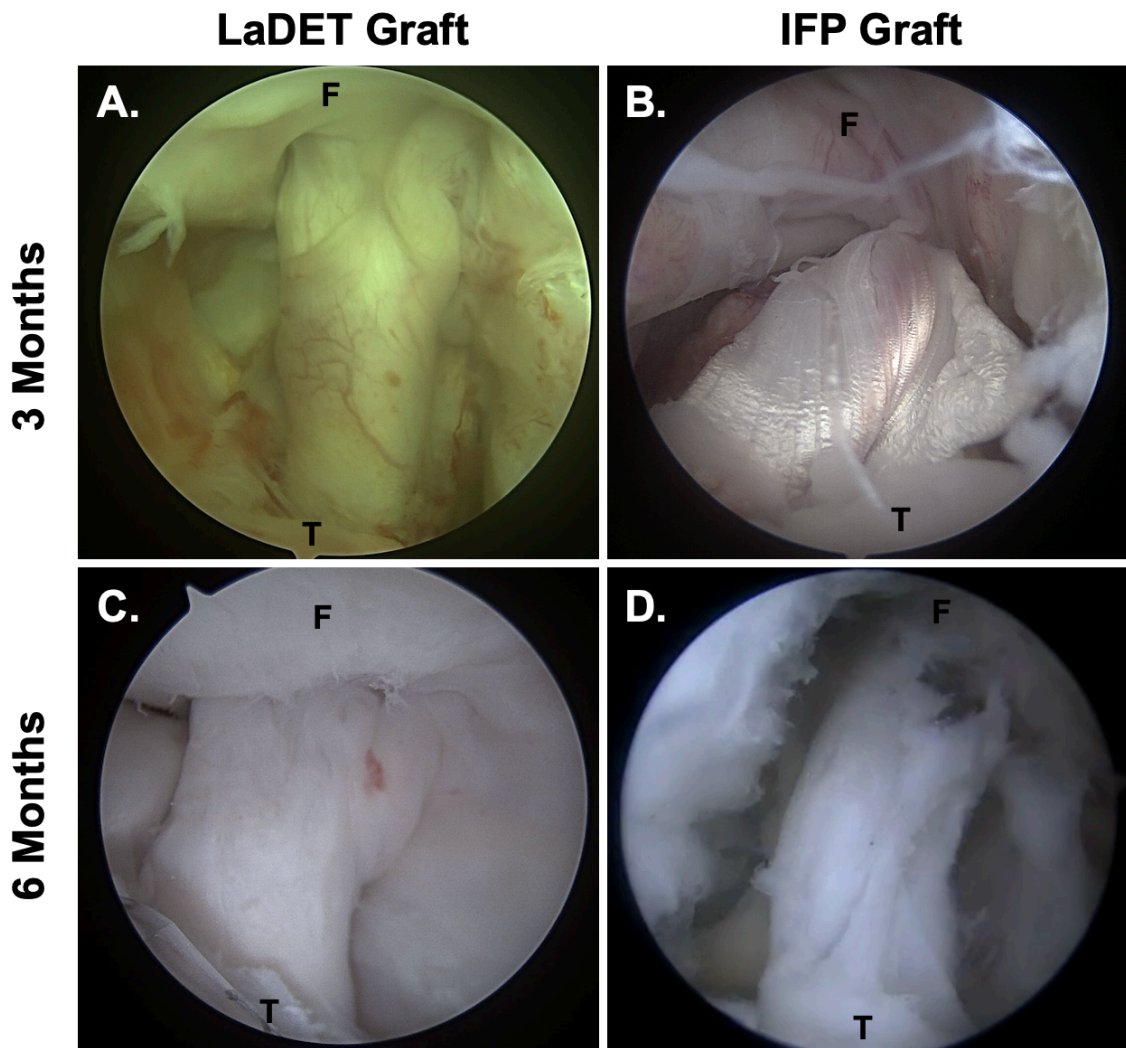


Figure 4.4. Arthroscopic evaluation in the right (surgical) stifles of the (A and C) LaDET and (B and D) IFP graft structures at three and six months following ACL reconstruction. F = Femoral side, T = Tibial side.

(Figure 4.4C). Mild synovial tissue expansion was noted in the joint space at the 6-month timepoint.

In the IFP graft animal, arthroscopy at 3 months showed a partially organized graft, consisting largely of fibrillated ACL remnant and loosely adhered tissue (Figure 4.4B). The FiberWire and LabralTape were identifiable and extended through the femoral tunnel. The FiberWire held slight tension, while the LabralTape was loose. The IFP graft itself was not clearly identifiable. Extensive synovial hyperplasia was present in the joint space. By 6 months, the remnant had further deteriorated and appeared retracted from the femoral tunnel, with increased synovial overgrowth (Figure 4.4D).

Radiographs taken at all timepoints showed no evidence of fractures or other notable abnormalities in either animal (Figures 4.5A, 4.5B). Additionally, no signs of bone tunnel widening or significant bone remodeling were observed.

MRI performed at 5 months post-surgery revealed distinguishable graft and/or ACL remnant material occupying the intercondylar notch in the LaDET graft animal on dorsal PDFS sequence (Figure 4.6A). The bone tunnel and PEEK interference screw in the lateral femoral condyle are also clearly visible. In contrast, the IFP graft animal showed disorganized soft tissue occupying the intercondylar notch, with poorly defined structure and unclear tissue composition (Figure 4.6B). The femoral bone tunnel and button on the lateral femoral condyle are also visible in the dorsal view. Sagittal T2-W images demonstrated visible tibial bone tunnels in both animals (Figures 4.6C, 4.6D).

Macroscopic evaluation of the stifles post-euthanasia confirmed graft continuity between the tibial and femoral tunnels in both animals. The LaDET graft appeared as a dense, fibrous band with similar properties and tension to the native ACL in the contralateral limb (Figure 4.7A). The ACL remnant and graft were indistinguishable by palpation. The IFP graft resembled suture material loosely surrounded by connective tissue and lacked significant tension (Figure

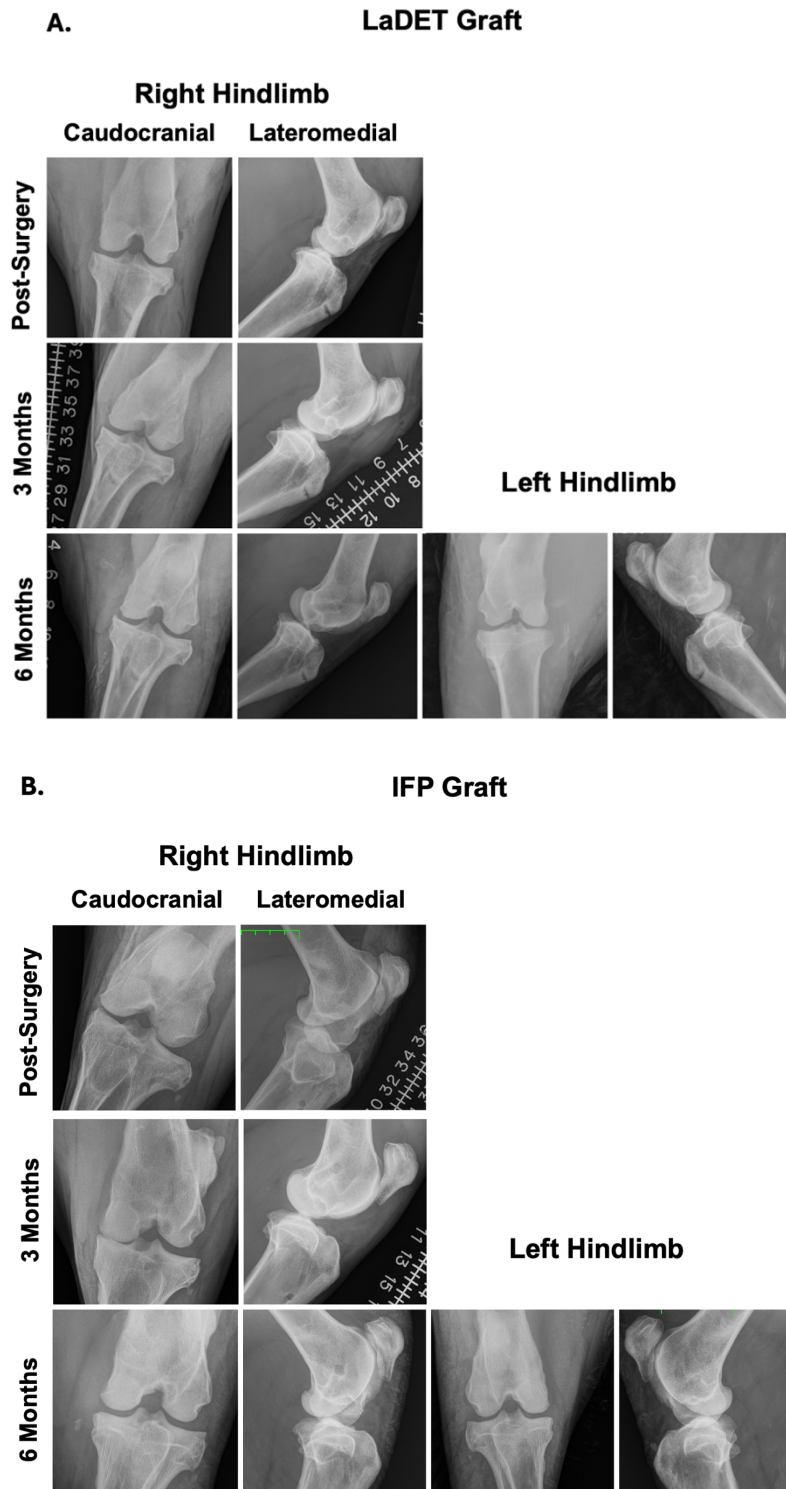


Figure 4.5. Radiographic imaging of right (surgical) stifles from the **(A)** LaDET graft and **(B)** IFP graft animals immediately following surgery and at timepoints of three and six months post-operatively. Contralateral left stifles were imaged at the six month timepoint to serve as controls. Stifles were imaged in both the caudocranial and lateromedial views.

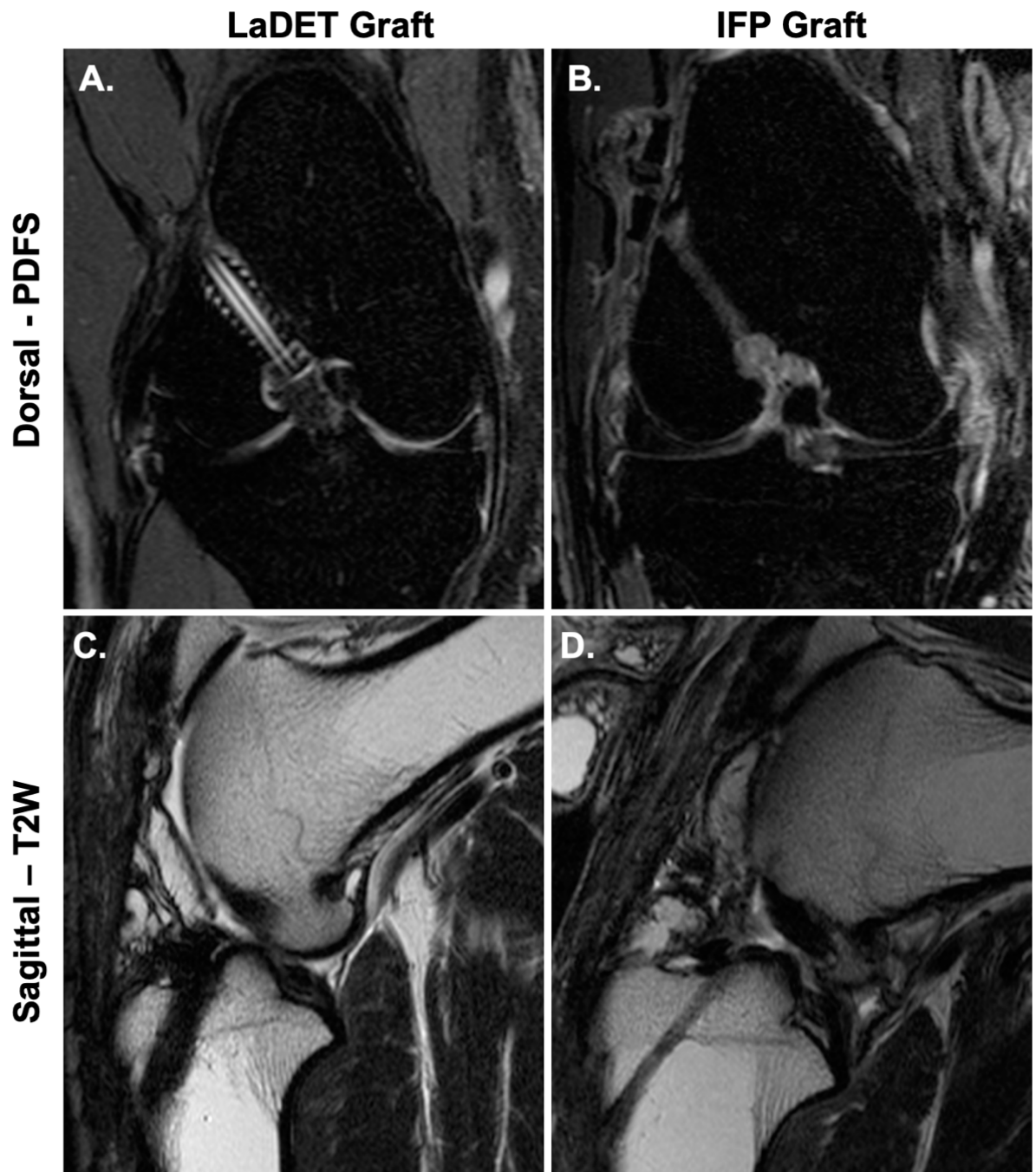


Figure 4.6. MRI of the right (surgical) stifle five months after ACL reconstruction. Dorsal plane images were acquired with a PDFS sequence are shown for the (A) LaDET and (B) IFP grafts. Sagittal plane images acquired using a T2W sequence are shown for the (C) LaDET and (D) IFP grafts.

A. LaDET Graft
Right Hind Left Hind



B. IFP Graft
Right Hind Left Hind



Figure 4.7. Macroscopic images of the right (surgical) and left (contralateral) stifles from the (A) LaDET graft animal and the (B) IFP graft animal. Surrounding tissues were removed to allow clear visualization of the ACL graft or native ACL.

4.7B). Palpation identified what was believed to be ACL remnant tissue, which did not extend into the femoral tunnel, although other soft tissue material was present within the tunnel.

Semi-quantitative macroscopic joint scoring showed greater PTOA in operated limbs compared to contralateral limbs for both animals (Table 4.3). The LaDET graft animal had PTOA characterized by cartilage changes ranging from surface roughening to small cartilage erosions, mild osteophyte development, and slight changes to the synovium (total score: 10/33).

The IFP limb had more severe PTOA with larger osteophytes and greater synovium changes (total score: 20/33). Osteophyte formation primarily accounted for the difference. The IFP graft animal also had a higher contralateral limb score than the LaDET animal (8/33, 1/33, respectively).

4.3.3 Histologic Graft Characterization

Histology in the LaDET graft animal revealed a continuous graft extending from tibia to femoral tunnel (Figure 4.8A). The graft exhibited low cellularity, minimal inflammation or vascularity, and tendon-like architecture (Figure 4.8B). These features were similar to the native ACL of the contralateral limb (Figures 4.8I, 4.8J). A seamless integration was observed of the graft with the distal ACL remnant (Figure 4.8C), and the proximal ACL remnant was indistinguishable from the graft. The graft in the tibial tunnel showed dense collagen, minimal vessels, no reactivity, and standard tendon architecture (Figure 4.8D). The graft demonstrated good integration within the femoral tunnel, with evidence of fibrous ossification of the LaDET graft in this region (Figure 4.8E). Broadly, the surrounding tissues appeared non-reactive and healthy. Images were selected from serial sections to represent distinct regions.

In the IFP graft animal, the graft extended from the tibia to femur, but the ACL remnant and graft were histologically distinct, and the ACL remnant did not continue into the femoral tunnel (Figure 4.8F). The ACL remnant exhibited substantial inflammation and reactive

Table 4.3. Macroscopic Joint Scoring

Category	Site	LaDET Graft Right Hind	LaDET Graft Left Hind	IFP Graft Right Hind	IFP Graft Left Hind
Gross Articular Cartilage	MFC	2	1	3	1
	LFC	1	0	1	1
	MTC	1	0	3	2
	LTC	3	0	1	1
Osteophytes	MFC	1	0	1	0
	LFC	0	0	3	0
	MTC	0	0	3	1
	LTC	1	0	3	1
Synovium	General	1	0	2	1
Total		10	1	20	8

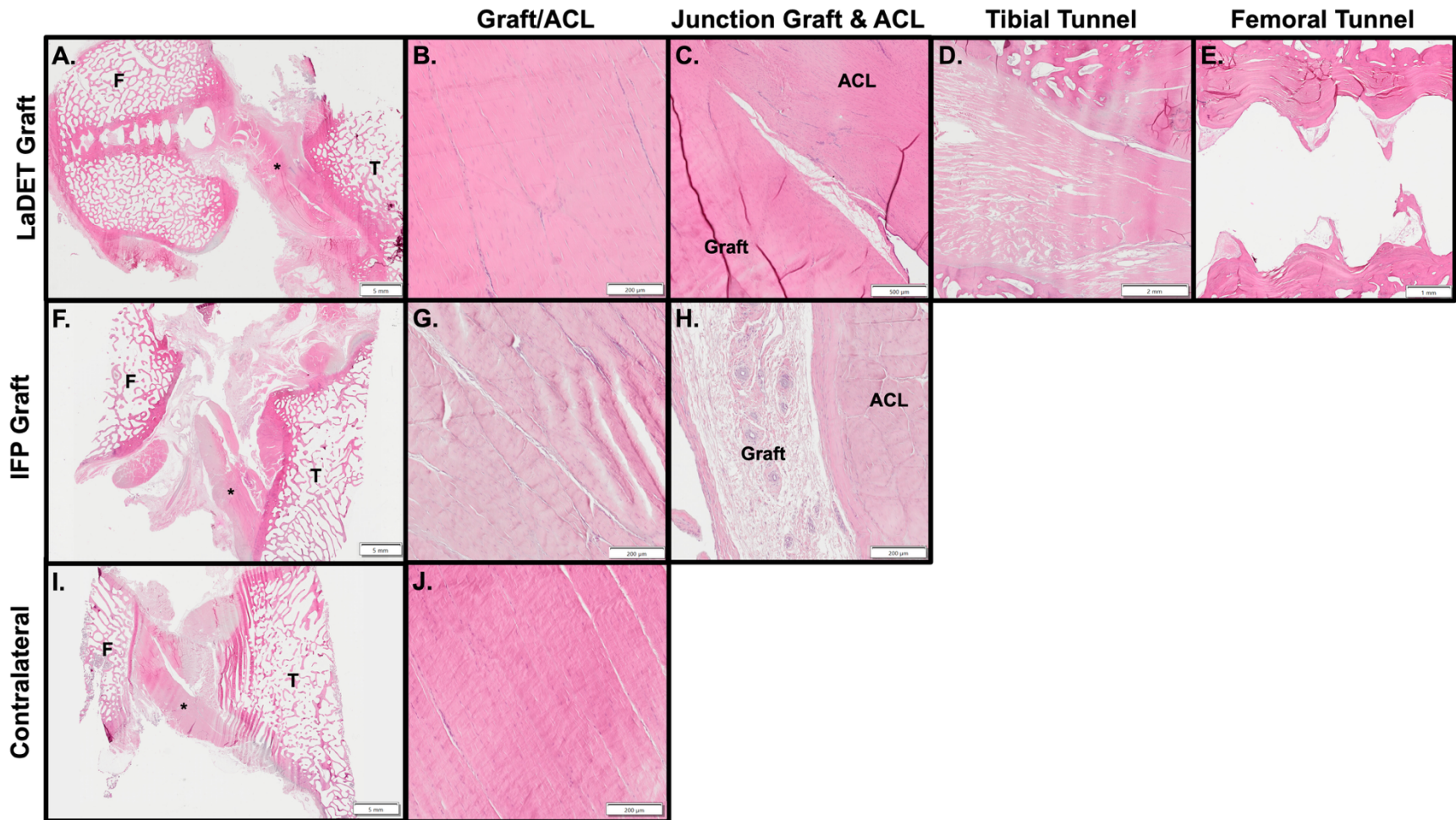


Figure 4.8. Histologic sections stained with hematoxylin and eosin for the (A – E) LaDET graft, (F – H) IFP graft, and (I – J) representative contralateral ACL. F = Femur, T = Tibia, * = ACL graft or native ACL

fibroplasia (Figure 4.8G). Compared to native ACL tissue, the remnant in the IFP graft animal was considered non-viable (Figure 4.8J). The IFP graft demonstrated poor integration with the ACL remnant and was only loosely associated with it (Figure 4.8H). Graft tissue showed synoviocyte hypertrophy and hyperplasia, neovascularization with degeneration, and moderate inflammation (Figure 4.8H). Adjacent tissues had reactive synovium, degenerating vasculature, and marked inflammatory cell infiltration.

4.4 Discussion

In this pilot study, we evaluated two novel techniques for ACL reconstruction to identify which, if any, warranted further investigation. The primary objective was to assess the feasibility of preserving vascular supply in an ACL graft and to explore its potential impact on reconstruction quality. To achieve this, we developed two surgical approaches in an ovine model, utilizing either the LaDET or the IFP as graft material. In both techniques, the grafts' native blood supply remained intact.

Histological evaluation of the LaDET graft demonstrated robust tissue spanning the femur and tibia, with a joint environment that appeared quiescent and non-reactive. Although we could not definitively determine if the native ACL remnants formed a continuous bridge, histologically, the mid-substance of the graft-remnant complex appeared to be a homogenous structure with no clear distinction between tendon and ligament. We were able to trace the distal ACL remnant from its tibial insertion into the graft, indicating at least partial integration. Compared to the contralateral limb, we did not observe substantial neovascularization or evidence of increased blood flow at the study endpoint. However, the relevant histologic sections did not include the vascular tunic observed arthroscopically, and any neovascularization that may have occurred earlier in the healing process could have resolved by this timepoint. This absence of abnormal or excessive vascularity could be a positive indicator, as persistent vascularization in tendons and ligaments is often associated with

persistent inflammation and impaired remodeling. To better characterize the vascular response, future studies will include earlier timepoints to capture transient increases in vascularization, along with cross-sectional histologic analyses to visualize peripheral vascularization and assess whether graft tissue can be differentiated from ACL remnants. Additionally, we are exploring the use of immunohistochemistry with markers such as elastin (greater expression in ligaments) and tenomodulin (greater expression in tendons) to determine tendon from ligament and CD31 to show neovascularization.^{34–38} Emerging techniques such as spatial proteomics may further help differentiate tissue type.

Functional assessments of the LaDET graft animal suggest that the graft contributed to provide mechanical support to the limb. In static weight-bearing tests, the animal not only returned to its baseline limb loading levels postoperatively, but also exceeded the limb loading observed in animals that had undergone ACL transection in a separate study. One confounding factor is that the LaDET graft animal displayed abnormal baseline loading, likely due to insufficient acclimation to the static weight-bearing system. In the original setup of this system, the handler stood at the right front side of the animal, which may have caused the animal to lean away from the handler and increase loading on the left hindlimb. The right hindlimb appeared to be minimally affected, as it demonstrated the ideal baseline loading at approximately 20% of body weight. For subsequent studies, including the IFP animal, the setup was modified so that the handler stood directly in front of the animal, and more time was spent on acclimation, likely contributing to more accurate baseline measurements. To further evaluate the mechanical contribution of the LaDET, future studies will include biomechanical testing of limbs reconstructed using our technique, with comparisons made to contralateral limbs to quantify the structural strength of the graft relative to native ACL. Taken together, the functional and histologic findings support continued evaluation of the LaDET graft as a promising technique for ACL reconstruction.

The IFP graft animal demonstrated histological evidence of inflammation and reactive synovium. Given that the posterior surface of the IFP is lined with synovial tissue, its incorporation into the graft may have disrupted synovial integrity and introduced inflamed synovium directly into the joint space, thereby perpetuating a pro-inflammatory environment. Both the synovium and IFP are recognized contributors to joint inflammation and have been implicated in the pathogenesis of OA. Based on MRI, arthroscopy, gross inspection, and histology, we believe that tissue bridged the femur and tibia in this animal. However, we did not observe continuity between the distal ACL remnant and its proximal counterpart, as the distal remnant was not associated with the femoral tunnel at study endpoint. This failure to bridge may explain the persistent offloading of the surgical limb and likely reflects insufficient mechanical contribution of the graft. The graft, composed primarily of adipose tissue, likely lacked the tensile strength necessary to withstand physiological loading and stabilize the joint. This structural insufficiency could have compromised functional recovery and contributed to altered joint mechanics. Interestingly, clinical evaluations such as lameness scoring and Lachman's testing did not show pronounced differences between the IFP and LaDET animals. However, lameness assessments in sheep are notoriously unreliable due to their tendency as prey animals to mask signs of pain.³⁹ Additionally, the long digital extensor tendon, originating on the craniolateral femoral condyle, has been shown to provide joint stability and may obscure deficits during Lachman's testing.^{40,41}

An important factor to consider is that sheep are weight bearing on their operated limb within a few hours after ACL reconstruction surgery, without the use of braces or external immobilization. This contrasts sharply with human ACL reconstruction protocols, which often involve non-weight bearing and bracing for at least several weeks following surgery.⁴² It is possible that the IFP graft in our procedure was too fragile to withstand immediate postoperative loading.

Another consideration with this procedure is that the observed synovitis and joint inflammation likely contributed to the higher osteoarthritis (OA) scores seen in this animal on macroscopic joint assessment. Inflammation is a well-established driver of OA progression^{43,44} Macroscopic evaluation also indicated degenerative changes in the contralateral limb. While we cannot determine the extent of pre-existing OA due to the absence of pre-surgical scoring, this finding is consistent with existing literature showing contralateral joint degeneration following unilateral ACL injury.^{45–47} This highlights a key limitation of the current study, the use of contralateral limbs as controls rather than including truly naïve animals. Future experiments will include a naïve control group to enable more accurate characterization of the injury response. Although the IFP graft may have succeeded in delivering blood flow to the ACL remnants, the combination of insufficient mechanical stability, lack of evidence of bridging of the ACL remnants, and persistent inflammation indicate that this technique does not merit continued investigation.

The primary limitation of this study is the small sample size, which was inherent to its design as a pilot study. The goal was not to reach statistical significance, but rather to determine which technique, if any, should be explored in future studies. Future studies exploring the LaDET graft technique will involve larger sample sizes, naïve controls, and comparison to the current gold-standard approach of reconstruction using an excised tendinous autograft. These future studies will also include qualitative biomechanical testing and molecular assessments to better characterize the graft healing response. One exciting aside is that the LaDET graft technique has already been successfully used in a clinical setting at the Colorado State University Veterinary Teaching Hospital in a ram with an ACL tear. This highlights the translational relevance of our approach, with potential applications in both veterinary and human medicine.

However, a key limitation regarding human translation is that the LaDET, as used in sheep, does not have a direct anatomical analog in humans. Thus, translation of the concept of

providing blood flow to the ACL remnants requires exploration of additional structures in humans. To address this, we have identified several candidate structures for exploration in future studies including the popliteus, gracilis, tibialis anterior, fibularis longus, extensor digitorum longus, and biceps femoris tendons.⁴⁸ The iliotibial band may also warrant renewed investigation, particularly since it was historically used in ACL reconstruction by Groves.⁶ Another limiting factor to human translation in this study is that only ewes were used. While this decision was based on the increased handling challenges posed by rams, future studies should include both sexes to evaluate potential sex-related differences in outcomes.

A final limitation to consider is that the LaDET graft used in this study did not recreate the double-bundle architecture of the native ACL, which consists of anteromedial and posterolateral bundles with distinct mechanical functions.⁴⁹ Although single-bundle reconstruction remains the clinical standard, there is growing interest in double-bundle techniques.⁵⁰ One recent study introduced a novel approach wherein one bundle consisted of repaired ACL tissue while the second was reconstructed with a hamstring autograft.⁵¹ Each bundle was tensioned independently to mimic native biomechanics. A similar approach could be adopted in our model by using SutureTape (Arthrex, AR-7534) to repair the ACL remnants as one bundle, while using the LaDET graft as a second, vascularized bundle. This combined method could further enhance biomechanical performance and healing.

One benefit of the LaDET procedure that has not yet been discussed is the preservation of native ACL remnants, which may support the maintenance of proprioceptive function. The ACL is rich in mechanoreceptors that detect changes in joint position, speed, and tension, key components of proprioception.⁵² After ACL injury, patients frequently exhibit proprioceptive deficits, which can contribute to impaired neuromuscular control and increased risk of reinjury.⁵³ Standard ACL reconstruction typically involves complete removal of the torn ligament to allow optimal graft placement, which may delay the restoration of proprioceptive function. Although proprioception can eventually return to near-normal levels, this often takes six months or

longer.⁵⁴ Importantly, studies have demonstrated that mechanoreceptors can persist in ACL remnants for up to three years post-injury.⁵⁵ Thus, retaining these remnants in our LaDET reconstruction technique may facilitate reinnervation of the graft and improve proprioceptive outcomes.^{51,56,57} In future work, we plan to investigate this using immunohistochemistry for neurofilament proteins as markers of nerve regeneration within the graft.

In conclusion, the findings of this pilot study support our hypothesis that the LaDET graft provides superior healing outcomes compared to the IFP graft. We believe that the LaDET technique warrants further investigation as a novel strategy for ACL reconstruction. A crucial next step will be to determine whether this technique offers improved healing compared to standard ACL reconstruction using an excised autograph. We are particularly enthusiastic about future studies exploring the biomechanical, immunohistochemical, and proteomic characteristics of this graft to achieve our overall goal of enhancing ACL graft healing and reducing the incidence of post-traumatic osteoarthritis following ACL reconstruction.

References

1. Bollen S. Epidemiology of knee injuries: diagnosis and triage. *Br J Sports Med*. 2000;34(3):227.2-228. doi:10.1136/bjsm.34.3.227-a
2. Kaeding CC, Léger-St-Jean B, Magnussen RA. Epidemiology and Diagnosis of Anterior Cruciate Ligament Injuries. *Clin Sports Med*. 2017;36(1):1-8. doi:10.1016/j.csm.2016.08.001
3. Mahapatra P, Horriat S, Anand BS. Anterior cruciate ligament repair – past, present and future. *J Exp Orthop*. 2018;5(1). doi:10.1186/s40634-018-0136-6
4. Schindler OS. Surgery for anterior cruciate ligament deficiency: A historical perspective. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2012;20(1):5-47. doi:10.1007/s00167-011-1756-x

5. Mayo Robson AW. Ruptured Crucial Ligaments and Their Repair by Operation. Ann Surg. Published online 1903.
6. Groves EWH. Operation for the Repair of the Crucial Ligaments. The Lancet. Published online 1917.
7. Kraeutler MJ, Bravman JT, McCarty EC. Bone-patellar tendon-bone autograft versus allograft in outcomes of anterior cruciate ligament reconstruction: A meta-analysis of 5182 patients. American Journal of Sports Medicine. 2013;41(10):2439-2448. doi:10.1177/0363546513484127
8. Morrey BF. Why bone–patella tendon–bone grafts should still be considered the gold standard for anterior cruciate ligament reconstruction. Yearbook of Orthopedics. 2010;2010:164. doi:10.1016/s0276-1092(09)79651-8
9. Friel NA, Chu CR. The Role of ACL Injury in the Development of Posttraumatic Knee Osteoarthritis. Clin Sports Med. 2013;32(1):1-12. doi:10.1016/j.csm.2012.08.017
10. Webster KE, Feller JA, Leigh WB, Richmond AK. Younger patients are at increased risk for graft rupture and contralateral injury after anterior cruciate ligament reconstruction. American Journal of Sports Medicine. 2014;42(3):641-647. doi:10.1177/0363546513517540
11. Barber-Westin SD, Noyes FR. Objective criteria for return to athletics after anterior cruciate ligament reconstruction and subsequent reinjury rates: a systematic review. Phys Sportsmed. 2011;39(3):100-110. doi:10.3810/psm.2011.09.1926
12. Nurden AT, Nurden P, Sanchez M, Andia I, Anitua E. Platelets and Wound Healing. Vol 13.; 2008.
13. Enoch S, Leaper DJ. Basic Science SURGeRY 26:2 31 Basic Science of Wound Healing.; 2007.

14. Wang Q, Shao G, Zhao X, Wong HH, Chin K, Zhao M, et al. Dysregulated fibrinolysis and plasmin activation promote the pathogenesis of osteoarthritis. *JCI Insight*. 2024;9(8). doi:10.1172/jci.insight.173603
15. Belcher C, Fawthrop F, Bunning R, Doherty M. Plasminogen Activators and Their Inhibitors in Synovial Fluids from Normal, Osteoarthritis, and Rheumatoid Arthritis Knees. Vol 55.; 1996. <http://ard.bmj.com/>
16. Rość D, Powierza W, Zastawna E, Drewniak W, Michalski A, Kotschy M. CR Post-Traumatic Plasminogenesis in Intraarticular Exudate in the Knee Joint. Vol 8.; 2002. http://www.MedSciMonit.com/pub/vol_8/no_5/1356.pdf
17. Murray MM. Current Status and Potential of Primary ACL Repair. *Clin Sports Med*. 2009;28(1):51-61. doi:10.1016/j.csm.2008.08.005
18. Van Zeeland EM, Kassel B, Montoya T, Saviola AJ, Burton LH, Easley JT, et al. Structural, functional, and proteomic based sex differences in murine post-traumatic osteoarthritis development following mechanical anterior cruciate ligament injury. *Osteoarthritis Cartilage*. Published online May 2025. doi:10.1016/j.joca.2025.05.004
19. Frank C, Amiel D, Akeson WH. HEALING OF THE MEDIAL COLLATERAL LIGAMENT OF THE KNEE A Morphological and Biochemical Assessment in Rabbits. Vol 54.; 1983.
20. Woo SL, Vogrin TM, Abramowitch SD. Healing and Repair of Ligament Injuries in the Knee. *Journal of the American Academy of Orthopaedic Surgeons*. Published online 2000:364-372.
21. Murray MM, Flutie BM, Kalish LA, Ecklund K, Fleming BC, Proffen BL, et al. The Bridge-Enhanced Anterior Cruciate Ligament Repair (BEAR) Procedure: An Early Feasibility Cohort Study. *Orthop J Sports Med*. 2016;4(11). doi:10.1177/2325967116672176

22. Shah AK, Neijna AG, Retzky JS, Gomoll AH, Strickland SM. Indications, Techniques, and Outcomes of Bridge-Enhanced ACL Restoration (BEAR). *Curr Rev Musculoskelet Med*. Published online April 1, 2025. doi:10.1007/s12178-025-09950-1
23. McMillan S, Putra J, Patel S, Kramer DE, Anthony S, Ford EA, et al. Histological Analysis of Bridge-Enhanced ACL Restoration (BEAR) Tissue in Ligament Retears. *Orthop J Sports Med*. 2025;13(4). doi:10.1177/23259671251331046
24. Abdelhakim GE. *ATLAS - Anatomy Of Sheep*.; 2006.
25. Parks A. Form and function of the equine digit. *Veterinary Clinics of North America - Equine Practice*. 2003;19(2):285-307. doi:10.1016/S0749-0739(03)00018-X
26. Bruce R, David M, Burr B, Sharkey NA, Fyhrie DP. Mechanical Properties of Ligament and Tendon. In: *Skeletal Tissue Mechanics*. ; 2015:175-225.
27. Gallagher J, Tierney P, Murray P, O'Brien M. The infrapatellar fat pad: Anatomy and clinical correlations. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2005;13(4):268-272. doi:10.1007/s00167-004-0592-7
28. Powers CM, Souza RB, Fulkerson JP. Patellofemoral Joint. In: *Pathology and Intervention in Musculoskeletal Rehabilitation*. Second. ; 2016:798-835.
29. Atkinson TS, Atkinson PJ, Mendenhall H V, Haut RC. Patellar Tendon and Infrapatellar Fat Pad Healing after Harvest of an ACL Graft 1.; 1998.
30. Shiraishi R, Ueda S. Relationship between the change in infrapatellar fat pad thickness assessed using ultrasonography and anterior knee pain on squatting after anterior cruciate ligament reconstruction. *Journal of Medical Ultrasonics*. 2023;50(2):237-243. doi:10.1007/s10396-023-01300-3
31. Montoya T, Bunten B, D'Amoto M, Graham K, Williams S, Ward T, et al. Design and Implementation of A Static Weight Bearing Device For Use In Ovine (Sheep) Preclinical Studies. In: *Rocky Mountain Bioengineering Symposium*. ; 2023.

32. Little CB, Smith MM, Cake MA, Read RA, Murphy MJ, Barry FP. The OARSI histopathology initiative - recommendations for histological assessments of osteoarthritis in sheep and goats. *Osteoarthritis Cartilage*. 2010;18(SUPPL. 3). doi:10.1016/j.joca.2010.04.016
33. Kim J, Breur GJ. Temporospacial and kinetic characteristics of sheep walking on a pressure sensing walkway. *Canadian Journal of Veterinary Research*. Published online 2008:50-55.
34. Hill JR, Eekhoff JD, Brophy RH, Lake SP. Elastic fibers in orthopedics: Form and function in tendons and ligaments, clinical implications, and future directions. *Journal of Orthopaedic Research*. 2020;38(11):2305-2317. doi:10.1002/jor.24695
35. Sawada T, Sugawara Y, Asai T, Aida N, Yanagisawa T, Ohta K, et al. Immunohistochemical characterization of elastic system fibers in rat molar periodontal ligament. *Journal of Histochemistry and Cytochemistry*. 2006;54(10):1095-1103. doi:10.1369/jhc.5A6905.2006
36. Shukunami C, Yoshimoto Y, Takimoto A, Yamashita H, Hiraki Y. Molecular characterization and function of tenomodulin, a marker of tendons and ligaments that integrate musculoskeletal components. *Japanese Dental Science Review*. 2016;52(4):84-92. doi:10.1016/j.jdsr.2016.04.003
37. Shukunami C, Takimoto A, Nishizaki Y, Yoshimoto Y, Tanaka S, Miura S, et al. Scleraxis is a transcriptional activator that regulates the expression of Tenomodulin, a marker of mature tenocytes and ligamentocytes. *Sci Rep*. 2018;8(1). doi:10.1038/s41598-018-21194-3
38. Kim H, Cho HJ, Kim SW, Liu B, Choi YJ, Lee J, et al. CD31+ cells represent highly angiogenic and vasculogenic cells in bone marrow: Novel role of nonendothelial CD31+ cells in neovascularization and their therapeutic effects on ischemic vascular disease. *Circ Res*. 2010;107(5):602-614. doi:10.1161/CIRCRESAHA.110.218396

39. Fitzpatrick J, Scott M, Nolan A. Assessment of pain and welfare in sheep. In: Small Ruminant Research. Vol 62. ; 2006:55-61. doi:10.1016/j.smallrumres.2005.07.028
40. Katie J. Sikes, Johnson JW, Michalko B, Brekhus C, Montoya T, Easley J, et al. Biomechanical Contributions of the LDE and ACL in the Ovine Stifle: Implications for a Novel Model of Post-Traumatic Osteoarthritis . In: Orthopaedic Research Society Annual Meeting. ; 2023.
41. Elliott CRB, Vasey JR, Russell TM. Transection of the lateral and long digital extensor tendons in racehorses. Aust Vet J. 2012;90(1-2):20-23. doi:10.1111/j.1751-0813.2011.00871.x
42. Bousquet BA, O'Brien L, Singleton S, Beggs M. POST-OPERATIVE CRITERION BASED REHABILITATION OF ACL REPAIRS: A CLINICAL COMMENTARY. Int J Sports Phys Ther. 2018;13(2):293-305. doi:10.26603/ijsp20180293
43. Knights AJ, Redding SJ, Maerz T. Inflammation in osteoarthritis: The latest progress and ongoing challenges. Curr Opin Rheumatol. 2023;35(2):128-134. doi:10.1097/BOR.0000000000000923
44. Sokolove J, Lepus CM. Role of inflammation in the pathogenesis of osteoarthritis: Latest findings and interpretations. Ther Adv Musculoskelet Dis. 2013;5(2):77-94. doi:10.1177/1759720X12467868
45. Metcalfe AJ, Andersson M Le, Goodfellow R, Thorstensson CA. Is knee osteoarthritis a symmetrical disease? Analysis of a 12year prospective cohort study. BMC Musculoskelet Disord. 2012;13. doi:10.1186/1471-2474-13-153
46. Christiansen BA, Anderson MJ, Lee CA, Williams JC, Yik JHN, Haudenschild DR. Musculoskeletal changes following non-invasive knee injury using a novel mouse model of post-traumatic osteoarthritis. Osteoarthritis Cartilage. 2012;20(7):773-782. doi:10.1016/j.joca.2012.04.014

47. Hislop BD, Devine C, June RK, Heveran CM. Subchondral bone structure and synovial fluid metabolism are altered in injured and contralateral limbs 7 days after non-invasive joint injury in skeletally-mature C57BL/6 mice. *Osteoarthritis Cartilage*. 2022;30(12):1593-1605. doi:10.1016/j.joca.2022.09.002
48. Gray H, Standring S, Borley NR. *Gray's Anatomy*. 40th ed. Livingstone/Elsevier; 2008.
49. Girgis FG, Marshall JL, Monajem A. The Cruciate Ligaments of the Knee Joint. *Clin Orthop Relat Res*. 1975;106:216-231. doi:10.1097/00003086-197501000-00033
50. Amis AA. The functions of the fibre bundles of the anterior cruciate ligament in anterior drawer, rotational laxity and the pivot shift. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2012;20(4):613-620. doi:10.1007/s00167-011-1864-7
51. Van de Velde SK. Double-Bundle Anterior Cruciate Ligament Reconstruction With Primary Repair and Hamstring Autograft Augmentation. *Arthrosc Tech*. 2023;12(5):e639-e645. doi:10.1016/j.eats.2022.12.021
52. Dhillon MS, Bali K, Prabhakar S. Proprioception in anterior cruciate ligament deficient knees and its relevance in anterior cruciate ligament reconstruction. *Indian J Orthop*. 2011;45(4):294-300. doi:10.4103/0019-5413.80320
53. Barrack RL, Skinner HB, Buckley SL. Proprioception in the anterior cruciate deficient knee. *Am J Sports Med*. 1989;17(1):1-6. doi:10.1177/036354658901700101
54. Angoules AG, Mavrogenis AF, Dimitriou R, Karzis K, Drakoulakis E, Michos J, et al. Knee proprioception following ACL reconstruction; a prospective trial comparing hamstrings with bone-patellar tendon-bone autograft. *Knee*. 2011;18(2):76-82. doi:10.1016/j.knee.2010.01.009
55. Georgoulis AD, Pappa L, Moebius U, Malamou-Mitsi V, Pappa S, Papageorgiou CO, et al. The presence of proprioceptive mechanoreceptors in the remnants of the ruptured ACL as a possible source of re-innervation of the ACL autograft. *Knee*

- Surgery, Sports Traumatology, Arthroscopy. 2001;9(6):364-368.
doi:10.1007/s001670100240
56. Lee BI, Min KD, Choi HS, Kim JB, Kim ST. Arthroscopic anterior cruciate ligament reconstruction with the tibial-remnant preserving technique using a hamstring graft. *Arthroscopy - Journal of Arthroscopic and Related Surgery*. 2006;22(3):340.e1-340.e7. doi:10.1016/j.arthro.2005.11.010
57. Kim SJ, Jo SB, Kim TW, Chang JH, Choi HS, Oh KS. A modified arthroscopic anterior cruciate ligament double-bundle reconstruction technique with autogenous quadriceps tendon graft: Remnant-preserving technique. *Arch Orthop Trauma Surg*. 2009;129(3):403-407. doi:10.1007/s00402-008-0764-x

CHAPTER 5: CONCLUSIONS AND FUTURE DIRECTIONS

The anterior cruciate ligament (ACL) is a critical stabilizer of the knee joint.¹ Despite its essential role in joint biomechanics, the ACL is highly susceptible to injury, particularly among young, active individuals, with a disproportionately high incidence in females due to a multifactorial interplay of anatomical, hormonal, and biomechanical risk factors.²⁻⁷ Following rupture, the ACL's limited healing capacity within the intra-articular environment often necessitates surgical reconstruction.^{8,9} However, even with successful repair, a striking proportion of patients, up to 87%, develop post-traumatic osteoarthritis (PTOA), a debilitating form of joint degeneration driven by chronic inflammation and irreversible tissue damage.¹⁰ This clinical trajectory, combined with the rising burden of ACL injuries and the limited effectiveness of current PTOA treatments, underscores all too well the critical need for research aimed at elucidating the mechanisms of PTOA and developing effective therapeutic strategies.¹¹ To address this need, the work of this dissertation focused on two broad areas to explore with high clinical potential: delaying PTOA onset and progression, and improving surgical ACL reconstruction techniques.

5.1 Overview of Findings

In the first aim of this study, we investigated sex differences in PTOA development using a preclinical mouse model of mechanical ACL rupture. We observed significant sex-based disparities. Male mice exhibited greater functional impairments and more severe histologic evidence of joint degeneration than females at 56 days post-injury. Proteomic analysis of ACL remnants revealed divergent responses between the sexes at early time-points. Specifically, female mice showed elevated expression of proteins related to fibrinolysis, coagulation, extracellular matrix remodeling, relaxin, and estrogen receptor (ER) signaling relative to male

mice. We hypothesize that these early molecular differences may underly the long-term variations in disease progression between sexes.

Given that male mice did not exhibit the early increase in ER signaling observed in females, we next sought to determine whether modulating this pathway could mitigate PTOA severity in males. Using our established preclinical model, we explored the role of estrogen signaling in PTOA development. Intra-articular delivery of 17 β -estradiol produced discernable protective effects at 35 days post-injury, improving mobility, static weight bearing, and reducing enthesophyte size compared to saline controls. However, the vehicle control, β -cyclodextrin, showed distinct effects on PTOA development relative to saline, affecting gait parameters, osteophyte maturity, and ER β expression. Therefore, interpretation of the protective effects observed with 17 β -estradiol should consider potential confounding factors, as β -cyclodextrin may not be biologically inert and could influence the results. Treatment with Fulvestrant, an ER antagonist, further suggested a role for ER signaling in male mice, with indications of worsened PTOA including reduced voluntary movement and more mature osteophyte formation. Collectively, these findings highlight the complex role of estrogen in joint health and the nuanced nature of hormone-based therapeutic interventions, pointing to multiple avenues for future research.

In the final aim, we investigated novel approaches to ACL reconstruction using an ovine preclinical model. As disruptions to the coagulation cascade appear to contribute significantly to the inability of the ACL to spontaneously heal, this pathway was of particular interest. Proteomic data from our first aim supported further investigation. We tested two autologous graft structures for ACL reconstruction, the lateral digital extensor tendon (LaDET) and the infrapatellar fat pad (IFP), which maintained a native blood supply. Among these, the LaDET graft showed promising outcomes, including complete recovery of functional mobility, seamless integration of the graft with ACL remnants, and reduced PTOA severity. These findings support the

hypothesis that increased vascularization promotes graft healing and lay the groundwork for future studies aimed at optimizing this technique.

5.2 Key Areas for Continued Study

The findings presented in this dissertation highlight several key areas that warrant further investigation. First, the role of sex in PTOA development must be fully elucidated. To achieve this, improved epidemiological studies are essential to establish clear sex-based differences in the progression of PTOA in humans. Additionally, further research into the molecular pathways underlying sex-specific PTOA progression are needed, with a focus on inflammation, pain, extracellular matrix remodeling, and hormonal signaling. Translation of findings from murine models to human clinical data is also necessary to validate relevance, with attention to developing sex-specific treatment strategies for osteoarthritis.

Second, our findings indicate a clear need to develop targeted hormone-based therapies for PTOA. Optimizing intra-articular delivery of estrogen and related modulators will require refinement of dosing, timing, and formulation strategies. Alternative delivery vehicles for steroid hormones should also be explored to avoid the confounding effects seen with β -cyclodextrin in this work. Further research into the distinct roles of estrogen receptors across joint tissues is also necessary, as these receptors may exert diverse functions and tissue-specific effects. In addition, other sex hormones, such as testosterone, may influence PTOA development. These effects should be examined in both males and females to understand sex-specific disease mechanisms.

Lastly, our findings suggest that improving blood flow to an ACL graft may enhance healing, paving the way for improved reconstruction techniques that promote graft integration and reduce long-term joint degeneration. Further studies on our LaDET graft technique are needed using larger cohorts, appropriate controls, and multiple timepoints. Biomechanical testing of the graft and long-term assessments of PTOA development following ACL

reconstruction are also necessary. Molecular analyses should examine the mechanisms involved, including whether a platelet-fibrin clot forms between ACL remnants with increased blood flow. More broadly, exploration for a human vascularized graft sources is needed. This work also challenges the field to investigate ACL reconstruction techniques that retain ACL remnants to preserve native biomechanics and proprioceptive function. Finally, therapeutic modulation of the intra-articular coagulation cascade represents another promising area for future research.

5.3 Conclusion

This dissertation offers new insights into the pathogenesis and treatment of ACL injury-induced PTOA, with a focus on sex-specific disease mechanisms and novel therapeutic strategies. Through preclinical experimentation, we identified sex-based differences in functional, structural, and proteomic responses to ACL injury, demonstrated preliminary support for estrogen signaling as a potential therapeutic avenue PTOA, and introduced a promising vascularized graft technique to improve ACL reconstruction outcomes.

While challenges remain, the findings presented here contribute important groundwork for advancing our understanding of joint degeneration following ACL injury. They highlight the necessity of a multifaceted approach that considers biological sex, molecular signaling, and surgical innovation. Continued research in these areas will be critical for translating preclinical findings into effective, targeted treatments. By building on these foundations, future work has the potential to meaningfully improve patient outcomes following ACL injury and reduce the long-term burden of PTOA.

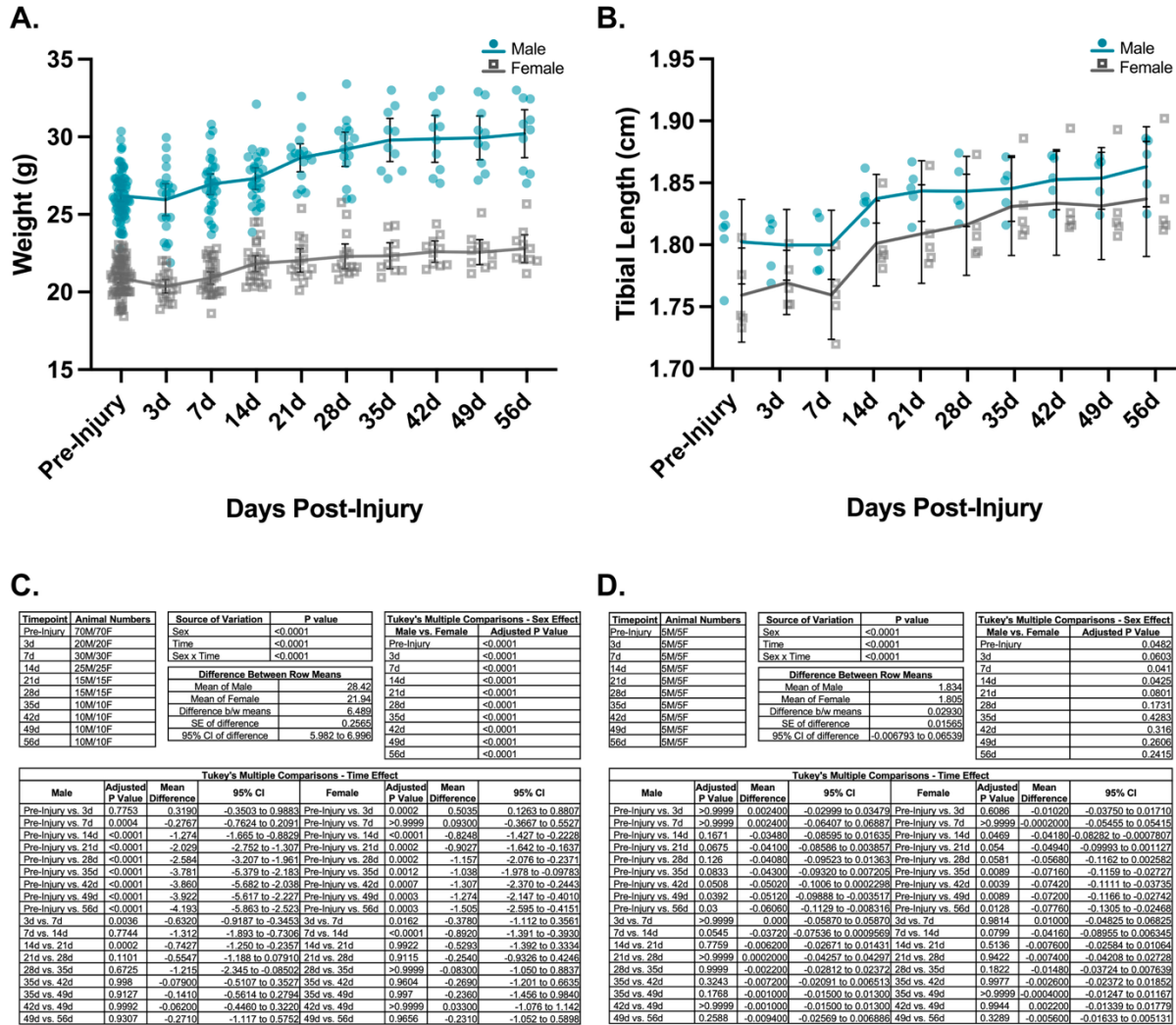
References

1. Zantop T, Petersen W, Fu FH. Anatomy of the anterior cruciate ligament. *Oper Tech Orthop.* 2005;15(1):20-28. doi:10.1053/j.oto.2004.11.011
2. Gornitzky AL, Lott A, Yellin JL, Fabricant PD, Lawrence JT, Ganley TJ. Sport-Specific Yearly Risk and Incidence of Anterior Cruciate Ligament Tears in High School Athletes: A Systematic Review and Meta-analysis. *American Journal of Sports Medicine.* 2016;44(10):2716-2723. doi:10.1177/0363546515617742
3. Murray MM, Vavken P, Fleming BC. *The ACL Handbook.* 1st ed. (Murray MM, Vavken P, Fleming B, eds.). Springer New York; 2013. doi:10.1007/978-1-4614-0760-7
4. Hutchinson MR, Ireland ML. *Knee Injuries in Female Athletes.* Vol 19.; 1995.
5. Arendt EA, Agel J, Dick R. Anterior Cruciate Ligament Injury Patterns Among Collegiate Men and Women. Vol 34.; 1999. www.nata.org/jat
6. Gwinn DE, Wilckens JH, Mcdevitt ER, Ross G, Kao TC. The Relative Incidence of Anterior Cruciate Ligament Injury in Men and Women at the United States Naval Academy*. Vol 28.; 2000.
7. Montalvo AM, Schneider DK, Webster KE, Yut L, Galloway MT, Heidt RS, et al. Anterior cruciate ligament injury risk in sport: A systematic review and meta-analysis of injury incidence by sex and sport classification. *J Athl Train.* 2019;54(5):472-482. doi:10.4085/1062-6050-407-16
8. Murray MM. Current Status and Potential of Primary ACL Repair. *Clin Sports Med.* 2009;28(1):51-61. doi:10.1016/j.csm.2008.08.005
9. Mahapatra P, Horriat S, Anand BS. Anterior cruciate ligament repair – past, present and future. *J Exp Orthop.* 2018;5(1). doi:10.1186/s40634-018-0136-6
10. Friel NA, Chu CR. The Role of ACL Injury in the Development of Posttraumatic Knee Osteoarthritis. *Clin Sports Med.* 2013;32(1):1-12. doi:10.1016/j.csm.2012.08.017

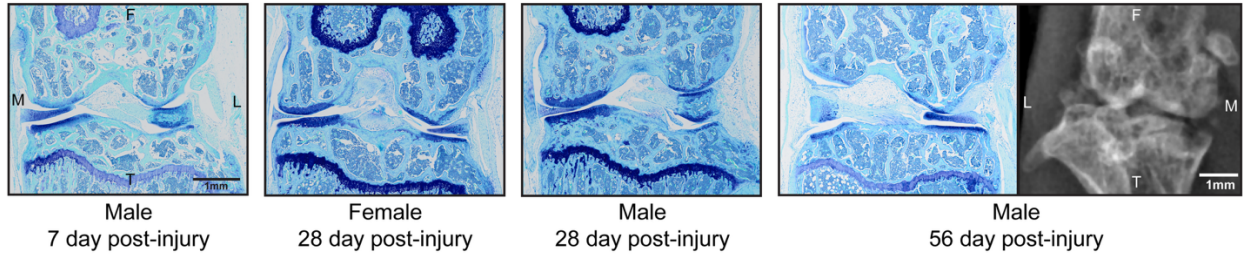
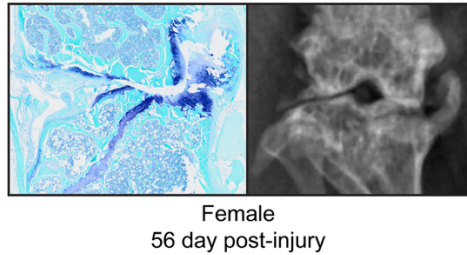
11. Punzi L, Galozzi P, Luisetto R, Favero M, Ramonda R, Oliviero F, et al. Post-traumatic arthritis: overview on pathogenic mechanisms and role of inflammation. RMD Open. 2016;2:279. doi:10.1136/rmdopen-2016

APPENDIX I

CHAPTER 2 SUPPLEMENTARY FIGURES

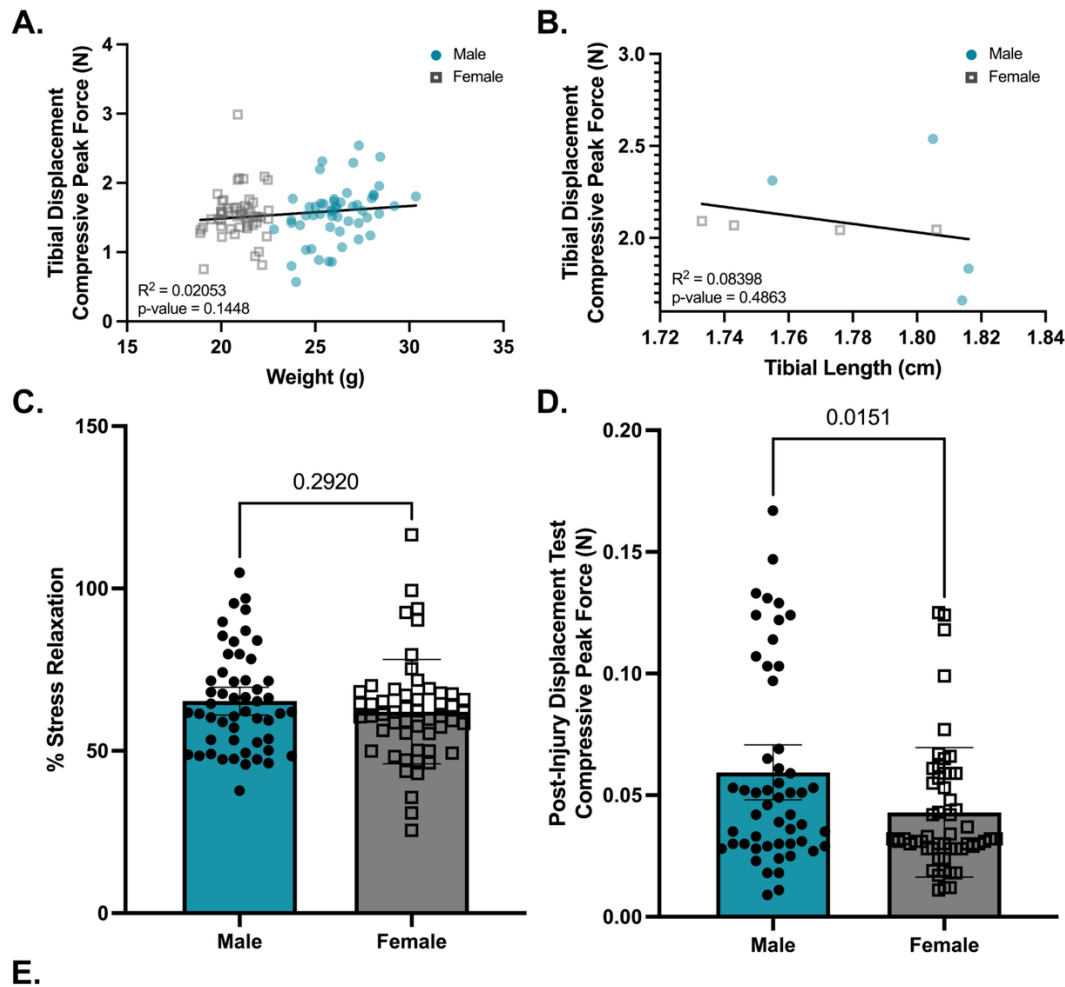


Appendix I.1. Longitudinal progression of (A) animal weights and (B) tibial lengths for male and female mice. Bars represent mean $\pm$ 95% confidence interval with individual animals represented by each datapoint. (C) Male mice consistently weighed more than female mice at all timepoints, and both sexes exhibited gradual weight increases throughout the study. A repeated measures mixed model with multiple comparisons was utilized and p-values calculated for sex, time, and sex/time interaction factors. Additionally, 95% confidence intervals were reported. (D) Male mice had longer tibial lengths compared to female mice prior to injury and at 7-days following injury. Tibial lengths also gradually increased throughout the study, particularly in female mice. Tibial lengths were measured longitudinally via radiographs and a repeated measures mixed model with multiple comparisons was utilized and p-values calculated for sex, time, and sex/time interaction factors. Additionally, 95% confidence intervals were reported.

A.**Excluded for Partial ACL Rupture (n=4)****B.****Excluded for Extreme Severity of Injury (n=1)****C.****ACL Rupture Parameters for Excluded Animals**

Animal	Tibial Displacement Peak Force (N)	Post-Injury Displacement Test Peak Force (N)
Excluded for Partial ACL Rupture		
Male 7d Post-Injury	1.935	0.166
Male 28d Post-Injury	1.843	0.174
Female 28d Post-Injury	0.763	0.129
Male 56d Post-Injury	2.042	0.035
Excluded for Extreme Severity of Injury		
Female 56d Post-Injury	2.365	0.043

Appendix I.2. Justification for excluding animals from the study. **(A)** Histology and radiograph images (if available) for four animals excluded for suspected partial ACL rupture. These animals showed minimal PTOA development and had **(C)** lower than average tibial displacement peak forces and/or higher than average post-injury displacement test peak forces. **(B)** One animal was excluded due to extreme severity of injury, thought to be the result of an extraneous MCL injury that occurred between 14- and 28-days post-injury. This was evidenced by erosion of the tibial plateau and calcification of the MCL. **(C)** This animal also exhibited a higher-than-average tibial displacement peak force.

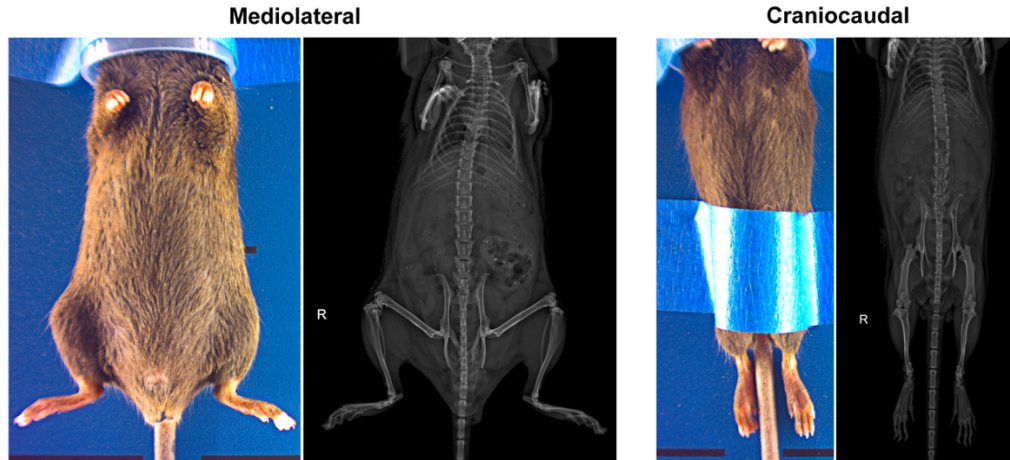


Unpaired t test – Male vs. Female					
Parameter	Group A	Group B	p-value	SEM	95% Confidence Interval
Tibial Displacement Compressive Force	Male (n=52)	Female (n=53)	0.8381	-0.01495 ± 0.07295	-0.1596 to 0.1297
% Stress Relaxation	Male (n=52)	Female (n=53)	0.292	-3.261 ± 3.079	-9.366 to 2.845
Post Injury Displacement Test	Male (n=52)	Female (n=53)	0.0151	-0.01648 ± 0.006669	-0.0297 to -0.003253

Simple Linear Regression						
Parameter	Number of Values	Slope	Y-intercept	R ²	p-value	Slope 95% Confidence Interval
Tibial Displacement Compressive Force Weight Correlation	105	0.01235	0.2925	0.02053	0.1448	-0.006347 to 0.04264
Tibial Displacement Compressive Force Tibial Length Correlation	8	-2.307	6.182	0.08398	0.4863	-9.916 to 5.303

Appendix I.3. Additional analyses of ACL rupture parameters. No correlation was found in mice between the force required to rupture the ACL (tibial displacement compressive peak force) and (A) bodyweight or (B) tibial length. Simple linear regression, individual animals represented by each datapoint. (C) There was no observed difference between male and female mice in the percent stress relaxation that occurred during preconditioning (preconditioning peak load/load at 200 cycles). (D) Interestingly, female mice exhibited a decrease in post-injury displacement test compressive peak force compared to males. Bars represent mean $\pm$ 95% confidence interval, with individual animals represented by each datapoint, two-tailed unpaired t-test. (E) Statistical report of ACL rupture parameters, including p-values and 95% confidence intervals for all analyses.

A. Animal Positioning for Radiographs



B. Radiograph Scoring Criteria

Scoring criteria were adapted from Hurley CR et al. Each factor was scored from 0 to 3, with 0 = not present, 1 = mild changes, 2 = moderate changes, and 3 = severe changes. Factors were summed to determine the total radiograph score.

Mediolateral	Craniocaudal
Intra-articular mineralized osseous fragments	Periarticular osteophytes, lateral femoral condyle
Intercondylar avulsion fracture fragments	Periarticular osteophytes, medial femoral condyle
Apical patellar osteophytes	Osteophytes, femoral intercondylar region
Basilar patellar osteophytes	Lateral collateral ligament enthesopathy
Stifle joint effusion or capsular thickening	Medial collateral ligament enthesopathy
Periarticular osteophytes, femoral trochlear groove	Lateral soft tissue thickening
Distal femoral condylar remodeling	Medial soft tissue thickening
Periarticular osteophytes, fabellae, and lateral and medial gastrocnemius and popliteal sesamoids	Periarticular osteophytes, proximolateral tibia
Cranial apical patellar enthesopathy	Periarticular osteophytes, proximomedial tibia
Periarticular osteophytes, cranioproximal tibia	Osteophytes, central tibial plateau
Periarticular osteophytes, caudoproximal tibia	Meniscal mineralization medial
Tibial condylar remodeling	Meniscal mineralization lateral
Femoral supratrochlear lysis	Subchondral cystic lucencies, femoral condyles medial
	Subchondral cystic lucencies, femoral condyles lateral
	Subchondral cystic lucencies, intercondyloid fossa
	Subchondral cystic lucencies, proximal medial tibial epiphysis
	Subchondral cystic lucencies, proximal lateral tibial epiphysis
	Subchondral sclerosis, proximolateral tibia
	Subchondral sclerosis proximal medial tibia
	Subchondral sclerosis medial femoral condyle
	Subchondral sclerosis lateral femoral condyle

Appendix I.4. (A) Protocol for mouse positioning for mediolateral and craniocaudal stifle radiographs. Tape was used in positioning for craniocaudal radiographs to align the femur and tibia and to maintain a consistent orientation for scoring of the stifle joint. **(B)** Overview of scoring system adapted from Hurley CR, et al²⁶ for use in mice.

Appendix I.5.

Toluidine Blue/Fast Green Stain

By: Katie Sikes 10/04/2023

Edited: Emily Van Zeeland 10/29/2023

Adapted from: <https://www.urmc.rochester.edu/MediaLibraries/URMCMedia/musculoskeletal-research/core-services/histology/documents/CMSR-Tol-Blue.pdf>

Sample Preparation: Fixation with 10% neutral buffered formalin, decalcification with 5% EDTA/PBS, paraffin embedded, sectioned at 5µm.

Samples: Mouse Stifles

Materials:

- 1) **100% EtOH**
- 2) **95% EtOH**
- 3) **70% EtOH**
- 4) **Xylene** (Fisher # X54)
- 5) **0.04% Toluidine Blue** (CAS# 92-31-9)
- 6) **0.02% Fast Green** (CAS# 2353-45-9)

Warm slides for approximately 1 hour at 60°C before beginning

Procedure Toluidine Blue/Fast Green staining:

- 1) Deparaffinize
 - a. Xylene: 3 min x 2
- 2) Hydrate slides
 - a. 100% ETOH: 2 min x 2
 - b. 95% ETOH: 2 min x 2
 - c. 70% ETOH: 2 min x 2
 - d. Room temperature deionized water: 2 min
- 3) Stain in **Toluidine Blue** solution: 20 min
- 4) Room temperature deionized water: 3 QUICK DIPS (approximately 30 seconds each)
- 5) Stain in **Fast Green** solution: 3 min 30 sec
- 6) Room temperature deionized water: 3 QUICK DIPS (approximately 30 seconds each)
- 7) Dehydrate
 - a. 95% ETOH: 30 seconds x 3
 - b. 100% ETOH: 30 seconds x 2
- 8) Clear
 - a. Xylene: 5 min x 2

Appendix I.5.

Histology Scoring Parameters

By: Kelly Santangelo & Emily Van Zeeland 11/29/2023

Adapted from: Patrick Haubruck, Raban Heller, Carina L. Blaker, Elizabeth C. Clarke, Susan M. Smith, Daniel Burkhardt, Yolanda Liu, Shihani Stoner, Sanaa Zaki, Cindy C. Shu, Christopher B. Little. *Streamlining quantitative joint-wide medial femoro-tibial histopathological scoring of mouse post-traumatic knee osteoarthritis models*, Osteoarthritis and Cartilage, Volume 31, Issue 12, 2023, Pages 1602-1611, <https://doi.org/10.1016/j.joca.2023.07.013>.

Samples: Coronal sections of anterior mouse stifles stained with toluidine blue & fast green.

Coronal were used instead of serial sagittal and thus medial and lateral compartments were scored separately for tibia and femur. Based on the histopathology that we observed, the following parameters within specific domains were updated:

DOMAIN 1: CARTILAGE

- The following was used in place of “CHONDROCYTE HYPERTROPHY/APOPTOSIS/CELL DEATH: ONLY SCORE NON-CALCIFIED ARTICULAR CARTILAGE”:
 - 0 Clinically unremarkable
 - 1 Hypercellularity, particularly with presence of chondrons
 - 2 Regions of hypercellularity via chondrons as well as cell clustering
 - 3 Any of the previous along with regions of hypocellularity
 - 4 Diffuse hypocellularity

DOMAIN 2: BONE

- For “OSTEOCYTE DEATH IN SUBCHONDRAL BONE”:
A score of 4 was included to represent severe subchondral bone pathology outside of the scoring system.
- For “SUBCHONDRAL BONE SCLEROSIS”:
A score of 4 was included to represent severe subchondral bone pathology outside of the scoring system.
- For “SUBCHONDRAL BONE Vascular Invasion/erosion”:
A score of 4 was included to represent severe subchondral bone pathology outside of the scoring system.

DOMAIN 3: MENISCUS

- For “BONE FORMATION – SCORE OUTER REGION (OUTER 1/3RD) ONLY”:
A score of 6 was included to represent severe meniscal pathology outside of the scoring system.

Appendix I.5. Protocol for staining of histology slides with toluidine blue and fast green. Adaptations made to murine PTOA scoring system are outlined.²⁷

Appendix I.6.

Proteomic Sample Preparation Protocol

By: Anthony Saviola 09/19/2023

Ligaments were resuspended in 8M urea, 0.1M Tris (pH 8.5), 5 mM TCEP (tris(2-carboxyethyl)phosphine) and incubated with constant agitation (1400 rpm) for 2 hrs at 37°C.^{1,2} Samples were then alkylated with 50 mM 2-chloroacetamide for 30 mins in the dark at room temperature. The solutions were diluted with four volumes of 100 mM Tris-HCl (pH 8.5) before digestion with Lys-C (1:100) (Pierce™) for 2 hrs at 37°C with constant shaking (1400 rpm). Samples were then digested overnight with trypsin (1:100) followed by a second treatment of trypsin for 2 hrs. Both steps were carried out with continuous agitation (1400 rpm) at 37°C. Following trypsin digestion, samples were acidified with formic acid (FA) to a final concentration of 1%, centrifuged at $16,000 \times g$ for 5 mins at room temperature, and the supernatant was collected. Aliquots containing 10 µg of digested peptides were purified using Pierce™ C18 Spin Tips (Thermo Scientific) according to the manufacturer's protocol, dried in a vacuum centrifuge, and resuspended in 0.1% FA in mass spectrometry-grade water.

Digested peptides were loaded onto Evotips and analyzed directly using an Evosep One liquid chromatography system (Evosep Biosystems, Denmark) coupled with a Bruker timsTOF SCP mass spectrometer (Bruker, Germany). Peptides were separated on a 75 µm i.d. $\times$ 15 cm separation column packed with 1.9 µm C18 beads (Evosep Biosystems, Denmark) and over a predetermined 44-minute gradient. Buffer A was 0.1% FA in water and buffer B was 0.1% FA in acetonitrile. Instrument control and data acquisition were performed using Compass Hystar (version 6.0) with the timsTOF SCP operating in parallel accumulation-serial fragmentation (PASEF) mode under the following settings: mass range 100-1700 m/z, 1/k/0 Start 0.7 V s cm⁻² End 1.3 V s cm⁻²; ramp accumulation times were 166 ms; capillary voltage was 4500 V, dry gas 8.0 L min⁻¹ and dry temp 200°C. The PASEF settings were: 5 MS/MS scans (total cycle time,

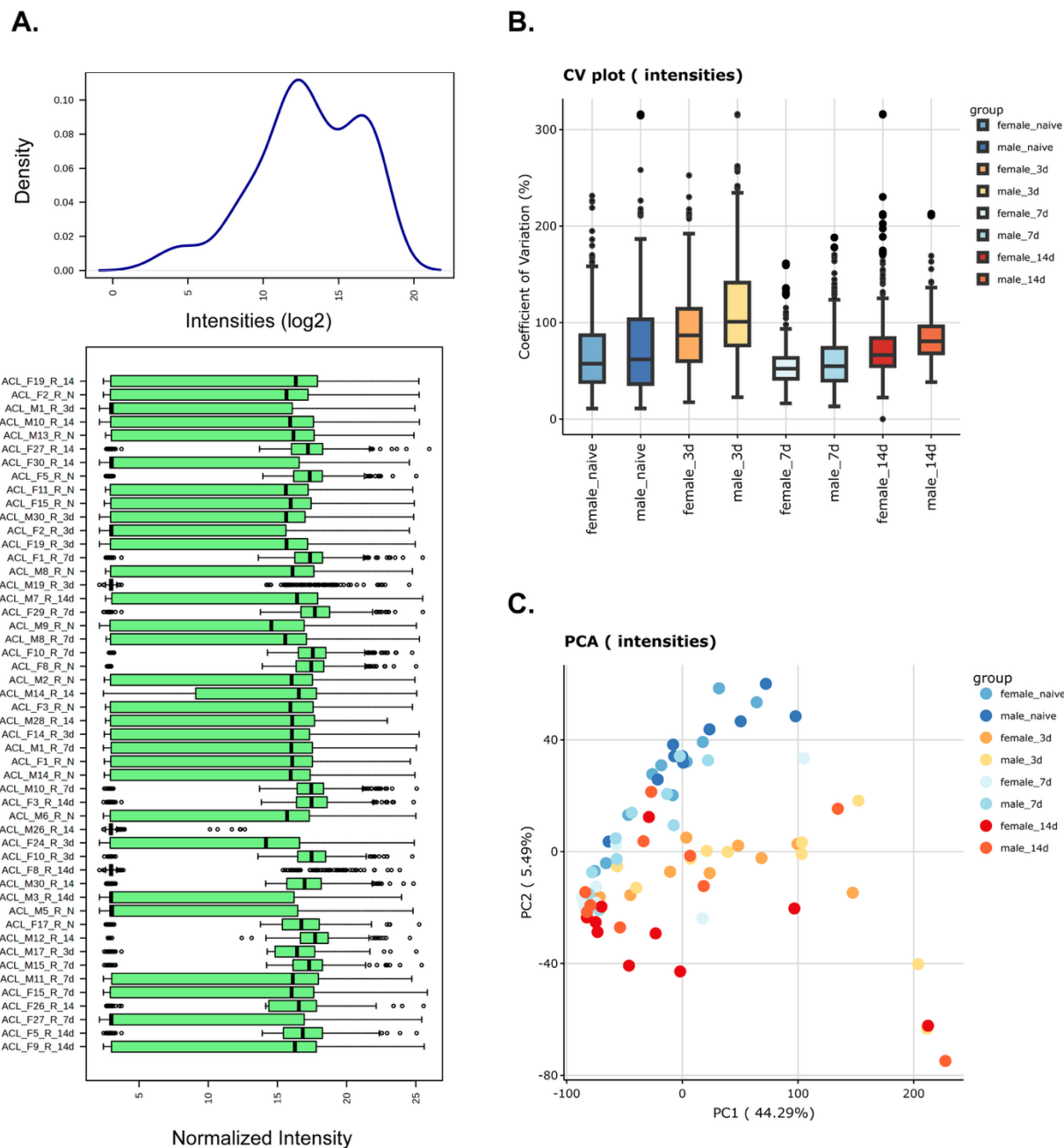
Appendix I.6.

1.03 s); charge range 0–5; active exclusion for 0.2 min; scheduling target intensity 20,000; intensity threshold 500; collision-induced dissociation energy 10 eV.

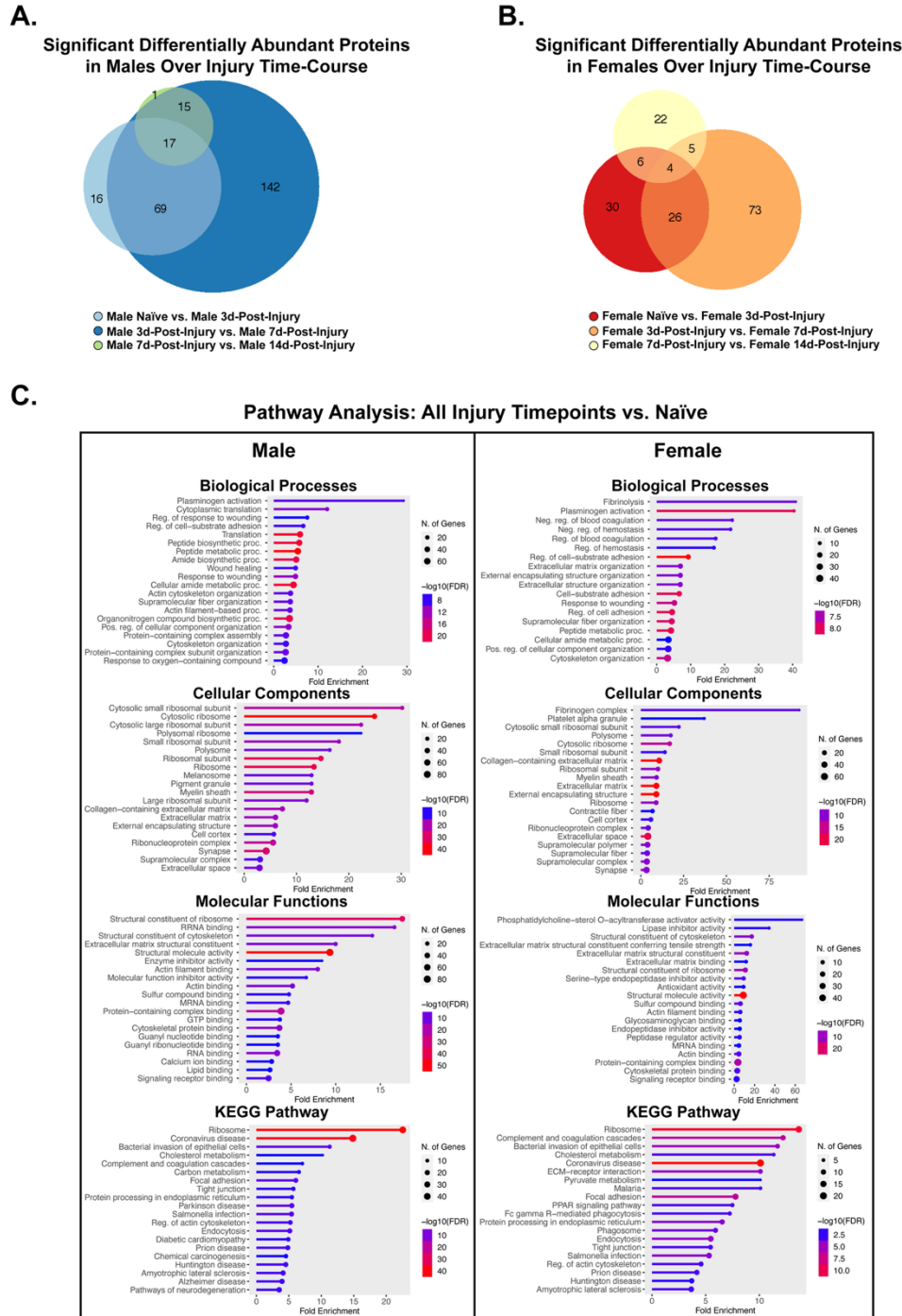
Fragmentation spectra were interpreted against the UniProt *Mus musculus* proteome database using the MSFragger-based FragPipe computational platform.³ Contaminants and reverse decoys were added to the database automatically. The precursor-ion mass tolerance and fragment-ion mass tolerance were set to 12 ppm and 20 ppm, respectively. Fixed modifications were set as carbamidomethyl (C), and variable modifications were set as oxidation (M), oxidation (P) (hydroxyproline), Gln->pyro- Glu (N-term), deamidated (NQ), and acetyl (Protein N-term). Two missed tryptic cleavages were allowed, and the protein-level false discovery rate (FDR) was $\leq 1\%$.

1. Naba A, Clauser KR, Hynes RO. Enrichment of extracellular matrix proteins from tissues and digestion into peptides for mass spectrometry analysis. *Journal of Visualized Experiments*. 2015;2015(101). doi:10.3791/53057
2. McCabe MC, Schmitt LR, Hill RC, et al. Evaluation and refinement of sample preparation methods for extracellular matrix proteome coverage. *Molecular and Cellular Proteomics*. 2021;20. doi:10.1016/J.MCPRO.2021.100079
3. Kong AT, Leprevost F V., Avtonomov DM, Mellacheruvu D, Nesvizhskii AI. MSFragger: Ultrafast and comprehensive peptide identification in mass spectrometry-based proteomics. *Nat Methods*. 2017;14(5):513-520. doi:10.1038/nmeth.4256

Appendix I.6. Detailed description of methods used for proteomic sample preparation and analysis.



Appendix I.7. Quality control figures generated during proteomic data analysis. **(A)** Kernal density plot and individual sample intensity box plots after data filtering, log2 normalization, and missing value imputation. The density plot is based on all 80 samples and the box plots show 50 samples. **(B)** Box plot displaying the coefficient of variation of sample intensities for each experimental group. Individual samples are marked. **(C)** PCA plot of all samples, organized by experimental group.



Appendix I.8. Additional findings from untargeted proteomic analyses of naïve and injured ACL tissue in male and female mice. Significant differentially abundant proteins were identified in (A) male and (B) female mice following injury at various timepoints throughout the study. A list of specific proteins can be found in Appendix I.17. (C) Pathway analyses were performed for male and female mice for all proteins that were significantly differentially abundant in an injured state compared to naïve for each sex. The figure displays the top 20 pathways with the highest Fold Enrichment, or all pathways identified if fewer than 20. Circle size indicates the number of genes associated with a pathway and color represents the False Discovery Rate (FDR).

Change in Time not Hidden (s)						Baseline Time not Hidden (s)		
Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means		Column B	Female
Time x Sex	8.463	0.3064	ns	No	Mean of Male	17.15	vs.	
Time	3.28	0.8215	ns	No	Mean of Female	45.15	Column A	Male
Sex	3.767	0.3423	ns	No	Difference between means	-28		
Subject	29.57	0.0051	**	Yes	SE of difference	27.74		
					95% CI of difference	-91.96 to 35.96	Unpaired t test	
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		P value	0.1787
7d							P value summary	ns
Male vs. Female	-47.27	-141.2 to 46.64	No	ns	0.3176		Significantly different (P < 0.05)?	No
21d							One- or two-tailed P value?	Two-tailed
Male vs. Female	-53.51	-147.4 to 40.40	No	ns	0.2585		t, df	t=1.474, df=8
28d							Mean of column A	499.3
Male vs. Female	-9.01	-102.9 to 84.90	No	ns	0.8483		Mean of column B	442.8
35d							Difference between means (B - A) ± SEM	-56.49 ± 38.33
Male vs. Female	-59.73	-153.6 to 34.18	No	ns	0.2079		95% confidence interval	-144.9 to 31.89
42d							R squared (eta squared)	0.2136
Male vs. Female	-59.87	-153.8 to 34.04	No	ns	0.2068			
49d								
Male vs. Female	66.33	-27.58 to 160.2	No	ns	0.1626			
56d								
Male vs. Female	-32.93	-126.8 to 60.98	No	ns	0.4853			
Male								
7d vs. 21d	-7.44	-133.0 to 118.2	No	ns	>0.9999			
7d vs. 28d	-31.34	-156.9 to 94.26	No	ns		0.987		
7d vs. 35d	-0.16	-125.8 to 125.4	No	ns	>0.9999			
7d vs. 42d	5.02	-120.6 to 130.6	No	ns	>0.9999			
7d vs. 49d	-37.16	-162.8 to 88.44	No	ns		0.9691		
7d vs. 56d	-33.72	-159.3 to 91.88	No	ns		0.981		
21d vs. 28d	-23.9	-149.5 to 101.7	No	ns		0.997		
21d vs. 35d	7.28	-118.3 to 132.9	No	ns	>0.9999			
21d vs. 42d	12.46	-113.1 to 138.1	No	ns	>0.9999			
21d vs. 49d	-29.72	-155.3 to 95.88	No	ns		0.9901		
21d vs. 56d	-26.28	-151.9 to 99.32	No	ns		0.9949		
28d vs. 35d	31.18	-94.42 to 156.8	No	ns		0.9873		
28d vs. 42d	36.36	-89.24 to 162.0	No	ns		0.9723		
28d vs. 49d	-5.82	-131.4 to 119.8	No	ns	>0.9999			
28d vs. 56d	-2.38	-128.0 to 123.2	No	ns	>0.9999			
35d vs. 42d	5.18	-120.4 to 130.8	No	ns	>0.9999			
35d vs. 49d	-37	-162.6 to 88.60	No	ns		0.9698		
35d vs. 56d	-33.56	-159.2 to 92.04	No	ns		0.9815		
42d vs. 49d	-42.18	-167.8 to 83.42	No	ns		0.9436		
42d vs. 56d	-38.74	-164.3 to 86.86	No	ns		0.9622		
49d vs. 56d	3.44	-122.2 to 129.0	No	ns	>0.9999			
Female								
7d vs. 21d	-13.68	-139.3 to 111.9	No	ns		0.9999		
7d vs. 28d	6.92	-118.7 to 132.5	No	ns	>0.9999			
7d vs. 35d	-12.62	-138.2 to 113.0	No	ns	>0.9999			
7d vs. 42d	-7.58	-133.2 to 118.0	No	ns	>0.9999			
7d vs. 49d	76.44	49.16 to 202.0	No	ns		0.5078		
7d vs. 56d	-19.38	-145.0 to 106.2	No	ns		0.9991		
21d vs. 28d	20.6	-105.0 to 146.2	No	ns		0.9987		
21d vs. 35d	1.06	-124.5 to 126.7	No	ns	>0.9999			
21d vs. 42d	6.1	-119.5 to 131.7	No	ns	>0.9999			
21d vs. 49d	90.12	-35.48 to 215.7	No	ns		0.3107		
21d vs. 56d	-5.7	-131.3 to 119.9	No	ns	>0.9999			
28d vs. 35d	-19.54	-145.1 to 106.1	No	ns		0.999		
28d vs. 42d	-14.5	-140.1 to 111.1	No	ns		0.9998		
28d vs. 49d	69.52	-56.08 to 195.1	No	ns		0.6174		
28d vs. 56d	-26.3	-151.9 to 99.30	No	ns		0.9949		
35d vs. 42d	5.04	-120.6 to 130.6	No	ns	>0.9999			
35d vs. 49d	89.06	-36.54 to 214.7	No	ns		0.3243		
35d vs. 56d	-6.76	-132.4 to 118.8	No	ns	>0.9999			
42d vs. 49d	84.02	-41.58 to 209.6	No	ns		0.3933		
42d vs. 56d	-11.8	-137.4 to 113.8	No	ns	>0.9999			
49d vs. 56d	-95.82	-221.4 to 29.78	No	ns		0.2436		

Change in Distance Traveled (m)						Baseline Distance Traveled (m)		
Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means		Column B vs. Column A	Female vs. Male
Time x Sex		3.799	0.4402 ns	No	Mean of Male	-1.528		
Time		14.04	0.0044 **	Yes	Mean of Female	1.005		
Sex		20.82	0.0484 *	Yes	Difference between means	-2.532		
Subject		30.76 <0.0001	****	Yes	SE of difference	1.088		
					95% CI of difference	-5.042 to -0.02291		
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.		Below threshold?	Summary	Adjusted P Value	Unpaired t test P value	0.2641
7d							P value summary	ns
Male vs. Female	-2.555	-5.633 to 0.5236		No	ns	0.102	Significantly different (P < 0.05)?	No
21d							One- or two-tailed P value?	Two-tailed
Male vs. Female	-2.372	-5.450 to 0.7068		No	ns	0.1284	t, df	t=1.201, df=8
28d							Mean of column A	9.209
Male vs. Female	-2.461	-5.539 to 0.6176		No	ns	0.1149	Mean of column B	7.456
35d							Difference between means (B - A) ± SEM	-1.753 ± 1.459
Male vs. Female	-4.306	-7.385 to -1.228		Yes	**	0.007	95% confidence interval	-5.118 to 1.613
42d							R squared (eta squared)	0.1528
Male vs. Female	-3.639	-6.717 to -0.5604		Yes	*	0.0214		
49d								
Male vs. Female	-0.8634	-3.942 to 2.215		No	ns	0.5765		
56d								
Male vs. Female	-1.531	-4.610 to 1.547		No	ns	0.3233		
Male								
7d vs. 21d	-0.8688	-4.475 to 2.737		No	ns	0.9891		
7d vs. 28d	-1.567	-5.173 to 2.039		No	ns	0.8309		
7d vs. 35d	-1.868	-5.474 to 1.738		No	ns	0.6868		
7d vs. 42d	-1.375	-4.980 to 2.231		No	ns	0.9008		
7d vs. 49d	-2.924	-6.530 to 0.6817		No	ns	0.1841		
7d vs. 56d	-3.806	-7.412 to -0.2005		Yes	*	0.0323		
21d vs. 28d	-0.6984	-4.304 to 2.907		No	ns	0.9966		
21d vs. 35d	-0.999	-4.605 to 2.607		No	ns	0.9777		
21d vs. 42d	-0.5058	-4.112 to 3.100		No	ns	0.9995		
21d vs. 49d	-2.055	-5.661 to 1.551		No	ns	0.5846		
21d vs. 56d	-2.937	-6.543 to 0.6683		No	ns	0.18		
28d vs. 35d	-0.3006	-3.906 to 3.305		No	ns	>0.9999		
28d vs. 42d	0.1926	-3.413 to 3.798		No	ns	>0.9999		
28d vs. 49d	-1.357	-4.963 to 2.249		No	ns	0.9062		
28d vs. 56d	-2.239	-5.845 to 1.367		No	ns	0.4836		
35d vs. 42d	0.4932	-3.113 to 4.099		No	ns	0.9995		
35d vs. 49d	-1.056	-4.662 to 2.550		No	ns	0.9706		
35d vs. 56d	-1.938	-5.544 to 1.667		No	ns	0.6488		
42d vs. 49d	-1.549	-5.155 to 2.056		No	ns	0.8382		
42d vs. 56d	-2.432	-6.037 to 1.174		No	ns	0.3836		
49d vs. 56d	-0.8822	-4.488 to 2.724		No	ns	0.9882		
Female								
7d vs. 21d	-0.6856	-4.291 to 2.920		No	ns	0.997		
7d vs. 28d	-1.473	-5.079 to 2.133		No	ns	0.8676		
7d vs. 35d	-3.619	-7.225 to -0.01369		Yes	*	0.0486		
7d vs. 42d	-2.459	-6.064 to 1.147		No	ns	0.3704		
7d vs. 49d	-1.233	-4.838 to 2.373		No	ns	0.9388		
7d vs. 56d	-2.783	-6.388 to 0.8231		No	ns	0.2318		
21d vs. 28d	-0.7876	-4.393 to 2.818		No	ns	0.9936		
21d vs. 35d	-2.934	-6.540 to 0.6719		No	ns	0.1811		
21d vs. 42d	-1.773	-5.379 to 1.833		No	ns	0.7358		
21d vs. 49d	-0.547	-4.153 to 3.059		No	ns	0.9991		
21d vs. 56d	-2.097	-5.703 to 1.509		No	ns	0.5615		
28d vs. 35d	-2.146	-5.752 to 1.460		No	ns	0.5343		
28d vs. 42d	-0.9854	-4.591 to 2.620		No	ns	0.9792		
28d vs. 49d	0.2406	-3.365 to 3.846		No	ns	>0.9999		
28d vs. 56d	-1.309	-4.915 to 2.296		No	ns	0.9197		
35d vs. 42d	1.161	-2.445 to 4.767		No	ns	0.9537		
35d vs. 49d	2.387	-1.219 to 5.993		No	ns	0.406		
35d vs. 56d	0.8368	-2.769 to 4.443		No	ns	0.9911		
42d vs. 49d	1.226	-2.380 to 4.832		No	ns	0.9403		
42d vs. 56d	-0.324	-3.930 to 3.282		No	ns	>0.9999		
49d vs. 56d	-1.55	-5.156 to 2.056		No	ns	0.838		

Change in Head Distance Traveled (m)										Baseline Head Distance Traveled (m)		
Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means					Column B vs. Column A	Female vs. Male	
Time x Sex	7.153	0.1628	ns	No	Mean of Male	-2.435						
Time	8.911	0.0818	ns	No	Mean of Female	1.916						
Sex	35.06	0.0019	**	Yes	Difference between means	-4.351						
Subject	13.5	0.0364	*	Yes	SE of difference	0.9545						
					95% CI of difference	-6.552 to -2.150						
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value					Unpaired t test	0.1385	
										P value		
										P value summary	ns	
										Significantly different (P < 0.05)?	No	
										One- or two-tailed P value?	Two-tailed	
										t, df	t=1.645, df=8	
7d										Mean of column A	17.06	
Male vs. Female	-4.114	-7.751 to -0.4755	Yes	*	0.0274					Mean of column B	14.04	
21d										Difference between means (B - A) ± SEM	-3.019 ± 1.935	
Male vs. Female	-4.282	-7.920 to -0.6437	Yes	*	0.0219					95% confidence interval	-7.250 to 1.212	
28d										R squared (eta squared)	0.2528	
Male vs. Female	-3.769	-7.406 to -0.1305	Yes	*	0.0426							
35d												
Male vs. Female	-7.082	-10.72 to -3.444	Yes	***	0.0003							
42d												
Male vs. Female	-6.701	-10.34 to -3.063	Yes	***	0.0005							
49d												
Male vs. Female	-0.6955	-4.333 to 2.942	No	ns	0.7032							
56d												
Male vs. Female	-3.814	-7.452 to -0.1757	Yes	*	0.0402							
Male												
7d vs. 21d	-0.8876	-6.022 to 4.247	No	ns	0.9982							
7d vs. 28d	-2.075	-7.210 to 3.059	No	ns	0.8733							
7d vs. 35d	-1.22	-6.354 to 3.915	No	ns	0.9899							
7d vs. 42d	-1.434	-6.568 to 3.701	No	ns	0.9768							
7d vs. 49d	-3.876	-9.010 to 1.258	No	ns	0.2547							
7d vs. 56d	-3.666	-8.801 to 1.468	No	ns	0.3162							
21d vs. 28d	-1.188	-6.322 to 3.947	No	ns	0.9912							
21d vs. 35d	-0.332	-5.466 to 4.802	No	ns	>0.9999							
21d vs. 42d	-0.546	-5.680 to 4.588	No	ns	0.9999							
21d vs. 49d	-2.988	-8.123 to 2.146	No	ns	0.5605							
21d vs. 56d	-2.779	-7.913 to 2.356	No	ns	0.6417							
28d vs. 35d	0.8556	-4.279 to 5.990	No	ns	0.9986							
28d vs. 42d	0.6416	-4.493 to 5.776	No	ns	0.9997							
28d vs. 49d	-1.801	-6.935 to 3.334	No	ns	0.9312							
28d vs. 56d	-1.591	-6.726 to 3.543	No	ns	0.9614							
35d vs. 42d	-0.214	-5.348 to 4.920	No	ns	>0.9999							
35d vs. 49d	-2.656	-7.791 to 2.478	No	ns	0.688							
35d vs. 56d	-2.447	-7.581 to 2.688	No	ns	0.7628							
42d vs. 49d	-2.442	-7.577 to 2.692	No	ns	0.7643							
42d vs. 56d	-2.233	-7.367 to 2.902	No	ns	0.8306							
49d vs. 56d	0.2096	-4.925 to 5.344	No	ns	>0.9999							
Female												
7d vs. 21d	-1.056	-6.190 to 4.079	No	ns	0.9953							
7d vs. 28d	-1.73	-6.865 to 3.404	No	ns	0.9427							
7d vs. 35d	-4.188	-9.323 to 0.9462	No	ns	0.1788							
7d vs. 42d	-4.021	-9.155 to 1.114	No	ns	0.2172							
7d vs. 49d	-0.458	-5.592 to 4.676	No	ns	>0.9999							
7d vs. 56d	-3.367	-8.501 to 1.768	No	ns	0.4175							
21d vs. 28d	-0.6744	-5.809 to 4.460	No	ns	0.9996							
21d vs. 35d	-3.132	-8.267 to 2.002	No	ns	0.5049							
21d vs. 42d	-2.965	-8.099 to 2.170	No	ns	0.5697							
21d vs. 49d	0.5978	-4.537 to 5.732	No	ns	0.9998							
21d vs. 56d	-2.311	-7.445 to 2.824	No	ns	0.8071							
28d vs. 35d	-2.458	-7.592 to 2.676	No	ns	0.759							
28d vs. 42d	-2.29	-7.425 to 2.844	No	ns	0.8134							
28d vs. 49d	1.272	-3.862 to 6.407	No	ns	0.9874							
28d vs. 56d	-1.636	-6.771 to 3.498	No	ns	0.9558							
35d vs. 42d	0.1676	-4.967 to 5.302	No	ns	>0.9999							
35d vs. 49d	3.73	-1.404 to 8.865	No	ns	0.2966							
35d vs. 56d	0.8216	-4.313 to 5.956	No	ns	0.9988							
42d vs. 49d	3.563	-1.572 to 8.697	No	ns	0.3407							
42d vs. 56d	0.654	-4.460 to 5.788	No	ns	0.9997							
49d vs. 56d	-2.909	-8.043 to 2.226	No	ns	0.5916							
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF				
7d												
Male vs. Female	-4.315	-0.2015	-4.114	1.816		5	5	3.203			56	
21d												
Male vs. Female	-3.427	0.8543	-4.282	1.816		5	5	3.334			56	
28d												
Male vs. Female	-2.24	1.529	-3.769	1.816		5	5	2.935			56	
35d												
Male vs. Female	-3.095	3.987	-7.082	1.816		5	5	5.515			56	
42d												
Male vs. Female	-2.881	3.819	-6.701	1.816		5	5	5.218			56	
49d												
Male vs. Female	-0.439	0.2565	-0.6955	1.816		5	5	0.5416			56	
56d												
Male vs. Female	-0.6486	3.165	-3.814	1.816		5	5	2.97			56	
Male												
7d vs. 21d	-4.315	-3.427	-0.8876	1.669		5	5	0.7522			48	
7d vs. 28d	-4.315	-2.24	-2.075	1.669		5	5	1.759			48	
7d vs. 35d	-4.315	-3.095	-1.22	1.669		5	5	1.034			48	
7d vs. 42d	-4.315	-2.881	-1.434	1.669		5	5	1.215			48	
7d vs. 49d	-4.315	-0.439	-3.876	1.669		5	5	3.285			48	
7d vs. 56d	-4.315	-0.6486	-3.666	1.669		5	5	3.107			48	
21d vs. 28d	-3.427	-2.24	-1.188	1.669		5	5	1.006			48	
21d vs. 35d	-3.427	-3.095	-0.332	1.669		5	5	0.2814			48	
21d vs. 42d	-3.427	-2.881	-0.546	1.669		5	5	0.4627			48	
21d vs. 49d	-3.427	-0.439	-2.988	1.669		5	5	2.533			48	
21d vs. 56d	-3.427	-0.6486	-2.779	1.669		5	5	2.355			48	
28d vs. 35d	-2.24	-3.095	0.8556	1.669		5	5	0.7251			48	
28d vs. 42d	-2.24	-2.881	0.6416	1.669		5	5	0.5437			48	
28d vs. 49d	-2.24	-0.439	-1.801	1.669		5	5	1.526			48	
28d vs. 56d	-2.24	-0.6486	-1.591	1.669		5	5	1.348			48	
35d vs. 42d	-3.095	-2.881	-0.214	1.669		5	5	0.1814			48	
35d vs. 49d	-3.095	-0.439	-2.656	1.669		5	5	2.251			48	
35d vs. 56d	-3.095	-0.6486	-2.447	1.669		5	5	2.074			48	
42d vs. 49d	-2.881	-0.439	-2.442	1.669		5	5	2.07			48	
42d vs. 56d	-2.881	-0.6486	-2.233	1.669		5	5	1.892			48	
49d vs. 56d	-0.439	-0.6486	0.2096	1.669		5	5	0.1776			48	
Female												
7d vs. 21d	-0.2015	0.8543	-1.056	1.669		5	5	0.8947			48	
7d vs. 28d	-0.2015	1.529	-1.73	1.669		5	5	1.466			48	
7d vs. 35d	-0.2015	3.987	-4.188	1.669		5	5	3.549			48	
7d vs. 42d	-0.2015	3.819	-4.021	1.669		5	5	3.407			48	
7d vs. 49d	-0.2015	0.2565	-0.458	1.669		5	5	0.3881			48	
7d vs. 56d	-0.2015	3.165	-3.367	1.669		5	5	2.853			48	
21d vs. 28d	0.8543	1.529	-0.6744	1.669		5	5	0.5715			48	
21d vs. 35d	0.8543	3.987	-3.132	1.669		5	5	2.655			48	
21d vs. 42d	0.8543	3.819	-2.965	1.669		5	5	2.513			48	
21d vs. 49d	0.8543	0.2565	-0.5978	1.669		5	5	0.5066			48	
21d vs. 56d	0.8543	3.165	-2.311	1.669		5	5	1.958			48	
28d vs. 35d	1.529	3.987	-2.458	1.669		5	5	2.083			48	
28d vs. 42d	1.529	3.819	-2.29	1.669		5	5	1.941			48	
28d vs. 49d	1.529	0.2565	-1.272	1.669		5	5	1.078			48	
28d vs. 56d	1.529	3.165	-1.636	1.669		5	5	1.387			48	
35d vs. 42d	3.987	3.819	-0.1674	1.669		5	5	0.142			48	
35d vs. 49d	3.987	0.2565	-3.73	1.669		5	5	3.161			48	
35d vs. 56d	3.987	3.165	-0.8216	1.669		5	5	0.6963			48	
42d vs. 49d	3.819	0.2565	-3.563	1.669		5	5	3.019			48	
42d vs. 56d	3.819	3.165	-0.654	1.669		5	5	0.5542			48	
49d vs. 56d	0.2565	3.165	-2.909	1.669		5	5	2.465			48	

Change in Mean Speed (m/s)						Baseline Mean Speed (m/s)					
Source of Variation	% of total variation	P value	P value summary	Significant?	Mean of Male	-0.002657	Column B	Female			
Time x Sex	3.913	0.4477 ns		No	Mean of Female	0.001529	vs.	Male			
Time	13.86	0.0062 **		Yes	Difference between means	-0.004186	Column A				
Sex	20.7	0.0458 *		Yes	SE of difference	0.001772					
Subject	29.66 <0.0001	****		Yes	95% CI of difference	-0.008271 to -0.0001003					
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		Unpaired t test			0.0321	
							P value	*			
							P value summary				
							Significantly different (P < 0.05)?	Yes			
							One- or two-tailed P value?	Two-tailed			
							t, df	t=2.591, df=8			
7d							Mean of column A			0.0184	
Male vs. Female	-0.0043	-0.009412 to 0.000	No	ns		0.0975	Mean of column B			0.0125	
21d							Difference between means (B - A) ± SEM	-0.005900 ± 0.002277			
Male vs. Female	-0.0041	-0.009212 to 0.001	No	ns		0.1137	95% confidence interval	-0.01115 to -0.0006491			
28d							R squared (eta squared)	0.4563			
Male vs. Female	-0.0041	-0.009212 to 0.001	No	ns		0.1137					
35d											
Male vs. Female	-0.0071	-0.01221 to -0.0015	Yes	**		0.0073					
42d											
Male vs. Female	-0.0059	-0.01101 to -0.0007	Yes	*		0.0245					
49d											
Male vs. Female	-0.0011	-0.006212 to 0.004	No	ns		0.6681					
56d											
Male vs. Female	-0.0027	-0.007812 to 0.002	No	ns		0.2946					
Male											
7d vs. 21d	-0.0014	-0.007503 to 0.004	No	ns		0.9916					
7d vs. 28d	-0.0026	-0.008703 to 0.003	No	ns		0.8436					
7d vs. 35d	-0.0032	-0.009303 to 0.002	No	ns		0.6746					
7d vs. 42d	-0.0022	-0.008303 to 0.003	No	ns		0.9223					
7d vs. 49d	-0.005	-0.01110 to 0.0011	No	ns		0.175					
7d vs. 56d	-0.0062	-0.01230 to -0.0009	Yes	*		0.0442					
21d vs. 28d	-0.0012	-0.007303 to 0.004	No	ns		0.9964					
21d vs. 35d	-0.0018	-0.007903 to 0.004	No	ns		0.9696					
21d vs. 42d	-0.0008	-0.006903 to 0.005	No	ns		0.9996					
21d vs. 49d	-0.0036	-0.009703 to 0.002	No	ns		0.5449					
21d vs. 56d	-0.0048	-0.01090 to 0.0013	No	ns		0.2129					
28d vs. 35d	-0.0006	-0.006703 to 0.005	No	ns	>0.9999						
28d vs. 42d	0.0004	-0.005703 to 0.006	No	ns	>0.9999						
28d vs. 49d	-0.0024	-0.008503 to 0.003	No	ns		0.8869					
28d vs. 56d	-0.0036	-0.009703 to 0.002	No	ns		0.5449					
35d vs. 42d	0.001	-0.005103 to 0.007	No	ns		0.9987					
35d vs. 49d	-0.0018	-0.007903 to 0.004	No	ns		0.9696					
35d vs. 56d	-0.003	-0.009103 to 0.003	No	ns		0.7361					
42d vs. 49d	-0.0028	-0.008903 to 0.003	No	ns		0.793					
42d vs. 56d	-0.004	-0.01010 to 0.0021	No	ns		0.4181					
49d vs. 56d	-0.0012	-0.007303 to 0.004	No	ns		0.9964					
Female											
7d vs. 21d	-0.0012	-0.007303 to 0.004	No	ns		0.9964					
7d vs. 28d	-0.0024	-0.008503 to 0.003	No	ns		0.8869					
7d vs. 35d	-0.006	-0.01210 to 0.0001	No	ns		0.0568					
7d vs. 42d	-0.0038	-0.009903 to 0.002	No	ns		0.4803					
7d vs. 49d	-0.0018	-0.007903 to 0.004	No	ns		0.9696					
7d vs. 56d	-0.0046	-0.01070 to 0.0015	No	ns		0.2564					
21d vs. 28d	-0.0012	-0.007303 to 0.004	No	ns		0.9964					
21d vs. 35d	-0.0048	-0.01090 to 0.0013	No	ns		0.2129					
21d vs. 42d	-0.0026	-0.008703 to 0.003	No	ns		0.8436					
21d vs. 49d	-0.0006	-0.006703 to 0.005	No	ns	>0.9999						
21d vs. 56d	-0.0034	-0.009503 to 0.002	No	ns		0.6103					
28d vs. 35d	-0.0036	-0.009703 to 0.002	No	ns		0.5449					
28d vs. 42d	-0.0014	-0.007503 to 0.004	No	ns		0.9916					
28d vs. 49d	0.0006	-0.005503 to 0.006	No	ns	>0.9999						
28d vs. 56d	-0.0022	-0.008303 to 0.003	No	ns		0.9223					
35d vs. 42d	0.0022	-0.003903 to 0.008	No	ns		0.9223					
35d vs. 49d	0.0042	-0.001903 to 0.010	No	ns		0.3594					
35d vs. 56d	0.0014	-0.004703 to 0.007	No	ns		0.9916					
42d vs. 49d	0.002	-0.004103 to 0.008	No	ns		0.9496					
42d vs. 56d	-0.0008	-0.006903 to 0.005	No	ns		0.9996					
49d vs. 56d	-0.0028	-0.008903 to 0.003	No	ns		0.793					
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF			
7d											
Male vs. Female	-0.0056	-0.0013	-0.0043	0.002552		5	5	2.383		56	
21d											
Male vs. Female	-0.0042	-0.0001	-0.0041	0.002552		5	5	2.272		56	
28d											
Male vs. Female	-0.003	0.0011	-0.0041	0.002552		5	5	2.272		56	
35d											
Male vs. Female	-0.0024	0.0047	-0.0071	0.002552		5	5	3.935		56	
42d											
Male vs. Female	-0.0034	0.0025	-0.0059	0.002552		5	5	3.27		56	
49d											
Male vs. Female	-0.0006	0.0005	-0.0011	0.002552		5	5	0.6096		56	
56d											
Male vs. Female	0.0006	0.0033	-0.0027	0.002552		5	5	1.496		56	
Male											
7d vs. 21d	-0.0056	-0.0042	-0.0014	0.001984		5	5	0.9981		48	
7d vs. 28d	-0.0056	-0.003	-0.0026	0.001984		5	5	1.854		48	
7d vs. 35d	-0.0056	-0.0024	-0.0032	0.001984		5	5	2.281		48	
7d vs. 42d	-0.0056	-0.0034	-0.0022	0.001984		5	5	1.568		48	
7d vs. 49d	-0.0056	-0.0006	-0.005	0.001984		5	5	3.565		48	
7d vs. 56d	-0.0056	0.0006	-0.0062	0.001984		5	5	4.42		48	
21d vs. 28d	-0.0042	-0.003	-0.0012	0.001984		5	5	0.8555		48	
21d vs. 35d	-0.0042	-0.0024	-0.0018	0.001984		5	5	1.283		48	
21d vs. 42d	-0.0042	-0.0034	-0.0008	0.001984		5	5	0.5704		48	
21d vs. 49d	-0.0042	-0.0006	-0.0036	0.001984		5	5	2.567		48	
21d vs. 56d	-0.0042	0.0006	-0.0048	0.001984		5	5	3.422		48	
28d vs. 35d	-0.003	-0.0024	-0.0006	0.001984		5	5	0.4278		48	
28d vs. 42d	-0.003	-0.0034	0.0004	0.001984		5	5	0.2852		48	
28d vs. 49d	-0.003	-0.0006	-0.0024	0.001984		5	5	1.711		48	
28d vs. 56d	-0.003	0.0006	-0.0036	0.001984		5	5	2.567		48	
35d vs. 42d	-0.0024	-0.0034	0.001	0.001984		5	5	0.7129		48	
35d vs. 49d	-0.0024	-0.0006	-0.0018	0.001984		5	5	1.283		48	
35d vs. 56d	-0.0024	0.0006	-0.003	0.001984		5	5	2.139		48	
42d vs. 49d	-0.0034	-0.0006	-0.0028	0.001984		5	5	1.996		48	
42d vs. 56d	-0.0034	0.0006	-0.004	0.001984		5	5	2.852		48	
49d vs. 56d	-0.0006	0.0006	-0.0012	0.001984		5	5	0.8555		48	
Female											
7d vs. 21d	-0.0013	-0.0001	-0.0012	0.001984		5	5	0.8555		48	
7d vs. 28d	-0.0013	0.0011	-0.0024	0.001984		5	5	1.711		48	
7d vs. 35d	-0.0013	0.0047	-0.006	0.001984		5	5	4.278		48	
7d vs. 42d	-0.0013	0.0025	-0.0038	0.001984		5	5	2.709		48	
7d vs. 49d	-0.0013	0.0005	-0.0018	0.001984		5	5	1.283		48	
7d vs. 56d	-0.0013	0.0033	-0.0046	0.001984		5	5	3.28		48	
21d vs. 28d	-0.0001	0.0011	-0.0012	0.001984		5	5	0.8555		48	
21d vs. 35d	-0.0001	0.0047	-0.0048	0.001984		5	5	3.422		48	
21d vs. 42d	-0.0001	0.0025	-0.0026	0.001984		5	5	1.854		48	
21d vs. 49d	-0.0001	0.0005	-0.0006	0.001984		5	5	0.4278		48	
21d vs. 56d	-0.0001	0.0033	-0.0034	0.001984		5	5	2.424		48	
28d vs. 35d	0.0011	0.0047	-0.0036	0.001984		5	5	2.567		48	
28d vs. 42d	0.0011	0.0025	-0.0014	0.001984		5	5	0.9981		48	
28d vs. 49d	0.0011	0.0005	0.0006	0.001984		5	5	0.4278		48	
28d vs. 56d	0.0011	0.0033	-0.0022	0.001984		5	5	1.568		48	
35d vs. 42d	0.0047	0.0025	0.0022	0.001984		5	5	1.568		48	
35d vs. 49d	0.0047	0.0005	0.0042	0.001984		5	5	2.994		48	
35d vs. 56d	0.0047	0.0033	0.0014	0.001984		5	5	0.9981		48	
42d vs. 49d	0.0025	0.0005									

Change in Mean Speed not Hidden (m/s)						Baseline Mean Speed not Hidden (m/s)				
Source of Variation	% of total variation	P value	P value summary	Significant?	Mean of Male	-0.003486	Column B vs. Column A	Female vs. Male		
Time x Sex	2.933	0.6407	ns	No	Mean of Female	-0.0003143				
Time	12.37	0.0141	*	Yes	Difference between means	-0.003171				
Sex	8.288	0.2521	ns	No	SE of difference	0.002569				
Subject	43.51	<0.0001	****	Yes	95% CI of difference	-0.009096 to 0.002753				
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		Unpaired t test	P value	0.665	
7d							P value summary	ns		
Male vs. Female	-0.0028	-0.009620 to 0.004	No	ns	0.4143		Significantly different (P < 0.05)?	No		
21d							One- or two-tailed P value?	Two-tailed t, df		
Male vs. Female	-0.0026	-0.009420 to 0.004	No	ns	0.4483		Mean of column A	0.0184		
28d							Mean of column B	0.0172		
Male vs. Female	-0.004	-0.01082 to 0.0028	No	ns	0.245		Difference between means (B - A) ± SEM	-0.001200 ± 0.002869		
35d							95% confidence interval	-0.007355 to 0.004955		
Male vs. Female	-0.0062	-0.01302 to 0.0006	No	ns	0.0739		R squared (eta squared)	0.02464		
42d										
Male vs. Female	-0.0048	-0.01162 to 0.0020	No	ns	0.1641					
49d										
Male vs. Female	-1.735E-18	-0.006820 to 0.006	No	ns	>0.9999					
56d										
Male vs. Female	-0.0018	-0.008620 to 0.005	No	ns	0.5991					
Male										
7d vs. 21d	-0.0012	-0.008624 to 0.006	No	ns	0.9988					
7d vs. 28d	-0.002	-0.009424 to 0.005	No	ns	0.9807					
7d vs. 35d	-0.0036	-0.01102 to 0.0038	No	ns	0.748					
7d vs. 42d	-0.003	-0.01042 to 0.0044	No	ns	0.8734					
7d vs. 49d	-0.0044	-0.01182 to 0.0030	No	ns	0.5393					
7d vs. 56d	-0.0062	-0.01362 to 0.0012	No	ns	0.1585					
21d vs. 28d	-0.0008	-0.008224 to 0.006	No	ns	0.9999					
21d vs. 35d	-0.0024	-0.009824 to 0.005	No	ns	0.9528					
21d vs. 42d	-0.0018	-0.009224 to 0.005	No	ns	0.9888					
21d vs. 49d	-0.0032	-0.01062 to 0.0042	No	ns	0.8363					
21d vs. 56d	-0.005	-0.01242 to 0.0024	No	ns	0.3851					
28d vs. 35d	-0.0016	-0.009024 to 0.005	No	ns	0.994					
28d vs. 42d	-0.001	-0.008424 to 0.006	No	ns	0.9996					
28d vs. 49d	-0.0024	-0.009824 to 0.005	No	ns	0.9528					
28d vs. 56d	-0.0042	-0.01162 to 0.0032	No	ns	0.593					
35d vs. 42d	0.0006	-0.006824 to 0.008	No	ns	>0.9999					
35d vs. 49d	-0.0008	-0.008224 to 0.006	No	ns	0.9999					
35d vs. 56d	-0.0026	-0.01002 to 0.0048	No	ns	0.9317					
42d vs. 49d	-0.0014	-0.008824 to 0.006	No	ns	0.9971					
42d vs. 56d	-0.0032	-0.01062 to 0.0042	No	ns	0.8363					
49d vs. 56d	-0.0018	-0.009224 to 0.005	No	ns	0.9888					
Female										
7d vs. 21d	-0.001	-0.008424 to 0.006	No	ns	0.9996					
7d vs. 28d	-0.0032	-0.01062 to 0.0042	No	ns	0.8363					
7d vs. 35d	-0.007	-0.01442 to 0.0004	No	ns	0.0764					
7d vs. 42d	-0.005	-0.01242 to 0.0024	No	ns	0.3851					
7d vs. 49d	-0.0016	-0.009024 to 0.005	No	ns	0.994					
7d vs. 56d	-0.0052	-0.01262 to 0.0022	No	ns	0.3386					
21d vs. 28d	-0.0022	-0.009624 to 0.005	No	ns	0.9689					
21d vs. 35d	-0.006	-0.01342 to 0.0014	No	ns	0.1871					
21d vs. 42d	-0.004	-0.01142 to 0.0034	No	ns	0.6464					
21d vs. 49d	-0.0006	-0.008024 to 0.006	No	ns	>0.9999					
21d vs. 56d	-0.0042	-0.01162 to 0.0032	No	ns	0.593					
28d vs. 35d	-0.0038	-0.01122 to 0.0036	No	ns	0.6985					
28d vs. 42d	-0.0018	-0.009224 to 0.005	No	ns	0.9888					
28d vs. 49d	0.0016	-0.005824 to 0.009	No	ns	0.994					
28d vs. 56d	-0.002	-0.009424 to 0.005	No	ns	0.9807					
35d vs. 42d	0.002	-0.005424 to 0.009	No	ns	0.9807					
35d vs. 49d	0.0054	-0.002024 to 0.012	No	ns	0.2952					
35d vs. 56d	0.0018	-0.005624 to 0.009	No	ns	0.9888					
42d vs. 49d	0.0034	-0.004024 to 0.010	No	ns	0.7943					
42d vs. 56d	-0.0002	-0.007624 to 0.007	No	ns	>0.9999					
49d vs. 56d	-0.0036	-0.01102 to 0.0038	No	ns	0.748					
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF		
7d										
Male vs. Female	-0.0064	-0.0036	-0.0028	0.003405		5	5	1.163	56	
21d										
Male vs. Female	-0.0052	-0.0026	-0.0026	0.003405		5	5	1.08	56	
28d										
Male vs. Female	-0.0044	-0.0004	-0.004	0.003405		5	5	1.662	56	
35d										
Male vs. Female	-0.0028	0.0034	-0.0062	0.003405		5	5	2.575	56	
42d										
Male vs. Female	-0.0034	0.0014	-0.0048	0.003405		5	5	1.994	56	
49d										
Male vs. Female	-0.002	-0.002	-1.735E-18	0.003405		5	5	7.21E-16	56	
56d										
Male vs. Female	-0.0002	0.0016	-0.0018	0.003405		5	5	0.7477	56	
Male										
7d vs. 21d	-0.0064	-0.0052	-0.0012	0.002413		5	5	0.7033	48	
7d vs. 28d	-0.0064	-0.0044	-0.002	0.002413		5	5	1.172	48	
7d vs. 35d	-0.0064	-0.0028	-0.0036	0.002413		5	5	2.11	48	
7d vs. 42d	-0.0064	-0.0034	-0.003	0.002413		5	5	1.758	48	
7d vs. 49d	-0.0064	-0.002	-0.0044	0.002413		5	5	2.579	48	
7d vs. 56d	-0.0064	-0.0002	-0.0062	0.002413		5	5	3.634	48	
21d vs. 28d	-0.0052	-0.0044	-0.0008	0.002413		5	5	0.4689	48	
21d vs. 35d	-0.0052	-0.0028	-0.0024	0.002413		5	5	1.407	48	
21d vs. 42d	-0.0052	-0.0034	-0.0018	0.002413		5	5	1.055	48	
21d vs. 49d	-0.0052	-0.002	-0.0032	0.002413		5	5	1.876	48	
21d vs. 56d	-0.0052	-0.0002	-0.005	0.002413		5	5	2.931	48	
28d vs. 35d	-0.0044	-0.0028	-0.0016	0.002413		5	5	0.9378	48	
28d vs. 42d	-0.0044	-0.0034	-0.001	0.002413		5	5	0.5861	48	
28d vs. 49d	-0.0044	-0.002	-0.0024	0.002413		5	5	1.407	48	
28d vs. 56d	-0.0044	-0.0002	-0.0042	0.002413		5	5	2.462	48	
35d vs. 42d	-0.0028	-0.0034	0.0006	0.002413		5	5	0.3517	48	
35d vs. 49d	-0.0028	-0.002	-0.0008	0.002413		5	5	0.4689	48	
35d vs. 56d	-0.0028	-0.0002	-0.0026	0.002413		5	5	1.524	48	
42d vs. 49d	-0.0034	-0.002	-0.0014	0.002413		5	5	0.8206	48	
42d vs. 56d	-0.0034	-0.0002	-0.0032	0.002413		5	5	1.876	48	
49d vs. 56d	-0.002	-0.0002	-0.0018	0.002413		5	5	1.055	48	
Female										
7d vs. 21d	-0.0036	-0.0026	-0.001	0.002413		5	5	0.5861	48	
7d vs. 28d	-0.0036	-0.0004	-0.0032	0.002413		5	5	1.876	48	
7d vs. 35d	-0.0036	0.0004	-0.007	0.002413		5	5	4.103	48	
7d vs. 42d	-0.0036	0.0014	-0.005	0.002413		5	5	2.931	48	
7d vs. 49d	-0.0036	-0.002	-0.0016	0.002413		5	5	0.9378	48	
7d vs. 56d	-0.0036	0.0016	-0.0052	0.002413		5	5	3.048	48	
21d vs. 28d	-0.0026	-0.0004	-0.0002	0.002413		5	5	1.289	48	
21d vs. 35d	-0.0026	0.0034	-0.006	0.002413		5	5	3.517	48	
21d vs. 42d	-0.0026	0.0014	-0.004	0.002413		5	5	2.344	48	
21d vs. 49d	-0.0026	-0.002	-0.0006	0.002413		5	5	0.3517	48	
21d vs. 56d	-0.0026	0.0016	-0.0042	0.002413		5	5	2.462	48	
28d vs. 35d	-0.0004	0.0034	-0.0038	0.002413		5	5	2.227	48	
28d vs. 42d	-0.0004	0.0014	-0.0018	0.002413		5	5	1.055	48	
28d vs. 49d	-0.0004	-0.002	0.0016	0.002413		5	5	0.9378	48	
28d vs. 56d	-0.0004	0.0016	-0.002	0.002413		5	5	1.172	48	
35d vs. 42d	0.0034	0.0014	0.002	0.002413		5	5	1.722	48	
35d vs. 49d	0.0034	-0.002	0.0054	0.002413		5	5	3.165	48	
35d vs. 56d	0.0034	0.0016	0.0018	0.002413		5	5	1.055	48	
42d vs. 49d	0.0014	0.002	0.0034	0.002413		5	5	1.993	48	
42d vs. 56d	0.0014	0.0016	-0.0002	0.002413		5	5	0.1172	48	
49d vs. 56d	-0.002	0.0016	-0.0036	0.002413		5	5	2.11	48	

Change in Max Speed (m/s)					Baseline Max Speed (m/s)				
Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means			Column B vs. Column A	Female vs. Male
Time x Sex	4.796	0.6642 ns		No	Mean of Male	-0.04077			
Time	5.928	0.5425 ns		No	Mean of Female	0.008557			
Sex	7.545	0.1628 ns		No	Difference between means	-0.04933			
Subject	25.54	0.0146 *		Yes	SE of difference	0.03209			
					95% CI of difference	-0.1233 to 0.02467		Unpaired t test	
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value			P value	0.0803
								P value summary	
								Significantly different (P < 0.05)?	ns
								One- or two-tailed P value?	No
								t, df	Two-tailed t=2.001, df=8
7d								Mean of column A	0.2614
Male vs. Female	-0.0097	-0.1247 to 0.1053	No	ns	0.8664			Mean of column B	0.2079
21d								Difference between means (B - A) ± SEM	-0.05350 ± 0.02673
Male vs. Female	-0.0209	-0.1359 to 0.09409	No	ns	0.7172			95% confidence interval	-0.1151 to 0.008144
28d								R squared (eta squared)	0.3336
Male vs. Female	-0.0551	-0.1701 to 0.05989	No	ns	0.3412				
35d									
Male vs. Female	-0.0913	-0.2063 to 0.02369	No	ns	0.1173				
42d									
Male vs. Female	-0.1197	-0.2347 to -0.00471	Yes	*	0.0416				
49d									
Male vs. Female	-0.0393	-0.1543 to 0.07569	No	ns	0.4964				
56d									
Male vs. Female	-0.0093	-0.1243 to 0.1057	No	ns	0.8719				
Male									
7d vs. 21d	-0.0294	-0.1876 to 0.1288	No	ns	0.9973				
7d vs. 28d	0.0111	-0.1472 to 0.1692	No	ns	>0.9999				
7d vs. 35d	0.0374	-0.1208 to 0.1956	No	ns	0.9902				
7d vs. 42d	0.0092	-0.1490 to 0.1674	No	ns	>0.9999				
7d vs. 49d	0.0162	-0.1420 to 0.1744	No	ns	>0.9999				
7d vs. 56d	-0.0558	-0.2140 to 0.1024	No	ns			0.9294		
21d vs. 28d	0.0404	-0.1178 to 0.1986	No	ns			0.9853		
21d vs. 35d	0.0668	-0.09137 to 0.2250	No	ns			0.8489		
21d vs. 42d	0.0386	-0.1196 to 0.1968	No	ns			0.9884		
21d vs. 49d	0.0456	-0.1126 to 0.2038	No	ns			0.9728		
21d vs. 56d	-0.0284	-0.1846 to 0.1318	No	ns			0.9985		
28d vs. 35d	0.0264	-0.1318 to 0.1846	No	ns			0.9985		
28d vs. 42d	-0.0018	-0.1600 to 0.1564	No	ns	>0.9999				
28d vs. 49d	0.0052	-0.1530 to 0.1634	No	ns	>0.9999				
28d vs. 56d	-0.0668	-0.2250 to 0.09137	No	ns			0.8489		
35d vs. 42d	-0.0282	-0.1864 to 0.1300	No	ns			0.9979		
35d vs. 49d	-0.0212	-0.1794 to 0.1370	No	ns			0.9996		
35d vs. 56d	-0.0932	-0.2514 to 0.06497	No	ns			0.5462		
42d vs. 49d	0.007	-0.1512 to 0.1652	No	ns	>0.9999				
42d vs. 56d	-0.065	-0.2232 to 0.09317	No	ns			0.8645		
49d vs. 56d	-0.072	-0.2302 to 0.08617	No	ns			0.7988		
Female									
7d vs. 21d	-0.0406	-0.1988 to 0.1176	No	ns	0.9849				
7d vs. 28d	-0.0344	-0.1926 to 0.1238	No	ns	0.9937				
7d vs. 35d	-0.0442	-0.2024 to 0.1140	No	ns	0.9767				
7d vs. 42d	-0.1008	-0.2590 to 0.05737	No	ns	0.4521				
7d vs. 49d	-0.0134	-0.1716 to 0.1448	No	ns	>0.9999				
7d vs. 56d	-0.0554	-0.2136 to 0.1028	No	ns	0.9316				
21d vs. 28d	0.0062	-0.1520 to 0.1644	No	ns	>0.9999				
21d vs. 35d	-0.0036	-0.1618 to 0.1546	No	ns	>0.9999				
21d vs. 42d	-0.0602	-0.2184 to 0.09797	No	ns	0.9015				
21d vs. 49d	0.0272	-0.1310 to 0.1854	No	ns	0.9983				
21d vs. 56d	-0.0148	-0.1730 to 0.1434	No	ns	>0.9999				
28d vs. 35d	-0.0098	-0.1680 to 0.1484	No	ns	>0.9999				
28d vs. 42d	-0.0664	-0.2246 to 0.09177	No	ns			0.8524		
28d vs. 49d	0.021	-0.1372 to 0.1792	No	ns			0.9996		
28d vs. 56d	-0.021	-0.1792 to 0.1372	No	ns			0.9996		
35d vs. 42d	-0.0566	-0.2148 to 0.1016	No	ns			0.9247		
35d vs. 49d	0.0308	-0.1274 to 0.1890	No	ns			0.9965		
35d vs. 56d	-0.0112	-0.1694 to 0.1470	No	ns	>0.9999				
42d vs. 49d	0.0874	-0.07077 to 0.2456	No	ns			0.6193		
42d vs. 56d	0.0454	-0.1128 to 0.2036	No	ns			0.9734		
49d vs. 56d	-0.042	-0.2002 to 0.1162	No	ns			0.982		
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF	
7d Male vs. Female	-0.0424	-0.0327	-0.0097	0.0574		5	5	0.239	56
21d Male vs. Female	-0.013	0.0079	-0.0209	0.0574		5	5	0.5149	56
28d Male vs. Female	-0.0534	0.0017	-0.0551	0.0574		5	5	1.358	56
35d Male vs. Female	-0.0798	0.0115	-0.0913	0.0574		5	5	2.249	56
42d Male vs. Female	-0.0516	0.0681	-0.1197	0.0574		5	5	2.949	56
49d Male vs. Female	-0.0586	-0.0193	-0.0393	0.0574		5	5	0.9682	56
56d Male vs. Female	0.0134	0.0227	-0.0093	0.0574		5	5	0.2291	56
Male									
7d vs. 21d	-0.0424	-0.013	-0.0294	0.05141		5	5	0.8088	48
7d vs. 28d	-0.0424	-0.0534	0.011	0.05141		5	5	0.3026	48
7d vs. 35d	-0.0424	-0.0798	0.0374	0.05141		5	5	1.029	48
7d vs. 42d	-0.0424	-0.0516	0.0092	0.05141		5	5	0.2531	48
7d vs. 49d	-0.0424	-0.0586	0.0162	0.05141		5	5	0.4456	48
7d vs. 56d	-0.0424	0.0134	-0.0558	0.05141		5	5	1.535	48
21d vs. 28d	-0.013	-0.0534	0.0404	0.05141		5	5	1.111	48
21d vs. 35d	-0.013	-0.0798	0.0668	0.05141		5	5	1.838	48
21d vs. 42d	-0.013	-0.0516	0.0386	0.05141		5	5	1.062	48
21d vs. 49d	-0.013	-0.0586	0.0456	0.05141		5	5	1.254	48
21d vs. 56d	-0.013	0.0134	-0.0264	0.05141		5	5	0.7262	48
28d vs. 35d	-0.0534	-0.0798	0.0264	0.05141		5	5	0.7262	48
28d vs. 42d	-0.0534	-0.0516	-0.0018	0.05141		5	5	0.04952	48
28d vs. 49d	-0.0534	-0.0586	0.0052	0.05141		5	5	0.143	48
28d vs. 56d	-0.0534	0.0134	-0.0668	0.05141		5	5	1.838	48
35d vs. 42d	-0.0798	-0.0516	-0.0282	0.05141		5	5	0.7758	48
35d vs. 49d	-0.0798	-0.0586	-0.0212	0.05141		5	5	0.5832	48
35d vs. 56d	-0.0798	0.0134	-0.0932	0.05141		5	5	2.564	48
42d vs. 49d	-0.0516	-0.0586	0.007	0.05141		5	5	0.1926	48
42d vs. 56d	-0.0516	0.0134	-0.065	0.05141		5	5	1.788	48
49d vs. 56d	-0.0586	0.0134	-0.072	0.05141		5	5	1.981	48
Female									
7d vs. 21d	-0.0327	0.0079	-0.0406	0.05141		5	5	1.117	48
7d vs. 28d	-0.0327	0.0017	-0.0344	0.05141		5	5	0.9463	48
7d vs. 35d	-0.0327	0.0115	-0.0442	0.05141		5	5	1.216	48
7d vs. 42d	-0.0327	0.0681	-0.1008	0.05141		5	5	2.773	48
7d vs. 49d	-0.0327	-0.0193	-0.0134	0.05141		5	5	0.3686	48
7d vs. 56d	-0.0327	0.0227	-0.0554	0.05141		5	5	1.524	48
21d vs. 28d	0.0079	0.0017	0.0062	0.05141		5	5	0.1706	48
21d vs. 35d	0.0079	0.0115	-0.0036	0.05141		5	5	0.09903	48
21d vs. 42d	0.0079	0.0681	-0.0602	0.05141		5	5	1.656	48
21d vs. 49d	0.0079	-0.0193	0.0272	0.05141		5	5	0.7482	48
21d vs. 56d	0.0079	0.0227	-0.0148	0.05141		5	5	0.4071	48
28d vs. 35d	0.0017	0.0115	-0.0098	0.05141		5	5	0.2696	48
28d vs. 42d	0.0017	0.0681	-0.0664	0.05141		5	5	1.827	48
28d vs. 49d	0.0017	-0.0193	0.021	0.05141		5	5	0.5777	48
28d vs. 56d	0.0017	0.0227	-0.021	0.05141		5	5	0.5777	48
35d vs. 42d	0.0115	-0.0681	-0.0566	0.05141		5	5	1.557	48
35d vs. 49d	0.0115	-0.0193	0.0308	0.05141		5	5	0.8473	48
35d vs. 56d	0.0115	0.0227	-0.0112	0.05141		5	5	0.3081	48
42d vs. 49d	0.0681	-0.0193	0.0874	0.05141		5	5	2.404	48
42d vs. 56d	0.0681	0.0227	0.0454	0.05141		5	5	1.249	48
49d vs. 56d	-0.0193	0.0227	-0.042	0.05141		5	5	1.155	48

Change in Freezing Episodes

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	3.413	0.5483 ns	No	No	Mean of Male
Time	15.28	0.0039 **	Yes	Yes	Mean of Female
Sex	5.975	0.3207 ns	No	No	Difference between means
Subject	42.66 <0.0001	****	Yes	Yes	SE of difference
					95% CI of difference

Baseline Freezing Episodes

Column B	Female
vs.	Male
Column A	
Unpaired t test	0.9015
P value	
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.1277, df=8

Tukey's multiple comparisons test Mean Diff. 95.00% CI of diff. Below threshold? Summary Adjusted P Value

7d									
Male vs. Female	6.1	-8.952 to 21.15	No	ns		0.4203			
21d									
Male vs. Female	-4.5	-19.55 to 10.55	No	ns		0.5517			
28d									
Male vs. Female	7.1	-7.952 to 22.15	No	ns		0.3488			
35d									
Male vs. Female	6.5	-8.552 to 21.55	No	ns		0.3907			
42d									
Male vs. Female	10.3	-4.752 to 25.35	No	ns		0.1759			
49d									
Male vs. Female	9.5	-5.552 to 24.55	No	ns		0.2114			
56d									
Male vs. Female	6.9	-8.152 to 21.95	No	ns		0.3624			
Male									
7d vs. 21d	9.2	-7.243 to 25.64	No	ns		0.6055			
7d vs. 28d	12.4	-4.043 to 28.84	No	ns		0.2558			
7d vs. 35d	12	-4.443 to 28.44	No	ns		0.2916			
7d vs. 42d	9	-7.443 to 25.44	No	ns		0.6296			
7d vs. 49d	10.4	-6.043 to 26.84	No	ns		0.4613			
7d vs. 56d	4.2	-12.24 to 20.64	No	ns		0.9853			
21d vs. 28d	3.2	-13.24 to 19.64	No	ns		0.9966			
21d vs. 35d	2.8	-13.64 to 19.24	No	ns		0.9984			
21d vs. 42d	-0.2	-16.64 to 16.24	No	ns	>0.9999				
21d vs. 49d	1.2	-15.24 to 17.64	No	ns	>0.9999				
21d vs. 56d	5	-21.44 to 11.44	No	ns		0.9647			
28d vs. 35d	-0.4	-16.84 to 16.04	No	ns	>0.9999				
28d vs. 42d	-3.4	-19.84 to 13.04	No	ns		0.9952			
28d vs. 49d	-2	-18.44 to 14.44	No	ns		0.9998			
28d vs. 56d	-8.2	-24.64 to 8.243	No	ns		0.7231			
35d vs. 42d	-3	-19.44 to 13.44	No	ns		0.9076			
35d vs. 49d	-1.6	-18.04 to 14.84	No	ns	>0.9999				
35d vs. 56d	-7.8	-24.24 to 8.643	No	ns		0.7666			
42d vs. 49d	1.4	-15.04 to 17.84	No	ns	>0.9999				
42d vs. 56d	-4.8	-21.24 to 11.64	No	ns		0.9711			
49d vs. 56d	-6.2	-22.64 to 10.24	No	ns		0.9054			
Female									
7d vs. 21d	-1.4	-17.84 to 15.04	No	ns	>0.9999				
7d vs. 28d	13.4	-3.043 to 29.84	No	ns		0.1797			
7d vs. 35d	12.4	-4.043 to 28.84	No	ns		0.2558			
7d vs. 42d	13.2	-3.243 to 29.64	No	ns		0.1934			
7d vs. 49d	13.8	-2.643 to 30.24	No	ns		0.1544			
7d vs. 56d	5	-11.44 to 21.44	No	ns		0.9647			
21d vs. 28d	14.8	-1.643 to 31.24	No	ns		0.1033			
21d vs. 35d	13.8	-2.643 to 30.24	No	ns		0.1544			
21d vs. 42d	14.6	-1.843 to 31.04	No	ns		0.1123			
21d vs. 49d	15.2	-1.243 to 31.64	No	ns		0.0872			
21d vs. 56d	6.4	-10.04 to 22.84	No	ns		0.8917			
28d vs. 35d	-1	-17.44 to 15.44	No	ns	>0.9999				
28d vs. 42d	-0.2	-16.64 to 16.24	No	ns	>0.9999				
28d vs. 49d	0.4	-16.04 to 16.84	No	ns	>0.9999				
28d vs. 56d	-8.4	-24.84 to 8.043	No	ns		0.7004			
35d vs. 42d	0.8	-15.64 to 17.24	No	ns	>0.9999				
35d vs. 49d	1.4	-15.04 to 17.84	No	ns	>0.9999				
35d vs. 56d	-7.4	-23.84 to 9.043	No	ns		0.8071			
42d vs. 49d	0.6	-15.84 to 17.04	No	ns	>0.9999				
42d vs. 56d	-8.2	-24.64 to 8.243	No	ns		0.7231			
49d vs. 56d	-8.8	-25.24 to 7.643	No	ns		0.6536			

Test details Mean 1 Mean 2 Mean Diff. SE of diff. N1 N2 q DF

7d									
Male vs. Female	12.6	6.5	6.1	7.514		5	5	1.148	56
21d									
Male vs. Female	3.4	7.9	-4.5	7.514		5	5	0.847	56
28d									
Male vs. Female	0.2	-6.9	7.1	7.514		5	5	1.336	56
35d									
Male vs. Female	0.6	-5.9	6.5	7.514		5	5	1.223	56
42d									
Male vs. Female	3.6	-6.7	10.3	7.514		5	5	1.939	56
49d									
Male vs. Female	2.2	-7.3	9.5	7.514		5	5	1.788	56
56d									
Male vs. Female	8.4	1.5	6.9	7.514		5	5	1.299	56
Male									
7d vs. 21d	12.6	3.4	9.2	5.344		5	5	2.434	48
7d vs. 28d	12.6	0.2	12.4	5.344		5	5	3.281	48
7d vs. 35d	12.6	0.6	12	5.344		5	5	3.175	48
7d vs. 42d	12.6	3.6	9	5.344		5	5	2.382	48
7d vs. 49d	12.6	2.2	10.4	5.344		5	5	2.752	48
7d vs. 56d	12.6	8.4	4.2	5.344		5	5	1.111	48
21d vs. 28d	3.4	0.2	3.2	5.344		5	5	0.8468	48
21d vs. 35d	3.4	0.6	2.8	5.344		5	5	0.7409	48
21d vs. 42d	3.4	3.6	-0.2	5.344		5	5	0.05292	48
21d vs. 49d	3.4	2.2	1.2	5.344		5	5	0.3175	48
21d vs. 56d	3.4	8.4	-5	5.344		5	5	1.323	48
28d vs. 35d	0.2	0.6	-0.4	5.344		5	5	0.1058	48
28d vs. 42d	0.2	3.6	-3.4	5.344		5	5	0.8997	48
28d vs. 49d	0.2	2.2	-2	5.344		5	5	0.5292	48
28d vs. 56d	0.2	8.4	-8.2	5.344		5	5	2.17	48
35d vs. 42d	0.6	3.6	-3	5.344		5	5	0.7939	48
35d vs. 49d	0.6	2.2	-1.6	5.344		5	5	0.4234	48
35d vs. 56d	0.6	8.4	-7.8	5.344		5	5	2.064	48
42d vs. 49d	3.6	2.2	1.4	5.344		5	5	0.3705	48
42d vs. 56d	3.6	8.4	-4.8	5.344		5	5	1.27	48
49d vs. 56d	2.2	8.4	-6.2	5.344		5	5	1.641	48
Female									
7d vs. 21d	6.5	7.9	-1.4	5.344		5	5	0.3705	48
7d vs. 28d	6.5	-6.9	13.4	5.344		5	5	3.546	48
7d vs. 35d	6.5	-5.9	12.4	5.344		5	5	3.281	48
7d vs. 42d	6.5	-6.7	13.2	5.344		5	5	3.493	48
7d vs. 49d	6.5	-7.3	13.8	5.344		5	5	3.652	48
7d vs. 56d	6.5	1.5	5	5.344		5	5	1.323	48
21d vs. 28d	7.9	-6.9	14.8	5.344		5	5	3.916	48
21d vs. 35d	7.9	-5.9	13.8	5.344		5	5	3.652	48
21d vs. 42d	7.9	-6.7	14.6	5.344		5	5	3.863	48
21d vs. 49d	7.9	-7.3	15.2	5.344		5	5	4.022	48
21d vs. 56d	7.9	1.5	6.4	5.344		5	5	1.694	48
28d vs. 35d	-6.9	-5.9	-1	5.344		5	5	0.2646	48
28d vs. 42d	-6.9	-6.7	-0.2	5.344		5	5	0.05292	48
28d vs. 49d	-6.9	-7.3	0.4	5.344		5	5	0.1058	48
28d vs. 56d	-6.9	1.5	-8.4	5.344		5	5	2.223	48
35d vs. 42d	-5.9	-6.7	0.8	5.344		5	5	0.2117	48
35d vs. 49d	-5.9	-7.3	1.4	5.344		5	5	0.3705	48
35d vs. 56d	-5.9	1.5	-7.4	5.344		5	5	1.958	48
42d vs. 49d	-6.7	-7.3	0.6	5.344		5	5	0.1588	48
42d vs. 56d	-6.7	1.5	-8.2	5.344		5	5	2.17	48
49d vs. 56d	-7.3	1.5	-8.8	5.344		5	5	2.329	48

Change in Time Freezing (s)					Difference between column means					Baseline Time Freezing (s)		
Source of Variation	% of total variation	P value	P value summary	Significant?	Mean of Male	Mean of Female	Difference between means	6.127	Column B	Female		
Time x Sex	2.636		0.7525 ns	No				0.3371	vs.	Male		
Time	17.47		0.0037 **	Yes				5.79	Column A			
Sex	1.733		0.5775 ns	No				8.973				
Subject	41.14 <0.0001		****	Yes				-17.21 to 28.79				
									Unpaired t test			
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value				P value	ns	0.7028	
									P value summary	No		
									Significantly different (P < 0.05)?	No		
									One- or two-tailed P value?	Two-tailed		
									t=0.3956, df=8			
7d									Mean of column A		38.27	
Male vs. Female	3.91	-23.63 to 31.45	No	ns	0.7771				Mean of column B		34.32	
21d									Difference between means (B - A) ± SEM		-3.950 ± 9.986	
Male vs. Female	-9.39	-36.93 to 18.15	No	ns	0.4974				95% confidence interval		-26.98 to 19.08	
28d									R squared (eta squared)		0.01918	
Male vs. Female	6.83	-20.71 to 34.37	No	ns	0.6212							
35d												
Male vs. Female	4.07	-23.47 to 31.61	No	ns	0.7683							
42d												
Male vs. Female	10.65	-16.89 to 38.19	No	ns	0.4418							
49d												
Male vs. Female	9.75	-17.79 to 37.29	No	ns	0.4811							
56d												
Male vs. Female	14.71	-12.83 to 42.25	No	ns	0.2892							
Male												
7d vs. 21d	13.46	-17.98 to 44.90	No	ns	0.8406							
7d vs. 28d	21.86	-9.582 to 53.30	No	ns	0.3473							
7d vs. 35d	24.38	-7.062 to 55.82	No	ns	0.227							
7d vs. 42d	17.64	-13.80 to 49.08	No	ns	0.6024							
7d vs. 49d	18.02	-13.42 to 49.46	No	ns	0.5783							
7d vs. 56d	1.26	-30.18 to 32.70	No	ns	>0.9999							
21d vs. 28d	8.4	-23.04 to 39.84	No	ns	0.9815							
21d vs. 35d	10.92	-20.52 to 42.36	No	ns	0.9342							
21d vs. 42d	4.18	-27.26 to 35.62	No	ns	0.9996							
21d vs. 49d	4.56	-26.88 to 36.00	No	ns	0.9993							
21d vs. 56d	-12.2	-43.64 to 19.24	No	ns	0.8931							
28d vs. 35d	2.52	-28.92 to 33.96	No	ns	>0.9999							
28d vs. 42d	-4.22	-35.66 to 27.22	No	ns	0.9996							
28d vs. 49d	-3.84	-35.28 to 27.60	No	ns	0.9998							
28d vs. 56d	-20.6	-52.04 to 10.84	No	ns	0.4185							
35d vs. 42d	-6.74	-38.18 to 24.70	No	ns	0.9942							
35d vs. 49d	-6.36	-37.80 to 25.08	No	ns	0.9957							
35d vs. 56d	-23.12	-64.56 to 8.322	No	ns	0.2832							
42d vs. 49d	0.38	-31.06 to 31.62	No	ns	>0.9999							
42d vs. 56d	-16.38	-47.82 to 15.06	No	ns	0.6811							
49d vs. 56d	-16.76	-48.20 to 14.68	No	ns	0.6577							
Female												
7d vs. 21d	0.16	-31.28 to 31.60	No	ns	>0.9999							
7d vs. 28d	24.78	-6.662 to 56.22	No	ns	0.2109							
7d vs. 35d	24.54	-6.902 to 55.98	No	ns	0.2205							
7d vs. 42d	24.38	-7.062 to 55.82	No	ns	0.227							
7d vs. 49d	23.86	-7.582 to 55.30	No	ns	0.2492							
7d vs. 56d	12.06	-19.38 to 43.50	No	ns	0.8982							
21d vs. 28d	24.62	-6.822 to 56.06	No	ns	0.2172							
21d vs. 35d	24.38	-7.062 to 55.82	No	ns	0.227							
21d vs. 42d	24.22	-7.222 to 55.66	No	ns	0.2337							
21d vs. 49d	23.7	-7.742 to 55.14	No	ns	0.2563							
21d vs. 56d	11.9	-19.54 to 43.34	No	ns	0.9038							
28d vs. 35d	-0.24	-31.68 to 31.20	No	ns	>0.9999							
28d vs. 42d	-0.4	-31.84 to 31.04	No	ns	>0.9999							
28d vs. 49d	-0.32	-32.36 to 30.52	No	ns	>0.9999							
28d vs. 56d	-12.72	-44.16 to 18.72	No	ns	0.8728							
35d vs. 42d	-0.16	-31.60 to 31.28	No	ns	>0.9999							
35d vs. 49d	-0.68	-32.12 to 30.76	No	ns	>0.9999							
35d vs. 56d	-12.48	-43.92 to 18.96	No	ns	0.8824							
42d vs. 49d	-0.52	-31.96 to 30.92	No	ns	>0.9999							
42d vs. 56d	-12.32	-43.76 to 19.12	No	ns	0.8886							
49d vs. 56d	-11.8	-43.24 to 19.64	No	ns	0.9073							
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF				
7d												
Male vs. Female	19.93	16.02	3.91	13.75		5	5	0.4023			56	
21d												
Male vs. Female	6.47	15.86	-9.39	13.75		5	5	0.966			56	
28d												
Male vs. Female	-1.93	-8.76	6.83	13.75		5	5	0.7027			56	
35d												
Male vs. Female	-4.45	-8.52	4.07	13.75		5	5	0.4187			56	
42d												
Male vs. Female	2.29	-8.36	10.65	13.75		5	5	1.096			56	
49d												
Male vs. Female	1.91	-7.84	9.75	13.75		5	5	1.003			56	
56d												
Male vs. Female	18.67	3.96	14.71	13.75		5	5	1.513			56	
Male												
7d vs. 21d	19.93	6.47	13.46	10.22		5	5	1.863			48	
7d vs. 28d	19.93	-1.93	21.86	10.22		5	5	3.025			48	
7d vs. 35d	19.93	-4.45	24.38	10.22		5	5	3.374			48	
7d vs. 42d	19.93	2.29	17.64	10.22		5	5	2.441			48	
7d vs. 49d	19.93	1.91	18.02	10.22		5	5	2.494			48	
7d vs. 56d	19.93	18.67	1.26	10.22		5	5	0.1744			48	
21d vs. 28d	6.47	-1.93	8.4	10.22		5	5	1.162			48	
21d vs. 35d	6.47	-4.45	10.92	10.22		5	5	1.511			48	
21d vs. 42d	6.47	2.29	4.18	10.22		5	5	0.5785			48	
21d vs. 49d	6.47	1.91	4.56	10.22		5	5	0.631			48	
21d vs. 56d	6.47	18.67	-12.2	10.22		5	5	1.688			48	
28d vs. 35d	-1.93	-4.45	2.52	10.22		5	5	0.3487			48	
28d vs. 42d	-1.93	2.29	-4.22	10.22		5	5	0.584			48	
28d vs. 49d	-1.93	1.91	-3.84	10.22		5	5	0.5314			48	
28d vs. 56d	-1.93	18.67	-20.6	10.22		5	5	2.851			48	
35d vs. 42d	-4.45	2.29	-6.74	10.22		5	5	0.9327			48	
35d vs. 49d	-4.45	1.91	-6.36	10.22		5	5	0.8801			48	
35d vs. 56d	-4.45	18.67	-23.12	10.22		5	5	3.2			48	
42d vs. 49d	2.29	1.91	0.38	10.22		5	5	0.05259			48	
42d vs. 56d	2.29	18.67	-16.38	10.22		5	5	2.267			48	
49d vs. 56d	1.91	18.67	-16.76	10.22		5	5	2.319			48	
Female												
7d vs. 21d	16.02	15.86	0.16	10.22		5	5	0.02214			48	
7d vs. 28d	16.02	-8.76	24.78	10.22		5	5	3.429			48	
7d vs. 35d	16.02	-8.52	24.54	10.22		5	5	3.396			48	
7d vs. 42d	16.02	-8.36	24.38	10.22		5	5	3.374			48	
7d vs. 49d	16.02	-7.84	23.86	10.22		5	5	3.302			48	
7d vs. 56d	16.02	3.96	12.06	10.22		5	5	1.689			48	
21d vs. 28d	15.86	-8.36	24.62	10.22		5	5	3.407			48	
21d vs. 35d	15.86	-8.52	24.38	10.22		5	5	3.374			48	
21d vs. 42d	15.86	-8.36	24.22	10.22		5	5	3.352			48	
21d vs. 49d	15.86	-7.84	23.7	10.22		5	5	3.28			48	
21d vs. 56d	15.86	3.96	11.9	10.22		5	5	1.647			48	
28d vs. 35d	-8.76	-8.36	-0.24	10.22		5	5	0.03321			48	
28d vs. 42d	-8.76	-8.36	-0.4	10.22		5	5	0.05536			48	
28d vs. 49d	-8.76	-7.84	-0.92	10.22		5	5	0.1273			48	
28d vs. 56d	-8.76	3.96	-12.72	10.22		5	5	1.76			48	
35d vs. 42d	-8.52	-8.36	-0.16	10.22		5	5	0.02214			48	
35d vs. 49d	-8.52	-7.84	-0.68	10.22		5	5	0.0941			48	
35d vs. 56d	-8.52	3.96	-12.48	10.22		5	5	1.727			48	
42d vs. 49d	-8.36	-7.84	-0.52	10.22		5	5	0.07196			48	
42d vs. 56d	-8.36	3.96	-12.32	10.22		5	5	1.705			48	
49d vs. 56d	-7.84	-3.96	-11.8	10.22		5	5	1.633			48	

Change in Time Mobile (s)							Baseline Time Mobile (s)			
Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means		Column B vs. Column A	Female vs. Male		
Time x Sex	2.492	0.777	ns	No	Mean of Male	-62.43				
Time	5.666	0.3116	ns	No	Mean of Female	-14.51				
Sex	11.76	0.1774	ns	No	Difference between means	-47.92				
Subject	43 <0.0001	****	****	Yes	SE of difference	32.4				
					95% CI of difference	-122.6 to 26.80				
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		Unpaired t test P value	0.3554		
7d							P value summary	ns		
Male vs. Female	-18.8	-107.4 to 69.78	No	ns	0.6724		Significantly different (P < 0.05)?	No		
21d							One- or two-tailed P value?	Two-tailed		
Male vs. Female	-35.5	-124.1 to 53.08	No	ns	0.4255		t, df	t=0.9809, df=8		
28d							Mean of column A	466.5		
Male vs. Female	-56.7	-145.3 to 31.88	No	ns	0.205		Mean of column B	490.5		
35d							Difference between means (B - A) ± SEM	24.00 ± 24.47		
Male vs. Female	-37.72	-126.3 to 50.86	No	ns	0.3973		95% confidence interval	-32.42 to 80.42		
42d							R squared (eta squared)	0.1074		
Male vs. Female	-71.86	-160.4 to 16.72	No	ns	0.1098					
49d										
Male vs. Female	-84.54	-173.1 to 4.042	No	ns	0.061					
56d										
Male vs. Female	-30.32	-118.9 to 58.26	No	ns	0.4957					
Male										
7d vs. 21d	4.58	-95.42 to 104.6	No	ns	>0.9999					
7d vs. 28d	12.54	-87.46 to 112.5	No	ns		0.9997				
7d vs. 35d	-38.26	-138.3 to 61.74	No	ns		0.8993				
7d vs. 42d	2.34	-97.66 to 102.3	No	ns	>0.9999					
7d vs. 49d	-4.12	-104.1 to 95.88	No	ns	>0.9999					
7d vs. 56d	-10.04	-110.0 to 89.96	No	ns	>0.9999					
21d vs. 28d	7.96	-92.04 to 108.0	No	ns	>0.9999					
21d vs. 35d	-42.84	-142.8 to 57.16	No	ns		0.8401				
21d vs. 42d	-2.24	-102.2 to 97.76	No	ns	>0.9999					
21d vs. 49d	-8.7	-108.7 to 91.30	No	ns	>0.9999					
21d vs. 56d	-14.62	-114.6 to 85.38	No	ns		0.9993				
28d vs. 35d	-50.8	-150.8 to 49.20	No	ns		0.7057				
28d vs. 42d	-10.2	-110.2 to 89.80	No	ns	>0.9999					
28d vs. 49d	-16.66	-116.7 to 83.34	No	ns		0.9986				
28d vs. 56d	-22.58	-122.6 to 77.42	No	ns		0.9923				
35d vs. 42d	40.6	-59.40 to 140.6	No	ns		0.871				
35d vs. 49d	34.14	-65.86 to 134.1	No	ns		0.9391				
35d vs. 56d	28.22	-71.78 to 128.2	No	ns		0.9756				
42d vs. 49d	-6.46	-106.5 to 93.54	No	ns	>0.9999					
42d vs. 56d	-12.38	-112.4 to 87.62	No	ns		0.9997				
49d vs. 56d	-5.92	-105.9 to 94.08	No	ns	>0.9999					
Female										
7d vs. 21d	-12.12	-112.1 to 87.88	No	ns		0.9998				
7d vs. 28d	-25.36	-125.4 to 74.64	No	ns		0.9858				
7d vs. 35d	-57.18	-157.2 to 42.82	No	ns		0.581				
7d vs. 42d	-50.72	-150.7 to 49.28	No	ns		0.7072				
7d vs. 49d	-69.86	-169.9 to 30.14	No	ns		0.3416				
7d vs. 56d	-21.56	-121.6 to 78.44	No	ns		0.594				
21d vs. 28d	-13.24	-113.2 to 86.76	No	ns		0.9996				
21d vs. 35d	-45.06	-145.1 to 54.94	No	ns		0.8062				
21d vs. 42d	-38.6	-138.6 to 61.40	No	ns		0.8954				
21d vs. 49d	-57.74	-157.7 to 42.26	No	ns		0.5698				
21d vs. 56d	-9.44	-109.4 to 90.56	No	ns	>0.9999					
28d vs. 35d	-31.82	-131.8 to 68.18	No	ns		0.9562				
28d vs. 42d	-25.36	-125.4 to 74.64	No	ns		0.9858				
28d vs. 49d	-44.5	-144.5 to 55.50	No	ns		0.8151				
28d vs. 56d	3.8	-96.20 to 103.8	No	ns	>0.9999					
35d vs. 42d	6.46	-93.54 to 106.5	No	ns	>0.9999					
35d vs. 49d	-12.68	-112.7 to 87.32	No	ns		0.9997				
35d vs. 56d	35.62	-64.38 to 135.6	No	ns		0.9263				
42d vs. 49d	-19.14	-119.1 to 80.86	No	ns		0.9969				
42d vs. 56d	29.16	-70.84 to 129.2	No	ns		0.9713				
49d vs. 56d	48.3	-51.70 to 148.3	No	ns		0.7515				
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF		
7d										
Male vs. Female	-67.14	-48.34	-18.8	44.22		5	5	0.6013		
21d										
Male vs. Female	-71.72	-36.22	-35.5	44.22		5	5	1.135		
28d										
Male vs. Female	-79.68	-22.98	-56.7	44.22		5	5	1.813		
35d										
Male vs. Female	-28.88	8.84	-37.72	44.22		5	5	1.206		
42d										
Male vs. Female	-69.48	2.38	-71.86	44.22		5	5	2.298		
49d										
Male vs. Female	-63.02	21.52	-84.54	44.22		5	5	2.704		
56d										
Male vs. Female	-57.1	-26.78	-30.32	44.22		5	5	0.9697		
Male										
7d vs. 21d	-67.14	-71.72	4.58	32.5		5	5	0.1993		
7d vs. 28d	-67.14	-79.68	12.54	32.5		5	5	0.5456		
7d vs. 35d	-67.14	-28.88	-38.26	32.5		5	5	1.665		
7d vs. 42d	-67.14	-69.48	2.34	32.5		5	5	0.1018		
7d vs. 49d	-67.14	-63.02	-4.12	32.5		5	5	0.1793		
7d vs. 56d	-67.14	-57.1	-10.04	32.5		5	5	0.4369		
21d vs. 28d	-71.72	-79.68	7.96	32.5		5	5	0.3464		
21d vs. 35d	-71.72	-28.88	-42.84	32.5		5	5	1.864		
21d vs. 42d	-71.72	-69.48	-2.24	32.5		5	5	0.09747		
21d vs. 49d	-71.72	-63.02	-8.7	32.5		5	5	0.3786		
21d vs. 56d	-71.72	-57.1	-14.62	32.5		5	5	0.6362		
28d vs. 35d	-79.68	-28.88	-50.8	32.5		5	5	2.21		
28d vs. 42d	-79.68	-69.48	-10.2	32.5		5	5	0.4438		
28d vs. 49d	-79.68	-63.02	-16.66	32.5		5	5	0.7249		
28d vs. 56d	-79.68	-57.1	-22.58	32.5		5	5	0.9825		
35d vs. 42d	-28.88	-69.48	40.6	32.5		5	5	1.767		
35d vs. 49d	-28.88	-63.02	34.14	32.5		5	5	1.466		
35d vs. 56d	-28.88	-57.1	28.22	32.5		5	5	1.228		
42d vs. 49d	-69.48	-63.02	-6.46	32.5		5	5	0.2811		
42d vs. 56d	-69.48	-57.1	-12.38	32.5		5	5	0.5387		
49d vs. 56d	-63.02	-57.1	-5.92	32.5		5	5	0.2576		
Female										
7d vs. 21d	-48.34	-36.22	-12.12	32.5		5	5	0.5274		
7d vs. 28d	-48.34	-22.98	-25.36	32.5		5	5	1.103		
7d vs. 35d	-48.34	8.84	-57.18	32.5		5	5	2.488		
7d vs. 42d	-48.34	2.38	-50.72	32.5		5	5	2.207		
7d vs. 49d	-48.34	21.52	-69.86	32.5		5	5	3.04		
7d vs. 56d	-48.34	-26.78	-21.56	32.5		5	5	0.9381		
21d vs. 28d	-36.22	-22.98	-13.24	32.5		5	5	0.5761		
21d vs. 35d	-36.22	8.84	-45.06	32.5		5	5	1.961		
21d vs. 42d	-36.22	2.38	-38.6	32.5		5	5	1.68		
21d vs. 49d	-36.22	21.52	-57.74	32.5		5	5	2.512		
21d vs. 56d	-36.22	-26.78	-9.44	32.5		5	5	0.4108		
28d vs. 35d	-22.98	8.84	-31.82	32.5		5	5	1.385		
28d vs. 42d	-22.98	2.38	-25.36	32.5		5	5	1.103		
28d vs. 49d	-22.98	21.52	-44.5	32.5		5	5	1.936		
28d vs. 56d	-22.98	-26.78	3.8	32.5		5	5	0.1653		
35d vs. 42d	8.84	2.38	6.46	32.5		5	5	0.2811		
35d vs. 49d	8.84	21.52	-12.68	32.5		5	5	0.5517		
35d vs. 56d	8.84	-26.78	35.62	32.5		5	5	1.55		
42d vs. 49d	2.38	21.52	-19.14	32.5		5	5	0.8328		
42d vs. 56d	2.38	-26.78	29.16	32.5		5	5	1.269		
49d vs. 56d	21.52	-26.78	48.3	32.5		5	5	2.102		

Change in Time Immobile (s)										Baseline Time Immobile (s)		
Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means					Column B vs. Column A	Female vs. Male	
Time x Sex	2.492	0.777 ns	No	No	Mean of Male	62.43						
Time	5.666	0.3116 ns	No	No	Mean of Female	14.51						
Sex	11.76	0.1774 ns	No	No	Difference between means	47.92						
Subject	43 <0.0001	****	Yes	Yes	SE of difference	32.4						
					95% CI of difference	-26.80 to 122.6						
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value					Unpaired t test P value	0.3554	
7d Male vs. Female	18.8	-69.78 to 107.4	No	ns	0.6724					P value summary	ns	
21d Male vs. Female	35.5	-53.08 to 124.1	No	ns	0.4255					Significantly different (P < 0.05)?	No	
28d Male vs. Female	56.7	-31.88 to 145.3	No	ns	0.205					One- or two-tailed P value?	Two-tailed t=0.9809, df=8	
35d Male vs. Female	37.72	-50.86 to 126.3	No	ns	0.3973					Mean of column A	133.5	
42d Male vs. Female	71.86	-16.72 to 160.4	No	ns	0.1098					Mean of column B	109.5	
49d Male vs. Female	84.54	-4.042 to 173.1	No	ns	0.061					Difference between means (B - A) ± SEM	-24.09 ± 24.47	
56d Male vs. Female	30.32	-58.26 to 118.9	No	ns	0.4957					95% confidence interval	-80.42 to 32.42	
										R squared (eta squared)	0.1074	
Male												
7d vs. 21d	-4.58	-104.6 to 95.42	No	ns	>0.9999							
7d vs. 28d	-12.54	-112.5 to 87.46	No	ns	0.9997							
7d vs. 35d	38.26	-61.74 to 138.3	No	ns	0.8993							
7d vs. 42d	-2.34	-102.3 to 97.66	No	ns	>0.9999							
7d vs. 49d	4.12	-95.88 to 104.1	No	ns	>0.9999							
7d vs. 56d	10.04	-89.96 to 110.0	No	ns	>0.9999							
21d vs. 28d	-7.96	-108.0 to 92.04	No	ns	>0.9999							
21d vs. 35d	42.84	-57.16 to 142.8	No	ns	0.8401							
21d vs. 42d	2.24	-97.76 to 102.2	No	ns	>0.9999							
21d vs. 49d	8.7	-91.30 to 108.7	No	ns	>0.9999							
21d vs. 56d	14.62	-85.38 to 114.6	No	ns	0.9993							
28d vs. 35d	50.8	-49.20 to 150.8	No	ns	0.7057							
28d vs. 42d	10.2	-89.80 to 110.2	No	ns	>0.9999							
28d vs. 49d	16.66	-83.34 to 116.7	No	ns	0.9986							
28d vs. 56d	22.58	-77.42 to 122.6	No	ns	0.9923							
35d vs. 42d	-40.6	-140.6 to 59.40	No	ns	0.871							
35d vs. 49d	-34.14	-134.1 to 65.86	No	ns	0.9391							
35d vs. 56d	-28.22	-128.2 to 71.78	No	ns	0.9756							
42d vs. 49d	6.46	-83.54 to 106.5	No	ns	>0.9999							
42d vs. 56d	12.38	-87.62 to 112.4	No	ns	0.9997							
49d vs. 56d	5.92	-94.08 to 105.9	No	ns	>0.9999							
Female												
7d vs. 21d	12.12	-87.88 to 112.1	No	ns	0.9998							
7d vs. 28d	25.36	-74.64 to 125.4	No	ns	0.9858							
7d vs. 35d	57.18	-42.82 to 157.2	No	ns	0.581							
7d vs. 42d	50.72	-49.28 to 150.7	No	ns	0.7072							
7d vs. 49d	69.86	-30.14 to 169.9	No	ns	0.3416							
7d vs. 56d	21.56	-78.44 to 121.6	No	ns	0.594							
21d vs. 28d	13.24	-86.76 to 113.2	No	ns	0.9996							
21d vs. 35d	45.06	-54.94 to 145.1	No	ns	0.8062							
21d vs. 42d	38.6	-81.40 to 138.6	No	ns	0.8954							
21d vs. 49d	57.74	-42.26 to 157.7	No	ns	0.5698							
21d vs. 56d	9.44	-90.56 to 109.4	No	ns	>0.9999							
28d vs. 35d	31.82	-68.18 to 131.8	No	ns	0.9562							
28d vs. 42d	25.36	-74.64 to 125.4	No	ns	0.9858							
28d vs. 49d	44.5	-55.50 to 144.5	No	ns	0.8151							
28d vs. 56d	-3.8	-103.8 to 96.20	No	ns	>0.9999							
35d vs. 42d	-6.46	-106.5 to 93.54	No	ns	>0.9999							
35d vs. 49d	12.68	-87.32 to 112.7	No	ns	0.9997							
35d vs. 56d	-35.62	-135.6 to 64.38	No	ns	0.9263							
42d vs. 49d	19.14	-80.86 to 119.1	No	ns	0.9969							
42d vs. 56d	-29.16	-129.2 to 70.84	No	ns	0.9713							
49d vs. 56d	-48.3	-148.3 to 51.70	No	ns	0.7515							
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF				
7d Male vs. Female	67.14	48.34	18.8	44.22		5	5	0.6013		56		
21d Male vs. Female	71.72	36.22	35.5	44.22		5	5	1.135		56		
28d Male vs. Female	79.68	22.98	56.7	44.22		5	5	1.813		56		
35d Male vs. Female	28.88	-8.84	37.72	44.22		5	5	1.206		56		
42d Male vs. Female	69.48	-2.38	71.86	44.22		5	5	2.298		56		
49d Male vs. Female	63.02	-21.52	84.54	44.22		5	5	2.704		56		
56d Male vs. Female	57.1	26.78	30.32	44.22		5	5	0.9697		56		
Male												
7d vs. 21d	67.14	71.72	-4.58	32.5		5	5	0.1993		48		
7d vs. 28d	67.14	79.68	-12.54	32.5		5	5	0.5456		48		
7d vs. 35d	67.14	28.88	38.26	32.5		5	5	1.665		48		
7d vs. 42d	67.14	69.48	-2.34	32.5		5	5	0.1018		48		
7d vs. 49d	67.14	63.02	4.12	32.5		5	5	0.1793		48		
7d vs. 56d	67.14	57.1	10.04	32.5		5	5	0.4369		48		
21d vs. 28d	71.72	79.68	-7.96	32.5		5	5	0.3464		48		
21d vs. 35d	71.72	28.88	42.84	32.5		5	5	1.864		48		
21d vs. 42d	71.72	69.48	2.24	32.5		5	5	0.09747		48		
21d vs. 49d	71.72	63.02	8.7	32.5		5	5	0.3786		48		
21d vs. 56d	71.72	57.1	14.62	32.5		5	5	0.6362		48		
28d vs. 35d	79.68	28.88	50.8	32.5		5	5	2.21		48		
28d vs. 42d	79.68	69.48	10.2	32.5		5	5	0.4438		48		
28d vs. 49d	79.68	63.02	16.66	32.5		5	5	0.7249		48		
28d vs. 56d	79.68	57.1	22.58	32.5		5	5	0.9825		48		
35d vs. 42d	28.88	69.48	-40.6	32.5		5	5	1.767		48		
35d vs. 49d	28.88	63.02	-34.14	32.5		5	5	1.466		48		
35d vs. 56d	28.88	57.1	-28.22	32.5		5	5	1.228		48		
42d vs. 49d	69.48	63.02	6.46	32.5		5	5	0.2811		48		
42d vs. 56d	69.48	57.1	12.38	32.5		5	5	0.5387		48		
49d vs. 56d	63.02	57.1	5.92	32.5		5	5	0.2576		48		
Female												
7d vs. 21d	48.34	36.22	12.12	32.5		5	5	0.5274		48		
7d vs. 28d	48.34	22.98	25.36	32.5		5	5	1.103		48		
7d vs. 35d	48.34	-8.84	57.18	32.5		5	5	2.488		48		
7d vs. 42d	48.34	-2.38	50.72	32.5		5	5	2.207		48		
7d vs. 49d	48.34	-21.52	69.86	32.5		5	5	3.04		48		
7d vs. 56d	48.34	26.78	21.56	32.5		5	5	0.9381		48		
21d vs. 28d	36.22	22.98	13.24	32.5		5	5	0.5761		48		
21d vs. 35d	36.22	-8.84	45.06	32.5		5	5	1.961		48		
21d vs. 42d	36.22	-2.38	38.6	32.5		5	5	1.68		48		
21d vs. 49d	36.22	-21.52	57.74	32.5		5	5	2.512		48		
21d vs. 56d	36.22	26.78	9.44	32.5		5	5	0.4108		48		
28d vs. 35d	22.98	-8.84	31.82	32.5		5	5	1.385		48		
28d vs. 42d	22.98	-2.38	25.36	32.5		5	5	1.103		48		
28d vs. 49d	22.98	-21.52	44.5	32.5		5	5	1.936		48		
28d vs. 56d	22.98	26.78	-3.8	32.5		5	5	0.1653		48		
35d vs. 42d	-8.84	-2.38	-6.46	32.5		5	5	0.2811		48		
35d vs. 49d	-8.84	-21.52	12.68	32.5		5	5	0.5517		48		
35d vs. 56d	-8.84	26.78	-35.62	32.5		5	5	1.55		48		
42d vs. 49d	-2.38	-21.52	19.14	32.5		5	5	0.8328		48		
42d vs. 56d	-2.38	26.78	-29.16	32.5		5	5	1.269		48		
49d vs. 56d	-21.52	26.78	-48.3	32.5		5	5	2.102		48		

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Change in Hut Entries

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	1.355	0.9349 ns	No	No	Mean of Male -1.829
Time	8.539	0.1041 ns	No	No	Mean of Female 0.1429
Sex	1.416	0.6541 ns	No	No	Difference between means -1.971
Subject	52.31 <0.0001	****	Yes	Yes	SE of difference 4.237
					95% CI of difference -11.74 to 7.798

Baseline Hut Entries

Column B vs. Column A	Female vs. Male
Unpaired t test P value P value summary Significantly different (P < 0.05)? One- or two-tailed P value? t, df	0.5507 ns No Two-tailed t=0.6229, df=8
Mean of column A Mean of column B Difference between means (B - A) ± SEM 95% confidence interval R squared (eta squared)	20.4 25.2 4.800 ± 4.120 -4.701 to 14.30 0.1451

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d Male vs. Female	-4.4	-15.45 to 6.651	No	ns	0.4285
21d Male vs. Female	0	-11.05 to 11.05	No	ns	>0.9999
28d Male vs. Female	-4.4	-15.45 to 6.651	No	ns	0.4285
35d Male vs. Female	-2.6	-13.65 to 8.451	No	ns	0.6393
42d Male vs. Female	-2.6	-13.65 to 8.451	No	ns	0.6393
49d Male vs. Female	0.8	-10.25 to 11.85	No	ns	0.8852
56d Male vs. Female	-0.6	-11.65 to 10.45	No	ns	0.9138
Male					
7d vs. 21d	-3.8	-15.54 to 7.941	No	ns	0.9525
7d vs. 28d	0.4	-11.34 to 12.14	No	ns	
7d vs. 35d	-4.4	-16.14 to 7.341	No	ns	0.9079
7d vs. 42d	-6.4	-18.14 to 5.341	No	ns	0.6341
7d vs. 49d	-5.2	-16.94 to 6.541	No	ns	0.8184
7d vs. 56d	-8.4	-20.14 to 3.341	No	ns	0.3141
21d vs. 28d	4.2	-7.541 to 15.94	No	ns	0.9249
21d vs. 35d	-0.6	-12.34 to 11.14	No	ns	>0.9999
21d vs. 42d	-2.6	-14.34 to 9.141	No	ns	0.9931
21d vs. 49d	-1.4	-13.14 to 10.34	No	ns	0.9998
21d vs. 56d	-4.6	-16.34 to 7.141	No	ns	0.8887
28d vs. 35d	-4.8	-16.54 to 6.941	No	ns	0.8673
28d vs. 42d	-6.8	-18.54 to 4.941	No	ns	0.5663
28d vs. 49d	-5.6	-17.34 to 6.141	No	ns	0.7621
28d vs. 56d	-8.8	-20.54 to 2.941	No	ns	0.2624
35d vs. 42d	-2	-13.74 to 9.741	No	ns	0.9984
35d vs. 49d	-0.8	-12.54 to 10.94	No	ns	>0.9999
35d vs. 56d	-4	-15.74 to 7.741	No	ns	0.9397
42d vs. 49d	1.2	-10.54 to 12.94	No	ns	>0.9999
42d vs. 56d	-2	-13.74 to 9.741	No	ns	0.9984
49d vs. 56d	-3.2	-14.94 to 8.541	No	ns	0.9795
Female					
7d vs. 21d	0.6	-11.14 to 12.34	No	ns	>0.9999
7d vs. 28d	0.4	-11.34 to 12.14	No	ns	>0.9999
7d vs. 35d	-2.6	-14.34 to 9.141	No	ns	0.9931
7d vs. 42d	-4.6	-16.34 to 7.141	No	ns	0.8887
7d vs. 49d	0	-11.74 to 11.74	No	ns	>0.9999
7d vs. 56d	-4.6	-16.34 to 7.141	No	ns	0.8887
21d vs. 28d	-0.2	-11.94 to 11.54	No	ns	>0.9999
21d vs. 35d	-3.2	-14.94 to 8.541	No	ns	0.9795
21d vs. 42d	-5.2	-16.94 to 6.541	No	ns	0.8184
21d vs. 49d	-0.6	-12.34 to 11.14	No	ns	>0.9999
21d vs. 56d	-5.2	-16.94 to 6.541	No	ns	0.8184
28d vs. 35d	-3	-14.74 to 8.741	No	ns	0.9853
28d vs. 42d	-5	-16.74 to 6.741	No	ns	0.8438
28d vs. 49d	-0.4	-12.14 to 11.34	No	ns	>0.9999
28d vs. 56d	-5	-16.74 to 6.741	No	ns	0.8438
35d vs. 42d	-2	-13.74 to 9.741	No	ns	0.9984
35d vs. 49d	2.6	-9.141 to 14.34	No	ns	0.9931
35d vs. 56d	-2	-13.74 to 9.741	No	ns	0.9984
42d vs. 49d	4.6	-7.141 to 16.34	No	ns	0.8887
42d vs. 56d	0	-11.74 to 11.74	No	ns	>0.9999
49d vs. 56d	-4.6	-16.34 to 7.141	No	ns	0.8887

Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF
7d Male vs. Female	-5.8	-1.4	-4.4	5.517		5	5	1.128
21d Male vs. Female	-2	-2	0	5.517		5	5	0
28d Male vs. Female	-6.2	-1.8	-4.4	5.517		5	5	1.128
35d Male vs. Female	-1.4	1.2	-2.6	5.517		5	5	0.6665
42d Male vs. Female	0.6	3.2	-2.6	5.517		5	5	0.6665
49d Male vs. Female	-0.6	-1.4	0.8	5.517		5	5	0.2051
56d Male vs. Female	2.6	3.2	-0.6	5.517		5	5	0.1538
Male								
7d vs. 21d	-5.8	-2	-3.8	3.816		5	5	1.408
7d vs. 28d	-5.8	-6.2	0.4	3.816		5	5	0.1482
7d vs. 35d	-5.8	-1.4	-4.4	3.816		5	5	1.631
7d vs. 42d	-5.8	0.6	-6.4	3.816		5	5	2.372
7d vs. 49d	-5.8	-0.6	-5.2	3.816		5	5	1.927
7d vs. 56d	-5.8	2.6	-8.4	3.816		5	5	3.113
21d vs. 28d	-2	-6.2	4.2	3.816		5	5	1.556
21d vs. 35d	-2	-1.4	-0.6	3.816		5	5	0.2223
21d vs. 42d	-2	0.6	-2.6	3.816		5	5	0.9635
21d vs. 49d	-2	-0.6	-1.4	3.816		5	5	0.5188
21d vs. 56d	-2	2.6	-4.6	3.816		5	5	1.705
28d vs. 35d	-6.2	-1.4	-4.8	3.816		5	5	1.779
28d vs. 42d	-6.2	0.6	-6.8	3.816		5	5	2.52
28d vs. 49d	-6.2	-0.6	-5.6	3.816		5	5	2.075
28d vs. 56d	-6.2	2.6	-8.8	3.816		5	5	3.261
35d vs. 42d	-1.4	0.6	-2	3.816		5	5	0.7412
35d vs. 49d	-1.4	-0.6	-0.8	3.816		5	5	0.2965
35d vs. 56d	-1.4	2.6	-4	3.816		5	5	1.482
42d vs. 49d	0.6	-0.6	1.2	3.816		5	5	0.4447
42d vs. 56d	0.6	2.6	-2	3.816		5	5	0.7412
49d vs. 56d	-0.6	2.6	-3.2	3.816		5	5	1.186
Female								
7d vs. 21d	-1.4	-2	0.6	3.816		5	5	0.2223
7d vs. 28d	-1.4	-1.8	0.4	3.816		5	5	0.1482
7d vs. 35d	-1.4	1.2	-2.6	3.816		5	5	0.9635
7d vs. 42d	-1.4	3.2	-4.6	3.816		5	5	1.705
7d vs. 49d	-1.4	-0.6	0	3.816		5	5	0
7d vs. 56d	-1.4	2.6	-4	3.816		5	5	1.705
21d vs. 28d	-2	-6.2	4.2	3.816		5	5	0.7412
21d vs. 35d	-2	1.2	-3.2	3.816		5	5	1.186
21d vs. 42d	-2	3.2	-5.2	3.816		5	5	1.927
21d vs. 49d	-2	-1.4	-0.6	3.816		5	5	0.2223
21d vs. 56d	-2	2.6	-4.6	3.816		5	5	1.927
28d vs. 35d	-1.8	1.2	-3	3.816		5	5	1.112
28d vs. 42d	-1.8	3.2	-5	3.816		5	5	1.853
28d vs. 49d	-1.8	-1.4	-0.4	3.816		5	5	0.1482
28d vs. 56d	-1.8	3.2	-5	3.816		5	5	1.853
35d vs. 42d	1.2	0.6	0.6	3.816		5	5	0.7412
35d vs. 49d	1.2	-1.4	2.6	3.816		5	5	0.9635
35d vs. 56d	1.2	3.2	-2	3.816		5	5	0.7412
42d vs. 49d	3.2	-1.4	4.6	3.816		5	5	1.705
42d vs. 56d	3.2	0	3.2	3.816		5	5	0
49d vs. 56d	-1.4	3.2	-4.6	3.816		5	5	1.705

Change in Hut Exits

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	1.483	0.9197 ns	No	No	Mean of Male -1.914
Time	8.436	0.1076 ns	No	No	Mean of Female 0.4
Sex	1.879	0.6051 ns	No	No	Difference between means -2.314
Subject	51.89 <0.0001	****	Yes	Yes	SE of difference 4.3
					95% CI of difference -12.23 to 7.601

Baseline Hut Exits

Column B vs. Column A	Female vs. Male
Unpaired t test P value P value summary Significantly different (P < 0.05)? One- or two-tailed P value? t, df	0.313 ns No Two-tailed t=1.077, df=8
Mean of column A Mean of column B Difference between means (B - A) ± SEM 95% confidence interval R squared (eta squared)	20.4 24.8 4.400 ± 4.087 -5.024 to 13.82 0.1266

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d Male vs. Female	-5	-16.23 to 6.230	No	ns	0.3762
21d Male vs. Female	-0.2	-11.43 to 11.03	No	ns	0.9717
28d Male vs. Female	-4.8	-16.03 to 6.430	No	ns	0.3955
35d Male vs. Female	-3	-14.23 to 8.230	No	ns	0.5947
42d Male vs. Female	-3	-14.23 to 8.230	No	ns	0.5947
49d Male vs. Female	0.6	-10.63 to 11.83	No	ns	0.9151
56d Male vs. Female	-0.8	-12.03 to 10.43	No	ns	0.887
Male					
7d vs. 21d	-4	-15.95 to 7.952	No	ns	0.9445
7d vs. 28d	0.4	-11.55 to 12.35	No	ns	0.9998
7d vs. 35d	-4.4	-16.35 to 7.552	No	ns	0.9147
7d vs. 42d	-6.6	-18.55 to 5.352	No	ns	0.62
7d vs. 49d	-5.4	-17.35 to 6.552	No	ns	0.8043
7d vs. 56d	-8.6	-20.55 to 3.352	No	ns	0.3075
21d vs. 28d	4.4	7.552 to 16.35	No	ns	0.9147
21d vs. 35d	-0.4	-12.35 to 11.55	No	ns	>0.9999
21d vs. 42d	-2.6	-14.55 to 9.352	No	ns	0.9937
21d vs. 49d	-1.4	-13.35 to 10.55	No	ns	0.9998
21d vs. 56d	-4.6	-16.55 to 7.352	No	ns	0.8967
28d vs. 35d	-4.8	-16.75 to 7.152	No	ns	0.8766
28d vs. 42d	-7	-18.95 to 4.952	No	ns	0.5533
28d vs. 49d	-5.8	-17.75 to 6.152	No	ns	0.7475
28d vs. 56d	-9	-20.95 to 2.952	No	ns	0.2574
35d vs. 42d	-2.2	-14.15 to 9.752	No	ns	0.9975
35d vs. 49d	-1	-12.95 to 10.95	No	ns	>0.9999
35d vs. 56d	-4.2	-16.15 to 7.752	No	ns	0.9306
42d vs. 49d	1.2	-10.75 to 13.15	No	ns	>0.9999
42d vs. 56d	-2	-13.95 to 9.952	No	ns	0.9985
49d vs. 56d	-3.2	-15.15 to 8.752	No	ns	0.9813
Female					
7d vs. 21d	0.8	-11.15 to 12.75	No	ns	>0.9999
7d vs. 28d	0.6	-11.35 to 12.55	No	ns	>0.9999
7d vs. 35d	-2.4	-14.35 to 9.552	No	ns	0.9959
7d vs. 42d	-4.6	-16.55 to 7.352	No	ns	0.8967
7d vs. 49d	0.2	-11.75 to 12.15	No	ns	>0.9999
7d vs. 56d	-4.4	-16.35 to 7.552	No	ns	0.9147
21d vs. 28d	-0.2	-12.15 to 11.75	No	ns	>0.9999
21d vs. 35d	-3.2	-15.15 to 8.752	No	ns	0.9813
21d vs. 42d	-5.4	-17.35 to 6.552	No	ns	0.8043
21d vs. 49d	-0.6	-12.55 to 11.35	No	ns	>0.9999
21d vs. 56d	-5.2	-17.15 to 6.752	No	ns	0.8303
28d vs. 35d	-3	-14.95 to 8.952	No	ns	0.9866
28d vs. 42d	-5.2	-17.15 to 6.752	No	ns	0.8303
28d vs. 49d	-0.4	-12.35 to 11.55	No	ns	>0.9999
28d vs. 56d	-5	-16.95 to 6.952	No	ns	0.8544
35d vs. 42d	-2.2	-14.15 to 9.752	No	ns	0.9975
35d vs. 49d	2.6	-9.352 to 14.55	No	ns	0.9937
35d vs. 56d	-2	-13.95 to 9.952	No	ns	0.9985
42d vs. 49d	4.8	7.152 to 16.75	No	ns	0.8766
42d vs. 56d	0.2	-11.75 to 12.15	No	ns	>0.9999
49d vs. 56d	-4.6	-16.55 to 7.352	No	ns	0.8967

Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF
7d Male vs. Female	-6	-1	-5	5.606		5	5	1.261
21d Male vs. Female	-2	-1.8	-0.2	5.606		5	5	0.05046
28d Male vs. Female	-6.4	-1.6	-4.8	5.606		5	5	1.211
35d Male vs. Female	-1.6	1.4	-3	5.606		5	5	0.7568
42d Male vs. Female	0.6	3.6	-3	5.606		5	5	0.7568
49d Male vs. Female	-0.6	-1.2	0.6	5.606		5	5	0.1514
56d Male vs. Female	2.6	3.4	-0.8	5.606		5	5	0.2018
Male								
7d vs. 21d	-6	-2	-4	3.885		5	5	1.456
7d vs. 28d	-6	-6.4	0.4	3.885		5	5	0.1456
7d vs. 35d	-6	-1.6	-4.4	3.885		5	5	1.602
7d vs. 42d	-6	0.6	-6.6	3.885		5	5	2.403
7d vs. 49d	-6	-0.6	-5.4	3.885		5	5	1.966
7d vs. 56d	-6	2.6	-8.6	3.885		5	5	3.131
21d vs. 28d	-2	-6.4	4.4	3.885		5	5	1.602
21d vs. 35d	-2	-1.8	-0.4	3.885		5	5	0.1456
21d vs. 42d	-2	0.6	-2.6	3.885		5	5	0.9465
21d vs. 49d	-2	-0.6	-1.4	3.885		5	5	0.5097
21d vs. 56d	-2	2.6	-4.6	3.885		5	5	1.675
28d vs. 35d	-6.4	-1.6	-4.8	3.885		5	5	1.747
28d vs. 42d	-6.4	0.6	-7	3.885		5	5	2.548
28d vs. 49d	-6.4	-0.6	-5.8	3.885		5	5	2.111
28d vs. 56d	-6.4	2.6	-9	3.885		5	5	3.276
35d vs. 42d	-1.6	0.6	-2.2	3.885		5	5	0.8009
35d vs. 49d	-1.6	-0.6	-1	3.885		5	5	0.364
35d vs. 56d	-1.6	2.6	-4.2	3.885		5	5	1.529
42d vs. 49d	0.6	-0.6	1.2	3.885		5	5	0.4368
42d vs. 56d	0.6	2.6	-2	3.885		5	5	0.7281
49d vs. 56d	-0.6	2.6	-3.2	3.885		5	5	1.165
Female								
7d vs. 21d	-1	-1.8	0.8	3.885		5	5	0.2912
7d vs. 28d	-1	-1.6	0.6	3.885		5	5	0.2184
7d vs. 35d	-1	1.4	-2.4	3.885		5	5	0.8737
7d vs. 42d	-1	3.6	-4.6	3.885		5	5	1.675
7d vs. 49d	-1	-1.2	0.2	3.885		5	5	0.07281
7d vs. 56d	-1	3.4	-4.4	3.885		5	5	1.602
21d vs. 28d	-1.8	-1.6	-0.2	3.885		5	5	0.07281
21d vs. 35d	-1.8	1.4	-3.2	3.885		5	5	1.165
21d vs. 42d	-1.8	3.6	-5.4	3.885		5	5	1.966
21d vs. 49d	-1.8	-1.2	-0.6	3.885		5	5	0.2184
21d vs. 56d	-1.8	3.4	-5.2	3.885		5	5	1.893
28d vs. 35d	-1.6	1.4	-3	3.885		5	5	1.092
28d vs. 42d	-1.6	3.6	-5.2	3.885		5	5	1.893
28d vs. 49d	-1.6	-1.2	-0.4	3.885		5	5	0.1456
28d vs. 56d	-1.6	3.4	-5	3.885		5	5	1.82
35d vs. 42d	1.4	1.4	-2.2	3.885		5	5	0.8009
35d vs. 49d	1.4	-1.2	2.6	3.885		5	5	0.9465
35d vs. 56d	1.4	3.4	-2	3.885		5	5	0.7281
42d vs. 49d	3.6	-1.2	4.8	3.885		5	5	1.747
42d vs. 56d	3.6	3.4	0.2	3.885		5	5	0.07281
49d vs. 56d	-1.2	3.4	-4.6	3.885		5	5	1.675

Change in Hut Time (s)										Baseline Hut Time (s)		
Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means					Column B vs. Column A	Female vs. Male	
Time x Sex	8.463	0.3064	ns	No	Mean of Male	-17.15						
Time	3.28	0.8215	ns	No	Mean of Female	-45.15						
Sex	3.767	0.3423	ns	No	Difference between means	28						
Subject	29.57	0.0051	**	Yes	SE of difference	27.74						
					95% CI of difference	-35.96 to 91.96						
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value					Unpaired t test P value	0.1787	
7d Male vs. Female	47.27	-46.64 to 141.2	No	ns	0.3176					P value summary	ns	
21d Male vs. Female	53.51	-40.40 to 147.4	No	ns	0.2585					Significantly different (P < 0.05)?	No	
28d Male vs. Female	9.01	-84.90 to 102.9	No	ns	0.8483					One- or two-tailed P value?	Two-tailed	
35d Male vs. Female	59.73	-34.18 to 153.6	No	ns	0.2079					t, df	t=1.474, df=8	
42d Male vs. Female	59.87	-34.04 to 153.8	No	ns	0.2068					Mean of column A	100.7	
49d Male vs. Female	-66.33	-160.2 to 27.58	No	ns	0.1626					Mean of column B	157.2	
56d Male vs. Female	32.93	-60.98 to 126.8	No	ns	0.4853					Difference between means (B - A) ± SEM	56.49 ± 38.33	
										95% confidence interval	-31.89 to 144.9	
										R squared (eta squared)	0.2136	
Male												
7d vs. 21d	7.44	-118.2 to 133.0	No	ns	>0.9999							
7d vs. 28d	31.34	-94.26 to 156.9	No	ns		0.987						
7d vs. 35d	0.16	-125.4 to 125.8	No	ns	>0.9999							
7d vs. 42d	-5.02	-130.6 to 120.6	No	ns	>0.9999							
7d vs. 49d	37.16	-88.44 to 162.8	No	ns		0.9691						
7d vs. 56d	33.72	-91.88 to 159.3	No	ns		0.981						
21d vs. 28d	23.9	-101.7 to 149.5	No	ns		0.997						
21d vs. 35d	-7.28	-132.9 to 118.3	No	ns	>0.9999							
21d vs. 42d	-12.46	-138.1 to 113.1	No	ns	>0.9999							
21d vs. 49d	29.72	-95.88 to 155.3	No	ns		0.9901						
21d vs. 56d	26.28	-99.32 to 151.9	No	ns		0.9949						
28d vs. 35d	-31.18	-156.8 to 94.42	No	ns		0.9873						
28d vs. 42d	-36.36	-162.0 to 89.24	No	ns		0.9723						
28d vs. 49d	5.82	-119.8 to 131.4	No	ns	>0.9999							
28d vs. 56d	2.38	-123.2 to 128.0	No	ns	>0.9999							
35d vs. 42d	-5.18	-130.8 to 120.4	No	ns	>0.9999							
35d vs. 49d	37	-88.60 to 162.6	No	ns		0.9698						
35d vs. 56d	33.56	-92.04 to 159.2	No	ns		0.9815						
42d vs. 49d	42.18	-83.42 to 167.8	No	ns		0.9436						
42d vs. 56d	38.74	-86.86 to 164.3	No	ns		0.9522						
49d vs. 56d	-3.44	-129.0 to 122.2	No	ns	>0.9999							
Female												
7d vs. 21d	13.68	-111.9 to 139.3	No	ns		0.9999						
7d vs. 28d	-6.92	-132.5 to 118.7	No	ns	>0.9999							
7d vs. 35d	12.62	-113.0 to 138.2	No	ns	>0.9999							
7d vs. 42d	7.58	-118.0 to 133.2	No	ns	>0.9999							
7d vs. 49d	-76.44	-202.0 to 49.16	No	ns		0.5078						
7d vs. 56d	19.38	-106.2 to 145.0	No	ns		0.9991						
21d vs. 28d	-20.6	-146.2 to 105.0	No	ns		0.9987						
21d vs. 35d	-1.06	-126.7 to 124.5	No	ns	>0.9999							
21d vs. 42d	-6.1	-131.7 to 119.5	No	ns	>0.9999							
21d vs. 49d	-90.12	-215.7 to 35.48	No	ns		0.3107						
21d vs. 56d	5.7	-119.9 to 131.3	No	ns	>0.9999							
28d vs. 35d	19.54	-106.1 to 145.1	No	ns		0.999						
28d vs. 42d	14.5	-111.1 to 140.1	No	ns		0.9998						
28d vs. 49d	-69.52	-195.1 to 56.08	No	ns		0.6174						
28d vs. 56d	26.3	-99.30 to 151.9	No	ns		0.9949						
35d vs. 42d	-5.04	-130.6 to 120.6	No	ns	>0.9999							
35d vs. 49d	-89.06	-214.7 to 36.54	No	ns		0.3243						
35d vs. 56d	6.76	-118.8 to 132.4	No	ns	>0.9999							
42d vs. 49d	-84.02	-209.6 to 41.58	No	ns		0.3933						
42d vs. 56d	11.8	-113.8 to 137.4	No	ns	>0.9999							
49d vs. 56d	95.82	-29.78 to 221.4	No	ns		0.2436						
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF				
7d Male vs. Female	-2.18	-49.45	47.27	46.88		5	5	1.426			56	
21d Male vs. Female	-9.62	-63.13	53.51	46.88		5	5	1.614			56	
28d Male vs. Female	-33.52	-42.53	9.01	46.88		5	5	0.2718			56	
35d Male vs. Female	-2.34	-62.07	59.73	46.88		5	5	1.802			56	
42d Male vs. Female	2.84	-57.03	59.87	46.88		5	5	1.806			56	
49d Male vs. Female	-39.34	26.99	-66.33	46.88		5	5	2.001			56	
56d Male vs. Female	-35.9	-68.83	32.93	46.88		5	5	0.9934			56	
Male												
7d vs. 21d	-2.18	-9.62	7.44	40.82		5	5	0.2577			48	
7d vs. 28d	-2.18	-33.52	31.34	40.82		5	5	1.086			48	
7d vs. 35d	-2.18	-2.34	0.16	40.82		5	5	0.005543			48	
7d vs. 42d	-2.18	2.84	-5.02	40.82		5	5	0.1739			48	
7d vs. 49d	-2.18	-39.34	37.16	40.82		5	5	1.287			48	
7d vs. 56d	-2.18	-35.9	33.72	40.82		5	5	1.168			48	
21d vs. 28d	-9.62	-33.52	23.9	40.82		5	5	0.828			48	
21d vs. 35d	-9.62	-2.34	7.28	40.82		5	5	0.2522			48	
21d vs. 42d	-9.62	2.84	-12.46	40.82		5	5	0.4317			48	
21d vs. 49d	-9.62	-39.34	29.72	40.82		5	5	1.03			48	
21d vs. 56d	-9.62	-35.9	26.28	40.82		5	5	0.9104			48	
28d vs. 35d	-33.52	-2.34	-31.18	40.82		5	5	1.08			48	
28d vs. 42d	-33.52	2.84	-36.36	40.82		5	5	1.26			48	
28d vs. 49d	-33.52	-39.34	5.82	40.82		5	5	0.2016			48	
28d vs. 56d	-33.52	-35.9	2.38	40.82		5	5	0.08245			48	
35d vs. 42d	-2.34	2.84	-5.18	40.82		5	5	0.1795			48	
35d vs. 49d	-2.34	-39.34	37	40.82		5	5	1.282			48	
35d vs. 56d	-2.34	-35.9	33.56	40.82		5	5	1.163			48	
42d vs. 49d	2.84	-39.34	42.18	40.82		5	5	1.461			48	
42d vs. 56d	2.84	-35.9	38.74	40.82		5	5	1.342			48	
49d vs. 56d	-39.34	-35.9	-3.44	40.82		5	5	0.1192			48	
Female												
7d vs. 21d	-49.45	-63.13	13.68	40.82		5	5	0.4739			48	
7d vs. 28d	-49.45	-42.53	-6.92	40.82		5	5	0.2397			48	
7d vs. 35d	-49.45	-62.07	12.62	40.82		5	5	0.4372			48	
7d vs. 42d	-49.45	-57.03	7.58	40.82		5	5	0.2626			48	
7d vs. 49d	-49.45	26.99	-76.44	40.82		5	5	2.648			48	
7d vs. 56d	-49.45	-68.83	19.38	40.82		5	5	0.6714			48	
21d vs. 28d	-63.13	-42.53	-20.6	40.82		5	5	0.7137			48	
21d vs. 35d	-63.13	-62.07	-1.06	40.82		5	5	0.03672			48	
21d vs. 42d	-63.13	-57.03	-6.1	40.82		5	5	0.2113			48	
21d vs. 49d	-63.13	26.99	-90.12	40.82		5	5	3.122			48	
21d vs. 56d	-63.13	-68.83	5.7	40.82		5	5	0.1975			48	
28d vs. 35d	-42.53	-62.07	19.54	40.82		5	5	0.6769			48	
28d vs. 42d	-42.53	-57.03	14.5	40.82		5	5	0.5023			48	
28d vs. 49d	-42.53	26.99	-69.52	40.82		5	5	2.408			48	
28d vs. 56d	-42.53	-68.83	26.3	40.82		5	5	0.9111			48	
35d vs. 42d	-62.07	-57.03	-5.04	40.82		5	5	0.1746			48	
35d vs. 49d	-62.07	26.99	-89.06	40.82		5	5	3.085			48	
35d vs. 56d	-62.07	-68.83	6.76	40.82		5	5	0.2342			48	
42d vs. 49d	-57.03	26.99	-84.02	40.82		5	5	2.911			48	
42d vs. 56d	-57.03	-68.83	11.8	40.82		5	5	0.4088			48	
49d vs. 56d	26.99	-68.83	95.82	40.82		5	5	3.32			48	

Change in Hut Mean Visit Time (s)										Baseline Hut Mean Visit Time (s)		
Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means					Column B	Female	
Time x Sex	10.1	0.3818 ns	No	No	Mean of Male	-0.33	1.189	Column A	Male			
Time	7.798	0.5442 ns	No	No	Mean of Female	-1.519						
Sex	0.2076	0.6563 ns	No	No	Difference between means	3.286						
Subject	7.775	0.749 ns	No	No	SE of difference	-9.095 to 6.058						
Tukey's multiple comparisons test										Unpaired t test		
	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value					P value	ns	0.3505
										P value summary	No	
										Significantly different (P < 0.05)?	Two-tailed	
										One- or two-tailed P value?	t=0.9914, df=8	
										t, df		
7d										Mean of column A	5.09	
Male vs. Female	3.85	-17.51 to 25.21	No	ns	0.7194					Mean of column B	6.86	
21d										Difference between means (B - A) ± SEM	1.770 ± 1.785	
Male vs. Female	2.89	-18.47 to 24.25	No	ns	0.7874					95% confidence interval	-2.347 to 5.887	
28d										R squared (eta squared)	0.1094	
Male vs. Female	1.09	-20.27 to 22.45	No	ns	0.919							
35d												
Male vs. Female	3.59	-17.77 to 24.95	No	ns	0.7376							
42d												
Male vs. Female	3.39	-17.97 to 24.75	No	ns	0.7517							
49d												
Male vs. Female	-27.37	-48.73 to -6.007	Yes	*	0.013							
56d												
Male vs. Female	1.93	-19.43 to 23.29	No	ns	0.857							
Male												
7d vs. 21d	1.76	-31.95 to 35.47	No	ns	>0.9999							
7d vs. 28d	2.08	-31.63 to 35.79	No	ns	>0.9999							
7d vs. 35d	1.4	-32.31 to 35.11	No	ns	>0.9999							
7d vs. 42d	1.84	-31.87 to 35.55	No	ns	>0.9999							
7d vs. 49d	3.8	-29.91 to 37.51	No	ns	0.9998							
7d vs. 56d	3.82	-29.89 to 37.53	No	ns	0.9998							
21d vs. 28d	0.32	-33.39 to 34.03	No	ns	>0.9999							
21d vs. 35d	-0.36	-34.07 to 33.35	No	ns	>0.9999							
21d vs. 42d	0.08	-33.63 to 33.79	No	ns	>0.9999							
21d vs. 49d	2.04	-31.87 to 35.75	No	ns	>0.9999							
21d vs. 56d	2.06	-31.65 to 35.77	No	ns	>0.9999							
28d vs. 35d	-0.68	-34.39 to 33.03	No	ns	>0.9999							
28d vs. 42d	-0.24	-33.95 to 33.47	No	ns	>0.9999							
28d vs. 49d	1.72	-31.99 to 35.43	No	ns	>0.9999							
28d vs. 56d	1.74	-31.97 to 35.45	No	ns	>0.9999							
35d vs. 42d	0.44	-33.27 to 34.15	No	ns	>0.9999							
35d vs. 49d	2.4	-31.31 to 36.11	No	ns	>0.9999							
35d vs. 56d	2.42	-31.29 to 36.13	No	ns	>0.9999							
42d vs. 49d	1.96	-31.75 to 35.67	No	ns	>0.9999							
42d vs. 56d	1.98	-31.73 to 35.69	No	ns	>0.9999							
49d vs. 56d	0.02	-33.69 to 33.73	No	ns	>0.9999							
Female												
7d vs. 21d	0.8	-32.81 to 34.51	No	ns	>0.9999							
7d vs. 28d	-0.68	-34.39 to 33.03	No	ns	>0.9999							
7d vs. 35d	1.14	-32.57 to 34.85	No	ns	>0.9999							
7d vs. 42d	1.38	-32.33 to 35.09	No	ns	>0.9999							
7d vs. 49d	-27.42	-51.13 to 6.295	No	ns	0.1815							
7d vs. 56d	1.9	-31.81 to 35.61	No	ns	>0.9999							
21d vs. 28d	-1.48	-35.19 to 32.23	No	ns	>0.9999							
21d vs. 35d	0.34	-33.37 to 34.05	No	ns	>0.9999							
21d vs. 42d	0.58	-33.13 to 34.29	No	ns	>0.9999							
21d vs. 49d	-28.22	-51.93 to 5.495	No	ns	0.1566							
21d vs. 56d	1.1	-32.81 to 34.81	No	ns	>0.9999							
28d vs. 35d	1.82	-31.89 to 35.53	No	ns	>0.9999							
28d vs. 42d	2.06	-31.65 to 35.77	No	ns	>0.9999							
28d vs. 49d	-26.74	-50.45 to 6.975	No	ns	0.2048							
28d vs. 56d	2.58	-31.13 to 36.29	No	ns	>0.9999							
35d vs. 42d	0.24	-33.47 to 33.95	No	ns	>0.9999							
35d vs. 49d	-28.56	-52.27 to 5.155	No	ns	0.1469							
35d vs. 56d	0.76	-32.95 to 34.47	No	ns	>0.9999							
42d vs. 49d	-28.8	-52.51 to 4.915	No	ns	0.1403							
42d vs. 56d	0.52	-33.19 to 34.23	No	ns	>0.9999							
49d vs. 56d	29.32	-4.395 to 63.03	No	ns	0.1269							
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF				
7d												
Male vs. Female	1.77	-2.08	3.85	10.66		5	5	0.5106		56		
21d												
Male vs. Female	0.01	-2.88	2.89	10.66		5	5	0.3833		56		
28d												
Male vs. Female	-0.31	-1.4	1.09	10.66		5	5	0.1446		56		
35d												
Male vs. Female	0.37	-3.22	3.59	10.66		5	5	0.4761		56		
42d												
Male vs. Female	-0.07	-3.46	3.39	10.66		5	5	0.4496		56		
49d												
Male vs. Female	-2.03	25.34	-27.37	10.66		5	5	3.63		56		
56d												
Male vs. Female	-2.05	-3.98	1.93	10.66		5	5	0.2559		56		
Male												
7d vs. 21d	1.77	0.01	1.76	10.96		5	5	0.2271		48		
7d vs. 28d	1.77	-0.31	2.08	10.96		5	5	0.2684		48		
7d vs. 35d	1.77	0.37	1.4	10.96		5	5	0.1807		48		
7d vs. 42d	1.77	-0.07	1.84	10.96		5	5	0.2375		48		
7d vs. 49d	1.77	-2.03	3.8	10.96		5	5	0.4904		48		
7d vs. 56d	1.77	-2.05	3.82	10.96		5	5	0.493		48		
21d vs. 28d	0.01	-0.31	0.32	10.96		5	5	0.0413		48		
21d vs. 35d	0.01	0.37	-0.36	10.96		5	5	0.04646		48		
21d vs. 42d	0.01	-0.07	0.08	10.96		5	5	0.01032		48		
21d vs. 49d	0.01	-2.03	2.04	10.96		5	5	0.2633		48		
21d vs. 56d	0.01	-2.05	2.06	10.96		5	5	0.2659		48		
28d vs. 35d	-0.31	0.37	-0.68	10.96		5	5	0.08776		48		
28d vs. 42d	-0.31	-0.07	-0.24	10.96		5	5	0.03097		48		
28d vs. 49d	-0.31	-2.03	1.72	10.96		5	5	0.222		48		
28d vs. 56d	-0.31	-2.05	1.74	10.96		5	5	0.2246		48		
35d vs. 42d	0.37	-0.07	0.44	10.96		5	5	0.05679		48		
35d vs. 49d	0.37	-2.03	2.4	10.96		5	5	0.3007		48		
35d vs. 56d	0.37	-2.05	2.42	10.96		5	5	0.3123		48		
42d vs. 49d	-0.07	-2.03	1.96	10.96		5	5	0.253		48		
42d vs. 56d	-0.07	-2.05	1.98	10.96		5	5	0.2555		48		
49d vs. 56d	-2.03	-2.05	0.02	10.96		5	5	0.002581		48		
Female												
7d vs. 21d	-2.08	-2.88	0.8	10.96		5	5	0.1032		48		
7d vs. 28d	-2.08	-1.4	-0.68	10.96		5	5	0.08776		48		
7d vs. 35d	-2.08	-3.22	1.14	10.96		5	5	0.1471		48		
7d vs. 42d	-2.08	-3.46	1.38	10.96		5	5	0.1781		48		
7d vs. 49d	-2.08	25.34	-27.42	10.96		5	5	3.539		48		
7d vs. 56d	-2.08	-3.98	1.9	10.96		5	5	0.2452		48		
21d vs. 28d	-2.88	-1.4	-1.48	10.96		5	5	0.191		48		
21d vs. 35d	-2.88	-3.22	0.34	10.96		5	5	0.04388		48		
21d vs. 42d	-2.88	-3.46	0.58	10.96		5	5	0.07485		48		
21d vs. 49d	-2.88	25.34	-28.22	10.96		5	5	3.642		48		
21d vs. 56d	-2.88	-3.98	1.1	10.96		5	5	0.142		48		
28d vs. 35d	-1.4	-3.22	1.82	10.96		5	5	0.2349		48		
28d vs. 42d	-1.4	-3.46	2.06	10.96		5	5	0.2659		48		
28d vs. 49d	-1.4	25.34	-26.74	10.96		5	5	3.451		48		
28d vs. 56d	-1.4	-3.98	2.58	10.96		5	5	0.333		48		
35d vs. 42d	-3.22	-3.46	0.24	10.96		5	5	0.03097		48		
35d vs. 49d	-3.22	25.34	-28.56	10.96		5	5	3.686		48		
35d vs. 56d	-3.22	-3.98	0.76	10.96		5	5	0.09808		48		
42d vs. 49d	-3.46	25.34	-28.8	10.96		5	5	3.717		48		
42d vs. 56d	-3.46	-3.98	0.52	10.96		5	5	0.06711		48		
49d vs. 56d	25.34	-3.98	29.32	10.96		5	5	3.784		48		

Change in Top of Hut Entries

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	4.292	0.5459	ns	No	Mean of Male -6.471
Time	8.504	0.1508	ns	No	Mean of Female 10.39
Sex	27.54	0.009	**	Yes	Difference between means -16.86
Subject	18.75	0.0139	*	Yes	SE of difference 4.918
					95% CI of difference -28.20 to -5.516

Baseline Top of Hut Entries

Column B vs. Column A	Female vs. Male
Unpaired t test	0.5507
P value	ns
P value summary	No
Significantly different (P < 0.05)?	Two-tailed
One- or two-tailed P value?	t=0.6229, df=8
Mean of column A	34.1
Mean of column B	29.7
Difference between means (B - A) ± SEM	-4.400 ± 7.064
95% confidence interval	-20.69 to 11.89
R squared (eta squared)	0.04625

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-19.4	-36.97 to -1.825	Yes	*	0.0311
21d					
Male vs. Female	-10.8	-28.37 to 6.775	No	ns	0.2235
28d					
Male vs. Female	-21.4	-38.97 to -3.825	Yes	*	0.0179
35d					
Male vs. Female	-18.8	-36.37 to -1.225	Yes	*	0.0365
42d					
Male vs. Female	-28.4	-45.97 to -10.83	Yes	**	0.002
49d					
Male vs. Female	-8.2	-25.77 to 9.375	No	ns	0.354
56d					
Male vs. Female	-11	-28.57 to 6.575	No	ns	0.2151
Male					
7d vs. 21d	-17.4	-41.54 to 6.743	No	ns	0.3057
7d vs. 28d	-8.2	-32.34 to 15.94	No	ns	0.9406
7d vs. 35d	-9.8	-33.94 to 14.34	No	ns	0.8711
7d vs. 42d	-9.2	-33.34 to 14.94	No	ns	0.901
7d vs. 49d	-17.4	-41.54 to 6.743	No	ns	0.3057
7d vs. 56d	-19.4	-43.54 to 4.743	No	ns	0.1925
21d vs. 28d	9.2	-14.94 to 33.34	No	ns	0.901
21d vs. 35d	7.6	-16.54 to 31.74	No	ns	0.9584
21d vs. 42d	8.2	-15.94 to 32.34	No	ns	0.9406
21d vs. 49d	0	-24.14 to 24.14	No	ns	>0.9999
21d vs. 56d	-2	-26.14 to 22.14	No	ns	>0.9999
28d vs. 35d	-1.6	-25.74 to 22.54	No	ns	>0.9999
28d vs. 42d	-1	-25.14 to 23.14	No	ns	>0.9999
28d vs. 49d	-9.2	-33.34 to 14.94	No	ns	0.901
28d vs. 56d	-11.2	-35.34 to 12.94	No	ns	0.7845
35d vs. 42d	0.6	-23.54 to 24.74	No	ns	>0.9999
35d vs. 49d	-7.6	-31.74 to 16.54	No	ns	0.9584
35d vs. 56d	-9.6	-33.74 to 14.54	No	ns	0.8816
42d vs. 49d	-8.2	-32.34 to 15.94	No	ns	0.9406
42d vs. 56d	-10.2	-34.34 to 13.94	No	ns	0.8486
49d vs. 56d	-2	-26.14 to 22.14	No	ns	>0.9999
Female					
7d vs. 21d	-8.8	-32.94 to 15.34	No	ns	0.9184
7d vs. 28d	-10.2	-34.34 to 13.94	No	ns	0.8486
7d vs. 35d	-9.2	-33.34 to 14.94	No	ns	0.901
7d vs. 42d	-18.2	-42.34 to 5.943	No	ns	0.2562
7d vs. 49d	-6.2	-30.34 to 17.94	No	ns	0.9849
7d vs. 56d	-11	-35.14 to 13.14	No	ns	0.7982
21d vs. 28d	-1.4	-25.54 to 22.74	No	ns	>0.9999
21d vs. 35d	-0.4	-24.54 to 23.74	No	ns	>0.9999
21d vs. 42d	-9.4	-33.54 to 14.74	No	ns	0.8915
21d vs. 49d	2.6	-21.54 to 26.74	No	ns	0.9999
21d vs. 56d	-2.2	-26.34 to 21.94	No	ns	>0.9999
28d vs. 35d	1	-23.14 to 25.14	No	ns	>0.9999
28d vs. 42d	-8	-32.14 to 16.14	No	ns	0.947
28d vs. 49d	4	-20.14 to 28.14	No	ns	0.9986
28d vs. 56d	-0.8	-24.94 to 23.34	No	ns	>0.9999
35d vs. 42d	-9	-33.14 to 15.14	No	ns	0.9099
35d vs. 49d	3	-21.14 to 27.14	No	ns	0.9997
35d vs. 56d	-1.8	-25.94 to 22.34	No	ns	>0.9999
42d vs. 49d	12	-12.14 to 36.14	No	ns	0.7261
42d vs. 56d	7.2	-16.94 to 31.34	No	ns	0.9679
49d vs. 56d	-4.8	-28.94 to 19.34	No	ns	0.9961

Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF
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7d								
Male vs. Female	-18.1	1.3	-19.4	8.773		5	5	3.127
21d								
Male vs. Female	-0.7	10.1	-10.8	8.773		5	5	1.741
28d								
Male vs. Female	-9.9	11.5	-21.4	8.773		5	5	3.45
35d								
Male vs. Female	-8.3	10.5	-18.8	8.773		5	5	3.031
42d								
Male vs. Female	-8.9	19.5	-28.4	8.773		5	5	4.578
49d								
Male vs. Female	-0.7	7.5	-8.2	8.773		5	5	1.322
56d								
Male vs. Female	1.3	12.3	-11	8.773		5	5	1.773
Male								
7d vs. 21d	-18.1	-0.7	-17.4	7.847		5	5	3.136
7d vs. 28d	-18.1	-9.9	-8.2	7.847		5	5	1.478
7d vs. 35d	-18.1	-8.3	-9.8	7.847		5	5	1.766
7d vs. 42d	-18.1	-8.9	-9.2	7.847		5	5	1.658
7d vs. 49d	-18.1	-0.7	-17.4	7.847		5	5	3.136
7d vs. 56d	-18.1	1.3	-19.4	7.847		5	5	3.496
21d vs. 28d	-0.7	-9.9	9.2	7.847		5	5	1.658
21d vs. 35d	-0.7	-8.3	7.6	7.847		5	5	1.37
21d vs. 42d	-0.7	-8.9	8.2	7.847		5	5	1.478
21d vs. 49d	-0.7	-0.7	0	7.847		5	5	0
21d vs. 56d	-0.7	1.3	-2	7.847		5	5	0.3604
28d vs. 35d	-9.9	-8.3	-1.6	7.847		5	5	0.2884
28d vs. 42d	-9.9	-8.9	-1	7.847		5	5	0.1802
28d vs. 49d	-9.9	-0.7	-9.2	7.847		5	5	1.658
28d vs. 56d	-9.9	1.3	-11.2	7.847		5	5	2.018
35d vs. 42d	-8.3	-8.9	0.6	7.847		5	5	0.1081
35d vs. 49d	-8.3	-0.7	-7.6	7.847		5	5	1.37
35d vs. 56d	-8.3	1.3	-9.6	7.847		5	5	1.73
42d vs. 49d	-8.9	-0.7	-8.2	7.847		5	5	1.478
42d vs. 56d	-8.9	1.3	-10.2	7.847		5	5	1.838
49d vs. 56d	-0.7	1.3	-2	7.847		5	5	0.3604
Female								
7d vs. 21d	1.3	10.1	-8.8	7.847		5	5	1.586
7d vs. 28d	1.3	11.5	-10.2	7.847		5	5	1.838
7d vs. 35d	1.3	10.5	-9.2	7.847		5	5	1.658
7d vs. 42d	1.3	19.5	-18.2	7.847		5	5	3.28
7d vs. 49d	1.3	7.5	-6.2	7.847		5	5	1.117
7d vs. 56d	1.3	12.3	-11	7.847		5	5	1.982
21d vs. 28d	10.1	11.5	-1.4	7.847		5	5	0.2523
21d vs. 35d	10.1	10.5	-0.4	7.847		5	5	0.07209
21d vs. 42d	10.1	19.5	-9.4	7.847		5	5	1.694
21d vs. 49d	10.1	7.5	2.6	7.847		5	5	0.4686
21d vs. 56d	10.1	12.3	-2.2	7.847		5	5	0.3965
28d vs. 35d	11.5	10.5	1	7.847		5	5	0.1802
28d vs. 42d	11.5	19.5	-8	7.847		5	5	1.442
28d vs. 49d	11.5	7.5	4	7.847		5	5	0.7209
28d vs. 56d	11.5	12.3	-0.8	7.847		5	5	0.1442
35d vs. 42d	10.5	19.5	-9	7.847		5	5	1.622
35d vs. 49d	10.5	7.5	3	7.847		5	5	0.5407
35d vs. 56d	10.5	12.3	-1.8	7.847		5	5	0.3244
42d vs. 49d	19.5	7.5	12	7.847		5	5	2.163
42d vs. 56d	19.5	12.3	7.2	7.847		5	5	1.298
49d vs. 56d	7.5	12.3	-4.8	7.847		5	5	0.8651

Change in Top of Hut Exits

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	4.164	0.5695 ns	No	No	Mean of Male Mean of Female
Time	8.444	0.1577 ns	No	No	Difference between means
Sex	27.77	0.0083 **	Yes	Yes	SE of difference
Subject	18.35	0.0165 *	Yes	Yes	95% CI of difference

Baseline Top of Hut Exits

Column B vs. Column A	Female vs. Male
-6.629	10.19
-16.81	4.832
-27.96 to -5.671	

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	Unpaired t test P value P value summary Significantly different (P < 0.05)? One- or two-tailed P value? t, df	0.5348 ns No Two-tailed t=0.6485, df=8
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7d Male vs. Female	-19.3	-36.75 to -1.849	Yes	*	0.0308		
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21d Male vs. Female	-11.3	-28.75 to 6.151	No	ns	0.1999		
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28d Male vs. Female	-21.3	-38.75 to -3.849	Yes	*	0.0177		
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35d Male vs. Female	-18.5	-35.95 to -1.049	Yes	*	0.0381		
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42d Male vs. Female	-28.1	-45.55 to -10.65	Yes	**	0.0021		
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49d Male vs. Female	-7.9	-25.35 to 9.551	No	ns	0.3684		
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56d Male vs. Female	-11.3	-28.75 to 6.151	No	ns	0.1999		
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Male							
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7d vs. 21d	-17.2	-41.29 to 6.888	No	ns	0.3163		
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7d vs. 28d	-8.2	-32.29 to 15.89	No	ns	0.9399		
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7d vs. 35d	-10	-34.09 to 14.09	No	ns	0.8588		
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7d vs. 42d	-9	-33.09 to 15.09	No	ns	0.909		
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7d vs. 49d	-17.6	-41.69 to 6.488	No	ns	0.2902		
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7d vs. 56d	-19	-43.09 to 5.088	No	ns	0.2101		
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21d vs. 28d	9	-15.09 to 33.09	No	ns	0.909		
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21d vs. 35d	7.2	-16.89 to 31.29	No	ns	0.9676		
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21d vs. 42d	8.2	-15.89 to 32.29	No	ns	0.9399		
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21d vs. 49d	-0.4	-24.49 to 23.69	No	ns	>0.9999		
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21d vs. 56d	-1.8	-25.89 to 22.29	No	ns	>0.9999		
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28d vs. 35d	-1.8	-25.89 to 22.29	No	ns	>0.9999		
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28d vs. 42d	-0.8	-24.89 to 23.29	No	ns	>0.9999		
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28d vs. 49d	-9.4	-33.49 to 14.69	No	ns	0.8905		
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28d vs. 56d	-10.8	-34.89 to 13.29	No	ns	0.8098		
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35d vs. 42d	1	-23.09 to 25.09	No	ns	>0.9999		
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35d vs. 49d	-7.6	-31.69 to 16.49	No	ns	0.9579		
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35d vs. 56d	-9	-33.09 to 15.09	No	ns	0.909		
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42d vs. 49d	-8.6	-32.69 to 15.49	No	ns	0.9255		
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42d vs. 56d	-10	-34.09 to 14.09	No	ns	0.8588		
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49d vs. 56d	-1.4	-25.49 to 22.69	No	ns	>0.9999		
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Female							
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7d vs. 21d	-9.2	-33.29 to 14.89	No	ns	0.9		
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7d vs. 28d	-10.2	-34.29 to 13.89	No	ns	0.8473		
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7d vs. 35d	-9.2	-33.29 to 14.89	No	ns	0.9		
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7d vs. 42d	-17.8	-41.89 to 6.288	No	ns	0.2777		
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7d vs. 49d	-6.2	-30.29 to 17.89	No	ns	0.9847		
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7d vs. 56d	-11	-35.09 to 13.09	No	ns	0.7964		
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21d vs. 28d	-1	-25.09 to 23.09	No	ns	>0.9999		
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21d vs. 35d	0	-24.09 to 24.09	No	ns	>0.9999		
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21d vs. 42d	-8.6	-32.69 to 15.49	No	ns	0.9255		
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21d vs. 49d	3	-21.09 to 27.09	No	ns	0.9997		
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21d vs. 56d	-1.8	-25.89 to 22.29	No	ns	>0.9999		
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28d vs. 35d	1	-23.09 to 25.09	No	ns	>0.9999		
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28d vs. 42d	-7.6	-31.69 to 16.49	No	ns	0.9579		
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28d vs. 49d	-4	-20.09 to 28.09	No	ns	0.9986		
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28d vs. 56d	-0.8	-24.89 to 23.29	No	ns	>0.9999		
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35d vs. 42d	-8.6	-32.69 to 15.49	No	ns	0.9255		
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35d vs. 49d	3	-21.09 to 27.09	No	ns	0.9997		
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35d vs. 56d	-1.8	-25.89 to 22.29	No	ns	>0.9999		
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42d vs. 49d	11.6	-12.49 to 35.69	No	ns	0.754		
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42d vs. 56d	6.8	-17.29 to 30.89	No	ns	0.9755		
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49d vs. 56d	-4.8	-28.89 to 19.29	No	ns	0.9961		
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Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF
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7d Male vs. Female	-18.2	1.1	-19.3	8.711		5	5	3.133
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21d Male vs. Female	-1	10.3	-11.3	8.711		5	5	1.834
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28d Male vs. Female	-10	11.3	-21.3	8.711		5	5	3.458
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35d Male vs. Female	-8.2	10.3	-18.5	8.711		5	5	3.003
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42d Male vs. Female	-9.2	18.9	-28.1	8.711		5	5	4.562
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49d Male vs. Female	-0.6	7.3	-7.9	8.711		5	5	1.283
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56d Male vs. Female	0.8	12.1	-11.3	8.711		5	5	1.834
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Male								
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7d vs. 21d	-18.2	-1	-17.2	7.829		5	5	3.107
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7d vs. 28d	-18.2	-10	-8.2	7.829		5	5	1.481
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7d vs. 35d	-18.2	-8.2	-10	7.829		5	5	1.806
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7d vs. 42d	-18.2	-9.2	-9	7.829		5	5	1.626
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7d vs. 49d	-18.2	-0.6	-17.6	7.829		5	5	3.179
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7d vs. 56d	-18.2	0.8	-19	7.829		5	5	3.432
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21d vs. 28d	-1	-10	9	7.829		5	5	1.626
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21d vs. 35d	-1	-8.2	7.2	7.829		5	5	1.301
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21d vs. 42d	-1	-9.2	8.2	7.829		5	5	1.481
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21d vs. 49d	-1	-0.6	-0.4	7.829		5	5	0.07226
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21d vs. 56d	-1	0.8	-1.8	7.829		5	5	0.3251
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28d vs. 35d	-10	-9.2	-1.8	7.829		5	5	0.3251
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28d vs. 42d	-10	-9.2	-0.8	7.829		5	5	0.1445
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28d vs. 49d	-10	-0.6	-9.4	7.829		5	5	1.698
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28d vs. 56d	-10	0.8	-10.8	7.829		5	5	1.951
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35d vs. 42d	-8.2	-9.2	1	7.829		5	5	0.1806
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35d vs. 49d	-8.2	0.6	-7.6	7.829		5	5	1.373
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35d vs. 56d	-8.2	0.8	-9	7.829		5	5	1.626
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42d vs. 49d	-9.2	-0.6	-8.6	7.829		5	5	1.553
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42d vs. 56d	-9.2	0.8	-10	7.829		5	5	1.806
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49d vs. 56d	-0.6	0.8	-1.4	7.829		5	5	0.2529
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Female								
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7d vs. 21d	1.1	10.3	-9.2	7.829		5	5	1.662
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7d vs. 28d	1.1	11.3	-10.2	7.829		5	5	1.943
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7d vs. 35d	1.1	10.3	-9.2	7.829		5	5	1.662
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7d vs. 42d	1.1	18.9	-17.8	7.829		5	5	3.215
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7d vs. 49d	1.1	7.3	-6.2	7.829		5	5	1.12
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7d vs. 56d	1.1	12.1	-11	7.829		5	5	1.987
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21d vs. 28d	10.3	11.3	-1	7.829		5	5	0.1806
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21d vs. 35d	10.3	10.3	0	7.829		5	5	0
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21d vs. 42d	10.3	18.9	-8.6	7.829		5	5	1.553
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21d vs. 49d	10.3	7.3	3	7.829		5	5	0.5419
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21d vs. 56d	10.3	12.1	-1.8	7.829		5	5	0.3251
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28d vs. 35d	11.3	10.3	1	7.829		5	5	0.1806
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28d vs. 42d	11.3	18.9	-7.6	7.829		5	5	1.373
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28d vs. 49d	11.3	7.3	4	7.829		5	5	0.7226
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28d vs. 56d	11.3	12.1	-0.8	7.829		5	5	0.1445
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35d vs. 42d	10.3	18.9	-8.6	7.829		5	5	1.553
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35d vs. 49d	10.3	7.3	3	7.829		5	5	0.5419
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35d vs. 56d	10.3	12.1	-1.8	7.829		5	5	0.3251
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42d vs. 49d	18.9	7.3	11.6	7.829		5	5	2.095
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42d vs. 56d	18.9	12.1	6.8	7.829		5	5	1.226
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49d vs. 56d	7.3	12.1	-4.8	7.829		5	5	0.867
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Change in Top of Hut Time (s)					Baseline Top of Hut Time (s)				
Source of Variation	% of total variation	P value	P value summary	Significant?	Mean of Male	2.97	Column B	Female	
Time x Sex	0.6497	0.9887 ns	0.0544 ns	No	Mean of Female	-0.7529	vs.	vs.	
Time	9.3968	No	No	No	Difference between means	3.763	Column A	Male	
Sex	5.489	0.3825 ns	No	No	SE of difference	1.615			
Subject	51.42 <0.0001	****	Yes	Yes	95% CI of difference	0.03819 to 7.488	Unpaired t test		
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		P value summary	0.4179	
7d							Significantly different (P < 0.05)?	ns	
Male vs. Female	17.75 -84.55 to 120.0	No	ns		0.7294		One- or two-tailed P value?	No	
21d							t df	t=0.8541, df=8	
Male vs. Female	32.05 -70.25 to 134.3	No	ns		0.5328		Mean of column A	95.11	
28d							Mean of column B	124	
Male vs. Female	27.25 -75.05 to 129.5	No	ns		0.5957		Difference between means (B - A) ± SEM	28.85 ± 33.78	
35d							95% confidence interval	-49.04 to 106.7	
Male vs. Female	34.71 -67.59 to 137.0	No	ns		0.4995		R squared (eta squared)	0.08357	
42d									
Male vs. Female	40.21 -62.09 to 142.5	No	ns		0.4344				
49d									
Male vs. Female	60.45 -41.85 to 162.7	No	ns		0.2415				
56d									
Male vs. Female	45.17 -57.13 to 147.5	No	ns		0.3802				
Male									
7d vs. 21d	-34.66 -140.9 to 71.58	No	ns		0.9507				
7d vs. 28d	-14.7 -120.9 to 91.54	No	ns		0.9995				
7d vs. 35d	11.6 -94.64 to 117.8	No	ns		0.9999				
7d vs. 42d	-51.98 -158.2 to 54.28	No	ns		0.7406				
7d vs. 49d	-35.54 -141.8 to 70.70	No	ns		0.8446				
7d vs. 56d	-71.2 -177.4 to 35.04	No	ns		0.3911				
21d vs. 28d	19.98 -86.28 to 126.2	No	ns		0.9972				
21d vs. 35d	46.26 -59.88 to 152.5	No	ns		0.8298				
21d vs. 42d	-17.3 -123.5 to 88.94	No	ns		0.9987				
21d vs. 49d	-6.88 -107.1 to 105.4	No	ns	>0.9999					
21d vs. 56d	-36.54 -142.8 to 69.70	No	ns		0.937				
28d vs. 35d	26.3 -79.94 to 132.5	No	ns		0.9875				
28d vs. 42d	-37.26 -143.5 to 68.98	No	ns		0.9312				
28d vs. 49d	-20.84 -127.1 to 85.40	No	ns		0.9964				
28d vs. 56d	-56.5 -162.7 to 49.74	No	ns		0.6601				
35d vs. 42d	-63.56 -169.8 to 42.68	No	ns		0.5282				
35d vs. 49d	-47.14 -153.4 to 59.10	No	ns		0.8171				
35d vs. 56d	-82.8 -189.0 to 23.44	No	ns		0.2219				
42d vs. 49d	16.42 -89.82 to 122.7	No	ns		0.9991				
42d vs. 56d	-19.24 -125.5 to 87.00	No	ns		0.9977				
49d vs. 56d	-35.66 -141.9 to 70.58	No	ns		0.9437				
Female									
7d vs. 21d	-20.36 -126.6 to 85.88	No	ns		0.9968				
7d vs. 28d	-6.2 -111.4 to 101.0	No	ns	>0.9999					
7d vs. 35d	28.56 -77.88 to 134.8	No	ns		0.9809				
7d vs. 42d	-29.5 -135.7 to 76.74	No	ns		0.9775				
7d vs. 49d	7.16 -99.08 to 113.4	No	ns	>0.9999					
7d vs. 56d	-43.78 -150.0 to 62.46	No	ns		0.8629				
21d vs. 28d	15.16 -91.98 to 121.4	No	ns		0.9994				
21d vs. 35d	48.92 -57.32 to 155.2	No	ns		0.7902				
21d vs. 42d	-9.14 -115.4 to 97.10	No	ns	>0.9999					
21d vs. 49d	27.52 -78.72 to 133.8	No	ns		0.9842				
21d vs. 56d	-23.42 -129.7 to 82.82	No	ns		0.9932				
28d vs. 35d	33.76 -72.48 to 140.0	No	ns		0.9564				
28d vs. 42d	-24.3 -130.5 to 81.94	No	ns		0.9917				
28d vs. 49d	12.36 -93.88 to 118.6	No	ns		0.9998				
28d vs. 56d	-38.58 -144.8 to 67.66	No	ns		0.9197				
35d vs. 42d	-58.06 -164.3 to 48.18	No	ns		0.6313				
35d vs. 49d	-21.4 -127.6 to 84.84	No	ns		0.9958				
35d vs. 56d	-72.34 -178.8 to 33.90	No	ns		0.372				
42d vs. 49d	36.66 -69.58 to 142.9	No	ns		0.8361				
42d vs. 56d	-14.28 -120.5 to 91.96	No	ns		0.9996				
49d vs. 56d	-50.94 -157.2 to 55.30	No	ns		0.7577				
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF	
7d									
Male vs. Female	17.51	-0.24	17.75	51.07		5	5	0.4916	56
21d									
Male vs. Female	52.17	20.12	32.05	51.07		5	5	0.8876	56
28d									
Male vs. Female	32.21	4.96	27.25	51.07		5	5	0.7547	56
35d									
Male vs. Female	5.91	-28.8	34.71	51.07		5	5	0.9613	56
42d									
Male vs. Female	69.47	29.26	40.21	51.07		5	5	1.114	56
49d									
Male vs. Female	53.05	-7.4	60.45	51.07		5	5	1.674	56
56d									
Male vs. Female	88.71	43.54	45.17	51.07		5	5	1.251	56
Male									
7d vs. 21d	17.51	52.17	-34.66	34.53		5	5	1.42	48
7d vs. 28d	17.51	32.21	-14.7	34.53		5	5	0.6021	48
7d vs. 35d	17.51	5.91	11.6	34.53		5	5	0.4751	48
7d vs. 42d	17.51	69.47	-51.96	34.53		5	5	2.128	48
7d vs. 49d	17.51	53.05	-35.54	34.53		5	5	1.456	48
7d vs. 56d	17.51	88.71	-71.2	34.53		5	5	2.916	48
21d vs. 28d	52.17	32.21	19.96	34.53		5	5	0.8175	48
21d vs. 35d	52.17	5.91	46.26	34.53		5	5	1.895	48
21d vs. 42d	52.17	69.47	-17.3	34.53		5	5	0.7085	48
21d vs. 49d	52.17	53.05	-0.88	34.53		5	5	0.03604	48
21d vs. 56d	52.17	88.71	-36.54	34.53		5	5	1.497	48
28d vs. 35d	32.21	5.91	26.3	34.53		5	5	1.077	48
28d vs. 42d	32.21	69.47	-37.26	34.53		5	5	1.526	48
28d vs. 49d	32.21	53.05	-20.84	34.53		5	5	0.8535	48
28d vs. 56d	32.21	88.71	-56.5	34.53		5	5	2.314	48
35d vs. 42d	5.91	69.47	-63.56	34.53		5	5	2.603	48
35d vs. 49d	5.91	53.05	-47.14	34.53		5	5	1.931	48
35d vs. 56d	5.91	88.71	-82.8	34.53		5	5	3.391	48
42d vs. 49d	69.47	53.05	16.42	34.53		5	5	0.6725	48
42d vs. 56d	69.47	88.71	-19.24	34.53		5	5	0.768	48
49d vs. 56d	53.05	88.71	-35.66	34.53		5	5	1.46	48
Female									
7d vs. 21d	-0.24	20.12	-20.36	34.53		5	5	0.8339	48
7d vs. 28d	-0.24	4.96	-5.2	34.53		5	5	0.213	48
7d vs. 35d	-0.24	-28.8	28.56	34.53		5	5	1.17	48
7d vs. 42d	-0.24	29.26	-29.5	34.53		5	5	1.208	48
7d vs. 49d	-0.24	-7.4	7.16	34.53		5	5	0.2932	48
7d vs. 56d	-0.24	43.54	-43.78	34.53		5	5	1.793	48
21d vs. 28d	20.12	4.96	15.16	34.53		5	5	0.6209	48
21d vs. 35d	20.12	-28.8	48.92	34.53		5	5	2.004	48
21d vs. 42d	20.12	29.26	-9.14	34.53		5	5	0.3743	48
21d vs. 49d	20.12	-7.4	27.52	34.53		5	5	1.127	48
21d vs. 56d	20.12	43.54	-23.42	34.53		5	5	0.9592	48
28d vs. 35d	4.96	-28.8	33.76	34.53		5	5	1.383	48
28d vs. 42d	4.96	29.26	-24.3	34.53		5	5	0.9952	48
28d vs. 49d	4.96	-7.4	12.36	34.53		5	5	0.5962	48
28d vs. 56d	4.96	43.54	-38.58	34.53		5	5	1.58	48
35d vs. 42d	-28.8	29.26	-58.06	34.53		5	5	2.378	48
35d vs. 49d	-28.8	-7.4	21.4	34.53		5	5	0.8765	48
35d vs. 56d	-28.8	43.54	-72.34	34.53		5	5	2.963	48
42d vs. 49d	29.26	-7.4	36.66	34.53		5	5	1.501	48
42d vs. 56d	29.26	43.54	-14.28	34.53		5	5	0.5849	48
49d vs. 56d	-7.4	43.54	-50.94	34.53		5	5	2.086	48

Change in Top of Hut Mean Visit Time (s)

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	1.433	0.9158 ns	No	No	Mean of Male	45.58
Time	5.242	0.3125 ns	No	No	Mean of Female	8.777
Sex	23.83	0.0482 *	Yes	Yes	Difference between means	36.8
Subject	35.13 <0.0001	****	Yes	Yes	SE of difference	39.82
					95% CI of difference	-55.03 to 126.6
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	
7d						
Male vs. Female	5.44	0.8890 to 9.991	Yes	*	0.02	
21d						
Male vs. Female	2.34	-2.211 to 6.891	No	ns	0.3074	
28d						
Male vs. Female	3.68	-0.8710 to 8.231	No	ns	0.1109	
35d						
Male vs. Female	3.42	-1.131 to 7.971	No	ns	0.1378	
42d						
Male vs. Female	4.48	-0.07100 to 9.031	No	ns	0.0536	
49d						
Male vs. Female	3.9	-0.6510 to 8.451	No	ns	0.0916	
56d						
Male vs. Female	3.08	-1.471 to 7.631	No	ns	0.1806	
Male						
7d vs. 21d	3.74	-1.569 to 9.049	No	ns	0.3319	
7d vs. 28d	3.06	-2.249 to 8.369	No	ns	0.5719	
7d vs. 35d	4.02	-1.289 to 9.329	No	ns	0.2515	
7d vs. 42d	2.24	-3.069 to 7.549	No	ns	0.8494	
7d vs. 49d	3.18	-2.129 to 8.489	No	ns	0.5268	
7d vs. 56d	2.66	-2.649 to 7.969	No	ns	0.7188	
21d vs. 28d	-0.68	-5.989 to 4.629	No	ns	0.9997	
21d vs. 35d	0.28	-5.029 to 5.589	No	ns	>0.9999	
21d vs. 42d	-1.5	-6.809 to 3.809	No	ns	0.9754	
21d vs. 49d	-0.56	-5.869 to 4.749	No	ns	0.9999	
21d vs. 56d	-1.08	-6.389 to 4.229	No	ns	0.9956	
28d vs. 35d	0.96	-4.349 to 6.269	No	ns	0.9977	
28d vs. 42d	-0.82	-6.129 to 4.489	No	ns	0.9991	
28d vs. 49d	0.12	-5.189 to 5.429	No	ns	>0.9999	
28d vs. 56d	-0.4	-5.709 to 4.909	No	ns	>0.9999	
35d vs. 42d	-1.78	-7.089 to 3.529	No	ns	0.944	
35d vs. 49d	-0.84	-6.149 to 4.469	No	ns	0.9989	
35d vs. 56d	-1.36	-6.669 to 3.949	No	ns	0.9851	
42d vs. 49d	0.94	-4.369 to 6.249	No	ns	0.998	
42d vs. 56d	0.42	-4.889 to 5.729	No	ns	>0.9999	
49d vs. 56d	-0.52	-5.829 to 4.789	No	ns	>0.9999	
Female						
7d vs. 21d	0.64	-4.669 to 5.949	No	ns	0.9998	
7d vs. 28d	1.3	-4.009 to 6.609	No	ns	0.9882	
7d vs. 35d	2	-3.309 to 7.309	No	ns	0.9057	
7d vs. 42d	1.28	-4.029 to 6.589	No	ns	0.9891	
7d vs. 49d	1.64	-3.669 to 6.949	No	ns	0.962	
7d vs. 56d	0.3	-5.009 to 5.609	No	ns	>0.9999	
21d vs. 28d	0.66	-4.649 to 5.969	No	ns	0.9997	
21d vs. 35d	1.36	-3.949 to 6.669	No	ns	0.9851	
21d vs. 42d	0.64	-4.669 to 5.949	No	ns	0.9998	
21d vs. 49d	1	-4.309 to 6.309	No	ns	0.9971	
21d vs. 56d	-0.34	-5.649 to 4.969	No	ns	>0.9999	
28d vs. 35d	0.7	-4.609 to 6.009	No	ns	0.9996	
28d vs. 42d	-0.02	-5.329 to 5.289	No	ns	>0.9999	
28d vs. 49d	0.34	-4.969 to 5.649	No	ns	>0.9999	
28d vs. 56d	-1	-5.309 to 4.309	No	ns	0.9971	
35d vs. 42d	-0.72	-6.029 to 4.589	No	ns	0.9996	
35d vs. 49d	-0.36	-5.669 to 4.949	No	ns	>0.9999	
35d vs. 56d	-1.7	-7.009 to 3.609	No	ns	0.9548	
42d vs. 49d	0.26	-4.949 to 5.669	No	ns	>0.9999	
42d vs. 56d	-0.98	-6.289 to 4.329	No	ns	0.9974	
49d vs. 56d	-1.34	-6.649 to 3.969	No	ns	0.9862	

Baseline Top of Hut Mean Visit Time (s)

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2296
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.301, df=8
Mean of column A	3.21
Mean of column B	4.27
Difference between means (B - A) ± SEM	1.060 ± 0.8150
95% confidence interval	-0.8194 to 2.939
R squared (eta squared)	0.1745

Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF
7d								
Male vs. Female	5.67	0.23	5.44	2.272		5	5	3.386
21d								
Male vs. Female	1.93	-0.41	2.34	2.272		5	5	1.457
28d								
Male vs. Female	2.61	-1.07	3.68	2.272		5	5	2.291
35d								
Male vs. Female	1.65	-1.77	3.42	2.272		5	5	2.129
42d								
Male vs. Female	3.43	-1.05	4.48	2.272		5	5	2.789
49d								
Male vs. Female	2.49	-1.41	3.9	2.272		5	5	2.428
56d								
Male vs. Female	3.01	-0.07	3.08	2.272		5	5	1.917
Male								
7d vs. 21d	5.67	1.93	3.74	1.726		5	5	3.065
7d vs. 28d	5.67	2.61	3.06	1.726		5	5	2.508
7d vs. 35d	5.67	1.65	4.02	1.726		5	5	3.295
7d vs. 42d	5.67	3.43	2.24	1.726		5	5	1.836
7d vs. 49d	5.67	2.49	3.18	1.726		5	5	2.606
7d vs. 56d	5.67	3.01	2.66	1.726		5	5	2.18
21d vs. 28d	1.93	2.61	-0.68	1.726		5	5	0.5573
21d vs. 35d	1.93	1.65	0.28	1.726		5	5	0.2295
21d vs. 42d	1.93	3.43	-1.5	1.726		5	5	1.229
21d vs. 49d	1.93	2.49	-0.56	1.726		5	5	0.459
21d vs. 56d	1.93	3.01	-1.08	1.726		5	5	0.8851
28d vs. 35d	2.61	1.65	0.96	1.726		5	5	0.7868
28d vs. 42d	2.61	3.43	-0.82	1.726		5	5	0.672
28d vs. 49d	2.61	2.49	0.12	1.726		5	5	0.09835
28d vs. 56d	2.61	3.01	-0.4	1.726		5	5	0.3278
35d vs. 42d	1.65	3.43	-1.78	1.726		5	5	1.459
35d vs. 49d	1.65	2.49	-0.84	1.726		5	5	0.6894
35d vs. 56d	1.65	3.01	-1.36	1.726		5	5	1.115
42d vs. 49d	3.43	2.49	0.94	1.726		5	5	0.7704
42d vs. 56d	3.43	3.01	0.42	1.726		5	5	0.3442
49d vs. 56d	2.49	3.01	-0.52	1.726		5	5	0.4262
Female								
7d vs. 21d	0.23	-0.41	0.64	1.726		5	5	0.5245
7d vs. 28d	0.23	-1.07	1.3	1.726		5	5	1.065
7d vs. 35d	0.23	-1.77	2	1.726		5	5	1.639
7d vs. 42d	0.23	-1.05	1.28	1.726		5	5	1.049
7d vs. 49d	0.23	-1.41	1.64	1.726		5	5	1.344
7d vs. 56d	0.23	-0.07	0.3	1.726		5	5	0.2459
21d vs. 28d	-0.41	-1.07	0.66	1.726		5	5	0.5409
21d vs. 35d	-0.41	-1.77	1.36	1.726		5	5	1.115
21d vs. 42d	-0.41	-1.05	0.64	1.726		5	5	0.5245
21d vs. 49d	-0.41	-1.41	1	1.726		5	5	0.8196
21d vs. 56d	-0.41	-0.07	-0.34	1.726		5	5	0.2786
28d vs. 35d	-1.07	-1.77	0.7	1.726		5	5	0.5737
28d vs. 42d	-1.07	-1.05	-0.02	1.726		5	5	0.01639
28d vs. 49d	-1.07	-1.41	0.34	1.726		5	5	0.2786
28d vs. 56d	-1.07	-0.07	-1	1.726		5	5	0.8196
35d vs. 42d	-1.77	-1.05	-0.72	1.726		5	5	0.5901
35d vs. 49d	-1.77	-1.41	-0.36	1.726		5	5	0.295
35d vs. 56d	-1.77	-0.07	-1.7	1.726		5	5	1.393
42d vs. 49d	-1.05	-1.41	0.36	1.726		5	5	0.295
42d vs. 56d	-1.05	-0.07	-0.98	1.726		5	5	0.8032
49d vs. 56d	-1.41	-0.07	-1.34	1.726		5	5	1.098

Change in Air Puffs

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	4.199	0.0479 ns	No	No	Mean of Male Mean of Female -2.571
Time	6.935	0.01844 ns	No	No	Difference between means 0.07143
Sex	0.01745	0.9603 ns	No	No	SE of difference 1.391
Subject	52.91	<0.0001	****	Yes	95% CI of difference -3.135 to 3.278

Baseline Air Puffs

Column B vs. Column A	Female vs. Male
Unpaired t test	0.5392
P value	ns
P value summary	No
Significantly different (P < 0.05)?	Two-tailed
One- or two-tailed P value?	t=0.6414, df=8
t, df	7.1
Mean of column A	5.6
Mean of column B	-1.500 ± 2.339
Difference between means (B - A) ± SEM	-6.893 to 3.893
95% confidence interval	0.0489
R squared (eta squared)	

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d Male vs. Female	0.9	-2.710 to 4.510	No	ns	0.6194
21d Male vs. Female	0.9	-2.710 to 4.510	No	ns	0.6194
28d Male vs. Female	0.1	-3.510 to 3.710	No	ns	0.9559
35d Male vs. Female	-2.1	-5.710 to 1.510	No	ns	0.2488
42d Male vs. Female	0.3	-3.310 to 3.910	No	ns	0.8684
49d Male vs. Female	-0.9	-4.510 to 2.710	No	ns	0.6194
56d Male vs. Female	1.3	-2.310 to 4.910	No	ns	0.4736
Male					
7d vs. 21d	-0.4	-4.209 to 3.409	No	ns	0.9999
7d vs. 28d	0.4	-3.409 to 4.209	No	ns	0.9999
7d vs. 35d	-0.2	-4.009 to 3.609	No	ns	>0.9999
7d vs. 42d	0.2	-3.609 to 4.009	No	ns	>0.9999
7d vs. 49d	1.4	-2.409 to 5.209	No	ns	0.9153
7d vs. 56d	-1.4	-5.209 to 2.409	No	ns	0.9153
21d vs. 28d	0.8	-3.009 to 4.609	No	ns	0.9948
21d vs. 35d	0.2	-3.609 to 4.009	No	ns	>0.9999
21d vs. 42d	0.6	-3.209 to 4.409	No	ns	0.9989
21d vs. 49d	1.8	-2.009 to 5.609	No	ns	0.7697
21d vs. 56d	-1.4	-4.809 to 2.809	No	ns	0.983
28d vs. 35d	-0.6	-4.409 to 3.209	No	ns	0.9989
28d vs. 42d	-0.2	-4.009 to 3.609	No	ns	>0.9999
28d vs. 49d	1	-2.809 to 4.809	No	ns	0.983
28d vs. 56d	-1.8	-5.609 to 2.009	No	ns	0.7697
35d vs. 42d	0.4	-3.409 to 4.209	No	ns	0.9999
35d vs. 49d	1.6	-2.209 to 5.409	No	ns	0.852
35d vs. 56d	-1.2	-5.009 to 2.609	No	ns	0.9582
42d vs. 49d	1.2	-2.609 to 5.009	No	ns	0.9582
42d vs. 56d	-1.6	-5.409 to 2.209	No	ns	0.852
49d vs. 56d	-2.8	-6.609 to 1.009	No	ns	0.2834
Female					
7d vs. 21d	-0.4	-4.209 to 3.409	No	ns	0.9999
7d vs. 28d	-0.4	-4.209 to 3.409	No	ns	0.9999
7d vs. 35d	-3.2	-7.009 to 0.6086	No	ns	0.1535
7d vs. 42d	-0.4	-4.209 to 3.409	No	ns	0.9999
7d vs. 49d	-0.4	-4.209 to 3.409	No	ns	0.9999
7d vs. 56d	-1.4	-5.209 to 2.409	No	ns	0.9999
21d vs. 28d	0	-3.809 to 3.809	No	ns	0.983
21d vs. 35d	-2.8	-6.609 to 1.009	No	ns	>0.9999
21d vs. 42d	0	-3.809 to 3.809	No	ns	0.2834
21d vs. 49d	0	-3.809 to 3.809	No	ns	>0.9999
21d vs. 56d	-0.6	-4.409 to 3.209	No	ns	>0.9999
28d vs. 35d	-2.8	-6.609 to 1.009	No	ns	0.9989
28d vs. 42d	-2.8	-6.609 to 1.009	No	ns	0.2834
28d vs. 49d	0	-3.809 to 3.809	No	ns	>0.9999
28d vs. 56d	0	-3.809 to 3.809	No	ns	>0.9999
35d vs. 42d	2.8	-1.009 to 6.609	No	ns	0.9989
35d vs. 49d	2.8	-1.009 to 6.609	No	ns	0.2834
35d vs. 56d	2.2	-1.609 to 6.009	No	ns	0.2834
42d vs. 49d	0	-3.809 to 3.809	No	ns	0.5693
42d vs. 56d	-0.6	-4.409 to 3.209	No	ns	>0.9999
49d vs. 56d	-0.6	-4.409 to 3.209	No	ns	0.9989

Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF
7d Male vs. Female	-2.5	-3.4	0.9	1.802		5	5	0.7063
21d Male vs. Female	-2.1	-3	0.9	1.802		5	5	0.7063
28d Male vs. Female	-2.9	-3	0.1	1.802		5	5	0.07848
35d Male vs. Female	-2.3	-0.2	-2.1	1.802		5	5	1.648
42d Male vs. Female	-2.7	-3	0.3	1.802		5	5	0.2354
49d Male vs. Female	-3.9	-3	-0.9	1.802		5	5	0.7063
56d Male vs. Female	-1.1	-2.4	1.3	1.802		5	5	1.02
Male								
7d vs. 21d	-2.5	-2.1	-0.4	1.238		5	5	0.457
7d vs. 28d	-2.5	-2.9	0.4	1.238		5	5	0.457
7d vs. 35d	-2.5	-2.3	-0.2	1.238		5	5	0.2285
7d vs. 42d	-2.5	-2.7	0.2	1.238		5	5	0.2285
7d vs. 49d	-2.5	-3.9	1.4	1.238		5	5	1.599
7d vs. 56d	-2.5	-1.1	-1.4	1.238		5	5	1.599
21d vs. 28d	-2.1	-2.9	0.8	1.238		5	5	0.9139
21d vs. 35d	-2.1	-2.3	0.2	1.238		5	5	0.2285
21d vs. 42d	-2.1	-2.7	0.6	1.238		5	5	0.6855
21d vs. 49d	-2.1	-3.9	1.8	1.238		5	5	2.056
21d vs. 56d	-2.1	-1.1	-1	1.238		5	5	1.142
28d vs. 35d	-2.9	-2.3	-0.6	1.238		5	5	0.6855
28d vs. 42d	-2.9	-2.7	-0.2	1.238		5	5	0.2285
28d vs. 49d	-2.9	-3.9	1	1.238		5	5	1.142
28d vs. 56d	-2.9	-1.1	-1.8	1.238		5	5	2.056
35d vs. 42d	-2.3	-2.7	0.4	1.238		5	5	0.457
35d vs. 49d	-2.3	-3.9	1.6	1.238		5	5	1.828
35d vs. 56d	-2.3	-1.1	-1.2	1.238		5	5	1.371
42d vs. 49d	-2.7	-3.9	1.2	1.238		5	5	1.371
42d vs. 56d	-2.7	-1.1	-1.6	1.238		5	5	1.828
49d vs. 56d	-3.9	-1.1	-2.8	1.238		5	5	3.199
Female								
7d vs. 21d	-3.4	-3	-0.4	1.238		5	5	0.457
7d vs. 28d	-3.4	-3	-0.4	1.238		5	5	0.457
7d vs. 35d	-3.4	-0.2	-3.2	1.238		5	5	3.656
7d vs. 42d	-3.4	-3	-0.4	1.238		5	5	0.457
7d vs. 49d	-3.4	-3	-0.4	1.238		5	5	0.457
7d vs. 56d	-3.4	-2.4	-1	1.238		5	5	1.142
21d vs. 28d	-3	-3	0	1.238		5	5	0
21d vs. 35d	-3	-0.2	-2.8	1.238		5	5	3.199
21d vs. 42d	-3	-3	0	1.238		5	5	0
21d vs. 49d	-3	-3	0	1.238		5	5	0
21d vs. 56d	-3	-2.4	-0.6	1.238		5	5	0.6855
28d vs. 35d	-3	-0.2	-2.8	1.238		5	5	3.199
28d vs. 42d	-3	-3	0	1.238		5	5	0
28d vs. 49d	-3	-3	0	1.238		5	5	0
28d vs. 56d	-3	-2.4	-0.6	1.238		5	5	0.6855
35d vs. 42d	-0.2	-3	2.8	1.238		5	5	3.199
35d vs. 49d	-0.2	-3	2.8	1.238		5	5	3.199
35d vs. 56d	-0.2	-2.4	2.2	1.238		5	5	2.513
42d vs. 49d	-3	-3	0	1.238		5	5	0
42d vs. 56d	-3	-2.4	-0.6	1.238		5	5	0.6855
49d vs. 56d	-3	-2.4	-0.6	1.238		5	5	0.6855

Appendix I.9. Statistical report of all ANY-maze parameters, comparing values prior to injury and over time following ACL rupture, including p-values and 95% confidence intervals for all analyses.

DigiGait Indices - Mouse Specifics, Inc.			
Index	Units	Definition	Example, Application, or Reference
Swing Time	s	Time duration of the swing phase (no paw contact with belt)	Swing duration decreases with increasing speed, and there is a limit on how brief swing duration can be. Arthritic animals may have increased swing duration because of loss of mobility of the joints. Swing duration increases with pain (Vrinten and Hamers, <i>Pain</i> 102:203-209, 2003). Longer swing in the forelimbs might provide mice with ample opportunity for limb placement prior to weight bearing (Clarke and Still, <i>Behav Res Methods</i> , 33:422-426, 2001, Budsberg et al. <i>Am J Vet Res</i> 48:915-918, 1987).
% Swing Stride	%	Percent of the total stride duration that the paw is in the air (swing phase).	If total stride duration is 100%, then X% is paw contact (stance) and Y% is no paw contact (swing). X% stance + Y% swing = 100% stride. % swing is typically around 35%; this value will typically increase with increasing speed.
Brake Time	s	Time duration of the braking phase (initial paw contact to maximum paw contact, commencing after the swing phase)	Time required for decelerating the motion and controlling the initiation of the stance phase. Could be longer or shorter depending on the pathology. A longer duration might indicate more precise control and distribution of loading during stance and reduced peak load.
% Brake Stride	%	Percent of the total stride duration that the paw is in the braking phase	If total stance duration is 100%, then B% is paw deceleration (braking) and P% is paw acceleration (propulsion).
Propel	s	Time duration of the propulsion phase (maximum paw contact to just before the swing phase)	Time required for accelerating the motion and continuing forward motion of the animal. This could be briefer or delayed depending on the phenotype. A shorter duration might indicate greater strength and better control.
% Propel Stride	%	% of the total stride duration that the paw is in the propulsion phase	If total stance duration is 100%, then B% is paw deceleration (braking) and P% is paw acceleration (propulsion). B%braking+P%propulsion=100%stance.
Stance	s	Time duration of the stance duration (paw contact with belt). Stance duration is equal to the sum of braking duration and propulsion duration).	Stance duration will decrease with increased speed. Moreover, with increased speed, stance duration will decrease to a greater extent than swing duration.
% Stance Stride	%	% of the total stride duration that the paw is in any contact with the belt.	As speed changes, the % of stride spent in stance changes more significantly than the % of stride spent in swing.
Stride Time	s	Time duration of one complete stride for one paw. Equal to the sum of stance duration and swing duration.	The predominate step pattern in mice at normal walking speed is alternate (forelimb contra-lateral hindlimb, in sequence). Stride duration is dependent on speed of motion and on stride frequency. Stride duration for all limbs are usually approximately equivalent (Clarke and Still, <i>Physiol & Behav</i> 66:723-729, 1999).
% Brake Stance	%	% of the stance phase (paw contact) that the paw is in the braking phase.	Braking constitutes about 50% of stance, is different in forelimbs compared to hind limbs, and changes with speed and pathology.
% Propel Stance	s	% of the stance phase (paw contact) that the paw is in the propulsion phase (paw coming off of belt)	Propulsion constitutes about 50% of stance, is different in forelimbs compared to hind limbs, and changes with pathology.
Swing/Stride	Real #	Ratio of swing phase time to stance phase time	An indicator of the temporal structure of gait at a given cadence. The ratio changes with stride frequency, and is approximately the same for both hind limbs and both forelimbs. In humans, at the point when walking changes over to running, the ratio is equal to one (Drillis, <i>Ann New York Acad. Sci.</i> 74: 86,1958). In disease conditions, the ratio for each limb may be different and represents a structural asymmetry of performance.
Stride Length	cm	The spatial length that a paw traverses through a given stride.	Distance between successive strides of the same paw. This number should normally be nearly equivalent among the 4 paws of a given animal (Hannigan
Stride Frequency	Steps per second	The cadence or the number of times each second that a paw takes a complete stride.	Stride frequency in mice ranges from ~2.5 Hz to ~8 Hz (Clarke and Still, <i>Physiol & Behav</i> 66:723-729, 1999, James RS et al. <i>J Exp Biol</i> 198:491-02, 1995). This is likely strain dependent and phenotype dependent.
Paw Angle	deg	The angle that the paw makes with the long axis of the direction of motion of the animal.	Otherwise known as "degree of external rotation", "high-foot angle" (in people), "toe in/out angle" (in people), or "spray angle". This value may decrease with walking speed (extent of which seems strain dependent). Normally, this value is ~5 deg in fore paws and ~15 deg in hind paws. More open angles of the hind paws are associated with ataxia, spinal cord injury, and demyelinating disease (Powell et al. <i>Physiol Behav</i> 67:819-21, 1999).
Stance Width	cm	The perpendicular distance between the centroids of either set of axial paws during peak stance	Normally, the stance width of the forelimbs is less than the hind limbs. These distances are size-dependent. Larger or smaller values may indicate postural adjustments for stability. Humans avoid narrow step widths because they are less stable (Donelan et al. <i>J Biomech</i> 37:827-35, 2004). It is sometimes referred to as the "base of support". Barron and Irvine (<i>Neurotoxicol Teratol</i> 16:89-94, 1994) showed that prenatal cocaine narrowed stance width in developing rats. Recent unpublished observations indicate a narrow stance width in young SOD1 G93A mice, a mouse model of amyotrophic lateral sclerosis, dependent on the treadmill walking conditions [speed and incline].
Paw Area at Peak Stance	cm ²	The area seen by the camera, and reported at the time corresponding to peak stance (e.g., maximal paw area)	The paw area may indicate the extent of plantar placement as a function of nerve injury, ability to load the limb, and pain. Rats with chronic pain, for example, were shown to have alterations in fore and hind paw area (Coulthard et al. <i>J Neurosci Methods</i> 116:197-213, 2002). Hind limb paw area is smaller in a Huntington's transgenic model (unpublished), but unchanged in a Down syndrome model (Hampton et al. <i>Physiol Behav</i> 82:381-389, 2004).
% Shared Stance	%	% of stance hind paws contact belt at same time, otherwise known as % double support.	In humans with Parkinson's disease, this value is increased (<i>Brain Nerve</i> ; 62:1193-202, 2011).
Gait Symmetry	Real #	Coordination metric; Ratio of forelimb stepping frequency to hind limb stepping frequency (Right forelimb step frequency + left forelimb step frequency) / (Right hind limb step frequency + left hind limb step frequency)	In a healthy subject walking fluidly, the gait symmetry will be ~ unity. In animals recovering from spinal cord injury, the hind limbs often step more frequently to compensate for hind limb failure, in which case Gait symmetry > 1.0. Gait symmetry declined with age; treadmill training counteracted the decline of gait symmetry (Dorner et al., <i>Gerontology</i> 42:7-13, 1996).
MAX dA/dt	cm ² /s	Maximal rate of change of paw area in contact with the treadmill belt during the braking phase. How quickly the limb is loaded during the initial period of stance; how rapidly does the animal decelerate.	It remains to be determined to what extent this metric reflects alterations in muscle strength. Unpublished data suggest that forelimb loading is accelerated in mice with Huntington's disease.
MIN dA/dt	cm ² /s	Maximal rate of change of paw area in contact with the treadmill belt during the propulsion phase. How quickly the limb is unloaded during the later period of stance. How rapidly is the animal able to propel itself into the next step.	It remains to be determined to what extent this metric reflects alterations in muscle strength. Unpublished data suggest that there is a decrease in the rate of force development in the hind limbs of SOD1 G93A mice, a model of amyotrophic lateral sclerosis.
Paw Placement Positioning	cm	Balance metric. This is the extent of overlap between ipsilateral fore and hind paws during full stance	This number is usually small, close to zero if forelimb and hind limb stance widths are close to equal, and could be negative if the width of the forelimbs during stance exceeds that of the hind limbs.
Paw drag		Propulsion metric. Area under the curve from time of full stance to the time the paw lifts off from the belt.	This metric may reflect the robustness of the lift off stage of the paw from the belt. If a hind limb is impaired from lifting the paw off of the belt during early propulsion, then this area may be higher, for example.

Change in Swing (s) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	0.7874	0.8874	ns	No	Mean of Male	0.002654
Time	2.368	0.2889	ns	No	Mean of Female	-0.00426
Sex	3.41	0.5714	ns	No	Difference between means	0.006914
Subject	78.35	<0.0001	****	Yes	SE of difference	0.01172
					95% CI of difference	-0.02011 to 0.03393

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	0.007693	-0.01787 to 0.0332	No	ns	0.5498
14d					
Male vs. Female	0.003893	-0.02167 to 0.0294	No	ns	0.7619
21d					
Male vs. Female	0.007793	-0.01777 to 0.0333	No	ns	0.5446
28d					
Male vs. Female	0.00856	-0.01700 to 0.0341	No	ns	0.5059
35d					
Male vs. Female	0.007693	-0.01787 to 0.0332	No	ns	0.5498
42d					
Male vs. Female	0.00006001	-0.02550 to 0.0256	No	ns	0.9963
49d					
Male vs. Female	0.01213	-0.01344 to 0.0376	No	ns	0.3468
56d					
Male vs. Female	0.007493	-0.01807 to 0.0330	No	ns	0.5602
Male					
7d vs. 14d	0.0063	-0.01100 to 0.0236	No	ns	0.9433
7d vs. 21d	0.005533	-0.01177 to 0.0228	No	ns	0.9715
7d vs. 28d	-0.003733	-0.02104 to 0.0135	No	ns	0.9972
7d vs. 35d	0.004567	-0.01274 to 0.0218	No	ns	0.9905
7d vs. 42d	0.003967	-0.01334 to 0.0212	No	ns	0.996
7d vs. 49d	0.001633	-0.01567 to 0.0189	No	ns	>0.9999
7d vs. 56d	0.003967	-0.01334 to 0.0212	No	ns	0.996
14d vs. 21d	-0.0007667	-0.01807 to 0.0165	No	ns	>0.9999
14d vs. 28d	-0.01003	-0.02734 to 0.0072	No	ns	0.606
14d vs. 35d	-0.001733	-0.01904 to 0.0155	No	ns	>0.9999
14d vs. 42d	-0.002333	-0.01964 to 0.0149	No	ns	0.9999
14d vs. 49d	-0.004667	-0.02197 to 0.0126	No	ns	0.9892
14d vs. 56d	-0.002333	-0.01964 to 0.0149	No	ns	0.9999
21d vs. 28d	-0.009267	-0.02657 to 0.0080	No	ns	0.696
21d vs. 35d	-0.0009667	-0.01827 to 0.0163	No	ns	>0.9999
21d vs. 42d	-0.001567	-0.01887 to 0.0157	No	ns	>0.9999
21d vs. 49d	-0.0039	-0.02120 to 0.0134	No	ns	0.9964
21d vs. 56d	-0.001567	-0.01887 to 0.0157	No	ns	>0.9999
28d vs. 35d	0.0083	-0.009004 to 0.025	No	ns	0.7988
28d vs. 42d	0.0077	-0.009604 to 0.025	No	ns	0.853
28d vs. 49d	0.005367	-0.01194 to 0.0226	No	ns	0.976
28d vs. 56d	0.0077	-0.009604 to 0.025	No	ns	0.853
35d vs. 42d	-0.0006	-0.01790 to 0.0167	No	ns	>0.9999
35d vs. 49d	-0.002293	-0.02024 to 0.0143	No	ns	0.9994
35d vs. 56d	-0.0006	-0.01790 to 0.0167	No	ns	>0.9999
42d vs. 49d	-0.002333	-0.01964 to 0.0149	No	ns	0.9999
42d vs. 56d	1.735E-18	-0.01730 to 0.0173	No	ns	>0.9999
49d vs. 56d	0.002333	-0.01497 to 0.0196	No	ns	0.9999
Female					
7d vs. 14d	0.0025	-0.01480 to 0.0198	No	ns	0.9998
7d vs. 21d	0.005633	-0.01167 to 0.0229	No	ns	0.9686
7d vs. 28d	-0.002867	-0.02017 to 0.0144	No	ns	0.9995
7d vs. 35d	0.004567	-0.01274 to 0.0218	No	ns	0.9905
7d vs. 42d	-0.003667	-0.02097 to 0.0136	No	ns	0.9975
7d vs. 49d	0.006067	-0.01124 to 0.0233	No	ns	0.9534
7d vs. 56d	0.003767	-0.01354 to 0.0210	No	ns	0.9971
14d vs. 21d	0.003133	-0.01417 to 0.0204	No	ns	0.9991
14d vs. 28d	-0.005367	-0.02267 to 0.0119	No	ns	0.976
14d vs. 35d	0.002067	-0.01524 to 0.0193	No	ns	>0.9999
14d vs. 42d	-0.006167	-0.02347 to 0.0111	No	ns	0.9492
14d vs. 49d	0.003567	-0.01374 to 0.0208	No	ns	0.9979
14d vs. 56d	0.001267	-0.01604 to 0.0185	No	ns	>0.9999
21d vs. 28d	-0.0085	-0.02580 to 0.0088	No	ns	0.779
21d vs. 35d	-0.001067	-0.01837 to 0.0162	No	ns	>0.9999
21d vs. 42d	-0.0093	-0.02660 to 0.0080	No	ns	0.6922
21d vs. 49d	0.0004333	-0.01687 to 0.0177	No	ns	>0.9999
21d vs. 56d	-0.001867	-0.01917 to 0.0154	No	ns	>0.9999
28d vs. 35d	0.007433	-0.009871 to 0.024	No	ns	0.8743
28d vs. 42d	-0.0008	-0.01810 to 0.0165	No	ns	>0.9999
28d vs. 49d	0.008933	-0.008371 to 0.026	No	ns	0.7332
28d vs. 56d	0.006633	-0.01067 to 0.0239	No	ns	0.9265
35d vs. 42d	-0.008233	-0.02554 to 0.0090	No	ns	0.8053
35d vs. 49d	0.0015	-0.01580 to 0.0188	No	ns	>0.9999
35d vs. 56d	-0.0008	-0.01810 to 0.0165	No	ns	>0.9999
42d vs. 49d	0.009733	-0.007571 to 0.027	No	ns	0.6417
42d vs. 56d	0.007433	-0.009871 to 0.024	No	ns	0.8743
49d vs. 56d	-0.0023	-0.01960 to 0.0150	No	ns	0.9999

Baseline Swing (s) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.3633
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.9639, df=8
How big is the difference?	
Mean of column A	0.07993
Mean of column B	0.09053
Difference between means (B - A) ± 0.01059 ± 0.01099	
95% confidence interval	-0.01475 to 0.03594
R squared (eta squared)	0.1041
F test to compare variances	
F, DFn, Dfd	13.55, 4, 4
P value	0.027
P value summary	*
Significantly different (P < 0.05)?	Yes
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Swing (s) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	7.063	0.211 ns	No	No	Mean of Male	0.001575
Time	5.005	0.431 ns	No	No	Mean of Female	0.00357
Sex	0.6799	0.7445 ns	No	No	Difference between means	-0.001995
Subject	47.8	<0.0001	****	Yes	SE of difference	0.005914
					95% CI of difference	-0.01563 to 0.01164

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.001713	-0.01425 to 0.0176	No	ns	0.8309
14d					
Male vs. Female	0.007313	-0.008649 to 0.023	No	ns	0.3635
21d					
Male vs. Female	-0.01069	-0.02665 to 0.0052	No	ns	0.1858
28d					
Male vs. Female	-0.01149	-0.02745 to 0.0044	No	ns	0.1554
35d					
Male vs. Female	-0.0009867	-0.01695 to 0.0149	No	ns	0.9021
42d					
Male vs. Female	0.00328	-0.01268 to 0.0192	No	ns	0.6828
49d					
Male vs. Female	-0.006753	-0.02272 to 0.0092	No	ns	0.4012
56d					
Male vs. Female	0.001647	-0.01432 to 0.0176	No	ns	0.8374

Male					
7d vs. 14d	0.0013	-0.01678 to 0.0193	No	ns	>0.9999
7d vs. 21d	0.006767	-0.01132 to 0.0248	No	ns	0.9349
7d vs. 28d	0.0057	-0.01238 to 0.0237	No	ns	0.9737
7d vs. 35d	0.0061	-0.01198 to 0.0241	No	ns	0.962
7d vs. 42d	0.003733	-0.01435 to 0.0218	No	ns	0.9979
7d vs. 49d	0.007567	-0.01052 to 0.0256	No	ns	0.8884
7d vs. 56d	0.0077	-0.01038 to 0.0257	No	ns	0.8792
14d vs. 21d	0.005467	-0.01262 to 0.0235	No	ns	0.9792
14d vs. 28d	0.0044	-0.01368 to 0.0224	No	ns	0.9942
14d vs. 35d	0.0048	-0.01328 to 0.0228	No	ns	0.9902
14d vs. 42d	0.002433	-0.01565 to 0.0205	No	ns	0.9999
14d vs. 49d	0.006267	-0.01182 to 0.0243	No	ns	0.9561
14d vs. 56d	0.0064	-0.01168 to 0.0244	No	ns	0.951
21d vs. 28d	-0.001067	-0.01915 to 0.0170	No	ns	>0.9999
21d vs. 35d	-0.0006667	-0.01875 to 0.0174	No	ns	>0.9999
21d vs. 42d	-0.003033	-0.02112 to 0.0150	No	ns	0.9995
21d vs. 49d	0.0008	-0.01728 to 0.0188	No	ns	>0.9999
21d vs. 56d	0.0009333	-0.01715 to 0.0190	No	ns	>0.9999
28d vs. 35d	0.0004	-0.01768 to 0.0184	No	ns	>0.9999
28d vs. 42d	-0.001967	-0.02005 to 0.0161	No	ns	>0.9999
28d vs. 49d	0.001867	-0.01622 to 0.0199	No	ns	>0.9999
28d vs. 56d	0.002	-0.01608 to 0.0200	No	ns	>0.9999
35d vs. 42d	-0.002367	-0.02045 to 0.0157	No	ns	0.9999
35d vs. 49d	0.001467	-0.01662 to 0.0195	No	ns	>0.9999
35d vs. 56d	0.0016	-0.01648 to 0.0196	No	ns	>0.9999
42d vs. 49d	0.003833	-0.01425 to 0.0219	No	ns	0.9975
42d vs. 56d	0.003967	-0.01412 to 0.0220	No	ns	0.9969
49d vs. 56d	0.0001333	-0.01795 to 0.0182	No	ns	>0.9999

Female					
7d vs. 14d	0.0069	-0.01118 to 0.0249	No	ns	0.9282
7d vs. 21d	-0.005633	-0.02372 to 0.0124	No	ns	0.9754
7d vs. 28d	-0.0075	-0.02558 to 0.0105	No	ns	0.8929
7d vs. 35d	0.0034	-0.01468 to 0.0214	No	ns	0.9989
7d vs. 42d	0.0053	-0.01278 to 0.0233	No	ns	0.9825
7d vs. 49d	-0.0009	-0.01898 to 0.0171	No	ns	>0.9999
7d vs. 56d	0.007633	-0.01045 to 0.0257	No	ns	0.8839
14d vs. 21d	-0.01253	-0.03062 to 0.0055	No	ns	0.378
14d vs. 28d	-0.0144	-0.03248 to 0.0036	No	ns	0.2139
14d vs. 35d	-0.0035	-0.02158 to 0.0145	No	ns	0.9986
14d vs. 42d	-0.0016	-0.01968 to 0.0164	No	ns	>0.9999
14d vs. 49d	-0.0078	-0.02588 to 0.0102	No	ns	0.8719
14d vs. 56d	0.0007333	-0.01735 to 0.0188	No	ns	>0.9999
21d vs. 28d	-0.001867	-0.01995 to 0.0162	No	ns	>0.9999
21d vs. 35d	0.009033	-0.009051 to 0.027	No	ns	0.7642
21d vs. 42d	0.01093	-0.007151 to 0.029	No	ns	0.5545
21d vs. 49d	0.004733	-0.01335 to 0.0228	No	ns	0.991
21d vs. 56d	0.01327	-0.004817 to 0.031	No	ns	0.3069
28d vs. 35d	0.0109	-0.007184 to 0.028	No	ns	0.5583
28d vs. 42d	0.0128	-0.005284 to 0.030	No	ns	0.3512
28d vs. 49d	0.0066	-0.01148 to 0.0246	No	ns	0.9426
28d vs. 56d	0.01513	-0.002951 to 0.033	No	ns	0.1655
35d vs. 42d	0.0019	-0.01618 to 0.0199	No	ns	>0.9999
35d vs. 49d	-0.0043	-0.02238 to 0.0137	No	ns	0.995
35d vs. 56d	0.004233	-0.01385 to 0.0223	No	ns	0.9954
42d vs. 49d	-0.0062	-0.02428 to 0.0118	No	ns	0.9585
42d vs. 56d	0.002333	-0.01575 to 0.0204	No	ns	>0.9999
49d vs. 56d	0.008533	-0.009551 to 0.026	No	ns	0.8117

Baseline Swing (s) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.5983
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.5486, df=8
How big is the difference?	
Mean of column A	0.08047
Mean of column B	0.08385
Difference between means (B - A)	±0.003380 ± 0.006162
95% confidence interval	-0.01083 to 0.01759
R squared (eta squared)	0.03625
F test to compare variances	
F, DFn, Dfd	1.928, 4, 4
P value	0.5405
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Swing (s) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	8.383	0.0943	ns	No	Mean of Male	0.008082
Time	4.587	0.4301	ns	No	Mean of Female	0.00398
Sex	2.337	0.5523	ns	No	Difference between means	0.004102
Subject	48.58	<0.0001	****	Yes	SE of difference	0.006612
					95% CI of difference	-0.01115 to 0.01935

Tukey's multiple comparisons test Mean Diff. 95.00% CI of diff. Below threshold? Summary Adjusted P Value

7d						
Male vs. Female	0.01366	-0.003782 to 0.031	No	ns		0.1226
14d						
Male vs. Female	0.00236	-0.01508 to 0.0198	No	ns		0.7878
21d						
Male vs. Female	-0.00394	-0.02138 to 0.0135	No	ns		0.6533
28d						
Male vs. Female	-0.005673	-0.02311 to 0.0117	No	ns		0.5181
35d						
Male vs. Female	-0.00394	-0.02138 to 0.0135	No	ns		0.6533
42d						
Male vs. Female	0.01406	-0.003382 to 0.031	No	ns		0.1122
49d						
Male vs. Female	0.00416	-0.01328 to 0.0216	No	ns		0.6354
56d						
Male vs. Female	0.01213	-0.005315 to 0.029	No	ns		0.1697
Male						
7d vs. 14d	-0.001827	-0.02102 to 0.0173	No	ns	>0.9999	
7d vs. 21d	0.00124	-0.01795 to 0.0204	No	ns	>0.9999	
7d vs. 28d	0.001273	-0.01792 to 0.0204	No	ns	>0.9999	
7d vs. 35d	0.001273	-0.01792 to 0.0204	No	ns	>0.9999	
7d vs. 42d	-0.01043	-0.02962 to 0.0087	No	ns		0.6804
7d vs. 49d	-0.004027	-0.02322 to 0.0151	No	ns		0.9977
7d vs. 56d	-0.00736	-0.02655 to 0.0118	No	ns		0.9263
14d vs. 21d	0.003067	-0.01612 to 0.0222	No	ns		0.9996
14d vs. 28d	0.0031	-0.01609 to 0.0222	No	ns		0.9996
14d vs. 35d	0.0031	-0.01609 to 0.0222	No	ns		0.9996
14d vs. 42d	-0.0086	-0.02779 to 0.0105	No	ns		0.8484
14d vs. 49d	-0.0022	-0.02139 to 0.0169	No	ns	>0.9999	
14d vs. 56d	-0.005533	-0.02472 to 0.0136	No	ns		0.9841
21d vs. 28d	0.00003333	-0.01916 to 0.0192	No	ns	>0.9999	
21d vs. 35d	0.00003333	-0.01916 to 0.0192	No	ns	>0.9999	
21d vs. 42d	-0.01167	-0.03086 to 0.0075	No	ns		0.5473
21d vs. 49d	-0.005267	-0.02446 to 0.0139	No	ns		0.9881
21d vs. 56d	-0.0086	-0.02779 to 0.0105	No	ns		0.8484
28d vs. 35d	-0.000000012	-0.01919 to 0.0191	No	ns	>0.9999	
28d vs. 42d	-0.0117	-0.03089 to 0.0074	No	ns		0.5437
28d vs. 49d	-0.0053	-0.02449 to 0.0138	No	ns		0.9876
28d vs. 56d	-0.008633	-0.02782 to 0.0105	No	ns		0.8458
35d vs. 42d	-0.0117	-0.03089 to 0.0074	No	ns		0.5437
35d vs. 49d	-0.0053	-0.02449 to 0.0138	No	ns		0.9876
35d vs. 56d	-0.008633	-0.02782 to 0.0105	No	ns		0.8458
42d vs. 49d	0.0064	-0.01279 to 0.0255	No	ns		0.9642
42d vs. 56d	0.003067	-0.01612 to 0.0222	No	ns		0.9996
49d vs. 56d	-0.003333	-0.02252 to 0.0158	No	ns		0.9993
Female						
7d vs. 14d	-0.01313	-0.03232 to 0.0060	No	ns		0.3948
7d vs. 21d	-0.01636	-0.03555 to 0.0028	No	ns		0.1491
7d vs. 28d	-0.01806	-0.03725 to 0.0011	No	ns		0.0792
7d vs. 35d	-0.01633	-0.03552 to 0.0028	No	ns		0.1508
7d vs. 42d	-0.01003	-0.02922 to 0.0091	No	ns		0.7213
7d vs. 49d	-0.01353	-0.03272 to 0.0056	No	ns		0.3564
7d vs. 56d	-0.008893	-0.02808 to 0.0103	No	ns		0.8252
14d vs. 21d	-0.003233	-0.02242 to 0.0159	No	ns		0.9994
14d vs. 28d	-0.004933	-0.02412 to 0.0142	No	ns		0.9919
14d vs. 35d	-0.0032	-0.02239 to 0.0159	No	ns		0.9995
14d vs. 42d	0.0031	-0.01609 to 0.0222	No	ns		0.9996
14d vs. 49d	-0.0004	-0.01959 to 0.0187	No	ns	>0.9999	
14d vs. 56d	0.004233	-0.01496 to 0.0234	No	ns		0.9968
21d vs. 28d	-0.0017	-0.02089 to 0.0174	No	ns	>0.9999	
21d vs. 35d	0.00003333	-0.01916 to 0.0192	No	ns	>0.9999	
21d vs. 42d	0.006333	-0.01286 to 0.0255	No	ns		0.9662
21d vs. 49d	0.002833	-0.01636 to 0.0220	No	ns		0.9998
21d vs. 56d	0.007467	-0.01172 to 0.0266	No	ns		0.9209
28d vs. 35d	0.001733	-0.01746 to 0.0209	No	ns	>0.9999	
28d vs. 42d	0.008033	-0.01116 to 0.0272	No	ns		0.8881
28d vs. 49d	0.004533	-0.01466 to 0.0237	No	ns		0.9952
28d vs. 56d	0.009167	-0.01002 to 0.0283	No	ns		0.8021
35d vs. 42d	0.0063	-0.01289 to 0.0254	No	ns		0.9671
35d vs. 49d	0.0028	-0.01639 to 0.0219	No	ns		0.9998
35d vs. 56d	0.007433	-0.01176 to 0.0266	No	ns		0.9226
42d vs. 49d	-0.0035	-0.02269 to 0.0156	No	ns		0.9991
42d vs. 56d	0.001133	-0.01806 to 0.0203	No	ns	>0.9999	
49d vs. 56d	0.004633	-0.01456 to 0.0238	No	ns		0.9945

Baseline Swing (s) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.946
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.06987, df=8
How big is the difference?	
Mean of column A	0.07871
Mean of column B	0.0792
Difference between means (B - A)	±0.0004933 ± 0.007061
95% confidence interval	-0.01579 to 0.01678
R squared (eta squared)	0.0006099
F test to compare variances	
F, DFn, Dfd	1.442, 4, 4
P value	0.7315
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Swing Stride FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	1.473	0.8336	ns	No	Mean of Male	0.3722
Time	11.16	0.0021	**	Yes	Mean of Female	-1.805
Sex	5.627	0.4039	ns	No	Difference between means	2.177
Subject	57.97	<0.0001	****	Yes	SE of difference	2.471
					95% CI of difference	-3.520 to 7.875

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	2.275	-3.586 to 8.137	No	ns	0.4409
14d					
Male vs. Female	1.942	-3.919 to 7.803	No	ns	0.5104
21d					
Male vs. Female	1.862	-3.999 to 7.723	No	ns	0.5279
28d					
Male vs. Female	2.269	-3.593 to 8.130	No	ns	0.4422
35d					
Male vs. Female	2.402	-3.459 to 8.263	No	ns	0.416
42d					
Male vs. Female	-0.2547	-6.116 to 5.607	No	ns	0.9311
49d					
Male vs. Female	3.959	-1.903 to 9.820	No	ns	0.182
56d					
Male vs. Female	2.965	-2.896 to 8.827	No	ns	0.316
Male					
7d vs. 14d	3.863	-1.462 to 9.189	No	ns	0.3205
7d vs. 21d	4.043	-1.282 to 9.369	No	ns	0.2662
7d vs. 28d	1.437	-3.889 to 6.762	No	ns	0.9892
7d vs. 35d	4.12	-1.205 to 9.445	No	ns	0.2449
7d vs. 42d	3.53	-1.795 to 8.855	No	ns	0.4357
7d vs. 49d	3.713	-1.612 to 9.039	No	ns	0.3702
7d vs. 56d	4.007	-1.319 to 9.332	No	ns	0.2767
14d vs. 21d	0.18	-5.145 to 5.505	No	ns	>0.9999
14d vs. 28d	-2.427	-7.752 to 2.899	No	ns	0.8372
14d vs. 35d	0.2567	-5.069 to 5.582	No	ns	>0.9999
14d vs. 42d	-0.3333	-5.659 to 4.992	No	ns	>0.9999
14d vs. 49d	-0.15	-5.475 to 5.175	No	ns	>0.9999
14d vs. 56d	0.1433	-5.182 to 5.469	No	ns	>0.9999
21d vs. 28d	-2.607	-7.932 to 2.719	No	ns	0.7819
21d vs. 35d	0.07667	-5.249 to 5.402	No	ns	>0.9999
21d vs. 42d	-0.5133	-5.839 to 4.812	No	ns	>0.9999
21d vs. 49d	-0.33	-5.655 to 4.995	No	ns	>0.9999
21d vs. 56d	-0.03667	-5.362 to 5.289	No	ns	>0.9999
28d vs. 35d	2.683	-2.642 to 8.009	No	ns	0.7562
28d vs. 42d	2.093	-3.232 to 7.419	No	ns	0.9169
28d vs. 49d	2.277	-3.049 to 7.602	No	ns	0.8769
28d vs. 56d	2.57	-2.755 to 7.895	No	ns	0.7938
35d vs. 42d	0.59	-5.915 to 4.735	No	ns	>0.9999
35d vs. 49d	-0.4067	-5.732 to 4.919	No	ns	>0.9999
35d vs. 56d	-0.1133	-5.439 to 5.212	No	ns	>0.9999
42d vs. 49d	0.1833	-5.142 to 5.509	No	ns	>0.9999
42d vs. 56d	0.4767	-4.849 to 5.802	No	ns	>0.9999
49d vs. 56d	0.2933	-5.032 to 5.619	No	ns	>0.9999
Female					
7d vs. 14d	3.53	-1.795 to 8.855	No	ns	0.4357
7d vs. 21d	3.63	-1.695 to 8.955	No	ns	0.3994
7d vs. 28d	1.43	-3.895 to 6.755	No	ns	0.9895
7d vs. 35d	4.247	-1.079 to 9.572	No	ns	0.2124
7d vs. 42d	1	-4.325 to 6.325	No	ns	0.9989
7d vs. 49d	5.397	0.07145 to 10.72	Yes	*	0.0448
7d vs. 56d	4.697	-0.6286 to 10.02	No	ns	0.1219
14d vs. 21d	0.1	-5.225 to 5.425	No	ns	>0.9999
14d vs. 28d	-2.1	-7.425 to 3.225	No	ns	0.9156
14d vs. 35d	0.7167	-4.609 to 6.042	No	ns	0.9999
14d vs. 42d	-2.53	-7.855 to 2.795	No	ns	0.8064
14d vs. 49d	1.867	-3.459 to 7.192	No	ns	0.9534
14d vs. 56d	1.167	-4.159 to 6.492	No	ns	0.997
21d vs. 28d	-2.2	-7.525 to 3.125	No	ns	0.8948
21d vs. 35d	0.6167	-4.709 to 5.942	No	ns	>0.9999
21d vs. 42d	-2.63	-7.955 to 2.695	No	ns	0.7742
21d vs. 49d	1.767	-3.559 to 7.092	No	ns	0.9652
21d vs. 56d	1.067	-4.259 to 6.392	No	ns	0.9983
28d vs. 35d	2.817	-2.509 to 8.142	No	ns	0.7089
28d vs. 42d	-0.43	-5.755 to 4.895	No	ns	>0.9999
28d vs. 49d	3.967	-1.359 to 9.292	No	ns	0.2885
28d vs. 56d	3.267	-2.059 to 8.592	No	ns	0.5361
35d vs. 42d	-3.247	-8.572 to 2.079	No	ns	0.5439
35d vs. 49d	1.15	-4.175 to 6.475	No	ns	0.9972
35d vs. 56d	0.45	-4.875 to 5.775	No	ns	>0.9999
42d vs. 49d	4.397	-0.9286 to 9.722	No	ns	0.178
42d vs. 56d	3.697	-1.629 to 9.022	No	ns	0.376
49d vs. 56d	-0.7	-6.025 to 4.625	No	ns	0.9999

Baseline % Swing Stride FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2149
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.347, df=8
How big is the difference?	
Mean of column A	43.63
Mean of column B	46.41
Difference between means (B - A) ± 2.066	
95% confidence interval	-1.981 to 7.545
R squared (eta squared)	0.1848
F test to compare variances	
F, DFn, Dfd	1.539, 4, 4
P value	0.6866
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Swing Stride 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	5.547	0.1963	ns	No	Mean of Male	-0.06
Time	11.05	0.011	*	Yes	Mean of Female	-1.109
Sex	1.403	0.6541	ns	No	Difference between means	1.049
Subject	51.84	<0.0001	****	Yes	SE of difference	2.254
					95% CI of difference	-1.149 to 6.247

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	2.851	-2.812 to 8.514	No	ns	0.3184
14d					
Male vs. Female	3.994	-1.669 to 9.658	No	ns	0.1637
21d					
Male vs. Female	-1.762	-7.426 to 3.901	No	ns	0.5364
28d					
Male vs. Female	-1.476	-7.139 to 4.188	No	ns	0.6045
35d					
Male vs. Female	0.9043	-4.759 to 6.568	No	ns	0.7508
42d					
Male vs. Female	1.184	-4.479 to 6.848	No	ns	0.6775
49d					
Male vs. Female	-0.699	-6.362 to 4.964	No	ns	0.806
56d					
Male vs. Female	3.394	-2.269 to 9.058	No	ns	0.2356

Male					
7d vs. 14d	2.63	-3.157 to 8.417	No	ns	0.839
7d vs. 21d	4.033	-1.753 to 9.820	No	ns	0.3708
7d vs. 28d	3.697	-2.090 to 9.483	No	ns	0.4839
7d vs. 35d	5.023	-0.7633 to 10.81	No	ns	0.1342
7d vs. 42d	4.16	-1.627 to 9.947	No	ns	0.3318
7d vs. 49d	5.187	-0.6000 to 10.97	No	ns	0.1101
7d vs. 56d	4.617	-1.170 to 10.40	No	ns	0.2119
14d vs. 21d	1.403	-4.383 to 7.190	No	ns	0.9943
14d vs. 28d	1.067	-4.720 to 6.853	No	ns	0.999
14d vs. 35d	2.393	-3.393 to 8.180	No	ns	0.8943
14d vs. 42d	1.53	-4.257 to 7.317	No	ns	0.9904
14d vs. 49d	2.557	-3.230 to 8.343	No	ns	0.8575
14d vs. 56d	1.987	-3.800 to 7.773	No	ns	0.9582
21d vs. 28d	-0.3367	-6.123 to 5.450	No	ns	>0.9999
21d vs. 35d	0.99	-4.797 to 6.777	No	ns	0.9994
21d vs. 42d	0.1267	-5.660 to 5.913	No	ns	>0.9999
21d vs. 49d	1.153	-4.633 to 6.940	No	ns	0.9983
21d vs. 56d	0.5833	-5.203 to 6.370	No	ns	>0.9999
28d vs. 35d	1.327	-4.480 to 7.113	No	ns	0.996
28d vs. 42d	0.4633	-5.323 to 6.250	No	ns	>0.9999
28d vs. 49d	1.49	-4.297 to 7.277	No	ns	0.9918
28d vs. 56d	0.92	-4.867 to 6.707	No	ns	0.9996
35d vs. 42d	-0.8633	-6.650 to 4.923	No	ns	0.9997
35d vs. 49d	0.1633	-5.623 to 5.950	No	ns	>0.9999
35d vs. 56d	-0.4067	-6.193 to 5.380	No	ns	>0.9999
42d vs. 49d	1.027	-4.760 to 6.813	No	ns	0.9992
42d vs. 56d	0.4567	-5.330 to 6.243	No	ns	>0.9999
49d vs. 56d	-0.57	-6.357 to 5.217	No	ns	>0.9999

Female					
7d vs. 14d	3.773	-2.013 to 9.560	No	ns	0.4571
7d vs. 21d	-0.58	-6.367 to 5.207	No	ns	>0.9999
7d vs. 28d	-0.63	-6.417 to 5.157	No	ns	>0.9999
7d vs. 35d	3.077	-2.710 to 8.863	No	ns	0.7035
7d vs. 42d	2.493	-3.293 to 8.280	No	ns	0.8725
7d vs. 49d	1.637	-4.150 to 7.423	No	ns	0.9858
7d vs. 56d	5.16	-0.6267 to 10.95	No	ns	0.1138
14d vs. 21d	-4.353	-10.14 to 1.433	No	ns	0.2769
14d vs. 28d	-4.403	-10.19 to 1.383	No	ns	0.2636
14d vs. 35d	-0.6967	-6.483 to 5.090	No	ns	>0.9999
14d vs. 42d	-1.28	-7.067 to 4.507	No	ns	0.9968
14d vs. 49d	-2.137	-7.923 to 3.650	No	ns	0.9391
14d vs. 56d	1.387	-4.400 to 7.173	No	ns	0.9947
21d vs. 28d	-0.05	-5.837 to 5.737	No	ns	>0.9999
21d vs. 35d	3.657	-2.130 to 9.443	No	ns	0.498
21d vs. 42d	3.073	-2.713 to 8.860	No	ns	0.7047
21d vs. 49d	2.217	-3.570 to 8.003	No	ns	0.9268
21d vs. 56d	5.74	-0.04665 to 11.53	No	ns	0.0533
28d vs. 35d	3.707	-2.080 to 9.493	No	ns	0.4804
28d vs. 42d	3.123	-2.663 to 8.910	No	ns	0.6876
28d vs. 49d	2.267	-3.520 to 8.053	No	ns	0.9184
28d vs. 56d	5.79	0.003345 to 11.58	Yes	*	0.0498
35d vs. 42d	-0.5833	-6.370 to 5.203	No	ns	>0.9999
35d vs. 49d	-1.44	-7.227 to 4.347	No	ns	0.9933
35d vs. 56d	2.083	-3.703 to 7.870	No	ns	0.9465
42d vs. 49d	-0.8567	-6.643 to 4.930	No	ns	0.9998
42d vs. 56d	2.667	-3.120 to 8.453	No	ns	0.8293
49d vs. 56d	3.523	-2.263 to 9.310	No	ns	0.5456

Baseline % Swing Stride 10DegUp

Column B	Female
vs.	vs.
Column A	Male

Unpaired t test	
P value	0.3655
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.9594, df=8

How big is the difference?	
Mean of column A	43.89
Mean of column B	45.92
Difference between means (B - A) ± 2.034 ± 2.120	
95% confidence interval	-2.855 to 6.924
R squared (eta squared)	0.1032

F test to compare variances	
F, DFn, Dfd	1.728, 4, 4
P value	0.6092
P value summary	ns
Significantly different (P < 0.05)?	No

Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Swing Stride 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	7.882	0.0583	ns	No	Mean of Male	1.555
Time	4.939	0.2599	ns	No	Mean of Female	0.8713
Sex	0.6213	0.7744	ns	No	Difference between means	0.6841
Subject	56.54	<0.0001	****	Yes	SE of difference	2.307
					95% CI of difference	-4.636 to 6.005

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	2.225	-3.478 to 7.928	No	ns	0.4385
14d					
Male vs. Female	0.2087	-5.494 to 5.912	No	ns	0.942
21d					
Male vs. Female	-1.755	-7.458 to 3.948	No	ns	0.541
28d					
Male vs. Female	-1.628	-7.331 to 4.075	No	ns	0.5705
35d					
Male vs. Female	-1.758	-7.461 to 3.945	No	ns	0.5402
42d					
Male vs. Female	5.332	-0.3710 to 11.04	No	ns	0.0664
49d					
Male vs. Female	-0.148	-5.851 to 5.555	No	ns	0.9588
56d					
Male vs. Female	2.995	-2.708 to 8.698	No	ns	0.298
Male					
7d vs. 14d	3.293	-2.365 to 8.951	No	ns	0.6013
7d vs. 21d	4.037	-1.621 to 9.695	No	ns	0.3413
7d vs. 28d	4.303	-1.355 to 9.961	No	ns	0.2642
7d vs. 35d	4.98	-0.6781 to 10.64	No	ns	0.1234
7d vs. 42d	1.067	-4.591 to 6.725	No	ns	0.9988
7d vs. 49d	4.443	-1.215 to 10.10	No	ns	0.2286
7d vs. 56d	2.687	-2.971 to 8.345	No	ns	0.8069
14d vs. 21d	0.7433	-4.915 to 6.401	No	ns	0.9999
14d vs. 28d	1.01	-4.648 to 6.668	No	ns	0.9992
14d vs. 35d	1.687	-3.971 to 7.345	No	ns	0.9808
14d vs. 42d	-2.227	-7.885 to 3.431	No	ns	0.9165
14d vs. 49d	1.15	-4.508 to 6.808	No	ns	0.9981
14d vs. 56d	-0.6067	-6.265 to 5.051	No	ns	>0.9999
21d vs. 28d	0.2667	-5.391 to 5.925	No	ns	>0.9999
21d vs. 35d	0.9433	-4.715 to 6.601	No	ns	0.9995
21d vs. 42d	-2.97	-8.628 to 2.688	No	ns	0.7167
21d vs. 49d	0.4067	-5.251 to 6.065	No	ns	>0.9999
21d vs. 56d	-1.35	-7.008 to 4.308	No	ns	0.9948
28d vs. 35d	0.6767	-4.981 to 6.335	No	ns	>0.9999
28d vs. 42d	-3.237	-8.895 to 2.421	No	ns	0.6221
28d vs. 49d	0.14	-5.518 to 5.798	No	ns	>0.9999
28d vs. 56d	-1.617	-7.275 to 4.041	No	ns	0.9849
35d vs. 42d	-3.913	-9.571 to 1.745	No	ns	0.3807
35d vs. 49d	-0.5367	-6.195 to 5.121	No	ns	>0.9999
35d vs. 56d	-2.293	-7.951 to 3.365	No	ns	0.9038
42d vs. 49d	3.377	-2.281 to 9.035	No	ns	0.5707
42d vs. 56d	1.62	-4.038 to 7.278	No	ns	0.9847
49d vs. 56d	-1.757	-7.415 to 3.901	No	ns	0.9758
Female					
7d vs. 14d	1.277	-4.381 to 6.935	No	ns	0.9964
7d vs. 21d	0.05667	-5.601 to 5.715	No	ns	>0.9999
7d vs. 28d	0.45	-5.208 to 6.108	No	ns	>0.9999
7d vs. 35d	0.9967	-4.661 to 6.655	No	ns	0.9992
7d vs. 42d	4.173	-1.485 to 9.831	No	ns	0.3003
7d vs. 49d	2.07	-3.588 to 7.728	No	ns	0.9419
7d vs. 56d	3.457	-2.201 to 9.115	No	ns	0.5413
14d vs. 21d	-1.22	-6.878 to 4.438	No	ns	0.9973
14d vs. 28d	-0.8267	-6.485 to 4.831	No	ns	0.9998
14d vs. 35d	-0.28	-5.938 to 5.378	No	ns	>0.9999
14d vs. 42d	2.897	-2.761 to 8.555	No	ns	0.7413
14d vs. 49d	0.7933	-4.865 to 6.451	No	ns	0.9998
14d vs. 56d	2.18	-3.478 to 7.838	No	ns	0.9247
21d vs. 28d	0.3933	-5.265 to 6.051	No	ns	>0.9999
21d vs. 35d	0.94	-4.718 to 6.598	No	ns	0.9995
21d vs. 42d	4.117	-1.541 to 9.775	No	ns	0.3169
21d vs. 49d	2.013	-3.645 to 7.671	No	ns	0.9496
21d vs. 56d	3.4	-2.258 to 9.058	No	ns	0.5621
28d vs. 35d	0.5467	-5.111 to 6.205	No	ns	>0.9999
28d vs. 42d	3.723	-1.935 to 9.381	No	ns	0.4452
28d vs. 49d	1.62	-4.038 to 7.278	No	ns	0.9847
28d vs. 56d	3.007	-2.651 to 8.665	No	ns	0.7041
35d vs. 42d	3.177	-2.481 to 8.835	No	ns	0.6439
35d vs. 49d	1.073	-4.585 to 6.731	No	ns	0.9988
35d vs. 56d	2.46	-3.198 to 8.118	No	ns	0.8673
42d vs. 49d	-2.103	-7.761 to 3.555	No	ns	0.937
42d vs. 56d	-0.7167	-6.375 to 4.941	No	ns	>0.9999
49d vs. 56d	1.387	-4.271 to 7.045	No	ns	0.9939

Baseline % Swing Stride 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.9028
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.1260, df=8
How big is the difference?	
Mean of column A	43.68
Mean of column B	43.39
Difference between means (B - A) ±	±-0.2947 ± 2.338
95% confidence interval	-5.686 to 5.097
R squared (eta squared)	0.001981
F test to compare variances	
F, DFn, Dfd	4.252, 4, 4
P value	0.1899
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Brake (s) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	17.13	<0.0001	****	Yes	Mean of Male Mean of Female
Time	12.4	0.0002	***	Yes	Difference between means
Sex	6.335	0.3141	ns	No	SE of difference
Subject	43.94	<0.0001	****	Yes	95% CI of difference
					-0.0006883 0.003822 -0.00451 0.004199 -0.01419 to 0.005174
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.00056	-0.01070 to 0.0095	No	ns	0.9125
14d					
Male vs. Female	-0.02353	-0.03366 to -0.013	Yes	****	<0.0001
21d					
Male vs. Female	-0.005727	-0.01586 to 0.0044	No	ns	0.2632
28d					
Male vs. Female	0.0008733	-0.009262 to 0.011	No	ns	0.8639
35d					
Male vs. Female	-0.00136	-0.01150 to 0.0087	No	ns	0.7895
42d					
Male vs. Female	-0.0007934	-0.01093 to 0.0093	No	ns	0.8762
49d					
Male vs. Female	-0.002893	-0.01303 to 0.0072	No	ns	0.5705
56d					
Male vs. Female	-0.002093	-0.01223 to 0.0080	No	ns	0.6813
Male					
7d vs. 14d	0.005	-0.004582 to 0.014	No	ns	0.7226
7d vs. 21d	0.0041	-0.005482 to 0.013	No	ns	0.8764
7d vs. 28d	0.003133	-0.006449 to 0.012	No	ns	0.9678
7d vs. 35d	0.001833	-0.007749 to 0.011	No	ns	0.9987
7d vs. 42d	0.0046	-0.004982 to 0.014	No	ns	0.7981
7d vs. 49d	0.003133	-0.006449 to 0.012	No	ns	0.9678
7d vs. 56d	0.0006667	-0.008915 to 0.010	No	ns	>0.9999
14d vs. 21d	-0.0009	-0.01048 to 0.0086	No	ns	>0.9999
14d vs. 28d	-0.001867	-0.01145 to 0.0077	No	ns	0.9986
14d vs. 35d	-0.003167	-0.01275 to 0.0064	No	ns	0.9659
14d vs. 42d	-0.0004	-0.009982 to 0.009	No	ns	>0.9999
14d vs. 49d	-0.001867	-0.01145 to 0.0077	No	ns	0.9986
14d vs. 56d	-0.004333	-0.01392 to 0.0052	No	ns	0.8424
21d vs. 28d	-0.0009667	-0.01055 to 0.0086	No	ns	>0.9999
21d vs. 35d	-0.002267	-0.01185 to 0.0073	No	ns	0.9951
21d vs. 42d	0.0005	-0.009082 to 0.010	No	ns	>0.9999
21d vs. 49d	-0.0009667	-0.01055 to 0.0086	No	ns	>0.9999
21d vs. 56d	-0.003433	-0.01302 to 0.0061	No	ns	0.9478
28d vs. 35d	-0.0013	-0.01088 to 0.0082	No	ns	0.9999
28d vs. 42d	0.001467	-0.008115 to 0.011	No	ns	0.9997
28d vs. 49d	-0.000000014	-0.009582 to 0.009	No	ns	>0.9999
28d vs. 56d	-0.002467	-0.01205 to 0.0071	No	ns	0.9918
35d vs. 42d	0.002767	-0.006815 to 0.012	No	ns	0.984
35d vs. 49d	0.0013	-0.008282 to 0.010	No	ns	0.9999
35d vs. 56d	-0.001167	-0.01075 to 0.0084	No	ns	>0.9999
42d vs. 49d	-0.001467	-0.01105 to 0.0081	No	ns	0.9997
42d vs. 56d	-0.003933	-0.01352 to 0.0056	No	ns	0.8979
49d vs. 56d	-0.002467	-0.01205 to 0.0071	No	ns	0.9918
Female					
7d vs. 14d	-0.01797	-0.02755 to -0.008	Yes	****	<0.0001
7d vs. 21d	-0.001067	-0.01065 to 0.0085	No	ns	>0.9999
7d vs. 28d	0.004567	-0.005015 to 0.014	No	ns	0.8039
7d vs. 35d	0.001033	-0.008549 to 0.010	No	ns	>0.9999
7d vs. 42d	0.004367	-0.005215 to 0.013	No	ns	0.8372
7d vs. 49d	0.0008	-0.008782 to 0.010	No	ns	>0.9999
7d vs. 56d	-0.0008666	-0.01045 to 0.0087	No	ns	>0.9999
14d vs. 21d	0.0169	0.007318 to 0.0264	Yes	****	<0.0001
14d vs. 28d	0.02253	0.01295 to 0.03212	Yes	****	<0.0001
14d vs. 35d	0.019	0.009418 to 0.0285	Yes	****	<0.0001
14d vs. 42d	0.02233	0.01275 to 0.03192	Yes	****	<0.0001
14d vs. 49d	0.01877	0.009185 to 0.0283	Yes	****	<0.0001
14d vs. 56d	0.0171	0.007518 to 0.0266	Yes	****	<0.0001
21d vs. 28d	0.005633	-0.003949 to 0.015	No	ns	0.5892
21d vs. 35d	0.0021	-0.007482 to 0.011	No	ns	0.997
21d vs. 42d	0.005433	-0.004149 to 0.015	No	ns	0.6324
21d vs. 49d	0.001867	-0.007715 to 0.011	No	ns	0.9986
21d vs. 56d	0.0002	-0.009382 to 0.009	No	ns	>0.9999
28d vs. 35d	-0.003533	-0.01312 to 0.0060	No	ns	0.9395
28d vs. 42d	-0.0002	-0.009782 to 0.009	No	ns	>0.9999
28d vs. 49d	-0.003767	-0.01335 to 0.0058	No	ns	0.9169
28d vs. 56d	-0.005433	-0.01502 to 0.0041	No	ns	0.6324
35d vs. 42d	0.003333	-0.006249 to 0.012	No	ns	0.9552
35d vs. 49d	-0.0002333	-0.009815 to 0.009	No	ns	>0.9999
35d vs. 56d	-0.0019	-0.01148 to 0.0076	No	ns	0.9984
42d vs. 49d	-0.003567	-0.01315 to 0.0060	No	ns	0.9366
42d vs. 56d	-0.005233	-0.01482 to 0.0043	No	ns	0.6748
49d vs. 56d	-0.001667	-0.01125 to 0.0079	No	ns	0.9993

Baseline Brake (s) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2328
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.291, df=8
How big is the difference?	
Mean of column A	0.02521
Mean of column B	0.02882
Difference between means (B - A) ± 0.003607 ± 0.002794	
95% confidence interval	-0.002836 to 0.01005
R squared (eta squared)	0.1724
F test to compare variances	
F, DFn, Dfd	17.29, 4, 4
P value	0.0173
P value summary	*
Significantly different (P < 0.05)?	Yes
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Brake (s) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	-0.00003334
Time x Sex	31.36	<0.0001	****	Yes	Mean of Male	0.002327
Time	26.31	<0.0001	****	Yes	Mean of Female	-0.00236
Sex	1.747	0.4356	ns	No	Difference between means	0.002875
Subject	20.75	<0.0001	****	Yes	SE of difference	-0.008991 to 0.004271
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	
7d						
Male vs. Female	-0.006193	-0.01423 to 0.0018	No	ns	0.1285	
14d						
Male vs. Female	-0.02656	-0.03459 to -0.0181	Yes	****	<0.0001	
21d						
Male vs. Female	0.002207	-0.005828 to 0.010	No	ns	0.5851	
28d						
Male vs. Female	0.009073	0.001039 to 0.0171	Yes	*	0.0275	
35d						
Male vs. Female	-0.00156	-0.009595 to 0.006	No	ns	0.6994	
42d						
Male vs. Female	0.002807	-0.005228 to 0.010	No	ns	0.4878	
49d						
Male vs. Female	0.00174	-0.006295 to 0.009	No	ns	0.6667	
56d						
Male vs. Female	-0.0003933	-0.008428 to 0.007	No	ns	0.9224	
Male						
7d vs. 14d	0.0001	-0.009364 to 0.009	No	ns	>0.9999	
7d vs. 21d	0.0007667	-0.008697 to 0.010	No	ns	>0.9999	
7d vs. 28d	-0.003467	-0.01293 to 0.0059	No	ns	0.9415	
7d vs. 35d	-0.0005333	-0.009997 to 0.008	No	ns	>0.9999	
7d vs. 42d	0.0005667	-0.008897 to 0.010	No	ns	>0.9999	
7d vs. 49d	-0.0021	-0.01156 to 0.0073	No	ns	0.9967	
7d vs. 56d	-0.0024	-0.01186 to 0.0070	No	ns	0.9925	
14d vs. 21d	0.0006667	-0.008797 to 0.010	No	ns	>0.9999	
14d vs. 28d	-0.003567	-0.01303 to 0.0058	No	ns	0.9325	
14d vs. 35d	-0.0006334	-0.01010 to 0.0088	No	ns	>0.9999	
14d vs. 42d	0.0004667	-0.008997 to 0.009	No	ns	>0.9999	
14d vs. 49d	-0.0022	-0.01166 to 0.0072	No	ns	0.9956	
14d vs. 56d	-0.0025	-0.01196 to 0.0069	No	ns	0.9905	
21d vs. 28d	-0.004233	-0.01370 to 0.0052	No	ns	0.8497	
21d vs. 35d	-0.0013	-0.01076 to 0.0081	No	ns	0.9999	
21d vs. 42d	-0.0002	-0.009664 to 0.009	No	ns	>0.9999	
21d vs. 49d	-0.002867	-0.01233 to 0.0065	No	ns	0.979	
21d vs. 56d	-0.003167	-0.01263 to 0.0062	No	ns	0.9636	
28d vs. 35d	0.002933	-0.006531 to 0.012	No	ns	0.9761	
28d vs. 42d	0.004033	-0.005431 to 0.013	No	ns	0.8787	
28d vs. 49d	0.001367	-0.008097 to 0.010	No	ns	0.9998	
28d vs. 56d	0.001067	-0.008397 to 0.010	No	ns	>0.9999	
35d vs. 42d	0.0011	-0.008364 to 0.010	No	ns	>0.9999	
35d vs. 49d	-0.001567	-0.01103 to 0.0078	No	ns	0.9995	
35d vs. 56d	-0.001867	-0.01133 to 0.0075	No	ns	0.9984	
42d vs. 49d	-0.002667	-0.01213 to 0.0067	No	ns	0.9861	
42d vs. 56d	-0.002967	-0.01243 to 0.0064	No	ns	0.9745	
49d vs. 56d	-0.0003	-0.009764 to 0.009	No	ns	>0.9999	
Female						
7d vs. 14d	-0.02027	-0.02973 to -0.0101	Yes	****	<0.0001	
7d vs. 21d	0.009167	-0.0002974 to 0.01	No	ns	0.0642	
7d vs. 28d	0.0118	0.002336 to 0.0212	Yes	**	0.0055	
7d vs. 35d	0.0041	-0.005364 to 0.013	No	ns	0.8694	
7d vs. 42d	0.009567	0.0001026 to 0.015	Yes	*	0.0458	
7d vs. 49d	0.005833	-0.003631 to 0.015	No	ns	0.53	
7d vs. 56d	0.0034	-0.006064 to 0.012	No	ns	0.9471	
14d vs. 21d	0.02943	0.01997 to 0.0389	Yes	****	<0.0001	
14d vs. 28d	0.03207	0.02260 to 0.0415	Yes	****	<0.0001	
14d vs. 35d	0.02437	0.01490 to 0.0338	Yes	****	<0.0001	
14d vs. 42d	0.02983	0.02037 to 0.0393	Yes	****	<0.0001	
14d vs. 49d	0.0261	0.01664 to 0.0355	Yes	****	<0.0001	
14d vs. 56d	0.02367	0.01420 to 0.0331	Yes	****	<0.0001	
21d vs. 28d	0.002633	-0.006831 to 0.012	No	ns	0.9871	
21d vs. 35d	-0.005067	-0.01453 to 0.0043	No	ns	0.6963	
21d vs. 42d	0.0004	-0.009064 to 0.009	No	ns	>0.9999	
21d vs. 49d	-0.003333	-0.01280 to 0.0061	No	ns	0.9522	
21d vs. 56d	-0.005767	-0.01523 to 0.0036	No	ns	0.5446	
28d vs. 35d	-0.0077	-0.01716 to 0.0017	No	ns	0.1921	
28d vs. 42d	-0.002233	-0.01170 to 0.0072	No	ns	0.9952	
28d vs. 49d	-0.005967	-0.01543 to 0.0034	No	ns	0.501	
28d vs. 56d	-0.0084	-0.01786 to 0.0010	No	ns	0.1172	
35d vs. 42d	0.005467	-0.003997 to 0.014	No	ns	0.6105	
35d vs. 49d	0.001733	-0.007731 to 0.011	No	ns	0.999	
35d vs. 56d	-0.0007	-0.01016 to 0.0087	No	ns	>0.9999	
42d vs. 49d	-0.003733	-0.01320 to 0.0057	No	ns	0.9155	
42d vs. 56d	-0.006167	-0.01563 to 0.0032	No	ns	0.4581	
49d vs. 56d	-0.002433	-0.01190 to 0.0070	No	ns	0.9919	

Baseline Brake (s) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2571
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.220, df=8
How big is the difference?	
Mean of column A	0.02365
Mean of column B	0.02792
Difference between means (B - A)	±0.004273 ± 0.003502
95% confidence interval	-0.003802 to 0.01235
R squared (eta squared)	0.1569
F test to compare variances	
F, DFn, Dfd	1.230, 4, 4
P value	0.846
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Brake (s) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	17.15	0.0003	***	Yes	Mean of Male	0.003265
Time	10.68	0.0095	**	Yes	Mean of Female	0.0003192
Sex	2.951	0.4685	ns	No	Difference between means	0.002946
Subject	40.76	<0.0001	****	Yes	SE of difference	0.003871
					95% CI of difference	-0.005980 to 0.01187
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	
7d						
Male vs. Female	0.0061	-0.003977 to 0.016	No	ns	0.231	
14d						
Male vs. Female	-0.0142	-0.02428 to -0.0041	Yes	**	0.0065	
21d						
Male vs. Female	0.008667	-0.001410 to 0.018	No	ns	0.0906	
28d						
Male vs. Female	0.008733	-0.001344 to 0.018	No	ns	0.0882	
35d						
Male vs. Female	0.004667	-0.005410 to 0.014	No	ns	0.3584	
42d						
Male vs. Female	-0.001133	-0.01121 to 0.0089	No	ns	0.8229	
49d						
Male vs. Female	0.006367	-0.003710 to 0.016	No	ns	0.2115	
56d						
Male vs. Female	0.004367	-0.005710 to 0.014	No	ns	0.3899	
Male						
7d vs. 14d	0.001167	-0.009719 to 0.012	No	ns	>0.9999	
7d vs. 21d	-0.003267	-0.01415 to 0.0076	No	ns	0.98	
7d vs. 28d	-0.0025	-0.01339 to 0.0083	No	ns	0.9959	
7d vs. 35d	-0.00003334	-0.01092 to 0.0108	No	ns	>0.9999	
7d vs. 42d	0.002633	-0.008252 to 0.013	No	ns	0.9944	
7d vs. 49d	-0.004667	-0.01555 to 0.0062	No	ns	0.8754	
7d vs. 56d	-0.003667	-0.01455 to 0.0072	No	ns	0.9623	
14d vs. 21d	-0.004433	-0.01532 to 0.0064	No	ns	0.9016	
14d vs. 28d	-0.003667	-0.01455 to 0.0072	No	ns	0.9623	
14d vs. 35d	-0.0012	-0.01209 to 0.0096	No	ns	>0.9999	
14d vs. 42d	0.001467	-0.009419 to 0.012	No	ns	0.9999	
14d vs. 49d	-0.005833	-0.01672 to 0.0050	No	ns	0.8953	
14d vs. 56d	-0.004833	-0.01572 to 0.0060	No	ns	0.8544	
21d vs. 28d	0.0007667	-0.01012 to 0.0116	No	ns	>0.9999	
21d vs. 35d	0.003233	-0.007652 to 0.014	No	ns	0.9812	
21d vs. 42d	0.0059	-0.004986 to 0.016	No	ns	0.6832	
21d vs. 49d	-0.0014	-0.01229 to 0.0094	No	ns	>0.9999	
21d vs. 56d	-0.0004	-0.01129 to 0.0104	No	ns	>0.9999	
28d vs. 35d	0.002467	-0.008419 to 0.013	No	ns	0.9963	
28d vs. 42d	0.005133	-0.005752 to 0.016	No	ns	0.8122	
28d vs. 49d	-0.002167	-0.01305 to 0.0087	No	ns	0.9983	
28d vs. 56d	-0.001167	-0.01205 to 0.0097	No	ns	>0.9999	
35d vs. 42d	0.002667	-0.008219 to 0.013	No	ns	0.994	
35d vs. 49d	-0.004633	-0.01552 to 0.0062	No	ns	0.8794	
35d vs. 56d	-0.003633	-0.01452 to 0.0072	No	ns	0.9641	
42d vs. 49d	-0.0073	-0.01819 to 0.0035	No	ns	0.4206	
42d vs. 56d	-0.0063	-0.01719 to 0.0045	No	ns	0.6082	
49d vs. 56d	0.001	-0.009886 to 0.011	No	ns	>0.9999	
Female						
7d vs. 14d	-0.01913	-0.03002 to -0.0082	Yes	****	<0.0001	
7d vs. 21d	-0.0007	-0.01159 to 0.0101	No	ns	>0.9999	
7d vs. 28d	0.0001333	-0.01075 to 0.0110	No	ns	>0.9999	
7d vs. 35d	-0.001467	-0.01235 to 0.0094	No	ns	0.9999	
7d vs. 42d	-0.0046	-0.01549 to 0.0062	No	ns	0.8833	
7d vs. 49d	-0.0044	-0.01529 to 0.0064	No	ns	0.9051	
7d vs. 56d	-0.0054	-0.01629 to 0.0054	No	ns	0.7704	
14d vs. 21d	0.01843	0.007548 to 0.0293	Yes	****	<0.0001	
14d vs. 28d	0.01927	0.008381 to 0.0301	Yes	****	<0.0001	
14d vs. 35d	0.01767	0.006781 to 0.0285	Yes	***	0.0001	
14d vs. 42d	0.01453	0.003648 to 0.0254	Yes	**	0.0023	
14d vs. 49d	0.01473	0.003848 to 0.0256	Yes	**	0.0019	
14d vs. 56d	0.01373	0.002848 to 0.0246	Yes	**	0.0048	
21d vs. 28d	0.0008334	-0.01005 to 0.0117	No	ns	>0.9999	
21d vs. 35d	-0.0007667	-0.01165 to 0.0101	No	ns	>0.9999	
21d vs. 42d	-0.0039	-0.01479 to 0.0069	No	ns	0.9478	
21d vs. 49d	-0.0037	-0.01459 to 0.0071	No	ns	0.9604	
21d vs. 56d	-0.0047	-0.01559 to 0.0061	No	ns	0.8714	
28d vs. 35d	-0.0016	-0.01249 to 0.0092	No	ns	0.9998	
28d vs. 42d	-0.004733	-0.01562 to 0.0061	No	ns	0.8672	
28d vs. 49d	-0.004533	-0.01542 to 0.0063	No	ns	0.8908	
28d vs. 56d	-0.005533	-0.01642 to 0.0053	No	ns	0.7481	
35d vs. 42d	-0.003133	-0.01402 to 0.0077	No	ns	0.9843	
35d vs. 49d	-0.002933	-0.01382 to 0.0079	No	ns	0.9893	
35d vs. 56d	-0.003933	-0.01482 to 0.0069	No	ns	0.9455	
42d vs. 49d	0.0002	-0.01069 to 0.0110	No	ns	>0.9999	
42d vs. 56d	-0.0008	-0.01169 to 0.0100	No	ns	>0.9999	
49d vs. 56d	-0.001	-0.01189 to 0.0098	No	ns	>0.9999	

Baseline Brake (s) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0311
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=2.610, df=8
How big is the difference?	
Mean of column A	0.02226
Mean of column B	0.03166
Difference between means (B - A) ± 0.009400 ± 0.003601	
95% confidence interval	0.001095 to 0.01770
R squared (eta squared)	0.4599
F test to compare variances	
F, DFn, Dfd	1.722, 4, 4
P value	0.6114
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Brake Stride FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	13.52	0.0001	***	Yes	Mean of Male -0.5894
Time	13.25	0.0001	***	Yes	Mean of Female 1.199
Sex	3.426	0.4771	ns	No	Difference between means -1.788
Subject	49.27	<0.0001	****	Yes	SE of difference 2.398
					95% CI of difference -7.317 to 3.741

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	0.196	-5.505 to 5.897	No	ns	0.9455
14d					
Male vs. Female	-10.61	-16.31 to -4.907	Yes	***	0.0004
21d					
Male vs. Female	-3.221	-8.921 to 2.480	No	ns	0.2633
28d					
Male vs. Female	0.986	-4.715 to 6.687	No	ns	0.7308
35d					
Male vs. Female	-0.4773	-6.178 to 5.223	No	ns	0.8677
42d					
Male vs. Female	0.5027	-5.198 to 6.203	No	ns	0.8607
49d					
Male vs. Female	-1.457	-7.158 to 4.243	No	ns	0.6113
56d					
Male vs. Female	-0.2273	-5.928 to 5.473	No	ns	0.9368
Male					
7d vs. 14d	2.69	-2.518 to 7.898	No	ns	0.7328
7d vs. 21d	2.63	-2.578 to 7.838	No	ns	0.7543
7d vs. 28d	2.657	-2.552 to 7.865	No	ns	0.7448
7d vs. 35d	1.627	-3.582 to 6.835	No	ns	0.975
7d vs. 42d	3.097	-2.112 to 8.305	No	ns	0.5753
7d vs. 49d	2.6	-2.608 to 7.808	No	ns	0.7647
7d vs. 56d	1.063	-4.145 to 6.272	No	ns	0.9981
14d vs. 21d	-0.06	-5.268 to 5.148	No	ns	>0.9999
14d vs. 28d	-0.03333	-5.242 to 5.175	No	ns	>0.9999
14d vs. 35d	-1.063	-6.272 to 4.145	No	ns	0.9981
14d vs. 42d	0.4067	-4.802 to 5.615	No	ns	>0.9999
14d vs. 49d	-0.09	-5.298 to 5.118	No	ns	>0.9999
14d vs. 56d	-1.627	-6.835 to 3.582	No	ns	0.975
21d vs. 28d	0.02667	-5.182 to 5.235	No	ns	>0.9999
21d vs. 35d	-1.003	-6.212 to 4.205	No	ns	0.9987
21d vs. 42d	0.4667	-4.742 to 5.675	No	ns	>0.9999
21d vs. 49d	-0.03	-5.238 to 5.178	No	ns	>0.9999
21d vs. 56d	-1.567	-6.775 to 3.642	No	ns	0.9798
28d vs. 35d	-1.03	-6.238 to 4.178	No	ns	0.9984
28d vs. 42d	0.44	-4.768 to 5.648	No	ns	>0.9999
28d vs. 49d	-0.05667	-5.265 to 5.152	No	ns	>0.9999
28d vs. 56d	-1.593	-6.802 to 3.615	No	ns	0.9777
35d vs. 42d	1.47	-3.738 to 6.678	No	ns	0.986
35d vs. 49d	0.9733	-4.235 to 6.182	No	ns	0.9989
35d vs. 56d	-0.5633	-5.772 to 4.645	No	ns	>0.9999
42d vs. 49d	-0.4967	-5.705 to 4.712	No	ns	>0.9999
42d vs. 56d	-2.033	-7.242 to 3.175	No	ns	0.9197
49d vs. 56d	-1.537	-6.745 to 3.672	No	ns	0.9819
Female					
7d vs. 14d	-8.113	-13.32 to -2.905	Yes	***	0.0002
7d vs. 21d	-0.7867	-5.995 to 4.422	No	ns	0.9997
7d vs. 28d	3.447	-1.762 to 8.655	No	ns	0.4379
7d vs. 35d	0.9533	-4.255 to 6.162	No	ns	0.999
7d vs. 42d	3.403	-1.805 to 8.612	No	ns	0.4544
7d vs. 49d	0.9467	-4.262 to 6.155	No	ns	0.9991
7d vs. 56d	0.64	-4.568 to 5.848	No	ns	>0.9999
14d vs. 21d	7.327	2.118 to 12.54	Yes	**	0.0011
14d vs. 28d	11.56	6.352 to 16.77	Yes	****	<0.0001
14d vs. 35d	9.067	3.858 to 14.28	Yes	****	<0.0001
14d vs. 42d	11.52	6.308 to 16.73	Yes	****	<0.0001
14d vs. 49d	9.06	3.852 to 14.27	Yes	****	<0.0001
14d vs. 56d	8.753	3.545 to 13.96	Yes	****	<0.0001
21d vs. 28d	4.233	-0.9750 to 9.442	No	ns	0.1931
21d vs. 35d	1.74	-3.468 to 6.948	No	ns	0.9639
21d vs. 42d	4.19	-1.018 to 9.398	No	ns	0.2034
21d vs. 49d	1.733	-3.475 to 6.942	No	ns	0.9646
21d vs. 56d	1.427	-3.782 to 6.635	No	ns	0.9882
28d vs. 35d	-2.493	-7.702 to 2.715	No	ns	0.8004
28d vs. 42d	-0.04333	-5.252 to 5.165	No	ns	>0.9999
28d vs. 49d	-2.5	-7.708 to 2.708	No	ns	0.7982
28d vs. 56d	-2.807	-8.015 to 2.402	No	ns	0.6894
35d vs. 42d	2.45	-2.758 to 7.658	No	ns	0.8141
35d vs. 49d	-0.006667	-5.215 to 5.202	No	ns	>0.9999
35d vs. 56d	-0.3133	-5.522 to 4.895	No	ns	>0.9999
42d vs. 49d	-2.457	-7.665 to 2.752	No	ns	0.812
42d vs. 56d	-2.763	-7.972 to 2.445	No	ns	0.7057
49d vs. 56d	-0.3067	-5.515 to 4.902	No	ns	>0.9999

Baseline % Brake Stride FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.1709
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.504, df=8
How big is the difference?	
Mean of column A	13.73
Mean of column B	15.89
Difference between means (B - A) ± 2.159 ± 1.435	
95% confidence interval	-1.151 to 5.469
R squared (eta squared)	0.2205
F test to compare variances	
F, DFn, Dfd	2.670, 4, 4
P value	0.3646
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Brake Stride 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	29.85	<0.0001	****	Yes	-0.5192
Time	23.3	<0.0001	****	Yes	0.1845
Sex	0.4792	0.6975	ns	No	-0.7037
Subject	23.61	<0.0001	****	Yes	1.746
					95% CI of difference
					-4.730 to 3.323

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-2.687	-7.575 to 2.201	No	ns	0.2763
14d					
Male vs. Female	-14.08	-18.97 to -9.189	Yes	****	<0.0001
21d					
Male vs. Female	2.053	-2.835 to 6.941	No	ns	0.4046
28d					
Male vs. Female	6.013	1.125 to 10.90	Yes	*	0.0167
35d					
Male vs. Female	-0.4603	-5.349 to 4.428	No	ns	0.8514
42d					
Male vs. Female	1.26	-3.629 to 6.148	No	ns	0.6085
49d					
Male vs. Female	1.673	-3.215 to 6.561	No	ns	0.4966
56d					
Male vs. Female	0.5963	-4.292 to 5.485	No	ns	0.8082
Male					
7d vs. 14d	0.7667	-5.003 to 6.537	No	ns	0.9999
7d vs. 21d	0.67	-5.100 to 6.440	No	ns	>0.9999
7d vs. 28d	-1.633	-7.403 to 4.137	No	ns	0.9857
7d vs. 35d	0.3433	-5.427 to 6.113	No	ns	>0.9999
7d vs. 42d	1.133	-4.637 to 6.903	No	ns	0.9985
7d vs. 49d	-0.7367	-6.507 to 5.033	No	ns	>0.9999
7d vs. 56d	-0.9367	-6.707 to 4.833	No	ns	0.9996
14d vs. 21d	-0.09667	-5.867 to 5.673	No	ns	>0.9999
14d vs. 28d	-2.4	-8.170 to 3.370	No	ns	0.8915
14d vs. 35d	-0.4233	-6.193 to 5.347	No	ns	>0.9999
14d vs. 42d	0.3667	-5.403 to 6.137	No	ns	>0.9999
14d vs. 49d	-1.503	-7.273 to 4.267	No	ns	0.9912
14d vs. 56d	-1.703	-7.473 to 4.067	No	ns	0.9818
21d vs. 28d	-2.303	-8.073 to 3.467	No	ns	0.9106
21d vs. 35d	-0.3267	-6.097 to 5.443	No	ns	>0.9999
21d vs. 42d	0.4633	-5.307 to 6.233	No	ns	>0.9999
21d vs. 49d	-1.407	-7.177 to 4.363	No	ns	0.9941
21d vs. 56d	-1.607	-7.377 to 4.163	No	ns	0.987
28d vs. 35d	1.977	-3.793 to 7.747	No	ns	0.9587
28d vs. 42d	2.767	-3.003 to 8.537	No	ns	0.7991
28d vs. 49d	0.8967	-4.873 to 6.667	No	ns	0.9997
28d vs. 56d	0.8967	-5.073 to 6.467	No	ns	>0.9999
35d vs. 42d	0.79	-4.980 to 6.560	No	ns	0.9999
35d vs. 49d	-1.08	-6.850 to 4.690	No	ns	0.9989
35d vs. 56d	-1.28	-7.050 to 4.490	No	ns	0.9967
42d vs. 49d	-1.87	-7.640 to 3.900	No	ns	0.9694
42d vs. 56d	-2.07	-7.840 to 3.700	No	ns	0.9474
49d vs. 56d	-0.2	-5.970 to 5.570	No	ns	>0.9999
Female					
7d vs. 14d	-10.62	-16.39 to -4.853	Yes	****	<0.0001
7d vs. 21d	5.41	-0.3601 to 11.18	No	ns	0.0813
7d vs. 28d	7.067	1.297 to 12.84	Yes	**	0.0068
7d vs. 35d	2.57	-3.200 to 8.340	No	ns	0.8524
7d vs. 42d	5.08	-0.6901 to 10.85	No	ns	0.1232
7d vs. 49d	3.623	-2.147 to 9.393	No	ns	0.5061
7d vs. 56d	2.347	-3.423 to 8.117	No	ns	0.9023
14d vs. 21d	16.03	10.26 to 21.80	Yes	****	<0.0001
14d vs. 28d	17.69	11.92 to 23.46	Yes	****	<0.0001
14d vs. 35d	13.19	7.423 to 18.96	Yes	****	<0.0001
14d vs. 42d	15.7	9.933 to 21.47	Yes	****	<0.0001
14d vs. 49d	14.25	8.477 to 20.02	Yes	****	<0.0001
14d vs. 56d	12.97	7.200 to 18.74	Yes	****	<0.0001
21d vs. 28d	1.657	-4.113 to 7.427	No	ns	0.9845
21d vs. 35d	-2.84	-8.610 to 2.930	No	ns	0.7772
21d vs. 42d	-0.33	-6.100 to 5.440	No	ns	>0.9999
21d vs. 49d	-1.787	-7.557 to 3.983	No	ns	0.9762
21d vs. 56d	-3.063	-8.833 to 2.707	No	ns	0.7051
28d vs. 35d	-4.497	-10.27 to 1.273	No	ns	0.237
28d vs. 42d	-1.987	-7.757 to 3.783	No	ns	0.9576
28d vs. 49d	-3.443	-9.213 to 2.327	No	ns	0.5708
28d vs. 56d	-4.72	-10.49 to 1.050	No	ns	0.1869
35d vs. 42d	2.51	-3.260 to 8.280	No	ns	0.867
35d vs. 49d	1.053	-4.717 to 6.823	No	ns	0.9991
35d vs. 56d	-0.2233	-5.993 to 5.547	No	ns	>0.9999
42d vs. 49d	-1.457	-7.227 to 4.313	No	ns	0.9927
42d vs. 56d	-2.733	-8.503 to 3.037	No	ns	0.8087
49d vs. 56d	-1.277	-7.047 to 4.493	No	ns	0.9968

Baseline % Brake Stride 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2585
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.216, df=8
How big is the difference?	
Mean of column A	13.19
Mean of column B	15.6
Difference between means (B - A) ± 2.420 ± 1.989	
95% confidence interval	-2.168 to 7.007
R squared (eta squared)	0.1561
F test to compare variances	
F, DFn, Dfd	1.003, 4, 4
P value	0.998
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Brake Stride 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	15.34	0.0005	***	Yes	Mean of Male	2.182
Time	33.88	<0.0001	****	Yes	Mean of Female	0.5793
Sex	2.144	0.3981	ns	No	Difference between means	1.603
Subject	21.52	<0.0001	****	Yes	SE of difference	1.796
					95% CI of difference	-2.538 to 5.744

Tukey's multiple comparisons test Mean Diff. 95.00% CI of diff. Below threshold? Summary Adjusted P Value

7d						
Male vs. Female	4.049	-1.343 to 9.442	No	ns		0.1385
14d						
Male vs. Female	6.543	1.150 to 11.94	Yes	*		0.0182
21d						
Male vs. Female	4.729	-0.6633 to 10.12	No	ns		0.0846
28d						
Male vs. Female	-8.241	-13.63 to -2.848	Yes	**		0.0033
35d						
Male vs. Female	2.876	-2.517 to 8.269	No	ns		0.2907
42d						
Male vs. Female	-1.091	-6.483 to 4.302	No	ns		0.6875
49d						
Male vs. Female	2.663	-2.730 to 8.055	No	ns		0.3277
56d						
Male vs. Female	1.296	-4.097 to 6.689	No	ns		0.6328
Male						
7d vs. 14d	-10.88	-17.67 to -4.100	Yes	***		0.0001
7d vs. 21d	-1.017	-7.800 to 5.767	No	ns		0.9997
7d vs. 28d	1.653	-5.130 to 8.437	No	ns		0.9941
7d vs. 35d	0.8867	-5.897 to 7.670	No	ns		0.9999
7d vs. 42d	2.92	-3.863 to 9.703	No	ns		0.8731
7d vs. 49d	-0.7633	-7.547 to 6.020	No	ns	>0.9999	
7d vs. 56d	-0.3467	-7.130 to 6.437	No	ns	>0.9999	
14d vs. 21d	9.867	3.083 to 16.65	Yes	***		0.0007
14d vs. 28d	12.54	5.753 to 19.32	Yes	****	<0.0001	
14d vs. 35d	11.77	4.987 to 18.55	Yes	****	<0.0001	
14d vs. 42d	13.8	7.020 to 20.59	Yes	****	<0.0001	
14d vs. 49d	10.12	3.337 to 16.90	Yes	***		0.0004
14d vs. 56d	10.54	3.753 to 17.32	Yes	***		0.0002
21d vs. 28d	2.67	-4.113 to 9.453	No	ns		0.9164
21d vs. 35d	1.903	-4.880 to 8.687	No	ns		0.9864
21d vs. 42d	3.937	-2.847 to 10.72	No	ns		0.6049
21d vs. 49d	0.2533	-6.530 to 7.037	No	ns	>0.9999	
21d vs. 56d	0.67	-6.113 to 7.453	No	ns	>0.9999	
28d vs. 35d	-0.7667	-7.550 to 6.017	No	ns	>0.9999	
28d vs. 42d	1.267	-5.517 to 8.050	No	ns		0.9989
28d vs. 49d	-2.417	-9.200 to 4.367	No	ns		0.9493
28d vs. 56d	-2	-8.783 to 4.783	No	ns		0.9819
35d vs. 42d	2.033	-4.750 to 8.817	No	ns		0.9802
35d vs. 49d	-1.65	-8.433 to 5.133	No	ns		0.9942
35d vs. 56d	-1.233	-8.017 to 5.550	No	ns		0.9991
42d vs. 49d	-3.683	-10.47 to 3.100	No	ns		0.6811
42d vs. 56d	-3.267	-10.05 to 3.517	No	ns		0.7956
49d vs. 56d	0.4167	-6.367 to 7.200	No	ns	>0.9999	
Female						
7d vs. 14d	-8.39	-15.17 to -1.607	Yes	**		0.0061
7d vs. 21d	-0.3367	-7.120 to 6.447	No	ns	>0.9999	
7d vs. 28d	-10.64	-17.42 to -3.853	Yes	***		0.0002
7d vs. 35d	-0.2867	-7.070 to 6.497	No	ns	>0.9999	
7d vs. 42d	-2.22	-9.003 to 4.563	No	ns		0.9677
7d vs. 49d	-2.15	-8.933 to 4.633	No	ns		0.9729
7d vs. 56d	-3.1	-9.883 to 3.683	No	ns		0.8352
14d vs. 21d	8.053	1.270 to 14.84	Yes	**		0.0097
14d vs. 28d	-2.247	-9.030 to 4.537	No	ns		0.9655
14d vs. 35d	8.103	1.320 to 14.89	Yes	**		0.0091
14d vs. 42d	6.17	-0.6133 to 12.95	No	ns		0.1001
14d vs. 49d	6.24	-0.5433 to 13.02	No	ns		0.0928
14d vs. 56d	5.29	-1.493 to 12.07	No	ns		0.2362
21d vs. 28d	-10.3	-17.08 to -3.517	Yes	***		0.0003
21d vs. 35d	0.05	-6.733 to 6.833	No	ns	>0.9999	
21d vs. 42d	-1.883	-8.667 to 4.900	No	ns		0.9872
21d vs. 49d	-1.813	-8.597 to 4.970	No	ns		0.9898
21d vs. 56d	-2.763	-9.547 to 4.020	No	ns		0.9015
28d vs. 35d	10.35	3.567 to 17.13	Yes	***		0.0003
28d vs. 42d	8.417	1.633 to 15.20	Yes	**		0.0058
28d vs. 49d	8.487	1.703 to 15.27	Yes	**		0.0053
28d vs. 56d	7.537	0.7534 to 14.32	Yes	*		0.0195
35d vs. 42d	-1.933	-8.717 to 4.850	No	ns		0.9851
35d vs. 49d	-1.863	-8.647 to 4.920	No	ns		0.988
35d vs. 56d	-2.813	-9.597 to 3.970	No	ns		0.8929
42d vs. 49d	0.07	-6.713 to 6.853	No	ns	>0.9999	
42d vs. 56d	-0.88	-7.663 to 5.903	No	ns	>0.9999	
49d vs. 56d	-0.95	-7.733 to 5.833	No	ns		0.9998

Baseline % Brake Stride 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0126
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=3.202, df=8
How big is the difference?	
Mean of column A	12.46
Mean of column B	17.48
Difference between means (B - A)	$\pm 5.023 \pm 1.569$
95% confidence interval	1.405 to 8.640
R squared (eta squared)	0.5617
F test to compare variances	
F, DFn, Dfd	1.725, 4, 4
P value	0.6105
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Propel (s) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	9.172		0.0055 **	Yes	Mean of Male	0.002287
Time	27.74	<0.0001	****	Yes	Mean of Female	0.004162
Sex	0.8436		0.6915 ns	No	Difference between means	-0.001875
Subject	39.84	<0.0001	****	Yes	SE of difference	0.004556
					95% CI of difference	-0.01238 to 0.008631

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.005733	-0.01711 to 0.0056	No	ns	0.3178
14d					
Male vs. Female	0.01283	0.001458 to 0.0242	Yes	*	0.0276
21d					
Male vs. Female	0.002467	-0.008909 to 0.013	No	ns	0.6663
28d					
Male vs. Female	-0.0052	-0.01658 to 0.0061	No	ns	0.3646
35d					
Male vs. Female	-0.004	-0.01538 to 0.0073	No	ns	0.4849
42d					
Male vs. Female	-0.003567	-0.01494 to 0.0078	No	ns	0.5333
49d					
Male vs. Female	-0.004333	-0.01571 to 0.0070	No	ns	0.4495
56d					
Male vs. Female	-0.007467	-0.01884 to 0.0039	No	ns	0.1945
Male					
7d vs. 14d	-0.01193	-0.02343 to -0.0004	Yes	*	0.0366
7d vs. 21d	-0.01397	-0.02546 to -0.0024	Yes	**	0.0075
7d vs. 28d	-0.0132	-0.02470 to -0.0017	Yes	*	0.014
7d vs. 35d	-0.0138	-0.02530 to -0.0023	Yes	**	0.0086
7d vs. 42d	-0.01463	-0.02613 to -0.0031	Yes	**	0.0043
7d vs. 49d	-0.01667	-0.02816 to -0.0051	Yes	***	0.0007
7d vs. 56d	-0.0126	-0.02410 to -0.0011	Yes	*	0.0223
14d vs. 21d	-0.002033	-0.01353 to 0.0094	No	ns	0.9992
14d vs. 28d	-0.001267	-0.01276 to 0.0102	No	ns	>0.9999
14d vs. 35d	-0.001867	-0.01336 to 0.0096	No	ns	0.9996
14d vs. 42d	-0.0027	-0.01420 to 0.0087	No	ns	0.9953
14d vs. 49d	-0.004733	-0.01623 to 0.0067	No	ns	0.8965
14d vs. 56d	-0.006667	-0.01216 to 0.0108	No	ns	>0.9999
21d vs. 28d	0.0007667	-0.01073 to 0.0122	No	ns	>0.9999
21d vs. 35d	0.0001667	-0.01133 to 0.0116	No	ns	>0.9999
21d vs. 42d	-0.0006667	-0.01216 to 0.0108	No	ns	>0.9999
21d vs. 49d	-0.0027	-0.01420 to 0.0087	No	ns	0.9953
21d vs. 56d	0.001367	-0.01013 to 0.0128	No	ns	>0.9999
28d vs. 35d	-0.0006	-0.01210 to 0.0109	No	ns	>0.9999
28d vs. 42d	-0.001433	-0.01293 to 0.0100	No	ns	>0.9999
28d vs. 49d	-0.003467	-0.01496 to 0.0080	No	ns	0.9795
28d vs. 56d	0.0006	-0.01090 to 0.0121	No	ns	>0.9999
35d vs. 42d	-0.0008333	-0.01233 to 0.0106	No	ns	>0.9999
35d vs. 49d	-0.002867	-0.01436 to 0.0086	No	ns	0.9933
35d vs. 56d	0.0012	-0.01030 to 0.0127	No	ns	>0.9999
42d vs. 49d	-0.002033	-0.01353 to 0.0094	No	ns	0.9992
42d vs. 56d	0.002033	-0.009464 to 0.013	No	ns	0.9992
49d vs. 56d	0.004067	-0.007431 to 0.015	No	ns	0.9512
Female					
7d vs. 14d	0.006633	-0.004864 to 0.018	No	ns	0.612
7d vs. 21d	-0.005767	-0.01726 to 0.0057	No	ns	0.7605
7d vs. 28d	-0.01267	-0.02416 to -0.0011	Yes	*	0.0212
7d vs. 35d	-0.01207	-0.02356 to -0.0005	Yes	*	0.0332
7d vs. 42d	-0.01247	-0.02396 to -0.0009	Yes	*	0.0247
7d vs. 49d	-0.01527	-0.02676 to -0.0037	Yes	**	0.0025
7d vs. 56d	-0.01433	-0.02583 to -0.0028	Yes	**	0.0055
14d vs. 21d	-0.0124	-0.02390 to -0.0009	Yes	*	0.0259
14d vs. 28d	-0.0193	-0.03080 to -0.0078	Yes	****	<0.0001
14d vs. 35d	-0.0187	-0.03020 to -0.0072	Yes	***	0.0001
14d vs. 42d	-0.0191	-0.03060 to -0.0076	Yes	****	<0.0001
14d vs. 49d	-0.0219	-0.03340 to -0.0104	Yes	****	<0.0001
14d vs. 56d	-0.02097	-0.03246 to -0.0094	Yes	****	<0.0001
21d vs. 28d	-0.0069	-0.01840 to 0.0045	No	ns	0.5637
21d vs. 35d	-0.0063	-0.01780 to 0.0051	No	ns	0.6713
21d vs. 42d	-0.0067	-0.01820 to 0.0047	No	ns	0.5999
21d vs. 49d	-0.0095	-0.02100 to 0.0019	No	ns	0.1772
21d vs. 56d	-0.008567	-0.02006 to 0.0029	No	ns	0.2882
28d vs. 35d	0.0006	-0.01090 to 0.0121	No	ns	>0.9999
28d vs. 42d	0.0002	-0.01130 to 0.0117	No	ns	>0.9999
28d vs. 49d	-0.0026	-0.01410 to 0.0088	No	ns	0.9963
28d vs. 56d	-0.001867	-0.01316 to 0.0098	No	ns	0.9998
35d vs. 42d	-0.0004	-0.01190 to 0.0111	No	ns	>0.9999
35d vs. 49d	-0.0032	-0.01470 to 0.0082	No	ns	0.9871
35d vs. 56d	-0.002267	-0.01376 to 0.0092	No	ns	0.9984
42d vs. 49d	-0.0028	-0.01430 to 0.0086	No	ns	0.9942
42d vs. 56d	-0.001867	-0.01336 to 0.0096	No	ns	0.9996
49d vs. 56d	0.0009333	-0.01056 to 0.0124	No	ns	>0.9999

Baseline Propel (s) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0348
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=2.538, df=8
How big is the difference?	
Mean of column A	0.07775
Mean of column B	0.06961
Difference between means (B - A) ± 0.008133 ± 0.003205	
95% confidence interval	-0.01552 to -0.0007431
R squared (eta squared)	0.446
F test to compare variances	
F, DFn, Dfd	2.143, 4, 4
P value	0.4787
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Propel (s) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	16.92	<0.0001	****	Yes	Mean of Male	0.002746
Time	22.61	<0.0001	****	Yes	Mean of Female	0.006923
Sex	3.091	0.4078	ns	No	Difference between means	-0.004177
Subject	32.4	<0.0001	****	Yes	SE of difference	0.004782
					95% CI of difference	-0.01520 to 0.006850

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.00364	-0.01635 to 0.0090	No	ns	0.5693
14d					
Male vs. Female	0.01906	0.006347 to 0.0317	Yes	**	0.0039
21d					
Male vs. Female	-0.006807	-0.01952 to 0.0059	No	ns	0.2888
28d					
Male vs. Female	-0.01651	-0.02922 to -0.0037	Yes	*	0.0118
35d					
Male vs. Female	-0.00344	-0.01615 to 0.0092	No	ns	0.5907
42d					
Male vs. Female	-0.003373	-0.01609 to 0.0093	No	ns	0.5979
49d					
Male vs. Female	-0.007073	-0.01979 to 0.0056	No	ns	0.2705
56d					
Male vs. Female	-0.01164	-0.02435 to 0.0010	No	ns	0.072
Male					
7d vs. 14d	-0.0099	-0.02403 to 0.0042	No	ns	0.3643
7d vs. 21d	-0.0096	-0.02373 to 0.0045	No	ns	0.4038
7d vs. 28d	-0.004967	-0.01910 to 0.0091	No	ns	0.9528
7d vs. 35d	-0.0133	-0.02743 to 0.0008	No	ns	0.0792
7d vs. 42d	-0.01387	-0.02800 to 0.0002	No	ns	0.0581
7d vs. 49d	-0.009767	-0.02390 to 0.0043	No	ns	0.3816
7d vs. 56d	-0.0079	-0.02203 to 0.0062	No	ns	0.6488
14d vs. 21d	0.0003	-0.01383 to 0.0144	No	ns	>0.9999
14d vs. 28d	0.004933	-0.009198 to 0.019	No	ns	0.9544
14d vs. 35d	-0.0034	-0.01753 to 0.0107	No	ns	0.9946
14d vs. 42d	-0.003967	-0.01810 to 0.0101	No	ns	0.9864
14d vs. 49d	0.0001333	-0.01400 to 0.0142	No	ns	>0.9999
14d vs. 56d	0.002	-0.01213 to 0.0161	No	ns	0.9998
21d vs. 28d	0.004633	-0.009498 to 0.018	No	ns	0.9674
21d vs. 35d	-0.0037	-0.01783 to 0.0104	No	ns	0.991
21d vs. 42d	-0.004267	-0.01840 to 0.0098	No	ns	0.9793
21d vs. 49d	-0.0001667	-0.01430 to 0.0139	No	ns	>0.9999
21d vs. 56d	0.0017	-0.01243 to 0.0158	No	ns	>0.9999
28d vs. 35d	-0.008333	-0.02246 to 0.0057	No	ns	0.5855
28d vs. 42d	-0.0089	-0.02303 to 0.0052	No	ns	0.5023
28d vs. 49d	-0.0048	-0.01893 to 0.0093	No	ns	0.9605
28d vs. 56d	-0.002933	-0.01706 to 0.0112	No	ns	0.9978
35d vs. 42d	-0.0005667	-0.01470 to 0.0135	No	ns	>0.9999
35d vs. 49d	0.003533	-0.01060 to 0.0176	No	ns	0.9932
35d vs. 56d	0.0054	-0.008732 to 0.019	No	ns	0.9277
42d vs. 49d	0.0041	-0.01003 to 0.0182	No	ns	0.9835
42d vs. 56d	0.005967	-0.008165 to 0.020	No	ns	0.8837
49d vs. 56d	0.001867	-0.01226 to 0.0160	No	ns	0.9999
Female					
7d vs. 14d	0.0128	-0.001332 to 0.026	No	ns	0.1029
7d vs. 21d	-0.01277	-0.02690 to 0.0013	No	ns	0.1046
7d vs. 28d	-0.01783	-0.03196 to -0.0037	Yes	**	0.0047
7d vs. 35d	-0.0131	-0.02723 to 0.0010	No	ns	0.088
7d vs. 42d	-0.0136	-0.02773 to 0.0005	No	ns	0.0673
7d vs. 49d	-0.0132	-0.02733 to 0.0009	No	ns	0.0835
7d vs. 56d	-0.0159	-0.03003 to -0.0017	Yes	*	0.0172
14d vs. 21d	-0.02557	-0.03970 to -0.0114	Yes	****	<0.0001
14d vs. 28d	-0.03063	-0.04476 to -0.0165	Yes	****	<0.0001
14d vs. 35d	-0.0259	-0.04003 to -0.0117	Yes	****	<0.0001
14d vs. 42d	-0.0264	-0.04053 to -0.0122	Yes	****	<0.0001
14d vs. 49d	-0.026	-0.04013 to -0.0116	Yes	****	<0.0001
14d vs. 56d	-0.0287	-0.04283 to -0.0145	Yes	****	<0.0001
21d vs. 28d	-0.005067	-0.01920 to 0.0090	No	ns	0.9476
21d vs. 35d	-0.0003333	-0.01446 to 0.0138	No	ns	>0.9999
21d vs. 42d	-0.0008333	-0.01496 to 0.0133	No	ns	>0.9999
21d vs. 49d	-0.0004333	-0.01456 to 0.0137	No	ns	>0.9999
21d vs. 56d	-0.003133	-0.01726 to 0.0110	No	ns	0.9967
28d vs. 35d	0.004733	-0.009398 to 0.018	No	ns	0.9634
28d vs. 42d	0.004233	-0.009898 to 0.018	No	ns	0.9802
28d vs. 49d	0.004633	-0.009498 to 0.018	No	ns	0.9674
28d vs. 56d	0.001933	-0.01220 to 0.0160	No	ns	0.9999
35d vs. 42d	-0.0005	-0.01463 to 0.0136	No	ns	>0.9999
35d vs. 49d	-0.0001	-0.01423 to 0.0140	No	ns	>0.9999
35d vs. 56d	-0.0028	-0.01693 to 0.0113	No	ns	0.9984
42d vs. 49d	0.0004	-0.01373 to 0.0145	No	ns	>0.9999
42d vs. 56d	-0.0023	-0.01643 to 0.0118	No	ns	0.9996
49d vs. 56d	-0.0027	-0.01683 to 0.0114	No	ns	0.9987

Baseline Propel (s) 10DegUp

Column B vs. Column A	Female vs. Male
Unpaired t test	
P value	0.0524
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=2.276, df=8
How big is the difference?	
Mean of column A	0.07855
Mean of column B	0.06954
Difference between means (B - A) ± 0.009007 ± 0.003958	
95% confidence interval	-0.01813 to 0.0001206
R squared (eta squared)	0.3929
F test to compare variances	
F, DFn, Dfd	3.432, 4, 4
P value	0.2595
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Propel (s) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	21.29	<0.0001	****	Yes	Mean of Male	0.00128
Time	20.38	<0.0001	****	Yes	Mean of Female	0.003435
Sex	1.371		0.5794 ns	No	Difference between means	-0.002155
Subject	32.87	<0.0001	****	Yes	SE of difference	0.003731
					95% CI of difference	-0.01076 to 0.006448

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.01401	-0.02382 to -0.0042	Yes	**	0.0058
14d					
Male vs. Female	0.01749	0.007676 to 0.0273	Yes	***	0.0007
21d					
Male vs. Female	-0.005347	-0.01516 to 0.0044	No	ns	0.2804
28d					
Male vs. Female	-0.007747	-0.01756 to 0.0020	No	ns	0.1196
35d					
Male vs. Female	-0.001813	-0.01162 to 0.0079	No	ns	0.7132
42d					
Male vs. Female	-0.00398	-0.01379 to 0.0058	No	ns	0.4207
49d					
Male vs. Female	0.0001867	-0.009624 to 0.009	No	ns	0.9698
56d					
Male vs. Female	-0.002013	-0.01182 to 0.0077	No	ns	0.6832
Male					
7d vs. 14d	-0.013	-0.02375 to -0.0022	Yes	**	0.0079
7d vs. 21d	-0.0082	-0.01895 to 0.0025	No	ns	0.2608
7d vs. 28d	-0.01003	-0.02078 to 0.0007	No	ns	0.0839
7d vs. 35d	-0.01537	-0.02612 to -0.0046	Yes	***	0.0009
7d vs. 42d	-0.01467	-0.02542 to -0.0035	Yes	**	0.0017
7d vs. 49d	-0.01493	-0.02568 to -0.0041	Yes	**	0.0013
7d vs. 56d	-0.01153	-0.02228 to -0.0007	Yes	*	0.0272
14d vs. 21d	0.0048	-0.005949 to 0.015	No	ns	0.8508
14d vs. 28d	0.002967	-0.007782 to 0.013	No	ns	0.9877
14d vs. 35d	-0.002367	-0.01312 to 0.0083	No	ns	0.9969
14d vs. 42d	-0.001667	-0.01242 to 0.0090	No	ns	0.9997
14d vs. 49d	-0.001933	-0.01268 to 0.0088	No	ns	0.9991
14d vs. 56d	0.001467	-0.009283 to 0.012	No	ns	0.9999
21d vs. 28d	-0.001833	-0.01258 to 0.0089	No	ns	0.9994
21d vs. 35d	-0.007167	-0.01792 to 0.0035	No	ns	0.4282
21d vs. 42d	-0.006467	-0.01722 to 0.0042	No	ns	0.5607
21d vs. 49d	-0.006733	-0.01748 to 0.0040	No	ns	0.5093
21d vs. 56d	-0.003333	-0.01408 to 0.0074	No	ns	0.976
28d vs. 35d	-0.005333	-0.01608 to 0.0054	No	ns	0.7702
28d vs. 42d	-0.004633	-0.01538 to 0.0061	No	ns	0.8723
28d vs. 49d	-0.0049	-0.01565 to 0.0058	No	ns	0.837
28d vs. 56d	-0.0015	-0.01225 to 0.0092	No	ns	0.9998
35d vs. 42d	0.0007	-0.01005 to 0.0114	No	ns	>0.9999
35d vs. 49d	0.0004333	-0.01032 to 0.0111	No	ns	>0.9999
35d vs. 56d	0.003833	-0.006916 to 0.014	No	ns	0.949
42d vs. 49d	-0.0002667	-0.01102 to 0.0104	No	ns	>0.9999
42d vs. 56d	0.003133	-0.007616 to 0.013	No	ns	0.9831
49d vs. 56d	0.0034	-0.007349 to 0.014	No	ns	0.9732
Female					
7d vs. 14d	0.0185	0.007751 to 0.0292	Yes	****	<0.0001
7d vs. 21d	0.0004667	-0.01028 to 0.0112	No	ns	>0.9999
7d vs. 28d	-0.003767	-0.01452 to 0.0069	No	ns	0.9535
7d vs. 35d	-0.003167	-0.01392 to 0.0075	No	ns	0.982
7d vs. 42d	-0.004633	-0.01538 to 0.0061	No	ns	0.8723
7d vs. 49d	-0.0007333	-0.01148 to 0.0100	No	ns	>0.9999
7d vs. 56d	0.0004667	-0.01028 to 0.0112	No	ns	>0.9999
14d vs. 21d	-0.01803	-0.02878 to -0.0072	Yes	****	<0.0001
14d vs. 28d	-0.02227	-0.03302 to -0.0115	Yes	****	<0.0001
14d vs. 35d	-0.02167	-0.03242 to -0.0105	Yes	****	<0.0001
14d vs. 42d	-0.02313	-0.03388 to -0.0123	Yes	****	<0.0001
14d vs. 49d	-0.01923	-0.02998 to -0.0084	Yes	****	<0.0001
14d vs. 56d	-0.01803	-0.02878 to -0.0072	Yes	****	<0.0001
21d vs. 28d	-0.004233	-0.01498 to 0.0065	No	ns	0.9162
21d vs. 35d	-0.003633	-0.01438 to 0.0071	No	ns	0.9615
21d vs. 42d	-0.0051	-0.01585 to 0.0056	No	ns	0.8075
21d vs. 49d	-0.0012	-0.01195 to 0.0095	No	ns	>0.9999
21d vs. 56d	-0.000000012	-0.01075 to 0.0107	No	ns	>0.9999
28d vs. 35d	0.0006	-0.01015 to 0.0113	No	ns	>0.9999
28d vs. 42d	-0.0008667	-0.01162 to 0.0098	No	ns	>0.9999
28d vs. 49d	0.003033	-0.007716 to 0.013	No	ns	0.986
28d vs. 56d	0.004233	-0.006516 to 0.014	No	ns	0.9162
35d vs. 42d	-0.001467	-0.01222 to 0.0092	No	ns	0.9999
35d vs. 49d	0.002433	-0.006316 to 0.013	No	ns	0.9963
35d vs. 56d	0.003633	-0.007116 to 0.014	No	ns	0.9616
42d vs. 49d	0.0039	-0.006849 to 0.014	No	ns	0.9443
42d vs. 56d	0.0051	-0.005649 to 0.015	No	ns	0.8075
49d vs. 56d	0.0012	-0.009549 to 0.011	No	ns	>0.9999

Baseline Propel (s) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.021
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=2.864, df=8
How big is the difference?	
Mean of column A	0.07815
Mean of column B	0.07091
Difference between means (B - A) ± 0.002530	
95% confidence interval	-0.01308 to -0.001413
R squared (eta squared)	0.5063
F test to compare variances	
F, DFn, Dfd	2.310, 4, 4
P value	0.4374
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Propel Stride FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	19.18	<0.0001	****	Yes	Mean of Male	0.2202
Time	26.04	<0.0001	****	Yes	Mean of Female	0.592
Sex	0.1933	0.8193	ns	No	Difference between means	-0.3718
Subject	27.75	<0.0001	****	Yes	SE of difference	1.575
					95% CI of difference	-4.004 to 3.261

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-2.449	-6.863 to 1.965	No	ns	0.2718
14d					
Male vs. Female	8.657	4.243 to 13.07	Yes	***	0.0002
21d					
Male vs. Female	1.397	-3.017 to 5.811	No	ns	0.5294
28d					
Male vs. Female	-3.259	-7.673 to 1.155	No	ns	0.1451
35d					
Male vs. Female	-1.886	-6.300 to 2.528	No	ns	0.3965
42d					
Male vs. Female	-0.1993	-4.613 to 4.215	No	ns	0.9284
49d					
Male vs. Female	-2.489	-6.903 to 1.925	No	ns	0.2641
56d					
Male vs. Female	-2.746	-7.160 to 1.668	No	ns	0.2185
Male					
7d vs. 14d	-6.537	-11.75 to -1.322	Yes	**	0.0051
7d vs. 21d	-6.693	-11.91 to -1.479	Yes	**	0.0038
7d vs. 28d	-4.057	-9.271 to 1.158	No	ns	0.2388
7d vs. 35d	-5.773	-10.99 to -0.5590	Yes	*	0.0202
7d vs. 42d	-6.65	-11.86 to -1.436	Yes	**	0.0042
7d vs. 49d	-6.307	-11.52 to -1.092	Yes	**	0.0079
7d vs. 56d	-5.057	-10.27 to 0.1576	No	ns	0.0636
14d vs. 21d	-0.1567	-5.371 to 5.058	No	ns	>0.9999
14d vs. 28d	2.48	-2.734 to 7.694	No	ns	0.8056
14d vs. 35d	0.7633	-4.451 to 5.978	No	ns	0.9998
14d vs. 42d	-0.1133	-5.328 to 5.101	No	ns	>0.9999
14d vs. 49d	0.23	-4.984 to 5.444	No	ns	>0.9999
14d vs. 56d	1.48	-3.734 to 6.694	No	ns	0.9855
21d vs. 28d	2.637	-2.578 to 7.851	No	ns	0.753
21d vs. 35d	0.92	-4.294 to 6.134	No	ns	0.9992
21d vs. 42d	0.04333	-5.171 to 5.258	No	ns	>0.9999
21d vs. 49d	0.3867	-4.828 to 5.601	No	ns	>0.9999
21d vs. 56d	1.637	-3.578 to 6.851	No	ns	0.9743
28d vs. 35d	-1.717	-6.931 to 3.498	No	ns	0.9666
28d vs. 42d	-2.593	-7.808 to 2.621	No	ns	0.7681
28d vs. 49d	-2.25	-7.464 to 2.964	No	ns	0.8717
28d vs. 56d	-1	-6.214 to 4.214	No	ns	0.9987
35d vs. 42d	-0.8767	-6.091 to 4.338	No	ns	0.9994
35d vs. 49d	-0.5333	-5.748 to 4.681	No	ns	>0.9999
35d vs. 56d	0.7167	-4.498 to 5.931	No	ns	0.9999
42d vs. 49d	0.3433	-4.871 to 5.558	No	ns	>0.9999
42d vs. 56d	1.593	-3.621 to 6.808	No	ns	0.9779
49d vs. 56d	1.25	-3.964 to 6.464	No	ns	0.9947
Female					
7d vs. 14d	4.57	-0.6443 to 9.784	No	ns	0.1267
7d vs. 21d	-2.847	-8.061 to 2.368	No	ns	0.6753
7d vs. 28d	-4.867	-10.08 to 0.3476	No	ns	0.084
7d vs. 35d	-5.21	-10.42 to 0.004314	No	ns	0.0503
7d vs. 42d	-4.4	-9.614 to 0.8143	No	ns	0.158
7d vs. 49d	-6.347	-11.56 to -1.132	Yes	**	0.0073
7d vs. 56d	-5.353	-10.57 to -0.1390	Yes	*	0.0402
14d vs. 21d	-7.417	-12.63 to -2.202	Yes	***	0.0009
14d vs. 28d	-9.437	-14.65 to -4.222	Yes	****	<0.0001
14d vs. 35d	-9.78	-14.99 to -4.566	Yes	****	<0.0001
14d vs. 42d	-8.97	-14.18 to -3.756	Yes	****	<0.0001
14d vs. 49d	-10.92	-16.13 to -5.702	Yes	****	<0.0001
14d vs. 56d	-9.923	-15.14 to -4.709	Yes	****	<0.0001
21d vs. 28d	-2.02	-7.234 to 3.194	No	ns	0.9226
21d vs. 35d	-2.363	-7.578 to 2.851	No	ns	0.8409
21d vs. 42d	-1.553	-6.768 to 3.661	No	ns	0.9808
21d vs. 49d	-3.5	-8.714 to 1.714	No	ns	0.4194
21d vs. 56d	-2.507	-7.721 to 2.708	No	ns	0.797
28d vs. 35d	-0.3433	-5.558 to 4.871	No	ns	>0.9999
28d vs. 42d	0.4667	-4.748 to 5.681	No	ns	>0.9999
28d vs. 49d	-1.48	-6.694 to 3.734	No	ns	0.9855
28d vs. 56d	-0.4867	-5.701 to 4.728	No	ns	>0.9999
35d vs. 42d	0.81	-4.404 to 6.024	No	ns	0.9997
35d vs. 49d	-1.137	-6.351 to 4.078	No	ns	0.9971
35d vs. 56d	-0.1433	-5.358 to 5.071	No	ns	>0.9999
42d vs. 49d	-1.947	-7.161 to 3.268	No	ns	0.9356
42d vs. 56d	-0.9533	-6.168 to 4.261	No	ns	0.999
49d vs. 56d	0.9933	-4.221 to 6.208	No	ns	0.9987

Baseline % Propel Stride FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0465
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=2.352, df=8
How big is the difference?	
Mean of column A	42.64
Mean of column B	37.72
Difference between means (B - A) ±	± -4.919 ± 2.091
95% confidence interval	-9.742 to -0.09704
R squared (eta squared)	0.4089
F test to compare variances	
F, DFn, Dfd	3.345, 4, 4
P value	0.269
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Propel Stide 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	16.72	0.0003	***	Yes	Mean of Male	0.5592
Time	27.91	<0.0001	****	Yes	Mean of Female	0.9063
Sex	0.1112	0.8611	ns	No	Difference between means	-0.3471
Subject	27.22	<0.0001	****	Yes	SE of difference	1.92
					95% CI of difference	-4.775 to 4.081

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-0.1467	-5.612 to 5.319	No	ns	0.9574
14d					
Male vs. Female	10.1	4.634 to 15.57	Yes	***	0.0005
21d					
Male vs. Female	-0.3067	-5.772 to 5.159	No	ns	0.9111
28d					
Male vs. Female	-4.537	-10.00 to 0.9291	No	ns	0.1022
35d					
Male vs. Female	-0.4467	-5.912 to 5.019	No	ns	0.8708
42d					
Male vs. Female	-2.477	-7.942 to 2.989	No	ns	0.3687
49d					
Male vs. Female	-0.9767	-6.442 to 4.489	No	ns	0.7223
56d					
Male vs. Female	-3.987	-9.452 to 1.479	No	ns	0.15
Male					
7d vs. 14d	-3.39	-9.950 to 3.170	No	ns	0.7322
7d vs. 21d	-4.713	-11.27 to 1.846	No	ns	0.3324
7d vs. 28d	-2.063	-8.623 to 4.496	No	ns	0.974
7d vs. 35d	-5.373	-11.93 to 1.186	No	ns	0.1855
7d vs. 42d	-5.273	-11.83 to 1.286	No	ns	0.2042
7d vs. 49d	-4.45	-11.01 to 2.110	No	ns	0.4057
7d vs. 56d	-3.677	-10.24 to 2.883	No	ns	0.6458
14d vs. 21d	-1.323	-7.883 to 5.236	No	ns	0.9982
14d vs. 28d	1.327	-5.233 to 7.886	No	ns	0.9982
14d vs. 35d	-1.983	-8.543 to 4.576	No	ns	0.9792
14d vs. 42d	-1.883	-8.443 to 4.676	No	ns	0.9845
14d vs. 49d	-1.06	-7.620 to 5.500	No	ns	0.9996
14d vs. 56d	-0.2867	-6.846 to 6.273	No	ns	>0.9999
21d vs. 28d	2.65	-3.910 to 9.210	No	ns	0.9053
21d vs. 35d	-0.66	-7.220 to 5.900	No	ns	>0.9999
21d vs. 42d	-0.56	-7.120 to 6.000	No	ns	>0.9999
21d vs. 49d	0.2633	-6.296 to 6.823	No	ns	>0.9999
21d vs. 56d	1.037	-5.523 to 7.596	No	ns	0.9996
28d vs. 35d	-3.31	-9.870 to 3.250	No	ns	0.7549
28d vs. 42d	-3.21	-9.770 to 3.350	No	ns	0.7822
28d vs. 49d	-2.387	-8.946 to 4.173	No	ns	0.9435
28d vs. 56d	-1.613	-8.173 to 4.946	No	ns	0.9938
35d vs. 42d	0.1	-6.460 to 6.660	No	ns	>0.9999
35d vs. 49d	0.9233	-5.636 to 7.483	No	ns	0.9998
35d vs. 56d	1.697	-4.863 to 8.256	No	ns	0.9916
42d vs. 49d	0.8233	-5.736 to 7.383	No	ns	>0.9999
42d vs. 56d	1.597	-4.963 to 8.156	No	ns	0.9942
49d vs. 56d	0.7733	-5.786 to 7.333	No	ns	>0.9999
Female					
7d vs. 14d	6.857	0.2968 to 13.42	Yes	*	0.0344
7d vs. 21d	-4.873	-11.43 to 1.686	No	ns	0.2917
7d vs. 28d	-6.453	-13.01 to 0.1065	No	ns	0.0569
7d vs. 35d	-5.673	-12.23 to 0.8865	No	ns	0.1372
7d vs. 42d	-7.603	-14.16 to -1.044	Yes	*	0.0126
7d vs. 49d	-5.28	-11.84 to 1.280	No	ns	0.2029
7d vs. 56d	-7.517	-14.08 to -0.9568	Yes	*	0.0142
14d vs. 21d	-11.73	-18.29 to -5.170	Yes	****	<0.0001
14d vs. 28d	-13.31	-19.87 to -6.750	Yes	****	<0.0001
14d vs. 35d	-12.53	-19.09 to -5.970	Yes	****	<0.0001
14d vs. 42d	-14.46	-21.02 to -7.900	Yes	****	<0.0001
14d vs. 49d	-12.14	-18.70 to -5.577	Yes	****	<0.0001
14d vs. 56d	-14.37	-20.93 to -7.814	Yes	****	<0.0001
21d vs. 28d	-1.58	-8.140 to 4.980	No	ns	0.9945
21d vs. 35d	-0.8	-7.360 to 5.760	No	ns	>0.9999
21d vs. 42d	-2.73	-9.290 to 3.830	No	ns	0.8912
21d vs. 49d	-0.4067	-6.966 to 6.153	No	ns	>0.9999
21d vs. 56d	-2.643	-9.203 to 3.916	No	ns	0.9065
28d vs. 35d	0.78	-5.780 to 7.340	No	ns	>0.9999
28d vs. 42d	-1.15	-7.710 to 5.410	No	ns	0.9993
28d vs. 49d	1.173	-5.386 to 7.733	No	ns	0.9992
28d vs. 56d	-1.063	-7.623 to 5.496	No	ns	0.9996
35d vs. 42d	-1.93	-8.490 to 4.630	No	ns	0.9822
35d vs. 49d	0.3933	-6.166 to 6.953	No	ns	>0.9999
35d vs. 56d	-1.843	-8.403 to 4.716	No	ns	0.9863
42d vs. 49d	2.323	-4.236 to 8.883	No	ns	0.9508
42d vs. 56d	0.08667	-6.473 to 6.646	No	ns	>0.9999
49d vs. 56d	-2.237	-8.796 to 4.323	No	ns	0.9597

Baseline % Propel Stride 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0456
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=2.365, df=8
How big is the difference?	
Mean of column A	42.95
Mean of column B	38.49
Difference between means (B - A) ± 1.884	
95% confidence interval	-8.801 to -0.1119
R squared (eta squared)	0.4116
F test to compare variances	
F, DFn, Dfd	1.103, 4, 4
P value	0.9266
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Propel Stride 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	13.32	<0.0001	****	Yes	Mean of Male	-2.445
Time	8.913	<0.0001	****	Yes	Mean of Female	-0.3248
Sex	3.597	0.5227	ns	No	Difference between means	-2.12
Subject	64.39	<0.0001	****	Yes	SE of difference	3.172
					95% CI of difference	-9.435 to 5.194

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-6.277	-13.08 to 0.5231	No	ns	0.0698
14d					
Male vs. Female	8.016	1.216 to 14.82	Yes	*	0.0216
21d					
Male vs. Female	-2.981	-9.781 to 3.820	No	ns	0.3845
28d					
Male vs. Female	-3.521	-10.32 to 3.280	No	ns	0.3049
35d					
Male vs. Female	-1.117	-7.918 to 5.683	No	ns	0.7438
42d					
Male vs. Female	-4.257	-11.06 to 2.543	No	ns	0.2156
49d					
Male vs. Female	-2.517	-9.318 to 4.283	No	ns	0.4623
56d					
Male vs. Female	-4.307	-11.11 to 2.493	No	ns	0.2103
Male					
7d vs. 14d	-4.923	-9.083 to -0.7639	Yes	*	0.01
7d vs. 21d	-2.99	-7.149 to 1.169	No	ns	0.3318
7d vs. 28d	-3.837	-7.996 to 0.3228	No	ns	0.0911
7d vs. 35d	-5.867	-10.03 to -1.707	Yes	**	0.0011
7d vs. 42d	-3.947	-8.106 to 0.2128	No	ns	0.0747
7d vs. 49d	-3.67	-7.829 to 0.4895	No	ns	0.1216
7d vs. 56d	-2.31	-6.469 to 1.849	No	ns	0.6563
14d vs. 21d	1.933	-2.226 to 6.093	No	ns	0.8231
14d vs. 28d	1.087	-3.073 to 5.246	No	ns	0.9911
14d vs. 35d	-0.9433	-5.103 to 3.216	No	ns	0.9962
14d vs. 42d	0.9767	-3.183 to 5.136	No	ns	0.9953
14d vs. 49d	1.253	-2.906 to 5.413	No	ns	0.9796
14d vs. 56d	2.613	-1.546 to 6.773	No	ns	0.5054
21d vs. 28d	-0.8467	-5.006 to 3.313	No	ns	0.9981
21d vs. 35d	-2.877	-7.036 to 1.283	No	ns	0.3807
21d vs. 42d	-0.9567	-5.116 to 3.203	No	ns	0.9959
21d vs. 49d	-0.68	-4.839 to 3.479	No	ns	0.9995
21d vs. 56d	0.68	-3.479 to 4.839	No	ns	0.9995
28d vs. 35d	-2.03	-6.189 to 2.129	No	ns	0.7845
28d vs. 42d	-0.11	-4.269 to 4.049	No	ns	>0.9999
28d vs. 49d	0.1667	-3.993 to 4.326	No	ns	>0.9999
28d vs. 56d	1.527	-2.633 to 5.686	No	ns	0.9409
35d vs. 42d	1.92	-2.239 to 6.079	No	ns	0.8281
35d vs. 49d	2.197	-1.983 to 6.356	No	ns	0.7105
35d vs. 56d	3.557	-0.6028 to 7.716	No	ns	0.1466
42d vs. 49d	0.2767	-3.883 to 4.436	No	ns	>0.9999
42d vs. 56d	1.637	-2.523 to 5.796	No	ns	0.9165
49d vs. 56d	1.36	-2.799 to 5.519	No	ns	0.9679
Female					
7d vs. 14d	9.37	5.211 to 13.53	Yes	****	<0.0001
7d vs. 21d	0.3067	-3.853 to 4.466	No	ns	>0.9999
7d vs. 28d	-1.08	-5.239 to 3.079	No	ns	0.9914
7d vs. 35d	-0.7067	-4.866 to 3.453	No	ns	0.9994
7d vs. 42d	-1.927	-6.086 to 2.233	No	ns	0.8256
7d vs. 49d	0.09	-4.069 to 4.249	No	ns	>0.9999
7d vs. 56d	-0.34	-4.499 to 3.819	No	ns	>0.9999
14d vs. 21d	-9.063	-13.22 to -4.904	Yes	****	<0.0001
14d vs. 28d	-10.45	-14.61 to -6.291	Yes	****	<0.0001
14d vs. 35d	-10.08	-14.24 to -5.917	Yes	****	<0.0001
14d vs. 42d	-11.3	-15.46 to -7.137	Yes	****	<0.0001
14d vs. 49d	-9.28	-13.44 to -5.121	Yes	****	<0.0001
14d vs. 56d	-9.71	-13.87 to -5.551	Yes	****	<0.0001
21d vs. 28d	-1.387	-5.546 to 2.773	No	ns	0.9643
21d vs. 35d	-1.013	-5.173 to 3.146	No	ns	0.9941
21d vs. 42d	-2.233	-6.393 to 1.926	No	ns	0.6932
21d vs. 49d	-0.2167	-4.376 to 3.943	No	ns	>0.9999
21d vs. 56d	-0.6467	-4.806 to 3.513	No	ns	0.9997
28d vs. 35d	0.3733	-3.786 to 4.533	No	ns	>0.9999
28d vs. 42d	-0.8467	-5.006 to 3.313	No	ns	0.9981
28d vs. 49d	1.17	-2.989 to 5.329	No	ns	0.9862
28d vs. 56d	0.74	-3.419 to 4.899	No	ns	0.9992
35d vs. 42d	-1.22	-5.379 to 2.939	No	ns	0.9825
35d vs. 49d	0.7967	-3.363 to 4.956	No	ns	0.9987
35d vs. 56d	0.3667	-3.793 to 4.526	No	ns	>0.9999
42d vs. 49d	2.017	-2.143 to 6.176	No	ns	0.79
42d vs. 56d	1.587	-2.573 to 5.746	No	ns	0.9283
49d vs. 56d	-0.43	-4.589 to 3.729	No	ns	>0.9999

Baseline % Propel Stride 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.1041
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.834, df=8
How big is the difference?	
Mean of column A	43.87
Mean of column B	39.14
Difference between means (B - A) ±	±-4.731 ± 2.580
95% confidence interval	-10.68 to 1.219
R squared (eta squared)	0.2959
F test to compare variances	
F, DFn, Dfd	3.176, 4, 4
P value	0.2891
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stance (s) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	1.726		0.7663 ns	No	Mean of Male	0.001581
Time	18	<0.0001	****	Yes	Mean of Female	0.007816
Sex	10.78		0.2075 ns	No	Difference between means	-0.006235
Subject	45.84	<0.0001	****	Yes	SE of difference	0.004547
					95% CI of difference	-0.01672 to 0.004250

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-0.006127	-0.01731 to 0.0050	No	ns	0.2779
14d					
Male vs. Female	-0.01069	-0.02188 to 0.0004	No	ns	0.0606
21d					
Male vs. Female	-0.00346	-0.01464 to 0.0077	No	ns	0.5387
28d					
Male vs. Female	-0.00396	-0.01514 to 0.0072	No	ns	0.4819
35d					
Male vs. Female	-0.00526	-0.01644 to 0.0059	No	ns	0.351
42d					
Male vs. Female	-0.00396	-0.01514 to 0.0072	No	ns	0.4819
49d					
Male vs. Female	-0.00696	-0.01814 to 0.0042	No	ns	0.2183
56d					
Male vs. Female	-0.00946	-0.02064 to 0.0017	No	ns	0.0959
Male					
7d vs. 14d	-0.006833	-0.01783 to 0.0041	No	ns	0.5192
7d vs. 21d	-0.009667	-0.02066 to 0.0013	No	ns	0.1242
7d vs. 28d	-0.01013	-0.02113 to 0.0008	No	ns	0.0915
7d vs. 35d	-0.01183	-0.02283 to -0.0008	Yes	*	0.0264
7d vs. 42d	-0.0101	-0.02109 to 0.0008	No	ns	0.0936
7d vs. 49d	-0.01353	-0.02453 to -0.0025	Yes	**	0.0064
7d vs. 56d	-0.01167	-0.02266 to -0.0006	Yes	*	0.0301
14d vs. 21d	-0.002833	-0.01383 to 0.0081	No	ns	0.9918
14d vs. 28d	-0.0033	-0.01429 to 0.0076	No	ns	0.98
14d vs. 35d	-0.005	-0.01599 to 0.0059	No	ns	0.8385
14d vs. 42d	-0.003267	-0.01426 to 0.0077	No	ns	0.9811
14d vs. 49d	-0.0067	-0.01769 to 0.0042	No	ns	0.5444
14d vs. 56d	-0.004833	-0.01583 to 0.0061	No	ns	0.8606
21d vs. 28d	-0.0004667	-0.01146 to 0.0105	No	ns	>0.9999
21d vs. 35d	-0.002167	-0.01316 to 0.0088	No	ns	0.9984
21d vs. 42d	-0.0004333	-0.01143 to 0.0105	No	ns	>0.9999
21d vs. 49d	-0.003867	-0.01486 to 0.0071	No	ns	0.9526
21d vs. 56d	-0.002	-0.01299 to 0.0089	No	ns	0.9991
28d vs. 35d	-0.0017	-0.01269 to 0.0092	No	ns	0.9997
28d vs. 42d	0.00003334	-0.01096 to 0.0110	No	ns	>0.9999
28d vs. 49d	-0.0034	-0.01439 to 0.0075	No	ns	0.9763
28d vs. 56d	-0.001533	-0.01253 to 0.0094	No	ns	0.9998
35d vs. 42d	0.001733	-0.009260 to 0.012	No	ns	0.9996
35d vs. 49d	-0.0017	-0.01269 to 0.0092	No	ns	0.9997
35d vs. 56d	0.0001667	-0.01083 to 0.0111	No	ns	>0.9999
42d vs. 49d	-0.003433	-0.01443 to 0.0075	No	ns	0.975
42d vs. 56d	-0.001567	-0.01256 to 0.0094	No	ns	0.9998
49d vs. 56d	0.001867	-0.009127 to 0.012	No	ns	0.9994
Female					
7d vs. 14d	-0.0114	-0.02239 to -0.0004	Yes	*	0.0369
7d vs. 21d	-0.007	-0.01799 to 0.0039	No	ns	0.4881
7d vs. 28d	-0.007967	-0.01896 to 0.0030	No	ns	0.3219
7d vs. 35d	-0.01097	-0.02196 to 0.0099	No	ns	0.051
7d vs. 42d	-0.007933	-0.01893 to 0.0030	No	ns	0.327
7d vs. 49d	-0.01437	-0.02536 to -0.0033	Yes	**	0.003
7d vs. 56d	-0.015	-0.02599 to -0.004	Yes	**	0.0017
14d vs. 21d	0.0044	-0.006594 to 0.015	No	ns	0.9094
14d vs. 28d	0.003433	-0.007560 to 0.014	No	ns	0.975
14d vs. 35d	0.0004333	-0.01056 to 0.0114	No	ns	>0.9999
14d vs. 42d	0.003467	-0.007527 to 0.014	No	ns	0.9736
14d vs. 49d	-0.002967	-0.01396 to 0.0080	No	ns	0.9892
14d vs. 56d	-0.0036	-0.01459 to 0.0073	No	ns	0.9676
21d vs. 28d	-0.0009667	-0.01196 to 0.0100	No	ns	>0.9999
21d vs. 35d	-0.003967	-0.01496 to 0.0070	No	ns	0.9459
21d vs. 42d	-0.0009333	-0.01193 to 0.0100	No	ns	>0.9999
21d vs. 49d	-0.007367	-0.01836 to 0.0036	No	ns	0.4216
21d vs. 56d	-0.008	-0.01899 to 0.0029	No	ns	0.3167
28d vs. 35d	-0.003	-0.01399 to 0.0079	No	ns	0.9885
28d vs. 42d	0.00003333	-0.01096 to 0.0110	No	ns	>0.9999
28d vs. 49d	-0.0064	-0.01739 to 0.0045	No	ns	0.6011
28d vs. 56d	-0.007033	-0.01803 to 0.0039	No	ns	0.482
35d vs. 42d	0.003033	-0.007960 to 0.014	No	ns	0.9877
35d vs. 49d	-0.0034	-0.01439 to 0.0075	No	ns	0.9763
35d vs. 56d	-0.004033	-0.01503 to 0.0069	No	ns	0.941
42d vs. 49d	-0.006433	-0.01743 to 0.0045	No	ns	0.5948
42d vs. 56d	-0.007067	-0.01806 to 0.0039	No	ns	0.4758
49d vs. 56d	-0.0006333	-0.01163 to 0.0103	No	ns	>0.9999

Baseline Stance (s) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2086
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.368, df=8
How big is the difference?	
Mean of column A	0.103
Mean of column B	0.09855
Difference between means (B - A) ± 0.004460 ± 0.003261	
95% confidence interval	-0.01198 to 0.003060
R squared (eta squared)	0.1895
F test to compare variances	
F, DFn, Dfd	2.278, 4, 4
P value	0.4448
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stance (s) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	3.083		0.2638 ns	No	Mean of Male	0.002546
Time	13.1	<0.0001	****	Yes	Mean of Female	0.009118
Sex	11.99		0.2152 ns	No	Difference between means	-0.006572
Subject	52.97	<0.0001	****	Yes	SE of difference	0.004883
					95% CI of difference	-0.01783 to 0.004688

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.009827	-0.02119 to 0.0015	No	ns	0.0888
14d					
Male vs. Female	-0.00766	-0.01902 to 0.0037	No	ns	0.1827
21d					
Male vs. Female	-0.004327	-0.01569 to 0.0070	No	ns	0.4495
28d					
Male vs. Female	-0.007093	-0.01845 to 0.0042	No	ns	0.2168
35d					
Male vs. Female	-0.005293	-0.01665 to 0.0060	No	ns	0.3554
42d					
Male vs. Female	-0.00046	-0.01182 to 0.0109	No	ns	0.9358
49d					
Male vs. Female	-0.005693	-0.01705 to 0.0056	No	ns	0.3205
56d					
Male vs. Female	-0.01223	-0.02359 to -0.00007	Yes	*	0.0353
Male					
7d vs. 14d	-0.009633	-0.01944 to 0.0001	No	ns	0.0576
7d vs. 21d	-0.0091	-0.01891 to 0.0007	No	ns	0.0874
7d vs. 28d	-0.0087	-0.01851 to 0.0011	No	ns	0.1175
7d vs. 35d	-0.0137	-0.02351 to -0.0038	Yes	**	0.0012
7d vs. 42d	-0.01327	-0.02307 to -0.0034	Yes	**	0.0019
7d vs. 49d	-0.01167	-0.02147 to -0.0018	Yes	**	0.0095
7d vs. 56d	-0.0103	-0.02011 to -0.0004	Yes	*	0.033
14d vs. 21d	0.0005333	-0.009274 to 0.010	No	ns	>0.9999
14d vs. 28d	0.0009333	-0.008874 to 0.010	No	ns	>0.9999
14d vs. 35d	-0.004067	-0.01387 to 0.0057	No	ns	0.893
14d vs. 42d	-0.003633	-0.01344 to 0.0061	No	ns	0.938
14d vs. 49d	-0.002033	-0.01184 to 0.0077	No	ns	0.9979
14d vs. 56d	-0.0006667	-0.01047 to 0.0091	No	ns	>0.9999
21d vs. 28d	0.0004	-0.009407 to 0.010	No	ns	>0.9999
21d vs. 35d	-0.0046	-0.01441 to 0.0052	No	ns	0.8163
21d vs. 42d	-0.004167	-0.01397 to 0.0056	No	ns	0.8803
21d vs. 49d	-0.002567	-0.01237 to 0.0072	No	ns	0.991
21d vs. 56d	-0.0012	-0.01101 to 0.0086	No	ns	>0.9999
28d vs. 35d	-0.005	-0.01481 to 0.0048	No	ns	0.7452
28d vs. 42d	-0.004567	-0.01437 to 0.0052	No	ns	0.8217
28d vs. 49d	-0.002967	-0.01277 to 0.0068	No	ns	0.9791
28d vs. 56d	-0.0016	-0.01141 to 0.0082	No	ns	0.9995
35d vs. 42d	0.0004333	-0.009374 to 0.010	No	ns	>0.9999
35d vs. 49d	0.002033	-0.007774 to 0.011	No	ns	0.9979
35d vs. 56d	0.0034	-0.006407 to 0.013	No	ns	0.956
42d vs. 49d	0.0016	-0.008207 to 0.011	No	ns	0.9995
42d vs. 56d	0.002967	-0.006840 to 0.012	No	ns	0.9791
49d vs. 56d	0.001367	-0.008440 to 0.011	No	ns	0.9998
Female					
7d vs. 14d	-0.007467	-0.01727 to 0.0023	No	ns	0.263
7d vs. 21d	-0.0036	-0.01341 to 0.0062	No	ns	0.9409
7d vs. 28d	-0.005967	-0.01577 to 0.0038	No	ns	0.5465
7d vs. 35d	-0.009167	-0.01897 to 0.0006	No	ns	0.0831
7d vs. 42d	-0.0039	-0.01371 to 0.0059	No	ns	0.9122
7d vs. 49d	-0.007533	-0.01734 to 0.0022	No	ns	0.2529
7d vs. 56d	-0.0127	-0.02251 to -0.0028	Yes	**	0.0034
14d vs. 21d	0.003867	-0.005940 to 0.013	No	ns	0.9157
14d vs. 28d	0.0015	-0.008307 to 0.011	No	ns	0.9997
14d vs. 35d	-0.0017	-0.01151 to 0.0081	No	ns	0.9993
14d vs. 42d	0.003567	-0.006240 to 0.013	No	ns	0.9436
14d vs. 49d	-0.00006666	-0.009874 to 0.009	No	ns	>0.9999
14d vs. 56d	-0.005233	-0.01504 to 0.0045	No	ns	0.6997
21d vs. 28d	-0.002367	-0.01217 to 0.0074	No	ns	0.9945
21d vs. 35d	-0.005567	-0.01537 to 0.0042	No	ns	0.6312
21d vs. 42d	-0.0003	-0.01011 to 0.0095	No	ns	>0.9999
21d vs. 49d	-0.003933	-0.01374 to 0.0058	No	ns	0.9085
21d vs. 56d	-0.0091	-0.01891 to 0.0007	No	ns	0.0874
28d vs. 35d	-0.0032	-0.01301 to 0.0066	No	ns	0.9682
28d vs. 42d	0.002067	-0.007740 to 0.011	No	ns	0.9976
28d vs. 49d	-0.001567	-0.01137 to 0.0082	No	ns	0.9996
28d vs. 56d	-0.006733	-0.01654 to 0.0030	No	ns	0.3901
35d vs. 42d	0.005267	-0.004540 to 0.015	No	ns	0.693
35d vs. 49d	0.001633	-0.008174 to 0.011	No	ns	0.9995
35d vs. 56d	-0.003533	-0.01334 to 0.0062	No	ns	0.9463
42d vs. 49d	-0.003633	-0.01344 to 0.0061	No	ns	0.938
42d vs. 56d	-0.0088	-0.01861 to 0.0010	No	ns	0.1093
49d vs. 56d	-0.005167	-0.01497 to 0.0046	No	ns	0.713

Baseline Stance (s) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2706
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.183, df=8
How big is the difference?	
Mean of column A	0.1023
Mean of column B	0.09757
Difference between means (B - A) ±	-0.004727 ± 0.003994
95% confidence interval	-0.01394 to 0.004484
R squared (eta squared)	0.149
F test to compare variances	
F, DFn, Dfd	2.112, 4, 4
P value	0.4868
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stance (s) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	8.44	0.0451	*	Yes	Mean of Male	0.004606
Time	21.66	<0.0001	****	Yes	Mean of Female	0.003772
Sex	0.2867	0.8153	ns	No	Difference between means	0.0008333
Subject	39.33	<0.0001	****	Yes	SE of difference	0.003451
					95% CI of difference	-0.007125 to 0.008791

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.007933	-0.017110 to 0.0012	No	ns	0.0888
14d					
Male vs. Female	0.003167	-0.006005 to 0.012	No	ns	0.4928
21d					
Male vs. Female	0.0036	-0.005572 to 0.012	No	ns	0.4358
28d					
Male vs. Female	0.001	-0.008172 to 0.010	No	ns	0.8283
35d					
Male vs. Female	0.002933	-0.006238 to 0.012	No	ns	0.5251
42d					
Male vs. Female	-0.005	-0.01417 to 0.0041	No	ns	0.2802
49d					
Male vs. Female	0.006567	-0.002605 to 0.015	No	ns	0.1575
56d					
Male vs. Female	0.002333	-0.006838 to 0.011	No	ns	0.613
Male					
7d vs. 14d	-0.0118	-0.02199 to -0.0016	Yes	*	0.0128
7d vs. 21d	-0.01177	-0.02196 to -0.0015	Yes	*	0.0131
7d vs. 28d	-0.0126	-0.02279 to -0.0024	Yes	**	0.0061
7d vs. 35d	-0.01537	-0.02556 to -0.0051	Yes	***	0.0004
7d vs. 42d	-0.01233	-0.02252 to -0.0021	Yes	**	0.0078
7d vs. 49d	-0.01947	-0.02966 to -0.0092	Yes	****	<0.0001
7d vs. 56d	-0.01517	-0.02536 to -0.0045	Yes	***	0.0005
14d vs. 21d	0.00003334	-0.01016 to 0.0102	No	ns	>0.9999
14d vs. 28d	-0.0008	-0.01099 to 0.0093	No	ns	>0.9999
14d vs. 35d	-0.003567	-0.01376 to 0.0066	No	ns	0.9538
14d vs. 42d	-0.0005333	-0.01072 to 0.0096	No	ns	>0.9999
14d vs. 49d	-0.007867	-0.01786 to 0.0025	No	ns	0.2769
14d vs. 56d	-0.003367	-0.01356 to 0.0068	No	ns	0.966
21d vs. 28d	-0.0008333	-0.01102 to 0.0093	No	ns	>0.9999
21d vs. 35d	-0.0036	-0.01379 to 0.0065	No	ns	0.9515
21d vs. 42d	-0.0005667	-0.01076 to 0.0096	No	ns	>0.9999
21d vs. 49d	-0.0077	-0.01789 to 0.0024	No	ns	0.2718
21d vs. 56d	-0.0034	-0.01359 to 0.0067	No	ns	0.9641
28d vs. 35d	-0.002767	-0.01296 to 0.0074	No	ns	0.9888
28d vs. 42d	0.0002667	-0.009924 to 0.010	No	ns	>0.9999
28d vs. 49d	-0.006867	-0.01706 to 0.0033	No	ns	0.4144
28d vs. 56d	-0.002567	-0.01276 to 0.0076	No	ns	0.9928
35d vs. 42d	0.003033	-0.007158 to 0.013	No	ns	0.9809
35d vs. 49d	-0.0041	-0.01429 to 0.0060	No	ns	0.9072
35d vs. 56d	0.0002	-0.009991 to 0.010	No	ns	>0.9999
42d vs. 49d	-0.007133	-0.01732 to 0.0030	No	ns	0.3653
42d vs. 56d	-0.002833	-0.01302 to 0.0073	No	ns	0.9871
49d vs. 56d	0.0043	-0.005891 to 0.014	No	ns	0.8841

Female					
7d vs. 14d	-0.0007	-0.01089 to 0.0094	No	ns	>0.9999
7d vs. 21d	-0.0002333	-0.01042 to 0.0099	No	ns	>0.9999
7d vs. 28d	-0.003667	-0.01386 to 0.0065	No	ns	0.9466
7d vs. 35d	-0.0045	-0.01469 to 0.0056	No	ns	0.8579
7d vs. 42d	-0.0094	-0.01959 to 0.0007	No	ns	0.0911
7d vs. 49d	-0.004967	-0.01516 to 0.0052	No	ns	0.7856
7d vs. 56d	-0.0049	-0.01509 to 0.0052	No	ns	0.7968
14d vs. 21d	0.0004667	-0.009724 to 0.010	No	ns	>0.9999
14d vs. 28d	-0.002967	-0.01316 to 0.0072	No	ns	0.9832
14d vs. 35d	-0.0038	-0.01399 to 0.0063	No	ns	0.936
14d vs. 42d	-0.0087	-0.01889 to 0.0014	No	ns	0.148
14d vs. 49d	-0.004267	-0.01446 to 0.0059	No	ns	0.8881
14d vs. 56d	-0.0042	-0.01439 to 0.0059	No	ns	0.896
21d vs. 28d	-0.003433	-0.01362 to 0.0067	No	ns	0.9622
21d vs. 35d	-0.004267	-0.01446 to 0.0059	No	ns	0.8881
21d vs. 42d	-0.009167	-0.01936 to 0.0010	No	ns	0.1076
21d vs. 49d	-0.004733	-0.01492 to 0.0054	No	ns	0.8236
21d vs. 56d	-0.004667	-0.01486 to 0.0055	No	ns	0.8338
28d vs. 35d	-0.0008333	-0.01102 to 0.0093	No	ns	>0.9999
28d vs. 42d	-0.005733	-0.01592 to 0.0044	No	ns	0.6415
28d vs. 49d	-0.0013	-0.01149 to 0.0088	No	ns	>0.9999
28d vs. 56d	-0.001233	-0.01142 to 0.0089	No	ns	>0.9999
35d vs. 42d	-0.0049	-0.01509 to 0.0052	No	ns	0.7968
35d vs. 49d	-0.0004667	-0.01066 to 0.0097	No	ns	>0.9999
35d vs. 56d	-0.0004	-0.01059 to 0.0097	No	ns	>0.9999
42d vs. 49d	0.004433	-0.005758 to 0.014	No	ns	0.8669
42d vs. 56d	0.0045	-0.005691 to 0.014	No	ns	0.8579
49d vs. 56d	0.00006665	-0.01012 to 0.0102	No	ns	>0.9999

Baseline Stance (s) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.6149
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.5233, df=8
How big is the difference?	
Mean of column A	0.1004
Mean of column B	0.1025
Difference between means (B - A)	±0.002100 ± 0.004013
95% confidence interval	-0.007153 to 0.01135
R squared (eta squared)	0.0331
F test to compare variances	
F, DFn, Dfd	1.725, 4, 4
P value	0.6102
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Stance Stride FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	1.473	0.8336	ns	No	-0.3722
Time	11.16	0.0021	**	Yes	Mean of Female 1.805
Sex	5.627	0.4039	ns	No	Difference between means -2.177
Subject	57.97	<0.0001	****	Yes	SE of difference 2.471 95% CI of difference -7.875 to 3.520

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-2.275	-8.137 to 3.586	No	ns	0.4409
14d					
Male vs. Female	-1.942	-7.803 to 3.919	No	ns	0.5104
21d					
Male vs. Female	-1.862	-7.723 to 3.999	No	ns	0.5279
28d					
Male vs. Female	-2.269	-8.130 to 3.593	No	ns	0.4422
35d					
Male vs. Female	-2.402	-8.263 to 3.459	No	ns	0.416
42d					
Male vs. Female	0.2547	-5.607 to 6.116	No	ns	0.9311
49d					
Male vs. Female	-3.959	-9.820 to 1.903	No	ns	0.182
56d					
Male vs. Female	-2.965	-8.827 to 2.896	No	ns	0.316
Male					
7d vs. 14d	-3.863	-9.189 to 1.462	No	ns	0.3205
7d vs. 21d	-4.043	-9.369 to 1.282	No	ns	0.2662
7d vs. 28d	-1.437	-6.762 to 3.889	No	ns	0.9892
7d vs. 35d	-4.12	-9.445 to 1.205	No	ns	0.2449
7d vs. 42d	-3.53	-8.855 to 1.795	No	ns	0.4357
7d vs. 49d	-3.713	-9.039 to 1.612	No	ns	0.3702
7d vs. 56d	-4.007	-9.332 to 1.319	No	ns	0.2767
14d vs. 21d	-0.18	-5.505 to 5.145	No	ns	>0.9999
14d vs. 28d	2.427	-2.899 to 7.752	No	ns	0.8372
14d vs. 35d	-0.2567	-5.582 to 5.069	No	ns	>0.9999
14d vs. 42d	0.3333	-4.992 to 5.659	No	ns	>0.9999
14d vs. 49d	0.15	-5.175 to 5.475	No	ns	>0.9999
14d vs. 56d	-0.1433	-5.469 to 5.182	No	ns	>0.9999
21d vs. 28d	2.607	-2.719 to 7.932	No	ns	0.7819
21d vs. 35d	-0.07667	-5.402 to 5.249	No	ns	>0.9999
21d vs. 42d	0.5133	-4.812 to 5.839	No	ns	>0.9999
21d vs. 49d	0.33	-4.995 to 5.655	No	ns	>0.9999
21d vs. 56d	0.03667	-5.289 to 5.362	No	ns	>0.9999
28d vs. 35d	-2.683	-8.009 to 2.642	No	ns	0.7562
28d vs. 42d	-2.093	-7.419 to 3.232	No	ns	0.9169
28d vs. 49d	-2.277	-7.602 to 3.049	No	ns	0.8769
28d vs. 56d	-2.57	-7.895 to 2.755	No	ns	0.7938
35d vs. 42d	0.59	-4.735 to 5.915	No	ns	>0.9999
35d vs. 49d	0.4067	-4.919 to 5.732	No	ns	>0.9999
35d vs. 56d	0.1133	-5.212 to 5.439	No	ns	>0.9999
42d vs. 49d	-0.1833	-5.509 to 5.142	No	ns	>0.9999
42d vs. 56d	-0.4767	-5.802 to 4.849	No	ns	>0.9999
49d vs. 56d	-0.2933	-5.619 to 5.032	No	ns	>0.9999
Female					
7d vs. 14d	-3.53	-8.855 to 1.795	No	ns	0.4357
7d vs. 21d	-3.63	-8.955 to 1.695	No	ns	0.3994
7d vs. 28d	-1.43	-6.755 to 3.895	No	ns	0.9895
7d vs. 35d	-4.247	-9.572 to 1.079	No	ns	0.2124
7d vs. 42d	-1	-6.325 to 4.325	No	ns	0.9989
7d vs. 49d	-5.397	-10.72 to -0.07145	Yes	*	0.0448
7d vs. 56d	-4.697	-10.02 to 0.6286	No	ns	0.1219
14d vs. 21d	-0.1	-5.425 to 5.225	No	ns	>0.9999
14d vs. 28d	2.1	-3.225 to 7.425	No	ns	0.9156
14d vs. 35d	-0.7167	-6.042 to 4.609	No	ns	0.9999
14d vs. 42d	2.53	-2.795 to 7.855	No	ns	0.8064
14d vs. 49d	-1.867	-7.192 to 3.459	No	ns	0.9534
14d vs. 56d	-1.167	-6.492 to 4.159	No	ns	0.997
21d vs. 28d	2.2	-3.125 to 7.525	No	ns	0.8948
21d vs. 35d	-0.6167	-5.942 to 4.709	No	ns	>0.9999
21d vs. 42d	2.63	-2.695 to 7.955	No	ns	0.7742
21d vs. 49d	-1.767	-7.092 to 3.559	No	ns	0.9652
21d vs. 56d	-1.067	-6.392 to 4.259	No	ns	0.9983
28d vs. 35d	-2.817	-8.142 to 2.509	No	ns	0.7089
28d vs. 42d	0.43	-4.895 to 5.755	No	ns	>0.9999
28d vs. 49d	-3.967	-9.292 to 1.359	No	ns	0.2885
28d vs. 56d	-3.267	-8.592 to 2.059	No	ns	0.5361
35d vs. 42d	3.247	-2.079 to 8.572	No	ns	0.5439
35d vs. 49d	-1.15	-6.475 to 4.175	No	ns	0.9972
35d vs. 56d	-0.45	-5.775 to 4.875	No	ns	>0.9999
42d vs. 49d	-4.397	-9.722 to 0.9286	No	ns	0.178
42d vs. 56d	-3.697	-9.022 to 1.629	No	ns	0.376
49d vs. 56d	0.7	-4.625 to 6.025	No	ns	0.9999

Baseline % Stance Stride FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2149
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.347, df=8
How big is the difference?	
Mean of column A	56.37
Mean of column B	53.59
Difference between means (B - A) ±	-2.782 ± 2.066
95% confidence interval	-7.545 to 1.981
R squared (eta squared)	0.1848
F test to compare variances	
F, DFn, Dfd	1.539, 4, 4
P value	0.6866
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Stance Stide 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	0.06
Time x Sex	5.547	0.1963	ns	No	Mean of Male	1.109
Time	11.05	0.011	*	Yes	Mean of Female	-1.049
Sex	1.403	0.6541	ns	No	Difference between means	2.254
Subject	51.84	<0.0001	****	Yes	SE of difference	-6.247 to 4.149

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-2.851	-8.514 to 2.812	No	ns	0.3184
14d					
Male vs. Female	-3.994	-9.658 to 1.669	No	ns	0.1637
21d					
Male vs. Female	1.762	-3.901 to 7.426	No	ns	0.5364
28d					
Male vs. Female	1.476	-4.188 to 7.139	No	ns	0.6045
35d					
Male vs. Female	-0.9043	-6.568 to 4.759	No	ns	0.7508
42d					
Male vs. Female	-1.184	-6.848 to 4.479	No	ns	0.6775
49d					
Male vs. Female	0.699	-4.964 to 6.362	No	ns	0.806
56d					
Male vs. Female	-3.394	-9.058 to 2.269	No	ns	0.2356
Male					
7d vs. 14d	-2.63	-8.417 to 3.157	No	ns	0.839
7d vs. 21d	-4.033	-9.820 to 1.753	No	ns	0.3708
7d vs. 28d	-3.697	-9.483 to 2.090	No	ns	0.4839
7d vs. 35d	-5.023	-10.81 to 0.7633	No	ns	0.1342
7d vs. 42d	-4.16	-9.947 to 1.627	No	ns	0.3318
7d vs. 49d	-5.187	-10.97 to 0.6000	No	ns	0.1101
7d vs. 56d	-4.617	-10.40 to 1.170	No	ns	0.2119
14d vs. 21d	-1.403	-7.190 to 4.383	No	ns	0.9943
14d vs. 28d	-1.067	-6.853 to 4.720	No	ns	0.999
14d vs. 35d	-2.393	-8.180 to 3.393	No	ns	0.8943
14d vs. 42d	-1.53	-7.317 to 4.257	No	ns	0.9904
14d vs. 49d	-2.557	-8.343 to 3.230	No	ns	0.8575
14d vs. 56d	-1.987	-7.773 to 3.800	No	ns	0.9582
21d vs. 28d	0.3367	-5.450 to 6.123	No	ns	>0.9999
21d vs. 35d	-0.99	-6.777 to 4.797	No	ns	0.9994
21d vs. 42d	-0.1267	-5.913 to 5.660	No	ns	>0.9999
21d vs. 49d	-1.153	-6.940 to 4.633	No	ns	0.9983
21d vs. 56d	-0.5833	-6.370 to 5.203	No	ns	>0.9999
28d vs. 35d	-1.327	-7.113 to 4.460	No	ns	0.996
28d vs. 42d	-0.4633	-6.250 to 5.323	No	ns	>0.9999
28d vs. 49d	-1.49	-7.277 to 4.297	No	ns	0.9918
28d vs. 56d	-0.92	-6.707 to 4.867	No	ns	0.9996
35d vs. 42d	0.8633	-4.923 to 6.650	No	ns	0.9997
35d vs. 49d	-0.1633	-5.950 to 5.623	No	ns	>0.9999
35d vs. 56d	0.4067	-5.380 to 6.193	No	ns	>0.9999
42d vs. 49d	-1.027	-6.813 to 4.760	No	ns	0.9992
42d vs. 56d	-0.4567	-6.243 to 5.330	No	ns	>0.9999
49d vs. 56d	0.57	-5.217 to 6.357	No	ns	>0.9999
Female					
7d vs. 14d	-3.773	-9.560 to 2.013	No	ns	0.4571
7d vs. 21d	0.58	-5.207 to 6.367	No	ns	>0.9999
7d vs. 28d	0.63	-5.157 to 6.417	No	ns	>0.9999
7d vs. 35d	-3.077	-8.863 to 2.710	No	ns	0.7035
7d vs. 42d	-2.493	-8.280 to 3.293	No	ns	0.8725
7d vs. 49d	-1.637	-7.423 to 4.150	No	ns	0.9858
7d vs. 56d	-5.16	-10.95 to 0.6267	No	ns	0.1138
14d vs. 21d	4.353	-1.433 to 10.14	No	ns	0.2769
14d vs. 28d	4.403	-1.383 to 10.19	No	ns	0.2636
14d vs. 35d	0.6967	-5.090 to 6.483	No	ns	>0.9999
14d vs. 42d	1.28	-4.507 to 7.067	No	ns	0.9968
14d vs. 49d	2.137	-3.650 to 7.923	No	ns	0.9391
14d vs. 56d	-1.387	-7.173 to 4.400	No	ns	0.9947
21d vs. 28d	0.05	-5.737 to 5.837	No	ns	>0.9999
21d vs. 35d	-3.657	-9.443 to 2.130	No	ns	0.498
21d vs. 42d	-3.073	-8.860 to 2.713	No	ns	0.7047
21d vs. 49d	-2.217	-8.003 to 3.570	No	ns	0.9268
21d vs. 56d	-5.74	-11.53 to 0.04665	No	ns	0.0533
28d vs. 35d	-3.707	-9.493 to 2.080	No	ns	0.4804
28d vs. 42d	-3.123	-8.910 to 2.663	No	ns	0.6876
28d vs. 49d	-2.267	-8.053 to 3.520	No	ns	0.9184
28d vs. 56d	-5.79	-11.58 to -0.00334	Yes	*	0.0498
35d vs. 42d	0.5833	-5.203 to 6.370	No	ns	>0.9999
35d vs. 49d	1.44	-4.347 to 7.227	No	ns	0.9933
35d vs. 56d	-2.083	-7.870 to 3.703	No	ns	0.9465
42d vs. 49d	0.8567	-4.930 to 6.643	No	ns	0.9998
42d vs. 56d	-2.667	-8.453 to 3.120	No	ns	0.8293
49d vs. 56d	-3.523	-9.310 to 2.263	No	ns	0.5456

Baseline % Stance Stride 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.3655
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.9594, df=8
How big is the difference?	
Mean of column A	56.11
Mean of column B	54.08
Difference between means (B - A) ±	±2.034 ± 2.120
95% confidence interval	-6.924 to 2.855
R squared (eta squared)	0.1032
F test to compare variances	
F, DFn, Dfd	1.728, 4, 4
P value	0.6092
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Stance Stride 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	7.882	0.0583	ns	No	Mean of Male	-1.555
Time	4.939	0.2599	ns	No	Mean of Female	-0.8713
Sex	0.6213	0.7744	ns	No	Difference between means	-0.6841
Subject	56.54	<0.0001	****	Yes	SE of difference	2.307
					95% CI of difference	-6.005 to 4.636

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-2.225	-7.928 to 3.478	No	ns	0.4385
14d					
Male vs. Female	-0.2087	-5.912 to 5.494	No	ns	0.942
21d					
Male vs. Female	1.755	-3.948 to 7.458	No	ns	0.541
28d					
Male vs. Female	1.628	-4.075 to 7.331	No	ns	0.5705
35d					
Male vs. Female	1.758	-3.945 to 7.461	No	ns	0.5402
42d					
Male vs. Female	-5.332	-11.04 to 0.3710	No	ns	0.0664
49d					
Male vs. Female	0.148	-5.555 to 5.851	No	ns	0.9588
56d					
Male vs. Female	-2.995	-8.698 to 2.708	No	ns	0.298
Male					
7d vs. 14d	-3.293	-8.951 to 2.365	No	ns	0.6013
7d vs. 21d	-4.037	-9.695 to 1.621	No	ns	0.3413
7d vs. 28d	-4.303	-9.961 to 1.355	No	ns	0.2642
7d vs. 35d	-4.98	-10.64 to 0.6781	No	ns	0.1234
7d vs. 42d	-1.067	-6.725 to 4.591	No	ns	0.9988
7d vs. 49d	-4.443	-10.10 to 1.215	No	ns	0.2286
7d vs. 56d	-2.687	-8.345 to 2.971	No	ns	0.8069
14d vs. 21d	-0.7433	-6.401 to 4.915	No	ns	0.9999
14d vs. 28d	-1.01	-6.668 to 4.648	No	ns	0.9992
14d vs. 35d	-1.687	-7.345 to 3.971	No	ns	0.9808
14d vs. 42d	2.227	-3.431 to 7.885	No	ns	0.9165
14d vs. 49d	-1.15	-6.808 to 4.508	No	ns	0.9981
14d vs. 56d	0.6067	-5.051 to 6.265	No	ns	>0.9999
21d vs. 28d	-0.2667	-5.925 to 5.391	No	ns	>0.9999
21d vs. 35d	-0.9433	-6.601 to 4.715	No	ns	0.9995
21d vs. 42d	2.97	-2.688 to 8.628	No	ns	0.7167
21d vs. 49d	-0.4067	-6.065 to 5.251	No	ns	>0.9999
21d vs. 56d	1.35	-4.308 to 7.008	No	ns	0.9948
28d vs. 35d	-0.6767	-6.335 to 4.981	No	ns	>0.9999
28d vs. 42d	3.237	-2.421 to 8.895	No	ns	0.6221
28d vs. 49d	-0.14	-5.798 to 5.518	No	ns	>0.9999
28d vs. 56d	1.617	-4.041 to 7.275	No	ns	0.9849
35d vs. 42d	3.913	-1.745 to 9.571	No	ns	0.3807
35d vs. 49d	0.5367	-5.121 to 6.195	No	ns	>0.9999
35d vs. 56d	2.293	-3.365 to 7.951	No	ns	0.9038
42d vs. 49d	-3.377	-9.035 to 2.281	No	ns	0.5707
42d vs. 56d	-1.62	-7.278 to 4.038	No	ns	0.9847
49d vs. 56d	1.757	-3.901 to 7.415	No	ns	0.9758
Female					
7d vs. 14d	-1.277	-6.935 to 4.381	No	ns	0.9964
7d vs. 21d	-0.05667	-5.715 to 5.601	No	ns	>0.9999
7d vs. 28d	-0.45	-6.108 to 5.208	No	ns	>0.9999
7d vs. 35d	-0.9967	-6.655 to 4.661	No	ns	0.9992
7d vs. 42d	-4.173	-9.831 to 1.485	No	ns	0.3003
7d vs. 49d	-2.07	-7.728 to 3.588	No	ns	0.9419
7d vs. 56d	-3.457	-9.115 to 2.201	No	ns	0.5413
14d vs. 21d	1.22	-4.438 to 6.878	No	ns	0.9973
14d vs. 28d	0.8267	-4.831 to 6.485	No	ns	0.9998
14d vs. 35d	0.28	-5.378 to 5.938	No	ns	>0.9999
14d vs. 42d	-2.897	-8.555 to 2.761	No	ns	0.7413
14d vs. 49d	-0.7933	-6.451 to 4.865	No	ns	0.9998
14d vs. 56d	-2.18	-7.838 to 3.478	No	ns	0.9247
21d vs. 28d	-0.3933	-6.051 to 5.265	No	ns	>0.9999
21d vs. 35d	-0.94	-6.598 to 4.718	No	ns	0.9995
21d vs. 42d	-4.117	-9.775 to 1.541	No	ns	0.3169
21d vs. 49d	-2.013	-7.671 to 3.645	No	ns	0.9496
21d vs. 56d	-3.4	-9.058 to 2.258	No	ns	0.5621
28d vs. 35d	-0.5467	-6.205 to 5.111	No	ns	>0.9999
28d vs. 42d	-3.723	-9.381 to 1.935	No	ns	0.4452
28d vs. 49d	-1.62	-7.278 to 4.038	No	ns	0.9847
28d vs. 56d	-3.007	-8.665 to 2.651	No	ns	0.7041
35d vs. 42d	-3.177	-8.835 to 2.481	No	ns	0.6439
35d vs. 49d	-1.073	-6.731 to 4.585	No	ns	0.9988
35d vs. 56d	-2.46	-8.118 to 3.198	No	ns	0.8673
42d vs. 49d	2.103	-3.555 to 7.761	No	ns	0.937
42d vs. 56d	0.7167	-4.941 to 6.375	No	ns	>0.9999
49d vs. 56d	-1.387	-7.045 to 4.271	No	ns	0.9939

Baseline % Stance Stride 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.9028
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.1260, df=8
How big is the difference?	
Mean of column A	56.32
Mean of column B	56.61
Difference between means (B - A) ± 0.2947 ± 2.338	
95% confidence interval	-5.097 to 5.686
R squared (eta squared)	0.001981
F test to compare variances	
F, DFn, Dfd	4.252, 4, 4
P value	0.1899
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stride (s) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	0.9892	0.8902	ns	No	Mean of Male	0.004375
Time	3.401	0.2157	ns	No	Mean of Female	0.003715
Sex	0.02424	0.9611	ns	No	Difference between means	0.00066
Subject	76.43	<0.0001	****	Yes	SE of difference	0.0131
					95% CI of difference	-0.02955 to 0.03087

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.001627	-0.02765 to 0.0309	No	ns	0.912
14d					
Male vs. Female	-0.007207	-0.03648 to 0.0220	No	ns	0.6245
21d					
Male vs. Female	0.004693	-0.02458 to 0.0339	No	ns	0.7498
28d					
Male vs. Female	0.00426	-0.02501 to 0.0335	No	ns	0.7722
35d					
Male vs. Female	0.002293	-0.02698 to 0.0315	No	ns	0.8761
42d					
Male vs. Female	-0.00384	-0.03311 to 0.0254	No	ns	0.7941
49d					
Male vs. Female	0.00526	-0.02401 to 0.0345	No	ns	0.7208
56d					
Male vs. Female	-0.001807	-0.03108 to 0.0274	No	ns	0.9023
Male					
7d vs. 14d	-0.0002333	-0.02231 to 0.0218	No	ns	>0.9999
7d vs. 21d	-0.004233	-0.02631 to 0.0178	No	ns	0.9987
7d vs. 28d	-0.01363	-0.03571 to 0.0084	No	ns	0.5277
7d vs. 35d	-0.0073	-0.02938 to 0.0147	No	ns	0.9659
7d vs. 42d	-0.006167	-0.02825 to 0.0159	No	ns	0.9868
7d vs. 49d	-0.01203	-0.03411 to 0.0100	No	ns	0.6771
7d vs. 56d	-0.007933	-0.03001 to 0.0141	No	ns	0.947
14d vs. 21d	-0.004	-0.02608 to 0.0180	No	ns	0.9991
14d vs. 28d	-0.0134	-0.03548 to 0.0086	No	ns	0.5496
14d vs. 35d	-0.007067	-0.02915 to 0.0150	No	ns	0.9714
14d vs. 42d	-0.005933	-0.02801 to 0.0161	No	ns	0.9895
14d vs. 49d	-0.0118	-0.03388 to 0.0102	No	ns	0.6981
14d vs. 56d	-0.0077	-0.02978 to 0.0143	No	ns	0.9546
21d vs. 28d	-0.0094	-0.03148 to 0.0126	No	ns	0.8792
21d vs. 35d	-0.003067	-0.02515 to 0.0190	No	ns	0.9998
21d vs. 42d	-0.001933	-0.02401 to 0.0201	No	ns	>0.9999
21d vs. 49d	-0.0078	-0.02988 to 0.0142	No	ns	0.9515
21d vs. 56d	-0.0037	-0.02578 to 0.0183	No	ns	0.9995
28d vs. 35d	0.006333	-0.01575 to 0.0284	No	ns	0.9846
28d vs. 42d	0.007467	-0.01461 to 0.0295	No	ns	0.9614
28d vs. 49d	0.0016	-0.02048 to 0.0236	No	ns	>0.9999
28d vs. 56d	0.0057	-0.01638 to 0.0277	No	ns	0.9917
35d vs. 42d	0.001133	-0.02095 to 0.0232	No	ns	>0.9999
35d vs. 49d	-0.004733	-0.02681 to 0.0173	No	ns	0.9973
35d vs. 56d	-0.0006333	-0.02271 to 0.0214	No	ns	>0.9999
42d vs. 49d	-0.005867	-0.02795 to 0.0162	No	ns	0.9901
42d vs. 56d	-0.001767	-0.02385 to 0.0203	No	ns	>0.9999
49d vs. 56d	0.0041	-0.01798 to 0.0261	No	ns	0.9989
Female					
7d vs. 14d	-0.009067	-0.03115 to 0.0130	No	ns	0.8977
7d vs. 21d	-0.001167	-0.02325 to 0.0209	No	ns	>0.9999
7d vs. 28d	-0.011	-0.03308 to 0.0110	No	ns	0.7665
7d vs. 35d	-0.006633	-0.02871 to 0.0154	No	ns	0.9799
7d vs. 42d	-0.01163	-0.03371 to 0.0104	No	ns	0.7128
7d vs. 49d	-0.0084	-0.03048 to 0.0136	No	ns	0.9292
7d vs. 56d	-0.01137	-0.03345 to 0.0107	No	ns	0.7359
14d vs. 21d	0.0079	-0.01418 to 0.0299	No	ns	0.9481
14d vs. 28d	-0.001933	-0.02401 to 0.0201	No	ns	>0.9999
14d vs. 35d	0.002433	-0.01965 to 0.0245	No	ns	>0.9999
14d vs. 42d	-0.002567	-0.02465 to 0.0195	No	ns	>0.9999
14d vs. 49d	0.0006667	-0.02141 to 0.0227	No	ns	>0.9999
14d vs. 56d	-0.0023	-0.02438 to 0.0197	No	ns	>0.9999
21d vs. 28d	-0.009833	-0.03191 to 0.0122	No	ns	0.8525
21d vs. 35d	-0.005467	-0.02755 to 0.0166	No	ns	0.9935
21d vs. 42d	-0.01047	-0.03255 to 0.0116	No	ns	0.8081
21d vs. 49d	-0.007233	-0.02931 to 0.0148	No	ns	0.9675
21d vs. 56d	-0.0102	-0.03228 to 0.0118	No	ns	0.8275
28d vs. 35d	0.004367	-0.01771 to 0.0264	No	ns	0.9984
28d vs. 42d	-0.0006333	-0.02271 to 0.0214	No	ns	>0.9999
28d vs. 49d	0.0026	-0.01948 to 0.0246	No	ns	>0.9999
28d vs. 56d	-0.0003667	-0.02245 to 0.0217	No	ns	>0.9999
35d vs. 42d	-0.005	-0.02708 to 0.0170	No	ns	0.9963
35d vs. 49d	-0.001767	-0.02385 to 0.0203	No	ns	>0.9999
35d vs. 56d	-0.004733	-0.02681 to 0.0173	No	ns	0.9973
42d vs. 49d	0.003233	-0.01885 to 0.0253	No	ns	0.9998
42d vs. 56d	0.0002667	-0.02181 to 0.0223	No	ns	>0.9999
49d vs. 56d	-0.002967	-0.02505 to 0.0191	No	ns	0.9999

Baseline Stride (s) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.6469
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.4759, df=8
How big is the difference?	
Mean of column A	0.1828
Mean of column B	0.1889
Difference between means (B - A)	$\pm 0.006060 \pm 0.01273$
95% confidence interval	-0.02330 to 0.03542
R squared (eta squared)	0.02753
F test to compare variances	
F, DFn, Dfd	13.14, 4, 4
P value	0.0286
P value summary	*
Significantly different (P < 0.05)?	Yes
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stride (s) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	5.616	0.2723	ns	No	Mean of Male	0.004262
Time	2.557	0.7634	ns	No	Mean of Female	0.01289
Sex	9.03	0.2546	ns	No	Difference between means	-0.008625
Subject	47.96	<0.0001	****	Yes	SE of difference	0.007028
					95% CI of difference	-0.02483 to 0.007582

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.00805	-0.02650 to 0.0104	No	ns	0.3866
14d					
Male vs. Female	-0.0005833	-0.01903 to 0.0178	No	ns	0.9498
21d					
Male vs. Female	-0.01528	-0.03373 to 0.0031	No	ns	0.1028
28d					
Male vs. Female	-0.01888	-0.03733 to -0.0004	Yes	*	0.045
35d					
Male vs. Female	-0.00645	-0.02490 to 0.0120	No	ns	0.4874
42d					
Male vs. Female	0.002983	-0.01546 to 0.0214	No	ns	0.7477
49d					
Male vs. Female	-0.01208	-0.03053 to 0.0063	No	ns	0.1954
56d					
Male vs. Female	-0.01065	-0.02910 to 0.0077	No	ns	0.253
Male					
7d vs. 14d	-0.008233	-0.02839 to 0.0119	No	ns	0.9003
7d vs. 21d	-0.002167	-0.02232 to 0.0179	No	ns	>0.9999
7d vs. 28d	-0.002833	-0.02299 to 0.0173	No	ns	0.9998
7d vs. 35d	-0.007167	-0.02732 to 0.0129	No	ns	0.9498
7d vs. 42d	-0.009667	-0.02982 to 0.0104	No	ns	0.799
7d vs. 49d	-0.0042	-0.02436 to 0.0159	No	ns	0.9978
7d vs. 56d	-0.002367	-0.02252 to 0.0177	No	ns	>0.9999
14d vs. 21d	0.006067	-0.01409 to 0.0262	No	ns	0.9797
14d vs. 28d	0.0054	-0.01476 to 0.0255	No	ns	0.9897
14d vs. 35d	0.001067	-0.01909 to 0.0212	No	ns	>0.9999
14d vs. 42d	-0.001433	-0.02159 to 0.0187	No	ns	>0.9999
14d vs. 49d	0.004033	-0.01612 to 0.0241	No	ns	0.9983
14d vs. 56d	0.005867	-0.01429 to 0.0260	No	ns	0.9832
21d vs. 28d	-0.0006667	-0.02082 to 0.0194	No	ns	>0.9999
21d vs. 35d	-0.005	-0.02516 to 0.0151	No	ns	0.9935
21d vs. 42d	-0.0075	-0.02766 to 0.0126	No	ns	0.9367
21d vs. 49d	-0.002033	-0.02219 to 0.0181	No	ns	>0.9999
21d vs. 56d	-0.0002	-0.02036 to 0.0199	No	ns	>0.9999
28d vs. 35d	-0.004333	-0.02449 to 0.0158	No	ns	0.9973
28d vs. 42d	-0.006833	-0.02699 to 0.0133	No	ns	0.9609
28d vs. 49d	-0.001367	-0.02152 to 0.0187	No	ns	>0.9999
28d vs. 56d	0.0004667	-0.01969 to 0.0206	No	ns	>0.9999
35d vs. 42d	-0.0025	-0.02266 to 0.0176	No	ns	>0.9999
35d vs. 49d	0.002967	-0.01719 to 0.0231	No	ns	0.9998
35d vs. 56d	0.0048	-0.01536 to 0.0249	No	ns	0.9949
42d vs. 49d	0.005467	-0.01469 to 0.0256	No	ns	0.9889
42d vs. 56d	0.0073	-0.01286 to 0.0274	No	ns	0.9448
49d vs. 56d	0.001833	-0.01832 to 0.0219	No	ns	>0.9999
Female					
7d vs. 14d	-0.0007667	-0.02092 to 0.0193	No	ns	>0.9999
7d vs. 21d	-0.0094	-0.02956 to 0.0107	No	ns	0.8207
7d vs. 28d	-0.01367	-0.03382 to 0.0064	No	ns	0.4064
7d vs. 35d	-0.005567	-0.02572 to 0.0145	No	ns	0.9876
7d vs. 42d	0.001367	-0.01879 to 0.0215	No	ns	>0.9999
7d vs. 49d	-0.008233	-0.02839 to 0.0119	No	ns	0.9003
7d vs. 56d	-0.004967	-0.02512 to 0.0151	No	ns	0.9937
14d vs. 21d	-0.008633	-0.02879 to 0.0115	No	ns	0.8759
14d vs. 28d	-0.0129	-0.03306 to 0.0072	No	ns	0.4816
14d vs. 35d	-0.0048	-0.02496 to 0.0153	No	ns	0.9949
14d vs. 42d	0.002133	-0.01802 to 0.0222	No	ns	>0.9999
14d vs. 49d	-0.007467	-0.02762 to 0.0126	No	ns	0.9381
14d vs. 56d	-0.0042	-0.02436 to 0.0159	No	ns	0.9978
21d vs. 28d	-0.004267	-0.02442 to 0.0158	No	ns	0.9976
21d vs. 35d	0.003833	-0.01632 to 0.0239	No	ns	0.9988
21d vs. 42d	0.01077	-0.009391 to 0.030	No	ns	0.6987
21d vs. 49d	0.001167	-0.01899 to 0.0213	No	ns	>0.9999
21d vs. 56d	0.004433	-0.01572 to 0.0245	No	ns	0.9969
28d vs. 35d	0.0081	-0.01206 to 0.0282	No	ns	0.9077
28d vs. 42d	0.01503	-0.005124 to 0.035	No	ns	0.2871
28d vs. 49d	0.005433	-0.01472 to 0.0255	No	ns	0.9893
28d vs. 56d	0.0087	-0.01146 to 0.0288	No	ns	0.8716
35d vs. 42d	0.006933	-0.01322 to 0.0270	No	ns	0.9578
35d vs. 49d	-0.002867	-0.02282 to 0.0174	No	ns	0.9999
35d vs. 56d	0.0006	-0.01956 to 0.0207	No	ns	>0.9999
42d vs. 49d	-0.0096	-0.02976 to 0.0105	No	ns	0.8045
42d vs. 56d	-0.006333	-0.02649 to 0.0138	No	ns	0.9742
49d vs. 56d	0.003267	-0.01689 to 0.0234	No	ns	0.9996

Baseline Stride (s) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.8498
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.1955, df=8
How big is the difference?	
Mean of column A	0.1827
Mean of column B	0.1812
Difference between means (B - A)	-0.001450 ± 0.007415
95% confidence interval	-0.01855 to 0.01565
R squared (eta squared)	0.004757
F test to compare variances	
F, DFn, Dfd	1.178, 4, 4
P value	0.8775
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stride (s) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	5.398	0.2115	ns	No	Mean of Male	0.01308
Time	5.634	0.1885	ns	No	Mean of Female	0.009737
Sex	1.18	0.6963	ns	No	Difference between means	0.003338
Subject	57.61	<0.0001	****	Yes	SE of difference	0.008248
					95% CI of difference	-0.01568 to 0.02236

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.006587	-0.02693 to 0.0137	No	ns	0.52
14d					
Male vs. Female	0.005313	-0.01503 to 0.0256	No	ns	0.6036
21d					
Male vs. Female	-0.0004867	-0.02083 to 0.0198	No	ns	0.962
28d					
Male vs. Female	-0.00452	-0.02486 to 0.0158	No	ns	0.6586
35d					
Male vs. Female	-0.001153	-0.02149 to 0.0191	No	ns	0.9102
42d					
Male vs. Female	0.008947	-0.01139 to 0.0292	No	ns	0.3828
49d					
Male vs. Female	0.01085	-0.009493 to 0.031	No	ns	0.2907
56d					
Male vs. Female	0.01435	-0.005993 to 0.034	No	ns	0.1637
Male					
7d vs. 14d	-0.0098	-0.02989 to 0.0102	No	ns	0.785
7d vs. 21d	-0.006833	-0.02693 to 0.0132	No	ns	0.9603
7d vs. 28d	-0.007767	-0.02786 to 0.0123	No	ns	0.9235
7d vs. 35d	-0.0103	-0.03039 to 0.0097	No	ns	0.7401
7d vs. 42d	-0.01903	-0.03913 to 0.0010	No	ns	0.0756
7d vs. 49d	-0.01997	-0.04006 to 0.0001	No	ns	0.0526
7d vs. 56d	-0.0188	-0.03889 to 0.0012	No	ns	0.0825
14d vs. 21d	0.002967	-0.01713 to 0.0230	No	ns	0.9998
14d vs. 28d	0.002033	-0.01806 to 0.0221	No	ns	>0.9999
14d vs. 35d	-0.0005	-0.02059 to 0.0195	No	ns	>0.9999
14d vs. 42d	-0.009233	-0.02933 to 0.0108	No	ns	0.8313
14d vs. 49d	-0.01017	-0.03026 to 0.0099	No	ns	0.7524
14d vs. 56d	-0.009	-0.02909 to 0.0110	No	ns	0.8488
21d vs. 28d	-0.0009333	-0.02103 to 0.0191	No	ns	>0.9999
21d vs. 35d	-0.003467	-0.02356 to 0.0166	No	ns	0.9993
21d vs. 42d	-0.0122	-0.03229 to 0.0078	No	ns	0.5491
21d vs. 49d	-0.01313	-0.03323 to 0.0069	No	ns	0.454
21d vs. 56d	-0.01197	-0.03206 to 0.0081	No	ns	0.5732
28d vs. 35d	-0.002533	-0.02263 to 0.0175	No	ns	>0.9999
28d vs. 42d	-0.01127	-0.03136 to 0.0088	No	ns	0.6453
28d vs. 49d	-0.0122	-0.03229 to 0.0078	No	ns	0.5491
28d vs. 56d	-0.01103	-0.03113 to 0.0090	No	ns	0.6689
35d vs. 42d	-0.008733	-0.02883 to 0.0113	No	ns	0.8675
35d vs. 49d	-0.009667	-0.02976 to 0.0104	No	ns	0.7964
35d vs. 56d	-0.0085	-0.02859 to 0.0115	No	ns	0.8827
42d vs. 49d	-0.0009333	-0.02103 to 0.0191	No	ns	>0.9999
42d vs. 56d	0.0002333	-0.01986 to 0.0203	No	ns	>0.9999
49d vs. 56d	0.001167	-0.01893 to 0.0212	No	ns	>0.9999
Female					
7d vs. 14d	0.0021	-0.01799 to 0.0221	No	ns	>0.9999
7d vs. 21d	-0.0007333	-0.02083 to 0.0193	No	ns	>0.9999
7d vs. 28d	-0.0057	-0.02579 to 0.0143	No	ns	0.9855
7d vs. 35d	-0.004867	-0.02496 to 0.0152	No	ns	0.9944
7d vs. 42d	-0.0035	-0.02359 to 0.0165	No	ns	0.9993
7d vs. 49d	-0.002533	-0.02263 to 0.0175	No	ns	>0.9999
7d vs. 56d	0.002133	-0.01796 to 0.0222	No	ns	>0.9999
14d vs. 21d	-0.002833	-0.02293 to 0.0172	No	ns	0.9998
14d vs. 28d	-0.0078	-0.02789 to 0.0122	No	ns	0.9219
14d vs. 35d	-0.006967	-0.02706 to 0.0131	No	ns	0.956
14d vs. 42d	-0.0056	-0.02569 to 0.0144	No	ns	0.9869
14d vs. 49d	-0.004633	-0.02473 to 0.0154	No	ns	0.9958
14d vs. 56d	0.00003333	-0.02006 to 0.0201	No	ns	>0.9999
21d vs. 28d	-0.004967	-0.02506 to 0.0151	No	ns	0.9936
21d vs. 35d	-0.004133	-0.02423 to 0.0159	No	ns	0.998
21d vs. 42d	-0.002767	-0.02286 to 0.0173	No	ns	0.9999
21d vs. 49d	-0.0018	-0.02189 to 0.0182	No	ns	>0.9999
21d vs. 56d	0.002867	-0.01723 to 0.0229	No	ns	0.9998
28d vs. 35d	0.0008333	-0.01926 to 0.0209	No	ns	>0.9999
28d vs. 42d	0.0022	-0.01789 to 0.0222	No	ns	>0.9999
28d vs. 49d	0.003167	-0.01693 to 0.0232	No	ns	0.9996
28d vs. 56d	0.007833	-0.01226 to 0.0279	No	ns	0.9202
35d vs. 42d	0.001367	-0.01873 to 0.0214	No	ns	>0.9999
35d vs. 49d	0.002333	-0.01776 to 0.0224	No	ns	>0.9999
35d vs. 56d	0.007	-0.01309 to 0.0270	No	ns	0.9549
42d vs. 49d	0.0009667	-0.01913 to 0.0210	No	ns	>0.9999
42d vs. 56d	0.005633	-0.01446 to 0.0257	No	ns	0.9865
49d vs. 56d	0.004667	-0.01543 to 0.0247	No	ns	0.9956

Baseline Stride (s) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.7737
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.2974, df=8
How big is the difference?	
Mean of column A	0.1792
Mean of column B	0.1817
Difference between means (B - A)	$\pm 0.002580 \pm 0.008675$
95% confidence interval	-0.01742 to 0.02258
R squared (eta squared)	0.01094
F test to compare variances	
F, DFn, Dfd	1.307, 4, 4
P value	0.8013
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Brake Stance FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	17.72	<0.0001	****	Yes	Mean of Male Mean of Female Difference between means
Time	18.19	<0.0001	****	Yes	SE of difference
Sex	1.969	0.5536	ns	No	95% CI of difference
Subject	41.21	<0.0001	****	Yes	

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	0.914	-7.389 to 9.217	No	ns	0.8266
14d					
Male vs. Female	-17.99	-26.29 to -9.683	Yes	****	<0.0001
21d					
Male vs. Female	-4.166	-12.47 to 4.137	No	ns	0.32
28d					
Male vs. Female	2.511	-5.792 to 10.81	No	ns	0.5479
35d					
Male vs. Female	0.6873	-7.616 to 8.990	No	ns	0.8692
42d					
Male vs. Female	0.4607	-7.842 to 8.764	No	ns	0.9121
49d					
Male vs. Female	-0.3993	-8.702 to 7.904	No	ns	0.9238
56d					
Male vs. Female	1.237	-7.066 to 9.540	No	ns	0.7669
Male					
7d vs. 14d	6.51	-1.606 to 14.63	No	ns	0.2064
7d vs. 21d	6.42	-1.696 to 14.54	No	ns	0.2209
7d vs. 28d	5.563	-2.553 to 13.68	No	ns	0.3922
7d vs. 35d	4.79	-3.326 to 12.91	No	ns	0.5844
7d vs. 42d	7.29	-0.8260 to 15.41	No	ns	0.1086
7d vs. 49d	6.33	-1.786 to 14.45	No	ns	0.236
7d vs. 56d	3.627	-4.489 to 11.74	No	ns	0.8503
14d vs. 21d	-0.09	-8.206 to 8.026	No	ns	>0.9999
14d vs. 28d	-0.9467	-9.063 to 7.169	No	ns	>0.9999
14d vs. 35d	-1.72	-9.836 to 6.396	No	ns	0.9975
14d vs. 42d	0.78	-7.336 to 8.896	No	ns	>0.9999
14d vs. 49d	-0.18	-8.296 to 7.936	No	ns	>0.9999
14d vs. 56d	-2.883	-11.00 to 5.233	No	ns	0.95
21d vs. 28d	-0.8567	-8.973 to 7.259	No	ns	>0.9999
21d vs. 35d	-1.63	-9.746 to 6.486	No	ns	0.9982
21d vs. 42d	0.87	-7.246 to 8.986	No	ns	>0.9999
21d vs. 49d	-0.09	-8.206 to 8.026	No	ns	>0.9999
21d vs. 56d	-2.793	-10.91 to 5.323	No	ns	0.9577
28d vs. 35d	-0.7733	-8.889 to 7.343	No	ns	>0.9999
28d vs. 42d	1.727	-6.389 to 9.843	No	ns	0.9975
28d vs. 49d	0.7667	-7.349 to 8.883	No	ns	>0.9999
28d vs. 56d	-1.937	-10.05 to 6.179	No	ns	0.9948
35d vs. 42d	2.5	-5.616 to 10.62	No	ns	0.9769
35d vs. 49d	1.54	-6.576 to 9.656	No	ns	0.9988
35d vs. 56d	-1.163	-9.279 to 6.953	No	ns	0.9998
42d vs. 49d	-0.96	-9.076 to 7.156	No	ns	>0.9999
42d vs. 56d	-3.663	-11.78 to 4.453	No	ns	0.8437
49d vs. 56d	-2.703	-10.82 to 5.413	No	ns	0.9645
Female					
7d vs. 14d	-12.39	-20.51 to -4.274	Yes	***	0.0003
7d vs. 21d	1.34	-6.776 to 9.456	No	ns	0.9995
7d vs. 28d	7.16	-0.9560 to 15.28	No	ns	0.1217
7d vs. 35d	4.563	-3.553 to 12.68	No	ns	0.6422
7d vs. 42d	6.837	-1.279 to 14.95	No	ns	0.1596
7d vs. 49d	5.017	-3.099 to 13.13	No	ns	0.5264
7d vs. 56d	3.95	-4.166 to 12.07	No	ns	0.7868
14d vs. 21d	13.73	5.614 to 21.85	Yes	****	<0.0001
14d vs. 28d	19.55	11.43 to 27.67	Yes	****	<0.0001
14d vs. 35d	16.95	8.837 to 25.07	Yes	****	<0.0001
14d vs. 42d	19.23	11.11 to 27.34	Yes	****	<0.0001
14d vs. 49d	17.41	9.291 to 25.52	Yes	****	<0.0001
14d vs. 56d	16.34	8.224 to 24.46	Yes	****	<0.0001
21d vs. 28d	5.82	-2.296 to 13.94	No	ns	0.3349
21d vs. 35d	3.223	-4.893 to 11.34	No	ns	0.9127
21d vs. 42d	5.497	-2.619 to 13.61	No	ns	0.4078
21d vs. 49d	3.677	-4.439 to 11.79	No	ns	0.8412
21d vs. 56d	2.61	-5.506 to 10.73	No	ns	0.9706
28d vs. 35d	-2.597	-10.71 to 5.519	No	ns	0.9715
28d vs. 42d	-0.3233	-8.439 to 7.793	No	ns	>0.9999
28d vs. 49d	-2.143	-10.26 to 5.973	No	ns	0.9905
28d vs. 56d	-3.21	-11.33 to 4.906	No	ns	0.9144
35d vs. 42d	2.273	-5.843 to 10.39	No	ns	0.9866
35d vs. 49d	0.4533	-7.663 to 8.569	No	ns	>0.9999
35d vs. 56d	-0.6133	-8.729 to 7.503	No	ns	>0.9999
42d vs. 49d	-1.82	-9.936 to 6.296	No	ns	0.9965
42d vs. 56d	-2.887	-11.00 to 5.229	No	ns	0.9497
49d vs. 56d	-1.067	-9.183 to 7.049	No	ns	0.9999

Baseline % Brake Stance FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0619
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=2.169, df=8
How big is the difference?	
Mean of column A	24.34
Mean of column B	29.31
Difference between means (B - A) ± 2.291	
95% confidence interval	-0.3130 to 10.25
R squared (eta squared)	0.3704
F test to compare variances	
F, DFn, Dfd	9.456, 4, 4
P value	0.0514
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Brake Stance 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	29.57	<0.0001	****	Yes	Mean of Male -0.7308
Time	26.81	<0.0001	****	Yes	Mean of Female -0.05892
Sex	0.1573	0.8122	ns	No	Difference between means -0.6719
Subject	20.86	<0.0001	****	Yes	SE of difference 2.736
					95% CI of difference -6.981 to 5.637

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-3.736	-11.63 to 4.154	No	ns	0.3477
14d					
Male vs. Female	-23.09	-30.98 to -15.20	Yes	****	<0.0001
21d					
Male vs. Female	3.158	-4.732 to 11.05	No	ns	0.4269
28d					
Male vs. Female	10.1	2.212 to 17.99	Yes	*	0.0129
35d					
Male vs. Female	-0.2557	-8.145 to 7.634	No	ns	0.9486
42d					
Male vs. Female	2.828	-5.062 to 10.72	No	ns	0.4766
49d					
Male vs. Female	2.728	-5.162 to 10.62	No	ns	0.4923
56d					
Male vs. Female	2.888	-5.002 to 10.78	No	ns	0.4673
Male					
7d vs. 14d	2.493	-7.092 to 12.08	No	ns	0.9913
7d vs. 21d	2.963	-6.622 to 12.55	No	ns	0.9764
7d vs. 28d	-1.03	-10.61 to 8.555	No	ns	>0.9999
7d vs. 35d	2.753	-6.832 to 12.34	No	ns	0.9844
7d vs. 42d	3.88	-5.705 to 13.46	No	ns	0.9044
7d vs. 49d	1.03	-8.555 to 10.61	No	ns	>0.9999
7d vs. 56d	0.1433	-9.442 to 9.728	No	ns	>0.9999
14d vs. 21d	0.47	-9.115 to 10.05	No	ns	>0.9999
14d vs. 28d	-3.523	-13.11 to 6.062	No	ns	0.9405
14d vs. 35d	0.26	-9.325 to 9.845	No	ns	>0.9999
14d vs. 42d	1.387	-8.198 to 10.97	No	ns	0.9998
14d vs. 49d	-1.463	-11.05 to 8.122	No	ns	0.9997
14d vs. 56d	-2.35	-11.93 to 7.235	No	ns	0.9939
21d vs. 28d	-3.993	-13.58 to 5.592	No	ns	0.8906
21d vs. 35d	-0.21	-9.795 to 9.375	No	ns	>0.9999
21d vs. 42d	0.9167	-8.668 to 10.50	No	ns	>0.9999
21d vs. 49d	-1.933	-11.52 to 7.652	No	ns	0.9982
21d vs. 56d	-2.82	-12.40 to 6.765	No	ns	0.9822
28d vs. 35d	3.783	-5.802 to 13.37	No	ns	0.9153
28d vs. 42d	4.91	-4.675 to 14.49	No	ns	0.7407
28d vs. 49d	2.06	-7.525 to 11.64	No	ns	0.9973
28d vs. 56d	1.173	-8.412 to 10.76	No	ns	>0.9999
35d vs. 42d	1.127	-8.458 to 10.71	No	ns	>0.9999
35d vs. 49d	-1.723	-11.31 to 7.862	No	ns	0.9991
35d vs. 56d	-2.61	-12.19 to 6.975	No	ns	0.9886
42d vs. 49d	-2.85	-12.43 to 6.735	No	ns	0.981
42d vs. 56d	-3.737	-13.32 to 5.848	No	ns	0.9202
49d vs. 56d	-0.8867	-10.47 to 8.698	No	ns	>0.9999
Female					
7d vs. 14d	-16.86	-26.44 to -7.272	Yes	****	<0.0001
7d vs. 21d	9.857	0.2718 to 19.44	Yes	*	0.0397
7d vs. 28d	12.81	3.222 to 22.39	Yes	**	0.0023
7d vs. 35d	6.233	-3.352 to 15.82	No	ns	0.4606
7d vs. 42d	10.44	0.8585 to 20.03	Yes	*	0.0235
7d vs. 49d	7.493	-2.092 to 17.08	No	ns	0.2335
7d vs. 56d	6.767	-2.818 to 16.35	No	ns	0.3545
14d vs. 21d	26.71	17.13 to 36.30	Yes	****	<0.0001
14d vs. 28d	29.66	20.08 to 39.25	Yes	****	<0.0001
14d vs. 35d	23.09	13.51 to 32.67	Yes	****	<0.0001
14d vs. 42d	27.3	17.72 to 36.88	Yes	****	<0.0001
14d vs. 49d	24.35	14.77 to 33.93	Yes	****	<0.0001
14d vs. 56d	23.62	14.04 to 33.21	Yes	****	<0.0001
21d vs. 28d	2.95	-6.635 to 12.53	No	ns	0.977
21d vs. 35d	-3.623	-13.21 to 5.962	No	ns	0.9315
21d vs. 42d	0.5867	-8.998 to 10.17	No	ns	>0.9999
21d vs. 49d	-2.363	-11.95 to 7.222	No	ns	0.9937
21d vs. 56d	-3.09	-12.67 to 6.495	No	ns	0.9702
28d vs. 35d	-6.573	-16.16 to 3.012	No	ns	0.3916
28d vs. 42d	-2.363	-11.95 to 7.222	No	ns	0.9937
28d vs. 49d	-5.313	-14.90 to 4.272	No	ns	0.6583
28d vs. 56d	-6.04	-15.62 to 3.545	No	ns	0.5016
35d vs. 42d	4.21	-5.375 to 13.79	No	ns	0.8612
35d vs. 49d	1.26	-8.325 to 10.84	No	ns	0.9999
35d vs. 56d	0.5333	-9.052 to 10.12	No	ns	>0.9999
42d vs. 49d	-2.95	-12.53 to 6.635	No	ns	0.977
42d vs. 56d	-3.677	-13.26 to 5.908	No	ns	0.9263
49d vs. 56d	-0.7267	-10.31 to 8.858	No	ns	>0.9999

Baseline % Brake Stance 10DegUp

Column B vs. Column A	Female vs. Male
Unpaired t test	
P value	0.136
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.657, df=8
How big is the difference?	
Mean of column A	23.26
Mean of column B	28.43
Difference between means (B - A) ± 5.168 ± 3.118	
95% confidence interval	-2.022 to 12.36
R squared (eta squared)	0.2556
F test to compare variances	
F, DFn, Dfd	1.191, 4, 4
P value	0.8696
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Brake Stance 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	19.19	<0.0001	****	Yes	Mean of Male	2.3
Time	11.1	0.0033	**	Yes	Mean of Female	-0.6004
Sex	3.506	0.4324	ns	No	Difference between means	2.9
Subject	41.04	<0.0001	****	Yes	SE of difference	3.508
					95% CI of difference	-5.190 to 10.99

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	7.829	-1.073 to 16.73	No	ns	0.0837
14d					
Male vs. Female	-13.86	-22.77 to -4.963	Yes	**	0.0028
21d					
Male vs. Female	7.735	-1.166 to 16.64	No	ns	0.0874
28d					
Male vs. Female	8.189	-0.7128 to 17.09	No	ns	0.0707
35d					
Male vs. Female	4.345	-4.556 to 13.25	No	ns	0.3331
42d					
Male vs. Female	0.5153	-8.386 to 9.417	No	ns	0.9083
49d					
Male vs. Female	4.675	-4.226 to 13.58	No	ns	0.298
56d					
Male vs. Female	3.779	-5.123 to 12.68	No	ns	0.3996
Male					
7d vs. 14d	4.313	-4.932 to 13.56	No	ns	0.8203
7d vs. 21d	-0.1667	-9.412 to 9.078	No	ns	>0.9999
7d vs. 28d	0.9433	-8.302 to 10.19	No	ns	>0.9999
7d vs. 35d	3.683	-5.562 to 12.93	No	ns	0.9114
7d vs. 42d	5.69	-3.555 to 14.94	No	ns	0.5319
7d vs. 49d	0.66	-8.585 to 9.905	No	ns	>0.9999
7d vs. 56d	0.36	-8.885 to 9.605	No	ns	>0.9999
14d vs. 21d	-4.48	-13.73 to 4.765	No	ns	0.7904
14d vs. 28d	-3.37	-12.62 to 5.875	No	ns	0.9429
14d vs. 35d	-0.63	-9.875 to 8.615	No	ns	>0.9999
14d vs. 42d	1.377	-7.868 to 10.62	No	ns	0.9998
14d vs. 49d	-3.653	-12.90 to 5.592	No	ns	0.9148
14d vs. 56d	-3.953	-13.20 to 5.292	No	ns	0.8768
21d vs. 28d	1.11	-8.135 to 10.36	No	ns	>0.9999
21d vs. 35d	3.85	-5.395 to 13.10	No	ns	0.8908
21d vs. 42d	5.857	-3.388 to 15.10	No	ns	0.4947
21d vs. 49d	0.8267	-8.418 to 10.07	No	ns	>0.9999
21d vs. 56d	0.5267	-8.718 to 9.772	No	ns	>0.9999
28d vs. 35d	2.74	-6.505 to 11.99	No	ns	0.9814
28d vs. 42d	4.747	-4.498 to 13.99	No	ns	0.7385
28d vs. 49d	-0.2833	-9.528 to 8.962	No	ns	>0.9999
28d vs. 56d	-0.5833	-9.828 to 8.662	No	ns	>0.9999
35d vs. 42d	2.007	-7.238 to 11.25	No	ns	0.9971
35d vs. 49d	-3.023	-12.27 to 6.222	No	ns	0.9678
35d vs. 56d	-3.323	-12.57 to 5.922	No	ns	0.9469
42d vs. 49d	-5.03	-14.28 to 4.215	No	ns	0.679
42d vs. 56d	-5.33	-14.58 to 3.915	No	ns	0.6128
49d vs. 56d	-0.3	-9.545 to 8.945	No	ns	>0.9999
Female					
7d vs. 14d	-17.38	-26.63 to -8.135	Yes	****	<0.0001
7d vs. 21d	-0.26	-9.505 to 8.985	No	ns	>0.9999
7d vs. 28d	1.303	-7.942 to 10.55	No	ns	0.9998
7d vs. 35d	0.2	-9.045 to 9.445	No	ns	>0.9999
7d vs. 42d	-1.623	-10.87 to 7.622	No	ns	0.9993
7d vs. 49d	-2.493	-11.74 to 6.752	No	ns	0.9892
7d vs. 56d	-3.69	-12.94 to 5.555	No	ns	0.9106
14d vs. 21d	17.12	7.875 to 26.37	Yes	****	<0.0001
14d vs. 28d	18.68	9.438 to 27.93	Yes	****	<0.0001
14d vs. 35d	17.58	8.335 to 26.83	Yes	****	<0.0001
14d vs. 42d	15.76	6.512 to 25.00	Yes	****	<0.0001
14d vs. 49d	14.89	5.642 to 24.13	Yes	***	0.0001
14d vs. 56d	13.69	4.445 to 22.94	Yes	***	0.0005
21d vs. 28d	1.563	-7.682 to 10.81	No	ns	0.9994
21d vs. 35d	0.46	-8.785 to 9.705	No	ns	>0.9999
21d vs. 42d	-1.363	-10.61 to 7.882	No	ns	0.9998
21d vs. 49d	-2.233	-11.48 to 7.012	No	ns	0.9944
21d vs. 56d	-3.43	-12.68 to 5.815	No	ns	0.9376
28d vs. 35d	-1.103	-10.35 to 8.142	No	ns	>0.9999
28d vs. 42d	-2.927	-12.17 to 6.318	No	ns	0.9731
28d vs. 49d	-3.797	-13.04 to 5.448	No	ns	0.8977
28d vs. 56d	-4.993	-14.24 to 4.252	No	ns	0.6869
35d vs. 42d	-1.823	-11.07 to 7.422	No	ns	0.9984
35d vs. 49d	-2.693	-11.94 to 6.552	No	ns	0.9831
35d vs. 56d	-3.89	-13.14 to 5.355	No	ns	0.8855
42d vs. 49d	-0.87	-10.12 to 8.375	No	ns	>0.9999
42d vs. 56d	-2.067	-11.31 to 7.178	No	ns	0.9966
49d vs. 56d	-1.197	-10.44 to 8.048	No	ns	>0.9999

Baseline % Brake Stance 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0152
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=3.075, df=8
How big is the difference?	
Mean of column A	22.01
Mean of column B	30.6
Difference between means (B - A)	±8.589 ± 2.793
95% confidence interval	2.148 to 15.03
R squared (eta squared)	0.5417
F test to compare variances	
F, DFn, Dfd	1.962, 4, 4
P value	0.53
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Propel Stance FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	17.72	<0.0001	****	Yes	Mean of Male	0.9136
Time	18.19	<0.0001	****	Yes	Mean of Female	-1.179
Sex	1.969	0.5536	ns	No	Difference between means	2.093
Subject	41.21	<0.0001	****	Yes	SE of difference	3.385
					95% CI of difference	-5.714 to 9.899

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.914	-9.217 to 7.389	No	ns	0.8266
14d					
Male vs. Female	17.99	9.683 to 26.29	Yes	****	<0.0001
21d					
Male vs. Female	4.166	-4.137 to 12.47	No	ns	0.32
28d					
Male vs. Female	-2.511	-10.81 to 5.792	No	ns	0.5479
35d					
Male vs. Female	-0.6873	-8.990 to 7.616	No	ns	0.8692
42d					
Male vs. Female	-0.4607	-8.764 to 7.842	No	ns	0.9121
49d					
Male vs. Female	0.3993	-7.904 to 8.702	No	ns	0.9238
56d					
Male vs. Female	-1.237	-9.540 to 7.066	No	ns	0.7669
Male					
7d vs. 14d	-6.51	-14.63 to 1.606	No	ns	0.2064
7d vs. 21d	-6.42	-14.54 to 1.696	No	ns	0.2209
7d vs. 28d	-5.563	-13.68 to 2.553	No	ns	0.3922
7d vs. 35d	-4.79	-12.91 to 3.326	No	ns	0.5844
7d vs. 42d	-7.29	-15.41 to 0.8260	No	ns	0.1086
7d vs. 49d	-6.33	-14.45 to 1.786	No	ns	0.236
7d vs. 56d	-3.627	-11.74 to 4.489	No	ns	0.8503
14d vs. 21d	0.09	-8.026 to 8.206	No	ns	>0.9999
14d vs. 28d	0.9467	-7.169 to 9.063	No	ns	>0.9999
14d vs. 35d	1.72	-6.396 to 9.836	No	ns	0.9975
14d vs. 42d	-0.78	-8.896 to 7.336	No	ns	>0.9999
14d vs. 49d	0.18	-7.936 to 8.296	No	ns	>0.9999
14d vs. 56d	2.883	-5.233 to 11.00	No	ns	0.95
21d vs. 28d	0.8567	-7.259 to 8.973	No	ns	>0.9999
21d vs. 35d	1.63	-6.486 to 9.746	No	ns	0.9982
21d vs. 42d	-0.87	-8.986 to 7.246	No	ns	>0.9999
21d vs. 49d	0.09	-8.026 to 8.206	No	ns	>0.9999
21d vs. 56d	2.793	-5.323 to 10.91	No	ns	0.9577
28d vs. 35d	0.7733	-7.343 to 8.889	No	ns	>0.9999
28d vs. 42d	-1.727	-9.843 to 6.389	No	ns	0.9975
28d vs. 49d	-0.7667	-8.883 to 7.349	No	ns	>0.9999
28d vs. 56d	1.937	-6.179 to 10.05	No	ns	0.9948
35d vs. 42d	-2.5	-10.62 to 5.616	No	ns	0.9769
35d vs. 49d	-1.54	-9.656 to 6.576	No	ns	0.9988
35d vs. 56d	1.163	-6.953 to 9.279	No	ns	0.9998
42d vs. 49d	0.96	-7.156 to 9.076	No	ns	>0.9999
42d vs. 56d	3.663	-4.453 to 11.78	No	ns	0.8437
49d vs. 56d	2.703	-5.413 to 10.82	No	ns	0.9645
Female					
7d vs. 14d	12.39	4.274 to 20.51	Yes	***	0.0003
7d vs. 21d	-1.34	-9.456 to 6.776	No	ns	0.9995
7d vs. 28d	-7.16	-15.28 to 0.9560	No	ns	0.1217
7d vs. 35d	-4.563	-12.68 to 3.553	No	ns	0.6422
7d vs. 42d	-6.837	-14.95 to 1.279	No	ns	0.1596
7d vs. 49d	-5.017	-13.13 to 3.099	No	ns	0.5264
7d vs. 56d	-3.95	-12.07 to 4.166	No	ns	0.7868
14d vs. 21d	-13.73	-21.85 to -5.614	Yes	****	<0.0001
14d vs. 28d	-19.55	-27.67 to -11.43	Yes	****	<0.0001
14d vs. 35d	-16.95	-25.07 to -8.837	Yes	****	<0.0001
14d vs. 42d	-19.23	-27.34 to -11.11	Yes	****	<0.0001
14d vs. 49d	-17.41	-25.52 to -9.291	Yes	****	<0.0001
14d vs. 56d	-16.34	-24.46 to -8.224	Yes	****	<0.0001
21d vs. 28d	-5.82	-13.94 to 2.296	No	ns	0.3349
21d vs. 35d	-3.223	-11.34 to 4.893	No	ns	0.9127
21d vs. 42d	-5.497	-13.61 to 2.619	No	ns	0.4078
21d vs. 49d	-3.677	-11.79 to 4.439	No	ns	0.8412
21d vs. 56d	-2.61	-10.73 to 5.506	No	ns	0.9706
28d vs. 35d	2.597	-5.519 to 10.71	No	ns	0.9715
28d vs. 42d	0.3233	-7.793 to 8.439	No	ns	>0.9999
28d vs. 49d	2.143	-5.973 to 10.26	No	ns	0.9905
28d vs. 56d	3.21	-4.906 to 11.33	No	ns	0.9144
35d vs. 42d	-2.273	-10.39 to 5.843	No	ns	0.9866
35d vs. 49d	-0.4533	-8.569 to 7.663	No	ns	>0.9999
35d vs. 56d	0.6133	-7.503 to 8.729	No	ns	>0.9999
42d vs. 49d	1.82	-6.296 to 9.936	No	ns	0.9965
42d vs. 56d	2.887	-5.229 to 11.00	No	ns	0.9497
49d vs. 56d	1.067	-7.049 to 9.183	No	ns	0.9999

Baseline % Propel Stance FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0619
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=2.169, df=8
How big is the difference?	
Mean of column A	75.66
Mean of column B	70.69
Difference between means (B - A) ±	±-4.971 ± 2.291
95% confidence interval	-10.25 to 0.3130
R squared (eta squared)	0.3704
F test to compare variances	
F, DFn, Dfd	9.456, 4, 4
P value	0.0514
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Propel Stance 100degUp										Baseline % Propel Stance 100degUp									
Source of Variation	% of total variation	P value	P value summary	Significant?	Mean of Male	0.7308	Mean of Female	0.06017	Column B	Female									
Time x Sex	29.57	<0.0001	****	Yes	Mean of Female	0.6707	Column A	ns	Male										
Time	8.82	<0.0001	****	Yes	Difference between means	0.6707													
Sex	0.1567	0.8126	ns	No	SE of difference	2.736													
Subject	20.86	<0.0001	****	Yes	95% CI of difference	-5.639 to 6.981													
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value				Unpaired t test	0.136									
									P value	ns									
									Significantly different (P < 0.05)?	No									
									One- or two-tailed P value?	Two-tailed t=1.657, df=8									
7d Male vs. Female	3.736	-4.154 to 11.63	No	ns	0.3478				How big is the difference?	76.74									
14d Male vs. Female	23.09	15.20 to 30.98	Yes	****	<0.0001				Mean of column A	71.57									
21d Male vs. Female	-3.158	-11.05 to 4.732	No	ns	0.4269				Difference between means (B - A) ± 5.168 ± 3.118										
28d Male vs. Female	-1.158	-11.05 to 4.732	No	ns	0.4269				95% confidence interval	-12.36 to 2.022									
35d Male vs. Female	-1.158	-11.05 to 4.732	No	ns	0.4269				R squared (eta squared)	0.2556									
42d Male vs. Female	-2.838	-10.73 to 5.052	No	ns	0.4751				F test to compare variances	1.191, 4, 4									
49d Male vs. Female	-2.728	-10.62 to 5.162	No	ns	0.4923				F, DFn, DdF	0.8996									
56d Male vs. Female	-2.888	-10.78 to 5.002	No	ns	0.4673				P value	ns									
Male									P value summary	ns									
7d vs. 14d	-2.493	-12.08 to 7.091	No	ns	0.9913				Significantly different (P < 0.05)?	No									
7d vs. 21d	-2.963	-12.55 to 6.621	No	ns	0.8764				One- or two-tailed P value?	Two-tailed t=1.657, df=8									
7d vs. 28d	1.03	-8.555 to 10.61	No	ns	>0.9999				How big is the difference?	76.74									
7d vs. 35d	-2.753	-12.34 to 6.831	No	ns	0.9844				Mean of column A	71.57									
7d vs. 42d	-3.88	-13.46 to 5.705	No	ns	0.9044				Difference between means (B - A) ± 5.168 ± 3.118										
7d vs. 49d	-1.03	-10.61 to 8.555	No	ns	>0.9999				95% confidence interval	-12.36 to 2.022									
7d vs. 56d	-0.1433	-9.728 to 9.441	No	ns	>0.9999				R squared (eta squared)	0.2556									
14d vs. 21d	-0.47	-10.05 to 9.115	No	ns	>0.9999				F test to compare variances	1.191, 4, 4									
14d vs. 28d	3.523	6.061 to 13.11	No	ns	0.9405				F, DFn, DdF	0.8996									
14d vs. 35d	-0.26	-9.845 to 9.325	No	ns	>0.9999				P value	ns									
14d vs. 42d	-1.387	-10.97 to 8.198	No	ns	0.9998				P value summary	ns									
14d vs. 49d	-1.463	-8.121 to 11.05	No	ns	0.9997				Significantly different (P < 0.05)?	No									
14d vs. 56d	2.35	-7.235 to 11.93	No	ns	0.9659				One- or two-tailed P value?	Two-tailed t=1.657, df=8									
21d vs. 28d	3.993	6.591 to 13.58	No	ns	0.8906				How big is the difference?	76.74									
21d vs. 35d	0.21	-9.375 to 9.795	No	ns	>0.9999				Mean of column A	71.57									
21d vs. 42d	-0.9167	-10.50 to 8.668	No	ns	>0.9999				Difference between means (B - A) ± 5.168 ± 3.118										
21d vs. 49d	1.933	-7.651 to 11.52	No	ns	0.9882				95% confidence interval	-12.36 to 2.022									
21d vs. 56d	2.82	-6.765 to 12.40	No	ns	0.9822				R squared (eta squared)	0.2556									
28d vs. 35d	-3.783	-13.37 to 5.801	No	ns	0.9153				F test to compare variances	1.191, 4, 4									
28d vs. 42d	-4.81	-14.49 to 4.875	No	ns	0.7407				F, DFn, DdF	0.8996									
28d vs. 49d	-2.06	-11.64 to 7.565	No	ns	0.9973				P value	ns									
28d vs. 56d	-1.173	-10.76 to 8.411	No	ns	>0.9999				P value summary	ns									
35d vs. 42d	-1.127	-10.71 to 8.458	No	ns	>0.9999				Significantly different (P < 0.05)?	No									
35d vs. 49d	1.723	-7.861 to 11.31	No	ns	0.9991				Data analyzed	5									
35d vs. 56d	2.61	-6.975 to 12.19	No	ns	0.9886				Sample size, column A	5									
42d vs. 49d	2.85	-6.735 to 12.43	No	ns	0.981				Sample size, column B	5									
42d vs. 56d	3.737	-5.848 to 13.32	No	ns	0.9202														
49d vs. 56d	0.8867	-8.698 to 10.47	No	ns	>0.9999														
Female																			
7d vs. 14d	16.86	7.272 to 26.44	Yes	****	<0.0001														
7d vs. 21d	-8.857	-19.44 to -0.2719	Yes	*	0.0397														
7d vs. 28d	-12.81	-22.39 to -3.222	Yes	**	0.0023														
7d vs. 35d	-6.233	-15.82 to 3.351	No	ns	0.4608														
7d vs. 42d	-10.45	-20.04 to -0.8685	Yes	*	0.0233														
7d vs. 49d	-7.493	-17.08 to 2.091	No	ns	0.2335														
7d vs. 56d	-6.767	-16.35 to 2.818	No	ns	0.3545														
14d vs. 21d	-26.71	-36.30 to -17.13	Yes	****	<0.0001														
14d vs. 28d	-29.65	-39.25 to -20.08	Yes	****	<0.0001														
14d vs. 35d	-23.09	-32.67 to -13.51	Yes	****	<0.0001														
14d vs. 42d	-27.31	-36.89 to -17.73	Yes	****	<0.0001														
14d vs. 49d	-24.35	-33.93 to -14.77	Yes	****	<0.0001														
14d vs. 56d	-23.62	-33.21 to -14.04	Yes	****	<0.0001														
21d vs. 28d	-2.95	-12.53 to 6.635	No	ns	0.877														
21d vs. 35d	3.623	-6.961 to 15.21	No	ns	0.9315														
21d vs. 42d	-0.5967	-10.18 to 8.988	No	ns	>0.9999														
21d vs. 49d	2.363	-7.221 to 11.95	No	ns	0.9937														
21d vs. 56d	3.09	-6.495 to 12.67	No	ns	0.9702														
28d vs. 35d	6.573	-3.011 to 16.16	No	ns	0.3916														
28d vs. 42d	2.353	-7.231 to 11.94	No	ns	0.9939														
28d vs. 49d	5.313	-4.271 to 14.90	No	ns	0.6583														
28d vs. 56d	6.04	-3.945 to 16.02	No	ns	0.5016														
35d vs. 42d	-4.22	-13.80 to 5.365	No	ns	0.8597														
35d vs. 49d	-1.26	-10.84 to 8.325	No	ns	0.9999														
35d vs. 56d	-0.5333	-10.12 to 9.051	No	ns	>0.9999														
42d vs. 49d	2.96	-6.625 to 12.54	No	ns	0.9765														
42d vs. 56d	3.687	-5.898 to 13.27	No	ns	0.9253														
49d vs. 56d	0.7267	-8.658 to 10.31	No	ns	>0.9999														
Test details	Mean 1	Mean 2	Mean Diff.	SE of diff.	N1	N2	q	DF											
7d Male vs. Female	-0.7983	-4.534	3.736	3.949		5	5	1.338	64										
14d Male vs. Female	1.695	-21.39	23.09	3.949		5	5	8.267	64										
21d Male vs. Female	2.165	5.323	-3.158	3.949		5	5	1.131	64										
28d Male vs. Female	-1.828	8.273	-10.1	3.949		5	5	3.617	64										
35d Male vs. Female	1.955	1.699	0.2557	3.949		5	5	0.09155	64										
42d Male vs. Female	3.082	5.919	-2.838	3.949		5	5	1.016	64										
49d Male vs. Female	0.2317	2.959	-2.728	3.949		5	5	0.9767	64										
56d Male vs. Female	-0.655	2.233	-2.888	3.949		5	5	1.034	64										
Male																			
7d vs. 14d	-0.7983	1.695	-2.493	3.044		5	5	1.158	56										
7d vs. 21d	-0.7983	2.165	-2.963	3.044		5	5	1.377	56										
7d vs. 28d	-0.7983	-1.628	1.03	3.044		5	5	0.4765	56										
7d vs. 35d	-0.7983	1.955	-2.753	3.044		5	5	1.279	56										
7d vs. 42d	-0.7983	3.082	-3.88	3.044		5	5	1.892	56										
7d vs. 49d	-0.7983	0.2317	-1.03	3.044		5	5	0.4785	56										
7d vs. 56d	-0.7983	-0.655	-0.1433	3.044		5	5	0.08658	56										
14d vs. 21d	1.695	2.165	-0.47	3.044		5	5	0.2183	56										
14d vs. 28d	1.695	-1.828	3.523	3.044		5	5	1.637	56										
14d vs. 35d	1.695	1.955	-0.26	3.044		5	5	0.1208	56										
14d vs. 42d	1.695	3.082	-1.387	3.044		5	5	0.6441	56										
14d vs. 49d	1.695	0.2317	1.463	3.044		5	5	0.6797	56										
14d vs. 56d	1.695	-0.655	-0.26	3.044		5	5	1.092	56										
21d vs. 28d	2.165	-1.828	3.993	3.044		5	5	1.855	56										
21d vs. 35d	2.165	1.955	0.21	3.044		5	5	0.09755	56										
21d vs. 42d	2.165	3.082	-0.9167	3.044		5	5	0.4258	56										
21d vs. 49d	2.165	0.2317	1.933	3.044		5	5	0.8981	56										
21d vs. 56d	2.165	-0.655	2.82	3.044		5	5	1.31	56										
28d vs. 35d	-1.828	1.955	-3.783	3.044		5	5	1.757	56										
28d vs. 42d	-1.828	3.082	-4.91	3.044		5	5	2.281	56										
28d vs. 49d	-1.828	0.2317	-2.06	3.044		5	5	0.9599	56										
28d vs. 56d	-1.828	-0.655	-1.173	3.044		5	5	0.545	56										
35d vs. 42d	1.955	3.082	-1.127	3.044		5	5	0.5234	56										
35d vs. 49d	1.955	0.2317	1.723	3.044		5	5	0.8005	56										
35d vs. 56d	1.955	-0.655	2.61	3.044		5	5	1.212	56										
42d vs. 49d	3.082	0.2317	2.85	3.044		5	5	1.324	56										
42d vs. 56d	3.082	-0.655	3.737	3.044		5	5	1.736	56										
49d vs. 56d	0.2317	-0.655	0.8867	3.044		5	5	0.4719	56										
Female																			
7d vs. 14d	-4.534	-21.39	16.86	3.044		5	5	7.83	56										
7d vs. 21d	-4.534	5.323	-9.857	3.044		5	5	4.579	56										
7d vs. 28d	-4.534	8.273	-12.81	3.044		5	5	5.949	56										
7d vs. 35d	-4.534	1.699	-6.233	3.044		5	5	2.896	56										
7d vs. 42d	-4.534	5.919	-10.45	3.044		5	5	4.856	56										
7d vs. 49d	-4.534	2.959	-7.493	3.044		5	5	3.481	56										
7d vs. 56d	-4.534	2.233	-6.767	3.044		5	5	3.143	56										
14d vs. 21d	-21.39	5.323	-26.71	3.044		5	5	12.41	56										
14d vs. 28d	-21.39	8.273	-29.65	3.044		5	5	13.78	56										
14d vs. 35d	-21.39	1.699	-23.09	3.044		5	5	10.73	56										
14d vs. 42d	-21.39	5.919	-27.31	3.044		5	5	12.69	56										
14d vs. 49d	-21.39	2.959	-24.35	3.044		5	5	11.31	56										
14d vs. 56d	-21.39	2.233	-23.62	3.044		5	5	10.87	56										
21d vs. 28d	5.323	8.273	-2.95	3.044		5	5	1.37	56										
21d vs. 35d	5.323	1.699	3.623	3.044		5	5	1.683	56										
21d vs. 42d	5.323	5.919</																	

Change in % Propel Stance 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	19.19	<0.0001	****	Yes	Mean of Male Mean of Female
Time	11.1	0.0033	**	Yes	Difference between means
Sex	3.506	0.4324	ns	No	SE of difference
Subject	41.04	<0.0001	****	Yes	95% CI of difference

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-7.829	-16.73 to 1.073	No	ns	0.0837
14d					
Male vs. Female	13.86	4.963 to 22.77	Yes	**	0.0028
21d					
Male vs. Female	-7.735	-16.64 to 1.166	No	ns	0.0874
28d					
Male vs. Female	-8.189	-17.09 to 0.7128	No	ns	0.0707
35d					
Male vs. Female	-4.345	-13.25 to 4.556	No	ns	0.3331
42d					
Male vs. Female	-0.5153	-9.417 to 8.386	No	ns	0.9083
49d					
Male vs. Female	-4.675	-13.58 to 4.226	No	ns	0.298
56d					
Male vs. Female	-3.779	-12.68 to 5.123	No	ns	0.3996
Male					
7d vs. 14d	-4.313	-13.56 to 4.932	No	ns	0.8203
7d vs. 21d	0.1667	-9.078 to 9.412	No	ns	>0.9999
7d vs. 28d	-0.9433	-10.19 to 8.302	No	ns	>0.9999
7d vs. 35d	-3.683	-12.93 to 5.562	No	ns	0.9114
7d vs. 42d	-5.69	-14.94 to 3.555	No	ns	0.5319
7d vs. 49d	-0.66	-9.905 to 8.585	No	ns	>0.9999
7d vs. 56d	-0.36	-9.605 to 8.885	No	ns	>0.9999
14d vs. 21d	4.48	-4.765 to 13.73	No	ns	0.7904
14d vs. 28d	3.37	-5.875 to 12.62	No	ns	0.9429
14d vs. 35d	0.63	-8.615 to 9.875	No	ns	>0.9999
14d vs. 42d	-1.377	-10.62 to 7.868	No	ns	0.9998
14d vs. 49d	3.653	-5.592 to 12.90	No	ns	0.9148
14d vs. 56d	3.953	-5.292 to 13.20	No	ns	0.8768
21d vs. 28d	-1.11	-10.36 to 8.135	No	ns	>0.9999
21d vs. 35d	-3.85	-13.10 to 5.395	No	ns	0.8908
21d vs. 42d	-5.657	-15.10 to 3.388	No	ns	0.4947
21d vs. 49d	-0.8267	-10.07 to 8.418	No	ns	>0.9999
21d vs. 56d	-0.5267	-9.772 to 8.718	No	ns	>0.9999
28d vs. 35d	-2.74	-11.99 to 6.505	No	ns	0.9814
28d vs. 42d	-4.747	-13.99 to 4.498	No	ns	0.7385
28d vs. 49d	0.2833	-8.962 to 9.528	No	ns	>0.9999
28d vs. 56d	0.5833	-8.662 to 9.828	No	ns	>0.9999
35d vs. 42d	-2.007	-11.25 to 7.238	No	ns	0.9971
35d vs. 49d	3.023	-6.222 to 12.27	No	ns	0.9678
35d vs. 56d	3.323	-5.922 to 12.57	No	ns	0.9469
42d vs. 49d	5.03	-4.215 to 14.28	No	ns	0.679
42d vs. 56d	5.33	-3.915 to 14.58	No	ns	0.6128
49d vs. 56d	0.3	-8.945 to 9.545	No	ns	>0.9999
Female					
7d vs. 14d	17.38	8.135 to 26.63	Yes	****	<0.0001
7d vs. 21d	0.26	-8.985 to 9.505	No	ns	>0.9999
7d vs. 28d	-1.303	-10.55 to 7.942	No	ns	0.9998
7d vs. 35d	-0.2	-9.445 to 9.045	No	ns	>0.9999
7d vs. 42d	1.623	-7.622 to 10.87	No	ns	0.9993
7d vs. 49d	2.493	-6.752 to 11.74	No	ns	0.9892
7d vs. 56d	3.69	-5.555 to 12.94	No	ns	0.9106
14d vs. 21d	-17.12	-26.37 to -7.875	Yes	****	<0.0001
14d vs. 28d	-18.68	-27.93 to -9.438	Yes	****	<0.0001
14d vs. 35d	-17.58	-26.83 to -8.335	Yes	****	<0.0001
14d vs. 42d	-15.76	-25.00 to -6.512	Yes	****	<0.0001
14d vs. 49d	-14.89	-24.13 to -5.642	Yes	***	0.0001
14d vs. 56d	-13.69	-22.94 to -4.445	Yes	***	0.0005
21d vs. 28d	-1.563	-10.81 to 7.682	No	ns	0.9994
21d vs. 35d	-0.46	-9.705 to 8.785	No	ns	>0.9999
21d vs. 42d	1.363	-7.882 to 10.61	No	ns	0.9998
21d vs. 49d	2.233	-7.012 to 11.48	No	ns	0.9944
21d vs. 56d	3.43	-5.815 to 12.68	No	ns	0.9376
28d vs. 35d	1.103	-8.142 to 10.35	No	ns	>0.9999
28d vs. 42d	2.927	-6.318 to 12.17	No	ns	0.9731
28d vs. 49d	3.797	-5.448 to 13.04	No	ns	0.8977
28d vs. 56d	4.993	-4.252 to 14.24	No	ns	0.6869
35d vs. 42d	1.823	-7.422 to 11.07	No	ns	0.9984
35d vs. 49d	2.693	-6.552 to 11.94	No	ns	0.9831
35d vs. 56d	3.89	-5.355 to 13.14	No	ns	0.8855
42d vs. 49d	0.87	-8.375 to 10.12	No	ns	>0.9999
42d vs. 56d	2.067	-7.178 to 11.31	No	ns	0.9966
49d vs. 56d	1.197	-8.048 to 10.44	No	ns	>0.9999

Baseline % Propel Stance 10DegDown

Column B vs. Column A	Female vs. Male
Unpaired t test	
P value	0.0152
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=3.075, df=8
How big is the difference?	
Mean of column A	77.99
Mean of column B	69.4
Difference between means (B - A) ± SEM	-8.589 ± 2.793
95% confidence interval	-15.03 to -2.148
R squared (eta squared)	0.5417
F test to compare variances	
F, DFn, Dfd	1.962, 4, 4
P value	0.53
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stance/Swing (#) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	2.773	0.7153	ns	No	Mean of Male	-0.01833
Time	14.11	0.0053	**	Yes	Mean of Female	0.05825
Sex	3.174	0.4771	ns	No	Difference between means	-0.07658
Subject	45.64	<0.0001	****	Yes	SE of difference	0.1027
					95% CI of difference	-0.3134 to 0.1602

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.08867	-0.3601 to 0.1828	No	ns	0.5164
14d					
Male vs. Female	-0.02533	-0.2968 to 0.2461	No	ns	0.8527
21d					
Male vs. Female	-0.062	-0.3335 to 0.2095	No	ns	0.6497
28d					
Male vs. Female	-0.082	-0.3535 to 0.1895	No	ns	0.5483
35d					
Male vs. Female	-0.1153	-0.3868 to 0.1561	No	ns	0.3992
42d					
Male vs. Female	0.07467	-0.1968 to 0.3461	No	ns	0.5846
49d					
Male vs. Female	-0.1753	-0.4468 to 0.09613	No	ns	0.2016
56d					
Male vs. Female	-0.1387	-0.4101 to 0.1328	No	ns	0.3113
Male					
7d vs. 14d	-0.2267	-0.5262 to 0.07290	No	ns	0.2702
7d vs. 21d	-0.19	-0.4896 to 0.1096	No	ns	0.4932
7d vs. 28d	-0.06333	-0.3629 to 0.2362	No	ns	0.9976
7d vs. 35d	-0.2067	-0.5062 to 0.09290	No	ns	0.3839
7d vs. 42d	-0.1767	-0.4762 to 0.1229	No	ns	0.5854
7d vs. 49d	-0.1933	-0.4929 to 0.1062	No	ns	0.4706
7d vs. 56d	-0.1833	-0.4829 to 0.1162	No	ns	0.5391
14d vs. 21d	0.03667	-0.2629 to 0.3362	No	ns	>0.9999
14d vs. 28d	0.1633	-0.1362 to 0.4629	No	ns	0.6767
14d vs. 35d	0.02	-0.2796 to 0.3196	No	ns	>0.9999
14d vs. 42d	0.05	-0.2496 to 0.3496	No	ns	0.9995
14d vs. 49d	0.03333	-0.2662 to 0.3329	No	ns	>0.9999
14d vs. 56d	0.04333	-0.2562 to 0.3429	No	ns	0.9998
21d vs. 28d	0.1267	-0.1729 to 0.4262	No	ns	0.8829
21d vs. 35d	-0.01667	-0.3162 to 0.2829	No	ns	>0.9999
21d vs. 42d	0.01333	-0.2862 to 0.3129	No	ns	>0.9999
21d vs. 49d	-0.003333	-0.3029 to 0.2962	No	ns	>0.9999
21d vs. 56d	0.006667	-0.2929 to 0.3062	No	ns	>0.9999
28d vs. 35d	-0.1433	-0.4429 to 0.1562	No	ns	0.8008
28d vs. 42d	-0.1133	-0.4129 to 0.1862	No	ns	0.9312
28d vs. 49d	-0.13	-0.4296 to 0.1696	No	ns	0.8684
28d vs. 56d	-0.12	-0.4196 to 0.1796	No	ns	0.9091
35d vs. 42d	0.03	-0.2696 to 0.3296	No	ns	>0.9999
35d vs. 49d	0.01333	-0.2862 to 0.3129	No	ns	>0.9999
35d vs. 56d	0.02333	-0.2762 to 0.3229	No	ns	>0.9999
42d vs. 49d	-0.01667	-0.3162 to 0.2829	No	ns	>0.9999
42d vs. 56d	-0.006667	-0.3062 to 0.2929	No	ns	>0.9999
49d vs. 56d	0.01	-0.2896 to 0.3096	No	ns	>0.9999
Female					
7d vs. 14d	-0.1633	-0.4629 to 0.1362	No	ns	0.6767
7d vs. 21d	-0.1633	-0.4629 to 0.1362	No	ns	0.6767
7d vs. 28d	-0.05667	-0.3562 to 0.2429	No	ns	0.9988
7d vs. 35d	-0.2333	-0.5329 to 0.06623	No	ns	0.2375
7d vs. 42d	-0.01333	-0.3129 to 0.2862	No	ns	>0.9999
7d vs. 49d	-0.28	-0.5796 to 0.01956	No	ns	0.0831
7d vs. 56d	-0.2333	-0.5329 to 0.06623	No	ns	0.2375
14d vs. 21d	0.000000008	-0.2996 to 0.2996	No	ns	>0.9999
14d vs. 28d	0.1067	-0.1929 to 0.4062	No	ns	0.9494
14d vs. 35d	-0.07	-0.3696 to 0.2296	No	ns	0.9955
14d vs. 42d	0.15	-0.1496 to 0.4496	No	ns	0.762
14d vs. 49d	-0.1167	-0.4162 to 0.1829	No	ns	0.9206
14d vs. 56d	-0.07	-0.3696 to 0.2296	No	ns	0.9955
21d vs. 28d	0.1067	-0.1929 to 0.4062	No	ns	0.9494
21d vs. 35d	-0.07	-0.3696 to 0.2296	No	ns	0.9955
21d vs. 42d	0.15	-0.1496 to 0.4496	No	ns	0.762
21d vs. 49d	-0.1167	-0.4162 to 0.1829	No	ns	0.9206
21d vs. 56d	-0.07	-0.3696 to 0.2296	No	ns	0.9955
28d vs. 35d	-0.1767	-0.4762 to 0.1229	No	ns	0.5854
28d vs. 42d	0.04333	-0.2562 to 0.3429	No	ns	0.9998
28d vs. 49d	-0.2233	-0.5229 to 0.07623	No	ns	0.2875
28d vs. 56d	-0.1767	-0.4762 to 0.1229	No	ns	0.5854
35d vs. 42d	0.22	-0.07956 to 0.5196	No	ns	0.3056
35d vs. 49d	-0.04667	-0.3462 to 0.2529	No	ns	0.9997
35d vs. 56d	0.000000006	-0.2996 to 0.2996	No	ns	>0.9999
42d vs. 49d	-0.2667	-0.5662 to 0.03290	No	ns	0.115
42d vs. 56d	-0.22	-0.5196 to 0.07956	No	ns	0.3056
49d vs. 56d	0.04667	-0.2529 to 0.3462	No	ns	0.9997

Baseline Stance/Swing (#) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2924
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.127, df=8
How big is the difference?	
Mean of column A	1.313
Mean of column B	1.215
Difference between means (B - A) ±	±0.09867 ± 0.08754
95% confidence interval	-0.3005 to 0.1032
R squared (eta squared)	0.137
F test to compare variances	
F, DFn, Dfd	1.511, 4, 4
P value	0.6988
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stance/Swing (#) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	5.077	0.2722	ns	No	Mean of Male	0.003333
Time	12.02	0.0086	**	Yes	Mean of Female	0.05392
Sex	1.264	0.6654	ns	No	Difference between means	-0.05058
Subject	50.15	<0.0001	****	Yes	SE of difference	0.1127
					95% CI of difference	-0.3104 to 0.2092

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.1093	-0.3965 to 0.1778	No	ns	0.4497
14d					
Male vs. Female	-0.1893	-0.4765 to 0.09784	No	ns	0.1925
21d					
Male vs. Female	0.06067	-0.2265 to 0.3478	No	ns	0.6744
28d					
Male vs. Female	0.08733	-0.1998 to 0.3745	No	ns	0.5456
35d					
Male vs. Female	-0.036	-0.3232 to 0.2512	No	ns	0.8031
42d					
Male vs. Female	-0.076	-0.3632 to 0.2112	No	ns	0.5988
49d					
Male vs. Female	0.044	-0.2432 to 0.3312	No	ns	0.7605
56d					
Male vs. Female	-0.186	-0.4732 to 0.1012	No	ns	0.2003
Male					
7d vs. 14d	-0.1167	-0.4171 to 0.1838	No	ns	0.9218
7d vs. 21d	-0.18	-0.4805 to 0.1205	No	ns	0.566
7d vs. 28d	-0.1733	-0.4738 to 0.1271	No	ns	0.6121
7d vs. 35d	-0.23	-0.5305 to 0.07047	No	ns	0.2569
7d vs. 42d	-0.18	-0.4805 to 0.1205	No	ns	0.566
7d vs. 49d	-0.26	-0.5605 to 0.04047	No	ns	0.1368
7d vs. 56d	-0.2333	-0.5338 to 0.06714	No	ns	0.2408
14d vs. 21d	-0.06333	-0.3638 to 0.2371	No	ns	0.9976
14d vs. 28d	-0.05667	-0.3571 to 0.2438	No	ns	0.9988
14d vs. 35d	-0.1133	-0.4138 to 0.1871	No	ns	0.9322
14d vs. 42d	-0.06333	-0.3638 to 0.2371	No	ns	0.9976
14d vs. 49d	-0.1433	-0.4438 to 0.1571	No	ns	0.8032
14d vs. 56d	-0.1167	-0.4171 to 0.1838	No	ns	0.9218
21d vs. 28d	0.006667	-0.2938 to 0.3071	No	ns	>0.9999
21d vs. 35d	-0.05	-0.3505 to 0.2505	No	ns	0.9995
21d vs. 42d	2.082E-17	-0.3005 to 0.3005	No	ns	>0.9999
21d vs. 49d	-0.08	-0.3805 to 0.2205	No	ns	0.99
21d vs. 56d	-0.05333	-0.3538 to 0.2471	No	ns	0.9992
28d vs. 35d	-0.05667	-0.3571 to 0.2438	No	ns	0.9988
28d vs. 42d	-0.006667	-0.3071 to 0.2938	No	ns	>0.9999
28d vs. 49d	-0.08667	-0.3871 to 0.2138	No	ns	0.9841
28d vs. 56d	-0.06	-0.3605 to 0.2405	No	ns	0.9983
35d vs. 42d	0.05	-0.2505 to 0.3505	No	ns	0.9995
35d vs. 49d	-0.03	-0.3305 to 0.2705	No	ns	>0.9999
35d vs. 56d	-0.003333	-0.3038 to 0.2971	No	ns	>0.9999
42d vs. 49d	-0.08	-0.3805 to 0.2205	No	ns	0.99
42d vs. 56d	-0.05333	-0.3538 to 0.2471	No	ns	0.9992
49d vs. 56d	0.02667	-0.2738 to 0.3271	No	ns	>0.9999
Female					
7d vs. 14d	-0.1967	-0.4971 to 0.1038	No	ns	0.4523
7d vs. 21d	-0.01	-0.3105 to 0.2905	No	ns	>0.9999
7d vs. 28d	0.02333	-0.2771 to 0.3238	No	ns	>0.9999
7d vs. 35d	-0.1567	-0.4571 to 0.1438	No	ns	0.7234
7d vs. 42d	-0.1467	-0.4471 to 0.1538	No	ns	0.7843
7d vs. 49d	-0.1067	-0.4071 to 0.1938	No	ns	0.9502
7d vs. 56d	-0.31	-0.6105 to -0.00952	Yes	*	0.0386
14d vs. 21d	0.1867	-0.1138 to 0.4871	No	ns	0.5199
14d vs. 28d	0.22	-0.08047 to 0.5205	No	ns	0.3092
14d vs. 35d	0.04	-0.2605 to 0.3405	No	ns	0.9999
14d vs. 42d	0.05	-0.2505 to 0.3505	No	ns	0.9995
14d vs. 49d	0.09	-0.2105 to 0.3905	No	ns	0.9802
14d vs. 56d	-0.1133	-0.4138 to 0.1871	No	ns	0.9322
21d vs. 28d	0.03333	-0.2671 to 0.3338	No	ns	>0.9999
21d vs. 35d	-0.1467	-0.4471 to 0.1538	No	ns	0.7843
21d vs. 42d	-0.1367	-0.4371 to 0.1638	No	ns	0.8385
21d vs. 49d	-0.09667	-0.3971 to 0.2038	No	ns	0.9706
21d vs. 56d	-0.3	-0.6005 to 0.00047	No	ns	0.0506
28d vs. 35d	-0.18	-0.4805 to 0.1205	No	ns	0.566
28d vs. 42d	-0.17	-0.4705 to 0.1305	No	ns	0.635
28d vs. 49d	-0.13	-0.4305 to 0.1705	No	ns	0.8702
28d vs. 56d	-0.3333	-0.6338 to -0.0328	Yes	*	0.0198
35d vs. 42d	0.01	-0.2905 to 0.3105	No	ns	>0.9999
35d vs. 49d	0.05	-0.2505 to 0.3505	No	ns	0.9995
35d vs. 56d	-0.1533	-0.4538 to 0.1471	No	ns	0.7444
42d vs. 49d	0.04	-0.2605 to 0.3405	No	ns	0.9999
42d vs. 56d	-0.1633	-0.4638 to 0.1371	No	ns	0.68
49d vs. 56d	-0.2033	-0.5038 to 0.09714	No	ns	0.4089

Baseline Stance/Swing (#) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.3715
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.9468, df=8
How big is the difference?	
Mean of column A	1.305
Mean of column B	1.202
Difference between means (B - A) ±	± -0.1027 ± 0.1084
95% confidence interval	-0.3527 to 0.1474
R squared (eta squared)	0.1008
F test to compare variances	
F, DFn, Dfd	1.843, 4, 4
P value	0.5683
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stance/Swing (#) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	7.117	0.0944	ns	No	-0.1067
Time	4.495	0.3332	ns	No	-0.0375
Sex	1.913	0.6147	ns	No	-0.06917
Subject	55.81	<0.0001	****	Yes	0.1321
					95% CI of difference -0.3737 to 0.2354
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.1367	-0.4651 to 0.1917	No	ns	0.4089
14d					
Male vs. Female	-0.09667	-0.4251 to 0.2317	No	ns	0.5586
21d					
Male vs. Female	0.05	-0.2784 to 0.3784	No	ns	0.762
28d					
Male vs. Female	0.07333	-0.2551 to 0.4017	No	ns	0.657
35d					
Male vs. Female	0.08	-0.2484 to 0.4084	No	ns	0.6282
42d					
Male vs. Female	-0.3267	-0.6551 to 0.00175	No	ns	0.0512
49d					
Male vs. Female	-0.02	-0.3484 to 0.3084	No	ns	0.9036
56d					
Male vs. Female	-0.1767	-0.5051 to 0.1517	No	ns	0.2866
Male					
7d vs. 14d	-0.16	-0.4895 to 0.1695	No	ns	0.7887
7d vs. 21d	-0.2	-0.5295 to 0.1295	No	ns	0.5494
7d vs. 28d	-0.2167	-0.5462 to 0.1128	No	ns	0.4462
7d vs. 35d	-0.27	-0.5995 to 0.05949	No	ns	0.1851
7d vs. 42d	-0.05667	-0.3862 to 0.2728	No	ns	0.9994
7d vs. 49d	-0.2367	-0.5662 to 0.09282	No	ns	0.3328
7d vs. 56d	-0.14	-0.4695 to 0.1895	No	ns	0.8803
14d vs. 21d	-0.04	-0.3695 to 0.2895	No	ns	>0.9999
14d vs. 28d	-0.05667	-0.3862 to 0.2728	No	ns	0.9994
14d vs. 35d	-0.11	-0.4395 to 0.2195	No	ns	0.964
14d vs. 42d	0.1033	-0.2262 to 0.4328	No	ns	0.9744
14d vs. 49d	-0.07667	-0.4062 to 0.2528	No	ns	0.9956
14d vs. 56d	0.02	-0.3095 to 0.3495	No	ns	>0.9999
21d vs. 28d	-0.01667	-0.3462 to 0.3128	No	ns	>0.9999
21d vs. 35d	-0.07	-0.3995 to 0.2595	No	ns	0.9975
21d vs. 42d	0.1433	-0.1862 to 0.4728	No	ns	0.8669
21d vs. 49d	-0.03667	-0.3662 to 0.2928	No	ns	>0.9999
21d vs. 56d	0.06	-0.2695 to 0.3895	No	ns	0.9991
28d vs. 35d	-0.05333	-0.3828 to 0.2762	No	ns	0.9996
28d vs. 42d	0.16	-0.1695 to 0.4895	No	ns	0.7887
28d vs. 49d	-0.02	-0.3495 to 0.3095	No	ns	>0.9999
28d vs. 56d	0.07667	-0.2528 to 0.4062	No	ns	0.9956
35d vs. 42d	0.2133	-0.1162 to 0.5428	No	ns	0.4664
35d vs. 49d	0.03333	-0.2962 to 0.3628	No	ns	>0.9999
35d vs. 56d	0.13	-0.1995 to 0.4595	No	ns	0.9154
42d vs. 49d	-0.18	-0.5095 to 0.1495	No	ns	0.6745
42d vs. 56d	-0.08333	-0.4128 to 0.2462	No	ns	0.9927
49d vs. 56d	0.09667	-0.2328 to 0.4262	No	ns	0.9824
Female					
7d vs. 14d	-0.12	-0.4495 to 0.2095	No	ns	0.9432
7d vs. 21d	-0.01333	-0.3428 to 0.3162	No	ns	>0.9999
7d vs. 28d	-0.006667	-0.3362 to 0.3228	No	ns	>0.9999
7d vs. 35d	-0.05333	-0.3828 to 0.2762	No	ns	0.9996
7d vs. 42d	-0.2467	-0.5762 to 0.08282	No	ns	0.2826
7d vs. 49d	-0.12	-0.4495 to 0.2095	No	ns	0.9432
7d vs. 56d	-0.18	-0.5095 to 0.1495	No	ns	0.6745
14d vs. 21d	0.1067	-0.2228 to 0.4362	No	ns	0.9695
14d vs. 28d	0.1133	-0.2162 to 0.4428	No	ns	0.9578
14d vs. 35d	0.06667	-0.2628 to 0.3962	No	ns	0.9982
14d vs. 42d	-0.1267	-0.4562 to 0.2028	No	ns	0.9255
14d vs. 49d	0.000000008	-0.3295 to 0.3295	No	ns	>0.9999
14d vs. 56d	-0.06	-0.3895 to 0.2695	No	ns	0.9991
21d vs. 28d	0.006667	-0.3228 to 0.3362	No	ns	>0.9999
21d vs. 35d	-0.04	-0.3695 to 0.2895	No	ns	>0.9999
21d vs. 42d	-0.2333	-0.5628 to 0.09615	No	ns	0.3506
21d vs. 49d	-0.1067	-0.4362 to 0.2228	No	ns	0.9695
21d vs. 56d	-0.1667	-0.4962 to 0.1628	No	ns	0.7526
28d vs. 35d	-0.04667	-0.3762 to 0.2828	No	ns	0.9998
28d vs. 42d	-0.24	-0.5695 to 0.08949	No	ns	0.3155
28d vs. 49d	-0.1133	-0.4428 to 0.2162	No	ns	0.9578
28d vs. 56d	-0.1733	-0.5028 to 0.1562	No	ns	0.7144
35d vs. 42d	-0.1933	-0.5228 to 0.1362	No	ns	0.5915
35d vs. 49d	-0.06667	-0.3962 to 0.2628	No	ns	0.9982
35d vs. 56d	-0.1267	-0.4562 to 0.2028	No	ns	0.9255
42d vs. 49d	0.1267	-0.2028 to 0.4562	No	ns	0.9255
42d vs. 56d	0.06667	-0.2628 to 0.3962	No	ns	0.9982
49d vs. 56d	-0.06	-0.3895 to 0.2695	No	ns	0.9991

Baseline Stance/Swing (#) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.96
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.05173, df=8
How big is the difference?	
Mean of column A	1.337
Mean of column B	1.33
Difference between means (B - A) ± SEM	-0.006667 ± 0.1289
95% confidence interval	-0.3038 to 0.2905
R squared (eta squared)	0.0003344
F test to compare variances	
F, DFn, Dfd	5.762, 4, 4
P value	0.1183
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stride Length (cm) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	0.8812	0.9157	ns	No	Mean of Male	0.1603
Time	3.304	0.2281	ns	No	Mean of Female	0.1403
Sex	0.01375	0.9707	ns	No	Difference between means	0.02
Subject	76.78	<0.0001	****	Yes	SE of difference	0.5285
					95% CI of difference	-1.199 to 1.239

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	0.05667	-1.123 to 1.236	No	ns	0.9238
14d					
Male vs. Female	-0.2767	-1.456 to 0.9026	No	ns	0.6409
21d					
Male vs. Female	0.1567	-1.023 to 1.336	No	ns	0.7916
28d					
Male vs. Female	0.17	-1.009 to 1.349	No	ns	0.7743
35d					
Male vs. Female	0.07667	-1.103 to 1.256	No	ns	0.8971
42d					
Male vs. Female	-0.1467	-1.326 to 1.033	No	ns	0.8046
49d					
Male vs. Female	0.2033	-0.9760 to 1.383	No	ns	0.7316
56d					
Male vs. Female	-0.08	-1.259 to 1.099	No	ns	0.8926
Male					
7d vs. 14d	-0.03333	-0.9187 to 0.8521	No	ns	>0.9999
7d vs. 21d	-0.1667	-1.052 to 0.7187	No	ns	0.9988
7d vs. 28d	-0.5533	-1.439 to 0.3321	No	ns	0.5123
7d vs. 35d	-0.2867	-1.172 to 0.5987	No	ns	0.9695
7d vs. 42d	-0.2567	-1.142 to 0.6287	No	ns	0.9836
7d vs. 49d	-0.49	-1.375 to 0.3954	No	ns	0.6602
7d vs. 56d	-0.3067	-1.192 to 0.5787	No	ns	0.9562
14d vs. 21d	-0.1333	-1.019 to 0.7521	No	ns	0.9997
14d vs. 28d	-0.52	-1.405 to 0.3654	No	ns	0.5904
14d vs. 35d	-0.2533	-1.139 to 0.6321	No	ns	0.9848
14d vs. 42d	-0.2233	-1.109 to 0.6621	No	ns	0.9928
14d vs. 49d	-0.4567	-1.342 to 0.4287	No	ns	0.7341
14d vs. 56d	-0.2733	-1.159 to 0.6121	No	ns	0.9766
21d vs. 28d	-0.3867	-1.272 to 0.4987	No	ns	0.8646
21d vs. 35d	-0.12	-1.005 to 0.7654	No	ns	0.9999
21d vs. 42d	-0.09	-0.9754 to 0.7954	No	ns	>0.9999
21d vs. 49d	-0.3233	-1.209 to 0.5621	No	ns	0.9424
21d vs. 56d	-0.14	-1.025 to 0.7454	No	ns	0.9996
28d vs. 35d	0.2667	-0.6187 to 1.152	No	ns	0.9796
28d vs. 42d	0.2967	-0.5887 to 1.182	No	ns	0.9633
28d vs. 49d	0.06333	-0.8221 to 0.9487	No	ns	>0.9999
28d vs. 56d	0.2467	-0.6387 to 1.132	No	ns	0.987
35d vs. 42d	0.03	-0.8554 to 0.9154	No	ns	>0.9999
35d vs. 49d	-0.2033	-1.089 to 0.6821	No	ns	0.9959
35d vs. 56d	-0.02	-0.9054 to 0.8654	No	ns	>0.9999
42d vs. 49d	-0.2333	-1.119 to 0.6521	No	ns	0.9906
42d vs. 56d	-0.05	-0.9354 to 0.8354	No	ns	>0.9999
49d vs. 56d	0.1833	-0.7021 to 1.069	No	ns	0.9979
Female					
7d vs. 14d	-0.3667	-1.252 to 0.5187	No	ns	0.8936
7d vs. 21d	-0.06667	-0.9521 to 0.8187	No	ns	>0.9999
7d vs. 28d	-0.44	-1.325 to 0.4454	No	ns	0.7688
7d vs. 35d	-0.2667	-1.152 to 0.6187	No	ns	0.9796
7d vs. 42d	-0.46	-1.345 to 0.4254	No	ns	0.727
7d vs. 49d	-0.3433	-1.229 to 0.5421	No	ns	0.9223
7d vs. 56d	-0.4433	-1.329 to 0.4421	No	ns	0.762
14d vs. 21d	0.3	-0.5854 to 1.185	No	ns	0.9611
14d vs. 28d	-0.07333	-0.9587 to 0.8121	No	ns	>0.9999
14d vs. 35d	0.1	-0.7854 to 0.9854	No	ns	>0.9999
14d vs. 42d	-0.09333	-0.9787 to 0.7921	No	ns	>0.9999
14d vs. 49d	0.02333	-0.8621 to 0.9087	No	ns	>0.9999
14d vs. 56d	-0.07667	-0.9621 to 0.8087	No	ns	>0.9999
21d vs. 28d	-0.3733	-1.259 to 0.5121	No	ns	0.8844
21d vs. 35d	-0.2	-1.085 to 0.6854	No	ns	0.9963
21d vs. 42d	-0.3933	-1.279 to 0.4921	No	ns	0.8541
21d vs. 49d	-0.2767	-1.162 to 0.6087	No	ns	0.9749
21d vs. 56d	-0.3767	-1.262 to 0.5087	No	ns	0.8796
28d vs. 35d	0.1733	-0.7121 to 1.059	No	ns	0.9985
28d vs. 42d	-0.02	-0.9054 to 0.8654	No	ns	>0.9999
28d vs. 49d	0.09667	-0.7887 to 0.9821	No	ns	>0.9999
28d vs. 56d	-0.003333	-0.8887 to 0.8821	No	ns	>0.9999
35d vs. 42d	-0.1933	-1.079 to 0.6921	No	ns	0.997
35d vs. 49d	-0.07667	-0.9621 to 0.8087	No	ns	>0.9999
35d vs. 56d	-0.1767	-1.062 to 0.7087	No	ns	0.9983
42d vs. 49d	0.1167	-0.7687 to 1.002	No	ns	0.9999
42d vs. 56d	0.01667	-0.8687 to 0.9021	No	ns	>0.9999
49d vs. 56d	-0.1	-0.9854 to 0.7854	No	ns	>0.9999

Baseline Stride Length (cm) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.6488
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.4730, df=8
How big is the difference?	
Mean of column A	7.321
Mean of column B	7.565
Difference between means (B - A) ± 0.2433 ± 0.5144	
95% confidence interval	-0.9429 to 1.430
R squared (eta squared)	0.02721
F test to compare variances	
F, DFn, Dfd	12.67, 4, 4
P value	0.0305
P value summary	*
Significantly different (P < 0.05)?	Yes
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stride Length (cm) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	5.81	0.2643	ns	No	Mean of Male	0.1733
Time	2.383	0.8036	ns	No	Mean of Female	0.5055
Sex	8.524	0.2661	ns	No	Difference between means	-0.3322
Subject	47.71	<0.0001	****	Yes	SE of difference	0.2778
					95% CI of difference	-0.9729 to 0.3085

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.3113	-1.045 to 0.4220	No	ns	0.3995
14d					
Male vs. Female	0.012	-0.7213 to 0.7453	No	ns	0.974
21d					
Male vs. Female	-0.6047	-1.338 to 0.1287	No	ns	0.1044
28d					
Male vs. Female	-0.728	-1.461 to 0.005340	No	ns	0.0516
35d					
Male vs. Female	-0.2313	-0.9647 to 0.5020	No	ns	0.5308
42d					
Male vs. Female	0.122	-0.6113 to 0.8553	No	ns	0.7407
49d					
Male vs. Female	-0.5013	-1.235 to 0.2320	No	ns	0.1768
56d					
Male vs. Female	-0.4147	-1.148 to 0.3187	No	ns	0.2629
Male					
7d vs. 14d	-0.3533	-1.161 to 0.4542	No	ns	0.8635
7d vs. 21d	-0.07333	-0.8808 to 0.7342	No	ns	>0.9999
7d vs. 28d	-0.1067	-0.9142 to 0.7008	No	ns	0.9999
7d vs. 35d	-0.2933	-1.101 to 0.5142	No	ns	0.9439
7d vs. 42d	-0.3833	-1.191 to 0.4242	No	ns	0.807
7d vs. 49d	-0.1533	-0.9608 to 0.6542	No	ns	0.9988
7d vs. 56d	-0.1033	-0.9108 to 0.7042	No	ns	>0.9999
14d vs. 21d	0.28	-0.5275 to 1.087	No	ns	0.956
14d vs. 28d	0.2467	-0.5608 to 1.054	No	ns	0.9779
14d vs. 35d	0.06	-0.7475 to 0.8675	No	ns	>0.9999
14d vs. 42d	-0.03	-0.8375 to 0.7775	No	ns	>0.9999
14d vs. 49d	0.2	-0.6075 to 1.007	No	ns	0.9935
14d vs. 56d	0.25	-0.5575 to 1.057	No	ns	0.9762
21d vs. 28d	-0.03333	-0.8408 to 0.7742	No	ns	>0.9999
21d vs. 35d	-0.22	-1.027 to 0.5875	No	ns	0.9886
21d vs. 42d	-0.31	-1.117 to 0.4975	No	ns	0.926
21d vs. 49d	-0.08	-0.8875 to 0.7275	No	ns	>0.9999
21d vs. 56d	-0.03	-0.8375 to 0.7775	No	ns	>0.9999
28d vs. 35d	-0.1867	-0.9942 to 0.6208	No	ns	0.9958
28d vs. 42d	-0.2767	-1.084 to 0.5308	No	ns	0.9587
28d vs. 49d	-0.04667	-0.8542 to 0.7608	No	ns	>0.9999
28d vs. 56d	0.003333	-0.8042 to 0.8108	No	ns	>0.9999
35d vs. 42d	-0.09	-0.8975 to 0.7175	No	ns	>0.9999
35d vs. 49d	0.14	-0.6675 to 0.9475	No	ns	0.9993
35d vs. 56d	0.19	-0.6175 to 0.9975	No	ns	0.9953
42d vs. 49d	0.23	-0.5775 to 1.037	No	ns	0.9852
42d vs. 56d	0.28	-0.5275 to 1.087	No	ns	0.956
49d vs. 56d	0.05	-0.7575 to 0.8575	No	ns	>0.9999
Female					
7d vs. 14d	-0.03	-0.8375 to 0.7775	No	ns	>0.9999
7d vs. 21d	-0.3667	-1.174 to 0.4408	No	ns	0.8396
7d vs. 28d	-0.5233	-1.331 to 0.2842	No	ns	0.4651
7d vs. 35d	-0.2133	-1.021 to 0.5942	No	ns	0.9905
7d vs. 42d	0.05	-0.7575 to 0.8575	No	ns	>0.9999
7d vs. 49d	-0.3433	-1.151 to 0.4642	No	ns	0.8799
7d vs. 56d	-0.2067	-1.014 to 0.6008	No	ns	0.9921
14d vs. 21d	-0.3367	-1.144 to 0.4708	No	ns	0.8903
14d vs. 28d	-0.4933	-1.301 to 0.3142	No	ns	0.5412
14d vs. 35d	-0.1833	-0.9908 to 0.6242	No	ns	0.9962
14d vs. 42d	0.08	-0.7275 to 0.8875	No	ns	>0.9999
14d vs. 49d	-0.3133	-1.121 to 0.4942	No	ns	0.922
14d vs. 56d	-0.1767	-0.9842 to 0.6308	No	ns	0.997
21d vs. 28d	-0.1567	-0.9642 to 0.6508	No	ns	0.9986
21d vs. 35d	0.1533	-0.6542 to 0.9608	No	ns	0.9988
21d vs. 42d	0.4167	-0.3908 to 1.224	No	ns	0.7337
21d vs. 49d	0.02333	-0.7842 to 0.8308	No	ns	>0.9999
21d vs. 56d	0.16	-0.6475 to 0.9675	No	ns	0.9984
28d vs. 35d	0.31	-0.4975 to 1.117	No	ns	0.926
28d vs. 42d	0.5733	-0.2342 to 1.381	No	ns	0.3473
28d vs. 49d	0.18	-0.6275 to 0.9875	No	ns	0.9966
28d vs. 56d	0.3167	-0.4908 to 1.124	No	ns	0.9179
35d vs. 42d	0.2633	-0.5442 to 1.071	No	ns	0.9683
35d vs. 49d	-0.13	-0.9375 to 0.6775	No	ns	0.9996
35d vs. 56d	0.006667	-0.8008 to 0.8142	No	ns	>0.9999
42d vs. 49d	-0.3933	-1.201 to 0.4142	No	ns	0.7861
42d vs. 56d	-0.2567	-1.064 to 0.5508	No	ns	0.9725
49d vs. 56d	0.1367	-0.6708 to 0.9442	No	ns	0.9994

Baseline Stride Length (cm) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.8742
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.1635, df=8
How big is the difference?	
Mean of column A	7.303
Mean of column B	7.255
Difference between means (B - A) ±	-0.04800 ± 0.2936
95% confidence interval	-0.7249 to 0.6289
R squared (eta squared)	0.003331
F test to compare variances	
F, DFn, Dfd	1.145, 4, 4
P value	0.8989
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stride Length (cm) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	5.365	0.2134	ns	No	Mean of Male	0.5142
Time	5.291	0.2211	ns	No	Mean of Female	0.3933
Sex	0.9411	0.7286	ns	No	Difference between means	0.1208
Subject	58.3	<0.0001	****	Yes	SE of difference	0.3363
					95% CI of difference	-0.6546 to 0.8962

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-0.1367	-0.4651 to 0.1917	No	ns	0.4089
14d					
Male vs. Female	-0.09667	-0.4251 to 0.2317	No	ns	0.5586
21d					
Male vs. Female	0.05	-0.2784 to 0.3784	No	ns	0.762
28d					
Male vs. Female	0.07333	-0.2551 to 0.4017	No	ns	0.657
35d					
Male vs. Female	0.08	-0.2484 to 0.4084	No	ns	0.6282
42d					
Male vs. Female	-0.3267	-0.6551 to 0.00175	No	ns	0.0512
49d					
Male vs. Female	-0.02	-0.3484 to 0.3084	No	ns	0.9036
56d					
Male vs. Female	-0.1767	-0.5051 to 0.1517	No	ns	0.2866
Male					
7d vs. 14d	-0.16	-0.4895 to 0.1695	No	ns	0.7887
7d vs. 21d	-0.2	-0.5295 to 0.1295	No	ns	0.5494
7d vs. 28d	-0.2167	-0.5462 to 0.1128	No	ns	0.4462
7d vs. 35d	-0.27	-0.5995 to 0.05949	No	ns	0.1851
7d vs. 42d	-0.05667	-0.3862 to 0.2728	No	ns	0.9994
7d vs. 49d	-0.2367	-0.5662 to 0.09282	No	ns	0.3328
7d vs. 56d	-0.14	-0.4695 to 0.1895	No	ns	0.8803
14d vs. 21d	-0.04	-0.3695 to 0.2895	No	ns	>0.9999
14d vs. 28d	-0.05667	-0.3862 to 0.2728	No	ns	0.9994
14d vs. 35d	-0.11	-0.4395 to 0.2195	No	ns	0.964
14d vs. 42d	0.1033	-0.2262 to 0.4328	No	ns	0.9744
14d vs. 49d	-0.07667	-0.4062 to 0.2528	No	ns	0.9956
14d vs. 56d	0.02	-0.3095 to 0.3495	No	ns	>0.9999
21d vs. 28d	-0.01667	-0.3462 to 0.3128	No	ns	>0.9999
21d vs. 35d	-0.07	-0.3995 to 0.2595	No	ns	0.9975
21d vs. 42d	0.1433	-0.1862 to 0.4728	No	ns	0.8669
21d vs. 49d	-0.03667	-0.3662 to 0.2928	No	ns	>0.9999
21d vs. 56d	0.06	-0.2695 to 0.3895	No	ns	0.9991
28d vs. 35d	-0.05333	-0.3828 to 0.2762	No	ns	0.9996
28d vs. 42d	0.16	-0.1695 to 0.4895	No	ns	0.7887
28d vs. 49d	-0.02	-0.3495 to 0.3095	No	ns	>0.9999
28d vs. 56d	0.07667	-0.2528 to 0.4062	No	ns	0.9956
35d vs. 42d	0.2133	-0.1162 to 0.5428	No	ns	0.4664
35d vs. 49d	0.03333	-0.2962 to 0.3628	No	ns	>0.9999
35d vs. 56d	0.13	-0.1995 to 0.4595	No	ns	0.9154
42d vs. 49d	-0.18	-0.5095 to 0.1495	No	ns	0.6745
42d vs. 56d	-0.08333	-0.4128 to 0.2462	No	ns	0.9927
49d vs. 56d	0.09667	-0.2328 to 0.4262	No	ns	0.9824
Female					
7d vs. 14d	-0.12	-0.4495 to 0.2095	No	ns	0.9432
7d vs. 21d	-0.01333	-0.3428 to 0.3162	No	ns	>0.9999
7d vs. 28d	-0.006667	-0.3362 to 0.3228	No	ns	>0.9999
7d vs. 35d	-0.05333	-0.3828 to 0.2762	No	ns	0.9996
7d vs. 42d	-0.2467	-0.5762 to 0.08282	No	ns	0.2826
7d vs. 49d	-0.12	-0.4495 to 0.2095	No	ns	0.9432
7d vs. 56d	-0.18	-0.5095 to 0.1495	No	ns	0.6745
14d vs. 21d	0.1067	-0.2228 to 0.4362	No	ns	0.9695
14d vs. 28d	0.1133	-0.2162 to 0.4428	No	ns	0.9578
14d vs. 35d	0.06667	-0.2628 to 0.3962	No	ns	0.9982
14d vs. 42d	-0.1267	-0.4562 to 0.2028	No	ns	0.9255
14d vs. 49d	0.000000008	-0.3295 to 0.3295	No	ns	>0.9999
14d vs. 56d	-0.06	-0.3895 to 0.2695	No	ns	0.9991
21d vs. 28d	0.006667	-0.3228 to 0.3362	No	ns	>0.9999
21d vs. 35d	-0.04	-0.3695 to 0.2895	No	ns	>0.9999
21d vs. 42d	-0.2333	-0.5628 to 0.09615	No	ns	0.3506
21d vs. 49d	-0.1067	-0.4362 to 0.2228	No	ns	0.9695
21d vs. 56d	-0.1667	-0.4962 to 0.1628	No	ns	0.7526
28d vs. 35d	-0.04667	-0.3762 to 0.2828	No	ns	0.9998
28d vs. 42d	-0.24	-0.5695 to 0.08949	No	ns	0.3155
28d vs. 49d	-0.1133	-0.4428 to 0.2162	No	ns	0.9578
28d vs. 56d	-0.1733	-0.5028 to 0.1562	No	ns	0.7144
35d vs. 42d	-0.1933	-0.5228 to 0.1362	No	ns	0.5915
35d vs. 49d	-0.06667	-0.3962 to 0.2628	No	ns	0.9982
35d vs. 56d	-0.1267	-0.4562 to 0.2028	No	ns	0.9255
42d vs. 49d	0.1267	-0.2028 to 0.4562	No	ns	0.9255
42d vs. 56d	0.06667	-0.2628 to 0.3962	No	ns	0.9982
49d vs. 56d	-0.06	-0.3895 to 0.2695	No	ns	0.9991

Baseline Stride Length (cm) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.7973
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.2655, df=8
How big is the difference?	
Mean of column A	7.177
Mean of column B	7.27
Difference between means (B - A) ± SEM	0.09333 ± 0.3515
95% confidence interval	-0.7173 to 0.9040
R squared (eta squared)	0.008734
F test to compare variances	
F, DFn, Dfd	1.281, 4, 4
P value	0.8162
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stride Frequency (steps/s) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	1.9	0.7739	ns	No	Mean of Male Mean of Female Difference between means SE of difference 95% CI of difference
Time	3.295	0.444	ns	No	-0.102 -0.2326 0.1306 0.304 -0.5703 to 0.8315
Sex	1.541	0.6788	ns	No	
Subject	66.79	<0.0001	****	Yes	

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.096	-0.6216 to 0.8136	No	ns	0.7901
14d					
Male vs. Female	0.3627	-0.3549 to 1.080	No	ns	0.3164
21d					
Male vs. Female	0.07267	-0.6449 to 0.7902	No	ns	0.8403
28d					
Male vs. Female	-0.1107	-0.8282 to 0.6069	No	ns	0.759
35d					
Male vs. Female	0.226	-0.4916 to 0.9436	No	ns	0.5315
42d					
Male vs. Female	0.2493	-0.4682 to 0.9669	No	ns	0.4901
49d					
Male vs. Female	-0.03067	-0.7482 to 0.6869	No	ns	0.9322
56d					
Male vs. Female	0.1793	-0.5382 to 0.8969	No	ns	0.6193
Male					
7d vs. 14d	0.05333	-0.5908 to 0.6974	No	ns	>0.9999
7d vs. 21d	0.08333	-0.5608 to 0.7274	No	ns	>0.9999
7d vs. 28d	0.4233	-0.2208 to 1.067	No	ns	0.4468
7d vs. 35d	0.1	-0.5441 to 0.7441	No	ns	0.9997
7d vs. 42d	0.1333	-0.5108 to 0.7774	No	ns	0.9979
7d vs. 49d	0.33	-0.3141 to 0.9741	No	ns	0.7406
7d vs. 56d	0.1033	-0.5408 to 0.7474	No	ns	0.9996
14d vs. 21d	0.03	-0.6141 to 0.6741	No	ns	>0.9999
14d vs. 28d	0.37	-0.2741 to 1.014	No	ns	0.6171
14d vs. 35d	0.04667	-0.5974 to 0.6908	No	ns	>0.9999
14d vs. 42d	0.08	-0.5641 to 0.7241	No	ns	>0.9999
14d vs. 49d	0.2767	-0.3674 to 0.9208	No	ns	0.8743
14d vs. 56d	0.05	-0.5941 to 0.6941	No	ns	>0.9999
21d vs. 28d	0.34	-0.3041 to 0.9841	No	ns	0.711
21d vs. 35d	0.01667	-0.6274 to 0.6608	No	ns	>0.9999
21d vs. 42d	0.05	-0.5941 to 0.6941	No	ns	>0.9999
21d vs. 49d	0.2467	-0.3974 to 0.8908	No	ns	0.9269
21d vs. 56d	0.02	-0.6241 to 0.6641	No	ns	>0.9999
28d vs. 35d	-0.3233	-0.9674 to 0.3208	No	ns	0.7597
28d vs. 42d	-0.29	-0.9341 to 0.3541	No	ns	0.8454
28d vs. 49d	-0.09333	-0.7374 to 0.5508	No	ns	0.9998
28d vs. 56d	-0.32	-0.9641 to 0.3241	No	ns	0.769
35d vs. 42d	0.03333	-0.6108 to 0.6774	No	ns	>0.9999
35d vs. 49d	0.23	-0.4141 to 0.8741	No	ns	0.9487
35d vs. 56d	0.003333	-0.6408 to 0.6474	No	ns	>0.9999
42d vs. 49d	0.1967	-0.4474 to 0.8408	No	ns	0.978
42d vs. 56d	-0.03	-0.6741 to 0.6141	No	ns	>0.9999
49d vs. 56d	-0.2267	-0.8708 to 0.4174	No	ns	0.9524
Female					
7d vs. 14d	0.32	-0.3241 to 0.9641	No	ns	0.769
7d vs. 21d	0.06	-0.5841 to 0.7041	No	ns	>0.9999
7d vs. 28d	0.2167	-0.4274 to 0.8608	No	ns	0.9625
7d vs. 35d	0.23	-0.4141 to 0.8741	No	ns	0.9487
7d vs. 42d	0.2867	-0.3574 to 0.9308	No	ns	0.8529
7d vs. 49d	0.2033	-0.4408 to 0.8474	No	ns	0.9735
7d vs. 56d	0.1867	-0.4574 to 0.8308	No	ns	0.9836
14d vs. 21d	-0.26	-0.9041 to 0.3841	No	ns	0.9057
14d vs. 28d	-0.1033	-0.7474 to 0.5408	No	ns	0.9996
14d vs. 35d	-0.09	-0.7341 to 0.5541	No	ns	0.9998
14d vs. 42d	-0.03333	-0.6774 to 0.6108	No	ns	>0.9999
14d vs. 49d	-0.1167	-0.7608 to 0.5274	No	ns	0.9991
14d vs. 56d	-0.1333	-0.7774 to 0.5108	No	ns	0.9979
21d vs. 28d	0.1567	-0.4874 to 0.8008	No	ns	0.9942
21d vs. 35d	0.17	-0.4741 to 0.8141	No	ns	0.9905
21d vs. 42d	0.2267	-0.4174 to 0.8708	No	ns	0.9524
21d vs. 49d	0.1433	-0.5008 to 0.7874	No	ns	0.9967
21d vs. 56d	0.1267	-0.5174 to 0.7708	No	ns	0.9985
28d vs. 35d	0.01333	-0.6308 to 0.6574	No	ns	>0.9999
28d vs. 42d	0.07	-0.5741 to 0.7141	No	ns	>0.9999
28d vs. 49d	-0.01333	-0.6574 to 0.6308	No	ns	>0.9999
28d vs. 56d	-0.03	-0.6741 to 0.6141	No	ns	>0.9999
35d vs. 42d	0.05667	-0.5874 to 0.7008	No	ns	>0.9999
35d vs. 49d	-0.02667	-0.6708 to 0.6174	No	ns	>0.9999
35d vs. 56d	-0.04333	-0.6874 to 0.6008	No	ns	>0.9999
42d vs. 49d	-0.08333	-0.7274 to 0.5608	No	ns	>0.9999
42d vs. 56d	-0.1	-0.7441 to 0.5441	No	ns	0.9997
49d vs. 56d	-0.01667	-0.6608 to 0.6274	No	ns	>0.9999

Baseline Stride Frequency (steps/s) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.8948
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.1365, df=8
How big is the difference?	
Mean of column A	5.469
Mean of column B	5.428
Difference between means (B - A) ±	± 0.04067 ± 0.2980
95% confidence interval	-0.7278 to 0.6465
R squared (eta squared)	0.002323
F test to compare variances	
F, DFn, Dfd	13.50, 4, 4
P value	0.0272
P value summary	*
Significantly different (P < 0.05)?	Yes
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stride Frequency (steps/s) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	3.348	0.5281	ns	No	Mean of Male -0.1667
Time	2.061	0.799	ns	No	Mean of Female -0.3837
Sex	5.223	0.4242	ns	No	Difference between means 0.217
Subject	58.94	<0.0001	****	Yes	SE of difference 0.2577 95% CI of difference -0.3773 to 0.8113

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.2003	-0.4336 to 0.8343	No	ns	0.5301
14d					
Male vs. Female	0.08367	-0.5503 to 0.7176	No	ns	0.7929
21d					
Male vs. Female	0.2537	-0.3803 to 0.8876	No	ns	0.4271
28d					
Male vs. Female	0.5103	-0.1236 to 1.144	No	ns	0.1127
35d					
Male vs. Female	0.2403	-0.3936 to 0.8743	No	ns	0.4516
42d					
Male vs. Female	-0.133	-0.7670 to 0.5010	No	ns	0.6765
49d					
Male vs. Female	0.3237	-0.3103 to 0.9576	No	ns	0.3116
56d					
Male vs. Female	0.257	-0.3770 to 0.8910	No	ns	0.421
Male					
7d vs. 14d	0.1033	-0.5199 to 0.7266	No	ns	0.9995
7d vs. 21d	0.08667	-0.5366 to 0.7099	No	ns	0.9998
7d vs. 28d	0.006667	-0.6166 to 0.6299	No	ns	>0.9999
7d vs. 35d	-0.006667	-0.6299 to 0.6166	No	ns	>0.9999
7d vs. 42d	0.1267	-0.4966 to 0.7499	No	ns	0.9981
7d vs. 49d	-0.05333	-0.6766 to 0.5699	No	ns	>0.9999
7d vs. 56d	-0.07667	-0.6999 to 0.5466	No	ns	>0.9999
14d vs. 21d	-0.01667	-0.6399 to 0.6066	No	ns	>0.9999
14d vs. 28d	-0.09667	-0.7199 to 0.5266	No	ns	0.9997
14d vs. 35d	-0.11	-0.7333 to 0.5133	No	ns	0.9992
14d vs. 42d	0.02333	-0.5999 to 0.6466	No	ns	>0.9999
14d vs. 49d	-0.1567	-0.7799 to 0.4666	No	ns	0.9929
14d vs. 56d	-0.18	-0.8033 to 0.4433	No	ns	0.984
21d vs. 28d	-0.08	-0.7033 to 0.5433	No	ns	>0.9999
21d vs. 35d	-0.09333	-0.7166 to 0.5299	No	ns	0.9997
21d vs. 42d	0.04	-0.5833 to 0.6633	No	ns	>0.9999
21d vs. 49d	-0.14	-0.7633 to 0.4833	No	ns	0.9965
21d vs. 56d	-0.1633	-0.7866 to 0.4599	No	ns	0.9909
28d vs. 35d	-0.01333	-0.6366 to 0.6099	No	ns	>0.9999
28d vs. 42d	0.12	-0.5033 to 0.7433	No	ns	0.9987
28d vs. 49d	-0.06	-0.6833 to 0.5633	No	ns	>0.9999
28d vs. 56d	-0.08333	-0.7066 to 0.5399	No	ns	0.9999
35d vs. 42d	0.1333	-0.4899 to 0.7566	No	ns	0.9974
35d vs. 49d	-0.04667	-0.6699 to 0.5766	No	ns	>0.9999
35d vs. 56d	0.07	-0.6933 to 0.5533	No	ns	>0.9999
42d vs. 49d	-0.18	-0.8033 to 0.4433	No	ns	0.984
42d vs. 56d	-0.2033	-0.8266 to 0.4199	No	ns	0.9682
49d vs. 56d	-0.02333	-0.6466 to 0.5999	No	ns	>0.9999
Female					
7d vs. 14d	-0.01333	-0.6366 to 0.6099	No	ns	>0.9999
7d vs. 21d	0.14	-0.4833 to 0.7633	No	ns	0.9965
7d vs. 28d	0.3167	-0.3066 to 0.9399	No	ns	0.7485
7d vs. 35d	0.03333	-0.5899 to 0.6566	No	ns	>0.9999
7d vs. 42d	-0.2067	-0.8299 to 0.4166	No	ns	0.9653
7d vs. 49d	0.07	-0.5533 to 0.6933	No	ns	>0.9999
7d vs. 56d	-0.02	-0.6433 to 0.6033	No	ns	>0.9999
14d vs. 21d	0.1533	-0.4699 to 0.7766	No	ns	0.9938
14d vs. 28d	0.33	-0.2933 to 0.9533	No	ns	0.7079
14d vs. 35d	0.04667	-0.5766 to 0.6699	No	ns	>0.9999
14d vs. 42d	-0.1933	-0.8166 to 0.4299	No	ns	0.9759
14d vs. 49d	0.08333	-0.5399 to 0.7066	No	ns	0.9999
14d vs. 56d	-0.006667	-0.6299 to 0.6166	No	ns	>0.9999
21d vs. 28d	0.1767	-0.4466 to 0.7999	No	ns	0.9856
21d vs. 35d	-0.1067	-0.7299 to 0.5166	No	ns	0.9994
21d vs. 42d	-0.3467	-0.9699 to 0.2766	No	ns	0.6545
21d vs. 49d	-0.07	-0.6933 to 0.5533	No	ns	>0.9999
21d vs. 56d	-0.16	-0.7833 to 0.4633	No	ns	0.992
28d vs. 35d	-0.2833	-0.9066 to 0.3399	No	ns	0.8389
28d vs. 42d	-0.5233	-1.147 to 0.09994	No	ns	0.1625
28d vs. 49d	-0.2467	-0.8699 to 0.3766	No	ns	0.9142
28d vs. 56d	-0.3367	-0.9599 to 0.2866	No	ns	0.6868
35d vs. 42d	-0.24	-0.8633 to 0.3833	No	ns	0.9249
35d vs. 49d	0.03667	-0.5866 to 0.6599	No	ns	>0.9999
35d vs. 56d	-0.05333	-0.6766 to 0.5699	No	ns	>0.9999
42d vs. 49d	0.2767	-0.3466 to 0.8999	No	ns	0.8546
42d vs. 56d	0.1867	-0.4366 to 0.8099	No	ns	0.9803
49d vs. 56d	-0.09	-0.7133 to 0.5333	No	ns	0.9998

Baseline Stride Frequency (steps/s) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.9238
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.09865, df=8
How big is the difference?	
Mean of column A	5.51
Mean of column B	5.537
Difference between means (B - A)	$\pm 0.02700 \pm 0.2737$
95% confidence interval	-0.6041 to 0.6581
R squared (eta squared)	0.001215
F test to compare variances	
F, DFn, Dfd	1.175, 4, 4
P value	0.8795
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stride Frequency (steps/s) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	3.506	0.4932 ns	No	No	-0.3998
Time	3.568	0.4812 ns	No	No	-0.1743
Sex	4.582	0.4499 ns	No	No	-0.2255
Subject	58.08	<0.0001	****	Yes	0.2839
					95% CI of difference -0.8801 to 0.4291
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.02533	-0.6741 to 0.7247	No	ns	0.9425
14d					
Male vs. Female	-0.3713	-1.071 to 0.3281	No	ns	0.2928
21d					
Male vs. Female	-0.1613	-0.8607 to 0.5381	No	ns	0.6465
28d					
Male vs. Female	-0.02467	-0.7241 to 0.6747	No	ns	0.944
35d					
Male vs. Female	-0.018	-0.7174 to 0.6814	No	ns	0.9592
42d					
Male vs. Female	-0.2913	-0.9907 to 0.4081	No	ns	0.4084
49d					
Male vs. Female	-0.528	-1.227 to 0.1714	No	ns	0.1364
56d					
Male vs. Female	-0.4347	-1.134 to 0.2647	No	ns	0.2189
Male					
7d vs. 14d	0.28	-0.4096 to 0.9696	No	ns	0.903
7d vs. 21d	0.25	-0.4396 to 0.9396	No	ns	0.9445
7d vs. 28d	0.25	-0.4396 to 0.9396	No	ns	0.9445
7d vs. 35d	0.28	-0.4096 to 0.9696	No	ns	0.903
7d vs. 42d	0.42	-0.2696 to 1.110	No	ns	0.5452
7d vs. 49d	0.6033	-0.08629 to 1.293	No	ns	0.128
7d vs. 56d	0.4433	-0.2463 to 1.133	No	ns	0.4757
14d vs. 21d	-0.03	-0.7196 to 0.6596	No	ns	>0.9999
14d vs. 28d	-0.03	-0.7196 to 0.6596	No	ns	>0.9999
14d vs. 35d	0.000000006	-0.6896 to 0.6896	No	ns	>0.9999
14d vs. 42d	0.14	-0.5496 to 0.8296	No	ns	0.9981
14d vs. 49d	0.3233	-0.3663 to 1.013	No	ns	0.8166
14d vs. 56d	0.1633	-0.5263 to 0.8530	No	ns	0.9951
21d vs. 28d	-0.000000006	-0.6896 to 0.6896	No	ns	>0.9999
21d vs. 35d	0.03	-0.6596 to 0.7196	No	ns	>0.9999
21d vs. 42d	0.17	-0.5196 to 0.8596	No	ns	0.9937
21d vs. 49d	0.3533	-0.3363 to 1.043	No	ns	0.7405
21d vs. 56d	0.1933	-0.4963 to 0.8830	No	ns	0.9865
28d vs. 35d	0.03	-0.6596 to 0.7196	No	ns	>0.9999
28d vs. 42d	0.17	-0.5196 to 0.8596	No	ns	0.9937
28d vs. 49d	0.3533	-0.3363 to 1.043	No	ns	0.7405
28d vs. 56d	0.1933	-0.4963 to 0.8830	No	ns	0.9865
35d vs. 42d	0.14	-0.5496 to 0.8296	No	ns	0.9981
35d vs. 49d	0.3233	-0.3663 to 1.013	No	ns	0.8166
35d vs. 56d	0.1633	-0.5263 to 0.8530	No	ns	0.9951
42d vs. 49d	0.1833	-0.5063 to 0.8730	No	ns	0.9901
42d vs. 56d	0.02333	-0.6663 to 0.7130	No	ns	>0.9999
49d vs. 56d	-0.16	-0.8496 to 0.5296	No	ns	0.9957
Female					
7d vs. 14d	-0.1167	-0.8063 to 0.5730	No	ns	0.9994
7d vs. 21d	0.06333	-0.6263 to 0.7530	No	ns	>0.9999
7d vs. 28d	0.2	-0.4896 to 0.8896	No	ns	0.9836
7d vs. 35d	0.2367	-0.4530 to 0.9263	No	ns	0.9583
7d vs. 42d	0.1033	-0.5863 to 0.7930	No	ns	0.9997
7d vs. 49d	0.05	-0.6396 to 0.7396	No	ns	>0.9999
7d vs. 56d	-0.01667	-0.7063 to 0.6730	No	ns	>0.9999
14d vs. 21d	0.18	-0.5096 to 0.8696	No	ns	0.9911
14d vs. 28d	0.3167	-0.3730 to 1.006	No	ns	0.8319
14d vs. 35d	0.3533	-0.3363 to 1.043	No	ns	0.7405
14d vs. 42d	0.22	-0.4696 to 0.9096	No	ns	0.9719
14d vs. 49d	0.1667	-0.5230 to 0.8563	No	ns	0.9944
14d vs. 56d	0.1	-0.5896 to 0.7896	No	ns	0.9998
21d vs. 28d	0.1367	-0.5530 to 0.8263	No	ns	0.9984
21d vs. 35d	0.1733	-0.5163 to 0.8630	No	ns	0.9929
21d vs. 42d	0.04	-0.6496 to 0.7296	No	ns	>0.9999
21d vs. 49d	-0.01333	-0.7030 to 0.6763	No	ns	>0.9999
21d vs. 56d	-0.08	-0.7696 to 0.6096	No	ns	>0.9999
28d vs. 35d	0.03667	-0.6530 to 0.7263	No	ns	>0.9999
28d vs. 42d	-0.09667	-0.7863 to 0.5930	No	ns	0.9998
28d vs. 49d	-0.15	-0.8396 to 0.5396	No	ns	0.9971
28d vs. 56d	-0.2167	-0.9063 to 0.4730	No	ns	0.9742
35d vs. 42d	-0.1333	-0.8230 to 0.5563	No	ns	0.9986
35d vs. 49d	-0.1867	-0.8763 to 0.5030	No	ns	0.989
35d vs. 56d	-0.2533	-0.9430 to 0.4363	No	ns	0.9407
42d vs. 49d	-0.05333	-0.7430 to 0.6363	No	ns	>0.9999
42d vs. 56d	-0.12	-0.8096 to 0.5696	No	ns	0.9993
49d vs. 56d	-0.06667	-0.7563 to 0.6230	No	ns	>0.9999

Baseline Stride Frequency (steps/s) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.5611
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.6064, df=8
How big is the difference?	
Mean of column A	5.597
Mean of column B	5.419
Difference between means (B - A) ± SEM	-0.1780 ± 0.2935
95% confidence interval	-0.8549 to 0.4989
R squared (eta squared)	0.04394
F test to compare variances	
F, DFn, Dfd	1.158, 4, 4
P value	0.8906
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Angle (deg) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	4.028	0.184	ns	No	Mean of Male	1.308
Time	21.09	<0.0001	****	Yes	Mean of Female	-1.828
Sex	12.23	0.1622	ns	No	Difference between means	3.136
Subject	41.26	<0.0001	****	Yes	SE of difference	2.036
					95% CI of difference	-1.560 to 7.831

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.3947	-4.618 to 5.407	No	ns	0.8755
14d					
Male vs. Female	5.605	0.5919 to 10.62	Yes	*	0.029
21d					
Male vs. Female	0.6447	-4.368 to 5.657	No	ns	0.7981
28d					
Male vs. Female	3.428	-1.585 to 8.441	No	ns	0.1767
35d					
Male vs. Female	3.311	-1.701 to 8.324	No	ns	0.1917
42d					
Male vs. Female	2.278	-2.735 to 7.291	No	ns	0.3674
49d					
Male vs. Female	5.085	0.07187 to 10.10	Yes	*	0.0469
56d					
Male vs. Female	4.338	-0.6748 to 9.351	No	ns	0.0887
Male					
7d vs. 14d	3.107	-1.828 to 8.041	No	ns	0.5028
7d vs. 21d	3.953	-0.9814 to 8.888	No	ns	0.2077
7d vs. 28d	1.603	-3.331 to 6.538	No	ns	0.9689
7d vs. 35d	1.993	-2.941 to 6.928	No	ns	0.9054
7d vs. 42d	2.94	-1.995 to 7.875	No	ns	0.5728
7d vs. 49d	5.103	0.1686 to 10.04	Yes	*	0.0378
7d vs. 56d	3.5	-1.435 to 8.435	No	ns	0.3487
14d vs. 21d	0.8467	-4.088 to 5.781	No	ns	0.9994
14d vs. 28d	-1.503	-6.438 to 3.431	No	ns	0.9783
14d vs. 35d	-1.113	-6.048 to 3.821	No	ns	0.9964
14d vs. 42d	-0.1667	-5.101 to 4.768	No	ns	>0.9999
14d vs. 49d	1.997	-2.938 to 6.931	No	ns	0.9046
14d vs. 56d	0.3933	-4.541 to 5.328	No	ns	>0.9999
21d vs. 28d	-2.35	-7.285 to 2.585	No	ns	0.8046
21d vs. 35d	-1.96	-6.895 to 2.975	No	ns	0.9127
21d vs. 42d	-1.013	-5.948 to 3.921	No	ns	0.998
21d vs. 49d	1.15	-3.785 to 6.085	No	ns	0.9955
21d vs. 56d	-0.4533	-5.388 to 4.481	No	ns	>0.9999
28d vs. 35d	0.39	-4.545 to 5.325	No	ns	>0.9999
28d vs. 42d	1.337	-3.598 to 6.271	No	ns	0.989
28d vs. 49d	3.5	-1.435 to 8.435	No	ns	0.3487
28d vs. 56d	1.897	-3.038 to 6.831	No	ns	0.9256
35d vs. 42d	0.9467	-3.988 to 5.891	No	ns	0.9987
35d vs. 49d	3.11	-1.825 to 8.045	No	ns	0.5014
35d vs. 56d	1.507	-3.428 to 6.441	No	ns	0.978
42d vs. 49d	2.163	-2.771 to 7.098	No	ns	0.8623
42d vs. 56d	0.56	-4.375 to 5.495	No	ns	>0.9999
49d vs. 56d	-1.603	-6.538 to 3.331	No	ns	0.9689
Female					
7d vs. 14d	8.317	3.382 to 13.25	Yes	****	<0.0001
7d vs. 21d	4.203	-0.7314 to 9.138	No	ns	0.1499
7d vs. 28d	4.637	-0.2981 to 9.571	No	ns	0.0801
7d vs. 35d	4.91	-0.02476 to 9.845	No	ns	0.0521
7d vs. 42d	4.823	-0.1114 to 9.758	No	ns	0.0599
7d vs. 49d	9.793	4.859 to 14.73	Yes	****	<0.0001
7d vs. 56d	7.443	2.509 to 12.38	Yes	***	0.0004
14d vs. 21d	-4.113	-9.048 to 0.8214	No	ns	0.1691
14d vs. 28d	-3.68	-8.615 to 1.255	No	ns	0.2872
14d vs. 35d	-3.407	-8.341 to 1.528	No	ns	0.3831
14d vs. 42d	-3.493	-8.428 to 1.441	No	ns	0.3511
14d vs. 49d	1.477	-3.458 to 6.411	No	ns	0.9804
14d vs. 56d	-0.8733	-5.808 to 4.061	No	ns	0.9992
21d vs. 28d	0.4333	-4.501 to 5.368	No	ns	>0.9999
21d vs. 35d	0.7067	-4.228 to 5.641	No	ns	0.9998
21d vs. 42d	0.62	-4.315 to 5.555	No	ns	>0.9999
21d vs. 49d	5.59	0.6552 to 10.52	Yes	*	0.016
21d vs. 56d	3.24	-1.695 to 8.175	No	ns	0.4482
28d vs. 35d	0.2733	-4.661 to 5.208	No	ns	>0.9999
28d vs. 42d	0.1867	-4.748 to 5.121	No	ns	>0.9999
28d vs. 49d	5.157	0.2219 to 10.09	Yes	*	0.0345
28d vs. 56d	2.807	-2.128 to 7.741	No	ns	0.6288
35d vs. 42d	-0.08667	-5.021 to 4.848	No	ns	>0.9999
35d vs. 49d	4.883	-0.05143 to 9.818	No	ns	0.0544
35d vs. 56d	2.533	-2.401 to 7.468	No	ns	0.7387
42d vs. 49d	4.97	0.03524 to 9.905	Yes	*	0.0472
42d vs. 56d	2.62	-2.315 to 7.555	No	ns	0.705
49d vs. 56d	-2.35	-7.285 to 2.585	No	ns	0.8046

Baseline Paw Angle (deg) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0152
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=3.075, df=8
How big is the difference?	
Mean of column A	15.06
Mean of column B	18.54
Difference between means (B - A) ± 3.471 ± 1.129	
95% confidence interval	0.8678 to 6.075
R squared (eta squared)	0.5416
F test to compare variances	
F, DFn, Dfd	1.373, 4, 4
P value	0.7662
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Angle (deg) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	9.226	0.0034	**	Yes	Mean of Male	2.085
Time	17.37	<0.0001	****	Yes	Mean of Female	0.2496
Sex	4.205	0.4279	ns	No	Difference between means	1.836
Subject	48.23	<0.0001	****	Yes	SE of difference	2.198
					95% CI of difference	-3.233 to 6.905

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-2.538	-7.799 to 2.722	No	ns	0.3387
14d					
Male vs. Female	7.468	2.208 to 12.73	Yes	**	0.0061
21d					
Male vs. Female	0.5283	-4.732 to 5.789	No	ns	0.8416
28d					
Male vs. Female	1.425	-3.835 to 6.685	No	ns	0.5903
35d					
Male vs. Female	-0.045	-5.305 to 5.215	No	ns	0.9864
42d					
Male vs. Female	2.418	-2.842 to 7.679	No	ns	0.3619
49d					
Male vs. Female	3.422	-1.839 to 8.682	No	ns	0.1985
56d					
Male vs. Female	2.008	-3.252 to 7.269	No	ns	0.4484
Male					
7d vs. 14d	0.7867	-4.093 to 5.666	No	ns	0.9996
7d vs. 21d	0.8267	-4.053 to 5.706	No	ns	0.9994
7d vs. 28d	1.787	-3.093 to 6.666	No	ns	0.9416
7d vs. 35d	1.643	-3.236 to 6.523	No	ns	0.9623
7d vs. 42d	1.88	-2.999 to 6.759	No	ns	0.9247
7d vs. 49d	2.643	-2.236 to 7.523	No	ns	0.6836
7d vs. 56d	3.23	-1.649 to 8.109	No	ns	0.4375
14d vs. 21d	0.04	-4.839 to 4.919	No	ns	>0.9999
14d vs. 28d	1	-3.879 to 5.879	No	ns	0.998
14d vs. 35d	0.8567	-4.023 to 5.736	No	ns	0.9993
14d vs. 42d	1.093	-3.786 to 5.973	No	ns	0.9965
14d vs. 49d	1.857	-3.023 to 6.736	No	ns	0.9292
14d vs. 56d	2.443	-2.436 to 7.323	No	ns	0.7619
21d vs. 28d	0.96	-3.919 to 5.839	No	ns	0.9985
21d vs. 35d	0.8167	-4.063 to 5.696	No	ns	0.9995
21d vs. 42d	1.053	-3.826 to 5.933	No	ns	0.9972
21d vs. 49d	1.817	-3.063 to 6.696	No	ns	0.9365
21d vs. 56d	2.403	-2.476 to 7.283	No	ns	0.7766
28d vs. 35d	-0.1433	-5.023 to 4.736	No	ns	>0.9999
28d vs. 42d	0.09333	-4.786 to 4.973	No	ns	>0.9999
28d vs. 49d	0.8567	-4.023 to 5.736	No	ns	0.9993
28d vs. 56d	1.443	-3.436 to 6.323	No	ns	0.9816
35d vs. 42d	0.2367	-4.843 to 5.116	No	ns	>0.9999
35d vs. 49d	1	-3.879 to 5.879	No	ns	0.998
35d vs. 56d	1.587	-3.293 to 6.466	No	ns	0.9688
42d vs. 49d	0.7633	-4.116 to 5.643	No	ns	0.9997
42d vs. 56d	1.35	-3.529 to 6.229	No	ns	0.9875
49d vs. 56d	0.5867	-4.293 to 5.466	No	ns	>0.9999
Female					
7d vs. 14d	10.79	5.914 to 15.67	Yes	****	<0.0001
7d vs. 21d	3.893	-0.9859 to 8.773	No	ns	0.2118
7d vs. 28d	5.75	0.8708 to 10.63	Yes	*	0.0105
7d vs. 35d	4.137	-0.7425 to 9.016	No	ns	0.1539
7d vs. 42d	6.837	1.957 to 11.72	Yes	**	0.0012
7d vs. 49d	8.603	3.724 to 13.48	Yes	****	<0.0001
7d vs. 56d	7.777	2.897 to 12.66	Yes	***	0.0001
14d vs. 21d	-6.9	-11.78 to -2.021	Yes	**	0.001
14d vs. 28d	-5.043	-9.923 to -0.1641	Yes	*	0.038
14d vs. 35d	-6.657	-11.54 to -1.777	Yes	**	0.0017
14d vs. 42d	-3.957	-8.836 to 0.9225	No	ns	0.1954
14d vs. 49d	-2.19	-7.069 to 2.689	No	ns	0.8474
14d vs. 56d	-3.017	-7.896 to 1.863	No	ns	0.5261
21d vs. 28d	1.857	-3.023 to 6.736	No	ns	0.9292
21d vs. 35d	0.2433	-4.636 to 5.123	No	ns	>0.9999
21d vs. 42d	2.943	-1.936 to 7.823	No	ns	0.5573
21d vs. 49d	4.71	-0.1692 to 9.589	No	ns	0.0658
21d vs. 56d	3.883	-0.9959 to 8.763	No	ns	0.2144
28d vs. 35d	-1.613	-6.493 to 3.266	No	ns	0.9658
28d vs. 42d	1.087	-3.793 to 5.966	No	ns	0.9966
28d vs. 49d	2.853	-2.026 to 7.733	No	ns	0.5956
28d vs. 56d	2.027	-2.853 to 6.906	No	ns	0.8921
35d vs. 42d	2.7	-2.179 to 7.579	No	ns	0.6603
35d vs. 49d	4.467	-0.4125 to 9.346	No	ns	0.0959
35d vs. 56d	3.64	-1.239 to 8.519	No	ns	0.2867
42d vs. 49d	1.767	-3.113 to 6.646	No	ns	0.9449
42d vs. 56d	0.94	-3.939 to 5.819	No	ns	0.9987
49d vs. 56d	-0.8267	-5.706 to 4.053	No	ns	0.9994

Baseline Paw Angle (deg) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.389
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.9108, df=8
How big is the difference?	
Mean of column A	13.71
Mean of column B	15.32
Difference between means (B - A) ± 1.605 ± 1.762	
95% confidence interval	-2.459 to 5.669
R squared (eta squared)	0.09395
F test to compare variances	
F, DFn, Dfd	2.869, 4, 4
P value	0.3317
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Angle (deg) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	6.684	0.0049	**	Yes	Mean of Male	2.63
Time	10.98	<0.0001	****	Yes	Mean of Female	-0.5808
Sex	11.25	0.2369	ns	No	Difference between means	3.211
Subject	55.04	<0.0001	****	Yes	SE of difference	2.512
					95% CI of difference	-2.581 to 9.003

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.3013	-6.004 to 5.401	No	ns	0.9163
14d					
Male vs. Female	8.795	3.093 to 14.50	Yes	**	0.003
21d					
Male vs. Female	1.932	-3.770 to 7.634	No	ns	0.5009
28d					
Male vs. Female	1.929	-3.774 to 7.631	No	ns	0.5017
35d					
Male vs. Female	4.372	-1.330 to 10.07	No	ns	0.1305
42d					
Male vs. Female	2.992	-2.710 to 8.694	No	ns	0.2985
49d					
Male vs. Female	3.589	-2.114 to 9.291	No	ns	0.2132
56d					
Male vs. Female	2.382	-3.320 to 8.084	No	ns	0.4071
Male					
7d vs. 14d	-0.4133	-4.978 to 4.152	No	ns	>0.9999
7d vs. 21d	0.4867	-4.078 to 5.052	No	ns	>0.9999
7d vs. 28d	0.39	-4.175 to 4.955	No	ns	>0.9999
7d vs. 35d	-2.997	-7.562 to 1.568	No	ns	0.4484
7d vs. 42d	0.3167	-4.248 to 4.882	No	ns	>0.9999
7d vs. 49d	1.927	-2.638 to 6.492	No	ns	0.8839
7d vs. 56d	1.477	-3.088 to 6.042	No	ns	0.9697
14d vs. 21d	0.9	-3.665 to 5.465	No	ns	0.9984
14d vs. 28d	0.8033	-3.762 to 5.368	No	ns	0.9993
14d vs. 35d	-2.583	-7.148 to 1.982	No	ns	0.6347
14d vs. 42d	0.73	-3.835 to 5.295	No	ns	0.9996
14d vs. 49d	2.34	-2.225 to 6.905	No	ns	0.7401
14d vs. 56d	1.89	-2.675 to 6.455	No	ns	0.8937
21d vs. 28d	-0.09667	-4.662 to 4.468	No	ns	>0.9999
21d vs. 35d	-3.483	-8.048 to 1.082	No	ns	0.2605
21d vs. 42d	-0.17	-4.735 to 4.395	No	ns	>0.9999
21d vs. 49d	1.44	-3.125 to 6.005	No	ns	0.9736
21d vs. 56d	0.99	-3.575 to 5.555	No	ns	0.9972
28d vs. 35d	-3.387	-7.952 to 1.178	No	ns	0.2933
28d vs. 42d	-0.07333	-4.638 to 4.492	No	ns	>0.9999
28d vs. 49d	1.537	-3.028 to 6.102	No	ns	0.9624
28d vs. 56d	1.087	-3.478 to 5.652	No	ns	0.9949
35d vs. 42d	3.313	-1.252 to 7.878	No	ns	0.3199
35d vs. 49d	4.923	0.3585 to 9.488	Yes	*	0.0259
35d vs. 56d	4.473	-0.09154 to 9.038	No	ns	0.0587
42d vs. 49d	1.61	-2.955 to 6.175	No	ns	0.9519
42d vs. 56d	1.16	-3.405 to 5.725	No	ns	0.9924
49d vs. 56d	-0.45	-5.015 to 4.115	No	ns	>0.9999
Female					
7d vs. 14d	8.683	4.118 to 13.25	Yes	****	<0.0001
7d vs. 21d	2.72	-1.845 to 7.285	No	ns	0.5726
7d vs. 28d	2.62	-1.945 to 7.185	No	ns	0.6181
7d vs. 35d	1.677	-2.888 to 6.242	No	ns	0.9407
7d vs. 42d	3.61	-0.9549 to 8.175	No	ns	0.2212
7d vs. 49d	5.817	1.252 to 10.38	Yes	**	0.0042
7d vs. 56d	4.16	-0.4049 to 8.725	No	ns	0.0988
14d vs. 21d	-5.963	-10.53 to -1.398	Yes	**	0.0031
14d vs. 28d	-6.063	-10.63 to -1.498	Yes	**	0.0025
14d vs. 35d	-7.007	-11.57 to -2.442	Yes	***	0.0003
14d vs. 42d	-5.073	-9.638 to -0.5085	Yes	*	0.0194
14d vs. 49d	-2.867	-7.432 to 1.698	No	ns	0.506
14d vs. 56d	-4.523	-9.088 to 0.04154	No	ns	0.0538
21d vs. 28d	-0.1	-4.665 to 4.465	No	ns	>0.9999
21d vs. 35d	-1.043	-5.608 to 3.522	No	ns	0.996
21d vs. 42d	0.89	-3.675 to 5.455	No	ns	0.9985
21d vs. 49d	3.097	-1.468 to 7.662	No	ns	0.4057
21d vs. 56d	1.44	-3.125 to 6.005	No	ns	0.9736
28d vs. 35d	-0.9433	-5.508 to 3.622	No	ns	0.9979
28d vs. 42d	0.99	-3.575 to 5.555	No	ns	0.9972
28d vs. 49d	3.197	-1.368 to 7.762	No	ns	0.3648
28d vs. 56d	1.54	-3.025 to 6.105	No	ns	0.9619
35d vs. 42d	1.933	-2.632 to 6.498	No	ns	0.8621
35d vs. 49d	4.14	-0.4249 to 8.705	No	ns	0.102
35d vs. 56d	2.483	-2.082 to 7.046	No	ns	0.6791
42d vs. 49d	2.207	-2.358 to 6.772	No	ns	0.7925
42d vs. 56d	0.55	-4.015 to 5.115	No	ns	>0.9999
49d vs. 56d	-1.657	-6.222 to 2.908	No	ns	0.9442

Baseline Paw Angle (deg) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0664
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=2.124, df=8
How big is the difference?	
Mean of column A	14.77
Mean of column B	17.95
Difference between means (B - A) ± SEM	3.175 ± 1.495
95% confidence interval	-0.2726 to 6.623
R squared (eta squared)	0.3605
F test to compare variances	
F, DFn, Dfd	1.857, 4, 4
P value	0.5635
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stance Width (cm) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	18.31	<0.0001	****	Yes	Mean of Male	0.1605
Time	6.7	0.0529	ns	No	Mean of Female	-0.1571
Sex	29.98	0.0086	**	Yes	Difference between means	0.3176
Subject	20.08	<0.0001	****	Yes	SE of difference	0.0919
					95% CI of difference	0.1057 to 0.5295

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.163	-0.1118 to 0.4378	No	ns	0.2405
14d					
Male vs. Female	0.953	0.6782 to 1.228	Yes	****	<0.0001
21d					
Male vs. Female	0.1663	-0.1085 to 0.4412	No	ns	0.2311
28d					
Male vs. Female	0.273	-0.001838 to 0.547	No	ns	0.0515
35d					
Male vs. Female	0.333	0.05816 to 0.6078	Yes	*	0.0183
42d					
Male vs. Female	0.143	-0.1318 to 0.4178	No	ns	0.3025
49d					
Male vs. Female	0.2263	-0.04851 to 0.5012	No	ns	0.1048
56d					
Male vs. Female	0.283	0.008162 to 0.5576	Yes	*	0.0438

Male					
7d vs. 14d	-0.3067	-0.6512 to 0.03792	No	ns	0.1152
7d vs. 21d	-0.07667	-0.4212 to 0.2679	No	ns	0.9967
7d vs. 28d	-0.1133	-0.4579 to 0.2312	No	ns	0.9668
7d vs. 35d	-0.27	-0.6146 to 0.07458	No	ns	0.231
7d vs. 42d	-0.06667	-0.4112 to 0.2779	No	ns	0.9986
7d vs. 49d	-0.14	-0.4846 to 0.2046	No	ns	0.9027
7d vs. 56d	-0.1533	-0.4979 to 0.1912	No	ns	0.853
14d vs. 21d	0.23	-0.1146 to 0.5746	No	ns	0.4267
14d vs. 28d	0.1933	-0.1512 to 0.5379	No	ns	0.6446
14d vs. 35d	0.03667	-0.3079 to 0.3812	No	ns	>0.9999
14d vs. 42d	0.24	-0.1046 to 0.5846	No	ns	0.3717
14d vs. 49d	0.1667	-0.1779 to 0.5112	No	ns	0.792
14d vs. 56d	0.1533	-0.1912 to 0.4979	No	ns	0.853
21d vs. 28d	-0.03667	-0.3812 to 0.3079	No	ns	>0.9999
21d vs. 35d	-0.1933	-0.5379 to 0.1512	No	ns	0.6446
21d vs. 42d	0.01	-0.3346 to 0.3546	No	ns	>0.9999
21d vs. 49d	-0.06333	-0.4079 to 0.2812	No	ns	0.999
21d vs. 56d	-0.07667	-0.4212 to 0.2679	No	ns	0.9967
28d vs. 35d	-0.1567	-0.5012 to 0.1879	No	ns	0.8388
28d vs. 42d	0.04667	-0.2979 to 0.3912	No	ns	0.9999
28d vs. 49d	-0.02667	-0.3712 to 0.3179	No	ns	>0.9999
28d vs. 56d	-0.04	-0.3846 to 0.3046	No	ns	>0.9999
35d vs. 42d	0.2033	-0.1412 to 0.5479	No	ns	0.5846
35d vs. 49d	0.13	-0.2146 to 0.4746	No	ns	0.9321
35d vs. 56d	0.1167	-0.2279 to 0.4612	No	ns	0.9612
42d vs. 49d	-0.07333	-0.4179 to 0.2712	No	ns	0.9975
42d vs. 56d	-0.08667	-0.4312 to 0.2579	No	ns	0.9929
49d vs. 56d	-0.01333	-0.3579 to 0.3312	No	ns	>0.9999

Female					
7d vs. 14d	0.4833	0.1388 to 0.8279	Yes	**	0.0011
7d vs. 21d	-0.07333	-0.4179 to 0.2712	No	ns	0.9975
7d vs. 28d	-0.003333	-0.3479 to 0.3412	No	ns	>0.9999
7d vs. 35d	-0.1	-0.4446 to 0.2446	No	ns	0.9835
7d vs. 42d	-0.08667	-0.4312 to 0.2579	No	ns	0.9929
7d vs. 49d	-0.07667	-0.4212 to 0.2679	No	ns	0.9967
7d vs. 56d	-0.03333	-0.3779 to 0.3112	No	ns	>0.9999
14d vs. 21d	-0.5567	-0.9012 to -0.2121	Yes	***	0.0001
14d vs. 28d	-0.4867	-0.8312 to -0.1421	Yes	**	0.001
14d vs. 35d	-0.5833	-0.9279 to -0.2388	Yes	****	<0.0001
14d vs. 42d	-0.57	-0.9146 to -0.2254	Yes	****	<0.0001
14d vs. 49d	-0.56	-0.9046 to -0.2154	Yes	***	0.0001
14d vs. 56d	-0.5167	-0.8612 to -0.1721	Yes	***	0.0004
21d vs. 28d	0.07	-0.2746 to 0.4146	No	ns	0.9981
21d vs. 35d	-0.02667	-0.3712 to 0.3179	No	ns	>0.9999
21d vs. 42d	-0.01333	-0.3579 to 0.3312	No	ns	>0.9999
21d vs. 49d	-0.003333	-0.3479 to 0.3412	No	ns	>0.9999
21d vs. 56d	0.04	-0.3046 to 0.3846	No	ns	>0.9999
28d vs. 35d	-0.09667	-0.4412 to 0.2479	No	ns	0.9864
28d vs. 42d	-0.08333	-0.4279 to 0.2612	No	ns	0.9944
28d vs. 49d	-0.07333	-0.4179 to 0.2712	No	ns	0.9975
28d vs. 56d	-0.03	-0.3746 to 0.3146	No	ns	>0.9999
35d vs. 42d	0.01333	-0.3312 to 0.3579	No	ns	>0.9999
35d vs. 49d	0.02333	-0.3212 to 0.3679	No	ns	>0.9999
35d vs. 56d	0.06667	-0.2779 to 0.4112	No	ns	0.9986
42d vs. 49d	0.01	-0.3346 to 0.3546	No	ns	>0.9999
42d vs. 56d	0.05333	-0.2912 to 0.3979	No	ns	0.9997
49d vs. 56d	0.04333	-0.3012 to 0.3879	No	ns	>0.9999

Baseline Stance Width (cm) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.6243
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.5092, df=8
How big is the difference?	
Mean of column A	2.26
Mean of column B	2.187
Difference between means (B - A) ±	±0.07367 ± 0.1447
95% confidence interval	-0.4073 to 0.2599
R squared (eta squared)	0.0314
F test to compare variances	
F, DFn, Dfd	1.623, 4, 4
P value	0.6505
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stance Width (cm) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	9.887	0.022	*	Yes	Mean of Male	-0.1042
Time	11.05	0.0119	*	Yes	Mean of Female	-0.1332
Sex	0.2189	0.8537	ns	No	Difference between means	0.029
Subject	48.27	<0.0001	****	Yes	SE of difference	0.1523
					95% CI of difference	-0.3221 to 0.3801

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-0.1943	-0.5831 to 0.1944	No	ns	0.3217
14d					
Male vs. Female	0.4723	0.08359 to 0.8611	Yes	*	0.018
21d					
Male vs. Female	-0.03433	-0.4231 to 0.3544	No	ns	0.8605
28d					
Male vs. Female	-0.09767	-0.4864 to 0.2911	No	ns	0.6175
35d					
Male vs. Female	0.1057	-0.2831 to 0.4944	No	ns	0.589
42d					
Male vs. Female	-0.06433	-0.4531 to 0.3244	No	ns	0.742
49d					
Male vs. Female	-0.08433	-0.4731 to 0.3044	No	ns	0.6662
56d					
Male vs. Female	0.129	-0.2597 to 0.5177	No	ns	0.5098
Male					
7d vs. 14d	-0.15	-0.5578 to 0.2578	No	ns	0.9403
7d vs. 21d	-0.1667	-0.5745 to 0.2411	No	ns	0.9
7d vs. 28d	-0.18	-0.5878 to 0.2278	No	ns	0.8581
7d vs. 35d	-0.2833	-0.6911 to 0.1245	No	ns	0.3749
7d vs. 42d	-0.1867	-0.5945 to 0.2211	No	ns	0.8341
7d vs. 49d	-0.1567	-0.5645 to 0.2511	No	ns	0.9258
7d vs. 56d	-0.2967	-0.7045 to 0.1111	No	ns	0.3171
14d vs. 21d	-0.01667	-0.4245 to 0.3911	No	ns	>0.9999
14d vs. 28d	-0.03	-0.4378 to 0.3778	No	ns	>0.9999
14d vs. 35d	-0.1333	-0.5411 to 0.2745	No	ns	0.9679
14d vs. 42d	-0.03667	-0.4445 to 0.3711	No	ns	>0.9999
14d vs. 49d	-0.006667	-0.4145 to 0.4011	No	ns	>0.9999
14d vs. 56d	-0.1467	-0.5545 to 0.2611	No	ns	0.9468
21d vs. 28d	-0.01333	-0.4211 to 0.3945	No	ns	>0.9999
21d vs. 35d	-0.1167	-0.5245 to 0.2911	No	ns	0.9848
21d vs. 42d	-0.02	-0.4278 to 0.3878	No	ns	>0.9999
21d vs. 49d	0.01	-0.3978 to 0.4178	No	ns	>0.9999
21d vs. 56d	-0.13	-0.5378 to 0.2778	No	ns	0.972
28d vs. 35d	-0.1033	-0.5111 to 0.3045	No	ns	0.9926
28d vs. 42d	-0.006667	-0.4145 to 0.4011	No	ns	>0.9999
28d vs. 49d	0.02333	-0.3845 to 0.4311	No	ns	>0.9999
28d vs. 56d	-0.1167	-0.5245 to 0.2911	No	ns	0.9848
35d vs. 42d	0.09667	-0.3111 to 0.5045	No	ns	0.9951
35d vs. 49d	0.1267	-0.2811 to 0.5345	No	ns	0.9758
35d vs. 56d	-0.01333	-0.4211 to 0.3945	No	ns	>0.9999
42d vs. 49d	0.03	-0.3778 to 0.4378	No	ns	>0.9999
42d vs. 56d	-0.11	-0.5178 to 0.2978	No	ns	0.9892
49d vs. 56d	-0.14	-0.5478 to 0.2678	No	ns	0.9582
Female					
7d vs. 14d	0.5167	0.1089 to 0.9245	Yes	**	0.0045
7d vs. 21d	-0.006667	-0.4145 to 0.4011	No	ns	>0.9999
7d vs. 28d	-0.08333	-0.4911 to 0.3245	No	ns	0.998
7d vs. 35d	0.01667	-0.3911 to 0.4245	No	ns	>0.9999
7d vs. 42d	-0.05667	-0.4645 to 0.3511	No	ns	0.9998
7d vs. 49d	-0.04667	-0.4545 to 0.3611	No	ns	>0.9999
7d vs. 56d	0.02667	-0.3811 to 0.4345	No	ns	>0.9999
14d vs. 21d	-0.5233	-0.9311 to -0.1155	Yes	**	0.0038
14d vs. 28d	-0.6	-1.008 to -0.1922	Yes	***	0.0006
14d vs. 35d	-0.5	-0.9078 to -0.0922	Yes	**	0.0067
14d vs. 42d	-0.5733	-0.9811 to -0.1655	Yes	**	0.0011
14d vs. 49d	-0.5633	-0.9711 to -0.1555	Yes	**	0.0014
14d vs. 56d	-0.49	-0.8978 to -0.0822	Yes	**	0.0085
21d vs. 28d	-0.07667	-0.4845 to 0.3311	No	ns	0.9989
21d vs. 35d	0.02333	-0.3845 to 0.4311	No	ns	>0.9999
21d vs. 42d	-0.05	-0.4578 to 0.3578	No	ns	>0.9999
21d vs. 49d	-0.04	-0.4478 to 0.3678	No	ns	>0.9999
21d vs. 56d	0.03333	-0.3745 to 0.4411	No	ns	>0.9999
28d vs. 35d	0.1	-0.3078 to 0.5078	No	ns	0.9939
28d vs. 42d	0.02667	-0.3811 to 0.4345	No	ns	>0.9999
28d vs. 49d	0.03667	-0.3711 to 0.4445	No	ns	>0.9999
28d vs. 56d	0.11	-0.2978 to 0.5178	No	ns	0.9892
35d vs. 42d	-0.07333	-0.4811 to 0.3345	No	ns	0.9991
35d vs. 49d	-0.06333	-0.4711 to 0.3445	No	ns	0.9997
35d vs. 56d	0.01	-0.3978 to 0.4178	No	ns	>0.9999
42d vs. 49d	0.01	-0.3978 to 0.4178	No	ns	>0.9999
42d vs. 56d	0.08333	-0.3245 to 0.4911	No	ns	0.998
49d vs. 56d	0.07333	-0.3345 to 0.4811	No	ns	0.9991

Baseline Stance Width (cm) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0586
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=2.204, df=8
How big is the difference?	
Mean of column A	2.372
Mean of column B	2.064
Difference between means (B - A) ±	±-0.3077 ± 0.1396
95% confidence interval	-0.6295 to 0.01418
R squared (eta squared)	0.3779
F test to compare variances	
F, DFn, Dfd	1.097, 4, 4
P value	0.9306
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Stance Width (cm) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	12.43		0.0218 *	Yes	-0.004583
Time	27.04	<0.0001	****	Yes	-0.04467
Sex	0.5142	0.6742	ns	No	0.04008
Subject	21.62	0.0009	***	Yes	0.0919
					95% CI of difference -0.1718 to 0.2520
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.03533	-0.3412 to 0.2705	No	ns	0.8182
14d					
Male vs. Female	0.5113	0.2055 to 0.8172	Yes	**	0.0014
21d					
Male vs. Female	-0.09867	-0.4045 to 0.2072	No	ns	0.5216
28d					
Male vs. Female	-0.082	-0.3879 to 0.2239	No	ns	0.5941
35d					
Male vs. Female	0.1747	-0.1312 to 0.4805	No	ns	0.2582
42d					
Male vs. Female	0.01133	-0.2945 to 0.3172	No	ns	0.9412
49d					
Male vs. Female	-0.05867	-0.3645 to 0.2472	No	ns	0.7028
56d					
Male vs. Female	-0.102	-0.4079 to 0.2039	No	ns	0.5077
Male					
7d vs. 14d	0.000000006	-0.4121 to 0.4121	No	ns	>0.9999
7d vs. 21d	-0.05	-0.4621 to 0.3621	No	ns	>0.9999
7d vs. 28d	-0.06667	-0.4788 to 0.3455	No	ns	0.9996
7d vs. 35d	-0.3167	-0.7288 to 0.09546	No	ns	0.2526
7d vs. 42d	-0.2	-0.6121 to 0.2121	No	ns	0.7892
7d vs. 49d	-0.1533	-0.5655 to 0.2588	No	ns	0.9367
7d vs. 56d	-0.11	-0.5221 to 0.3021	No	ns	0.9899
14d vs. 21d	-0.05	-0.4621 to 0.3621	No	ns	>0.9999
14d vs. 28d	-0.06667	-0.4788 to 0.3455	No	ns	0.9996
14d vs. 35d	-0.3167	-0.7288 to 0.09546	No	ns	0.2526
14d vs. 42d	-0.2	-0.6121 to 0.2121	No	ns	0.7892
14d vs. 49d	-0.1533	-0.5655 to 0.2588	No	ns	0.9367
14d vs. 56d	-0.11	-0.5221 to 0.3021	No	ns	0.9899
21d vs. 28d	-0.01667	-0.4288 to 0.3955	No	ns	>0.9999
21d vs. 35d	-0.2667	-0.6798 to 0.1455	No	ns	0.4672
21d vs. 42d	-0.15	-0.5621 to 0.2621	No	ns	0.9434
21d vs. 49d	-0.1033	-0.5155 to 0.3088	No	ns	0.993
21d vs. 56d	-0.06	-0.4721 to 0.3521	No	ns	0.9988
28d vs. 35d	-0.25	-0.6621 to 0.1621	No	ns	0.5503
28d vs. 42d	-0.1333	-0.5455 to 0.2788	No	ns	0.9697
28d vs. 49d	-0.08667	-0.4988 to 0.3255	No	ns	0.9977
28d vs. 56d	-0.04333	-0.4555 to 0.3688	No	ns	>0.9999
35d vs. 42d	0.1167	-0.2955 to 0.5288	No	ns	0.9857
35d vs. 49d	0.1633	-0.2488 to 0.5755	No	ns	0.9136
35d vs. 56d	0.2067	-0.2055 to 0.6188	No	ns	0.7606
42d vs. 49d	0.04667	-0.3655 to 0.4588	No	ns	>0.9999
42d vs. 56d	0.09	-0.3221 to 0.5021	No	ns	0.997
49d vs. 56d	0.04333	-0.3688 to 0.4555	No	ns	>0.9999
Female					
7d vs. 14d	0.5467	0.1345 to 0.9588	Yes	**	0.0025
7d vs. 21d	-0.1133	-0.5255 to 0.2988	No	ns	0.9879
7d vs. 28d	-0.1133	-0.5255 to 0.2988	No	ns	0.9879
7d vs. 35d	-0.1067	-0.5188 to 0.3055	No	ns	0.9916
7d vs. 42d	-0.1533	-0.5655 to 0.2588	No	ns	0.9367
7d vs. 49d	-0.1767	-0.5888 to 0.2355	No	ns	0.8754
7d vs. 56d	-0.1767	-0.5888 to 0.2355	No	ns	0.8754
14d vs. 21d	-0.66	-1.072 to -0.2479	Yes	***	0.0001
14d vs. 28d	-0.66	-1.072 to -0.2479	Yes	***	0.0001
14d vs. 35d	-0.6533	-1.065 to -0.2412	Yes	***	0.0002
14d vs. 42d	-0.7	-1.112 to -0.2879	Yes	****	<0.0001
14d vs. 49d	-0.7233	-1.135 to -0.3112	Yes	****	<0.0001
14d vs. 56d	-0.7233	-1.135 to -0.3112	Yes	****	<0.0001
21d vs. 28d	0.000000006	-0.4121 to 0.4121	No	ns	>0.9999
21d vs. 35d	0.006667	-0.4055 to 0.4188	No	ns	>0.9999
21d vs. 42d	-0.04	-0.4521 to 0.3721	No	ns	>0.9999
21d vs. 49d	-0.06333	-0.4755 to 0.3488	No	ns	0.9997
21d vs. 56d	-0.06333	-0.4755 to 0.3488	No	ns	0.9997
28d vs. 35d	0.006667	-0.4055 to 0.4188	No	ns	>0.9999
28d vs. 42d	-0.04	-0.4521 to 0.3721	No	ns	>0.9999
28d vs. 49d	-0.06333	-0.4755 to 0.3488	No	ns	0.9997
28d vs. 56d	-0.06333	-0.4755 to 0.3488	No	ns	0.9997
35d vs. 42d	-0.04667	-0.4588 to 0.3655	No	ns	>0.9999
35d vs. 49d	-0.07	-0.4821 to 0.3421	No	ns	0.9994
35d vs. 56d	-0.07	-0.4821 to 0.3421	No	ns	0.9994
42d vs. 49d	-0.02333	-0.4355 to 0.3888	No	ns	>0.9999
42d vs. 56d	-0.02333	-0.4355 to 0.3888	No	ns	>0.9999
49d vs. 56d	-0.000000002	-0.4121 to 0.4121	No	ns	>0.9999

Baseline Stance Width (cm) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0215
P value summary	*
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=2.848, df=8
How big is the difference?	
Mean of column A	2.493
Mean of column B	2.208
Difference between means (B - A) ± SEM	-0.2853 ± 0.1002
95% confidence interval	-0.5164 to -0.05432
R squared (eta squared)	0.5035
F test to compare variances	
F, DFn, Dfd	2.451, 4, 4
P value	0.04065
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Angle at Peak Stance (cm*2) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	17.44	<0.0001	****	Yes	Mean of Male -0.01078
Time	17.59	<0.0001	****	Yes	Mean of Female 0.0001083
Sex	0.1364	0.8775	ns	No	Difference between means -0.01089
Subject	43.1	<0.0001	****	Yes	SE of difference 0.06844
					95% CI of difference -0.1687 to 0.1469

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.0416	-0.2093 to 0.1261	No	ns	0.6219
14d					
Male vs. Female	0.2971	0.1294 to 0.4647	Yes	***	0.0008
21d					
Male vs. Female	-0.1076	-0.2753 to 0.06008	No	ns	0.2045
28d					
Male vs. Female	-0.09493	-0.2626 to 0.07275	No	ns	0.2623
35d					
Male vs. Female	0.02207	-0.1456 to 0.1897	No	ns	0.7935
42d					
Male vs. Female	-0.01393	-0.1816 to 0.1537	No	ns	0.8687
49d					
Male vs. Female	-0.07827	-0.2459 to 0.08942	No	ns	0.3546
56d					
Male vs. Female	-0.06993	-0.2376 to 0.09775	No	ns	0.4078
Male					
7d vs. 14d	-0.1053	-0.2689 to 0.05822	No	ns	0.4733
7d vs. 21d	-0.025	-0.1886 to 0.1386	No	ns	0.9997
7d vs. 28d	0.004	-0.1596 to 0.1676	No	ns	>0.9999
7d vs. 35d	-0.181	-0.3446 to -0.0174	Yes	*	0.0203
7d vs. 42d	-0.109	-0.2726 to 0.05455	No	ns	0.4287
7d vs. 49d	-0.05233	-0.2159 to 0.1112	No	ns	0.9714
7d vs. 56d	-0.08133	-0.2449 to 0.08222	No	ns	0.7682
14d vs. 21d	0.08033	-0.08322 to 0.2439	No	ns	0.779
14d vs. 28d	0.1093	-0.05422 to 0.2729	No	ns	0.4247
14d vs. 35d	-0.07567	-0.2392 to 0.08789	No	ns	0.8265
14d vs. 42d	-0.003667	-0.1672 to 0.1599	No	ns	>0.9999
14d vs. 49d	0.053	-0.1106 to 0.2166	No	ns	0.9694
14d vs. 56d	0.024	-0.1396 to 0.1876	No	ns	0.9998
21d vs. 28d	0.029	-0.1346 to 0.1926	No	ns	0.9992
21d vs. 35d	-0.156	-0.3196 to 0.00755	No	ns	0.0719
21d vs. 42d	-0.084	-0.2476 to 0.07955	No	ns	0.7382
21d vs. 49d	-0.02733	-0.1909 to 0.1362	No	ns	0.9995
21d vs. 56d	-0.05633	-0.2199 to 0.1072	No	ns	0.9575
28d vs. 35d	-0.185	-0.3486 to -0.0214	Yes	*	0.0163
28d vs. 42d	-0.113	-0.2766 to 0.05055	No	ns	0.382
28d vs. 49d	-0.05633	-0.2199 to 0.1072	No	ns	0.9575
28d vs. 56d	-0.08533	-0.2489 to 0.07822	No	ns	0.7228
35d vs. 42d	0.072	-0.09155 to 0.2366	No	ns	0.8598
35d vs. 49d	0.1287	-0.03489 to 0.2922	No	ns	0.2267
35d vs. 56d	0.09967	-0.06389 to 0.2632	No	ns	0.5445
42d vs. 49d	0.05667	-0.1069 to 0.2202	No	ns	0.9562
42d vs. 56d	0.02767	-0.1359 to 0.1912	No	ns	0.9994
49d vs. 56d	-0.029	-0.1926 to 0.1346	No	ns	0.9992
Female					
7d vs. 14d	0.2333	0.06978 to 0.3969	Yes	***	0.0009
7d vs. 21d	-0.091	-0.2546 to 0.07255	No	ns	0.6542
7d vs. 28d	-0.04933	-0.2129 to 0.1142	No	ns	0.9794
7d vs. 35d	-0.1173	-0.2809 to 0.04622	No	ns	0.3343
7d vs. 42d	-0.08133	-0.2449 to 0.08222	No	ns	0.7682
7d vs. 49d	-0.089	-0.2526 to 0.07455	No	ns	0.6788
7d vs. 56d	-0.1097	-0.2732 to 0.05389	No	ns	0.4208
14d vs. 21d	-0.3243	-0.4879 to -0.1608	Yes	****	<0.0001
14d vs. 28d	-0.2827	-0.4462 to -0.1191	Yes	****	<0.0001
14d vs. 35d	-0.3507	-0.5142 to -0.1871	Yes	****	<0.0001
14d vs. 42d	-0.3147	-0.4782 to -0.1511	Yes	****	<0.0001
14d vs. 49d	-0.3223	-0.4859 to -0.1588	Yes	****	<0.0001
14d vs. 56d	-0.343	-0.5066 to -0.1794	Yes	****	<0.0001
21d vs. 28d	0.04167	-0.1219 to 0.2052	No	ns	0.9923
21d vs. 35d	-0.02633	-0.1899 to 0.1372	No	ns	0.9996
21d vs. 42d	0.009667	-0.1539 to 0.1732	No	ns	>0.9999
21d vs. 49d	0.002	-0.1616 to 0.1656	No	ns	>0.9999
21d vs. 56d	-0.01867	-0.1822 to 0.1449	No	ns	>0.9999
28d vs. 35d	-0.068	-0.2316 to 0.09555	No	ns	0.8917
28d vs. 42d	-0.032	-0.1956 to 0.1316	No	ns	0.9985
28d vs. 49d	-0.03967	-0.2032 to 0.1239	No	ns	0.9943
28d vs. 56d	-0.06033	-0.2239 to 0.1032	No	ns	0.9394
35d vs. 42d	0.036	-0.1276 to 0.1996	No	ns	0.9969
35d vs. 49d	0.02833	-0.1352 to 0.1919	No	ns	0.9993
35d vs. 56d	0.007667	-0.1559 to 0.1712	No	ns	>0.9999
42d vs. 49d	-0.007667	-0.1712 to 0.1559	No	ns	>0.9999
42d vs. 56d	-0.02833	-0.1919 to 0.1352	No	ns	0.9993
49d vs. 56d	-0.02067	-0.1842 to 0.1429	No	ns	>0.9999

Baseline Paw Angle at Peak Stance (cm*2) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2164
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.342, df=8
How big is the difference?	
Mean of column A	0.7549
Mean of column B	0.6359
Difference between means (B - A) ±	± -0.1189 ± 0.08862
95% confidence interval	-0.3233 to 0.08541
R squared (eta squared)	0.1838
F test to compare variances	
F, DFn, Dfd	7.903, 4, 4
P value	0.07
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Angle at Peak Stance (cm*2) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	12.35	0.0005	***	Yes	Mean of Male -0.0175
Time	24.26	<0.0001	****	Yes	Mean of Female 0.02747
Sex	1.333	0.6207	ns	No	Difference between means -0.04497
Subject	40.25	<0.0001	****	Yes	SE of difference 0.08737
					95% CI of difference -0.2464 to 0.1565
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.03887	-0.1779 to 0.2556	No	ns	0.7213
14d					
Male vs. Female	0.2522	0.03547 to 0.4689	Yes	*	0.0233
21d					
Male vs. Female	-0.0708	-0.2875 to 0.1459	No	ns	0.5163
28d					
Male vs. Female	-0.1148	-0.3315 to 0.1019	No	ns	0.294
35d					
Male vs. Female	0.006867	-0.2099 to 0.2236	No	ns	0.9497
42d					
Male vs. Female	-0.2228	-0.4395 to -0.0060	Yes	*	0.0441
49d					
Male vs. Female	-0.0928	-0.3095 to 0.1239	No	ns	0.3955
56d					
Male vs. Female	-0.1565	-0.3732 to 0.06026	No	ns	0.1541
Male					
7d vs. 14d	0.106	-0.1105 to 0.3225	No	ns	0.7816
7d vs. 21d	-0.043	-0.2595 to 0.1735	No	ns	0.9984
7d vs. 28d	0.09867	-0.1178 to 0.3151	No	ns	0.837
7d vs. 35d	-0.04767	-0.2641 to 0.1688	No	ns	0.9969
7d vs. 42d	0.01	-0.2065 to 0.2265	No	ns	>0.9999
7d vs. 49d	0.06633	-0.1501 to 0.2828	No	ns	0.9775
7d vs. 56d	0.095	-0.1215 to 0.3115	No	ns	0.8616
14d vs. 21d	-0.149	-0.3655 to 0.06746	No	ns	0.3868
14d vs. 28d	-0.007333	-0.2238 to 0.2091	No	ns	>0.9999
14d vs. 35d	-0.1537	-0.3701 to 0.06279	No	ns	0.3475
14d vs. 42d	-0.096	-0.3125 to 0.1205	No	ns	0.8551
14d vs. 49d	-0.03967	-0.2561 to 0.1768	No	ns	0.999
14d vs. 56d	-0.011	-0.2275 to 0.2055	No	ns	>0.9999
21d vs. 28d	0.1417	-0.07479 to 0.3581	No	ns	0.4524
21d vs. 35d	-0.004667	-0.2211 to 0.2118	No	ns	>0.9999
21d vs. 42d	0.053	-0.1635 to 0.2695	No	ns	0.994
21d vs. 49d	0.1093	-0.1071 to 0.3258	No	ns	0.754
21d vs. 56d	0.138	-0.07846 to 0.3545	No	ns	0.4865
28d vs. 35d	-0.1463	-0.3628 to 0.07013	No	ns	0.4102
28d vs. 42d	-0.08867	-0.3051 to 0.1278	No	ns	0.8989
28d vs. 49d	-0.03233	-0.2488 to 0.1841	No	ns	0.9997
28d vs. 56d	-0.003667	-0.2201 to 0.2128	No	ns	>0.9999
35d vs. 42d	0.05767	-0.1588 to 0.2741	No	ns	0.99
35d vs. 49d	0.114	-0.1025 to 0.3305	No	ns	0.7133
35d vs. 56d	0.1427	-0.07379 to 0.3591	No	ns	0.4432
42d vs. 49d	0.05633	-0.1601 to 0.2728	No	ns	0.9913
42d vs. 56d	0.085	-0.1315 to 0.3015	No	ns	0.9174
49d vs. 56d	0.02867	-0.1878 to 0.2451	No	ns	0.9999
Female					
7d vs. 14d	0.3193	0.1029 to 0.5358	Yes	***	0.0005
7d vs. 21d	-0.1527	-0.3691 to 0.06379	No	ns	0.3557
7d vs. 28d	-0.055	-0.2715 to 0.1615	No	ns	0.9925
7d vs. 35d	-0.07967	-0.2961 to 0.1368	No	ns	0.9401
7d vs. 42d	-0.2517	-0.4681 to -0.0352	Yes	*	0.0122
7d vs. 49d	-0.06533	-0.2818 to 0.1511	No	ns	0.9794
7d vs. 56d	-0.1003	-0.3168 to 0.1161	No	ns	0.8251
14d vs. 21d	-0.472	-0.6885 to -0.2555	Yes	****	<0.0001
14d vs. 28d	-0.3743	-0.5908 to -0.1579	Yes	****	<0.0001
14d vs. 35d	-0.399	-0.6155 to -0.1825	Yes	****	<0.0001
14d vs. 42d	-0.571	-0.7875 to -0.3545	Yes	****	<0.0001
14d vs. 49d	-0.3847	-0.6011 to -0.1682	Yes	****	<0.0001
14d vs. 56d	-0.4197	-0.6361 to -0.2032	Yes	****	<0.0001
21d vs. 28d	0.09767	-0.1188 to 0.3141	No	ns	0.8439
21d vs. 35d	0.073	-0.1435 to 0.2895	No	ns	0.962
21d vs. 42d	-0.099	-0.3155 to 0.1175	No	ns	0.8347
21d vs. 49d	0.08733	-0.1291 to 0.3038	No	ns	0.9059
21d vs. 56d	0.05233	-0.1641 to 0.2688	No	ns	0.9944
28d vs. 35d	-0.02467	-0.2411 to 0.1918	No	ns	>0.9999
28d vs. 42d	-0.1967	-0.4131 to 0.01979	No	ns	0.1008
28d vs. 49d	-0.01033	-0.2268 to 0.2061	No	ns	>0.9999
28d vs. 56d	-0.04533	-0.2618 to 0.1711	No	ns	0.9977
35d vs. 42d	-0.172	-0.3885 to 0.04446	No	ns	0.2161
35d vs. 49d	0.01433	-0.2021 to 0.2308	No	ns	>0.9999
35d vs. 56d	-0.02067	-0.2371 to 0.1958	No	ns	>0.9999
42d vs. 49d	0.1863	-0.03013 to 0.4028	No	ns	0.141
42d vs. 56d	0.1513	-0.06513 to 0.3678	No	ns	0.3669
49d vs. 56d	-0.035	-0.2515 to 0.1815	No	ns	0.9996

Baseline Paw Angle at Peak Stance (cm*2) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2361
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.281, df=8
How big is the difference?	
Mean of column A	0.7435
Mean of column B	0.6214
Difference between means (B - A) ±	-0.1221 ± 0.09534
95% confidence interval	-0.3420 to 0.09772
R squared (eta squared)	0.1702
F test to compare variances	
F, DFn, Dfd	8.643, 4, 4
P value	0.0601
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Angle at Peak Stance (cm^2) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	11.5	0.0062	**	Yes	Mean of Male	-0.06456
Time	17.5	0.0002	***	Yes	Mean of Female	-0.02844
Sex	1.471	0.6063	ns	No	Difference between means	-0.03612
Subject	40.91	<0.0001	****	Yes	SE of difference	0.06734
					95% CI of difference	-0.1914 to 0.1192

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.01847	-0.1569 to 0.1939	No	ns	0.8341
14d					
Male vs. Female	0.1795	0.004082 to 0.3545	Yes	*	0.045
21d					
Male vs. Female	-0.1332	-0.3086 to 0.04218	No	ns	0.1341
28d					
Male vs. Female	-0.1165	-0.2919 to 0.05885	No	ns	0.1891
35d					
Male vs. Female	0.0418	-0.1336 to 0.2172	No	ns	0.6356
42d					
Male vs. Female	-0.1089	-0.2843 to 0.06652	No	ns	0.2195
49d					
Male vs. Female	-0.0792	-0.2546 to 0.09618	No	ns	0.3704
56d					
Male vs. Female	-0.09087	-0.2663 to 0.08452	No	ns	0.3046
Male					
7d vs. 14d	0.09467	-0.09489 to 0.2842	No	ns	0.7643
7d vs. 21d	0.1157	-0.07389 to 0.3052	No	ns	0.5428
7d vs. 28d	0.09133	-0.09822 to 0.2809	No	ns	0.7951
7d vs. 35d	-0.02	-0.2096 to 0.1696	No	ns	>0.9999
7d vs. 42d	0.03167	-0.1579 to 0.2212	No	ns	0.9995
7d vs. 49d	0.01667	-0.1729 to 0.2062	No	ns	>0.9999
7d vs. 56d	0.07233	-0.1172 to 0.2619	No	ns	0.9282
14d vs. 21d	0.021	-0.1686 to 0.2106	No	ns	>0.9999
14d vs. 28d	-0.003333	-0.1929 to 0.1862	No	ns	>0.9999
14d vs. 35d	-0.1147	-0.3042 to 0.07489	No	ns	0.5538
14d vs. 42d	-0.063	-0.2526 to 0.1266	No	ns	0.9649
14d vs. 49d	-0.078	-0.2676 to 0.1116	No	ns	0.8968
14d vs. 56d	-0.02233	-0.2119 to 0.1672	No	ns	>0.9999
21d vs. 28d	-0.02433	-0.2139 to 0.1652	No	ns	>0.9999
21d vs. 35d	-0.1357	-0.3252 to 0.05389	No	ns	0.3373
21d vs. 42d	-0.084	-0.2736 to 0.1056	No	ns	0.8557
21d vs. 49d	-0.099	-0.2886 to 0.09056	No	ns	0.7218
21d vs. 56d	-0.04333	-0.2329 to 0.1462	No	ns	0.996
28d vs. 35d	-0.1113	-0.3009 to 0.07822	No	ns	0.5904
28d vs. 42d	-0.05967	-0.2492 to 0.1299	No	ns	0.9739
28d vs. 49d	-0.07467	-0.2642 to 0.1149	No	ns	0.9161
28d vs. 56d	-0.019	-0.2086 to 0.1706	No	ns	>0.9999
35d vs. 42d	0.05167	-0.1379 to 0.2412	No	ns	0.9885
35d vs. 49d	0.03667	-0.1529 to 0.2262	No	ns	0.9986
35d vs. 56d	0.09233	-0.09722 to 0.2819	No	ns	0.7861
42d vs. 49d	-0.015	-0.2046 to 0.1746	No	ns	>0.9999
42d vs. 56d	0.04067	-0.1489 to 0.2302	No	ns	0.9973
49d vs. 56d	0.05567	-0.1339 to 0.2452	No	ns	0.9823
Female					
7d vs. 14d	0.2557	0.06611 to 0.4452	Yes	**	0.002
7d vs. 21d	-0.036	-0.2256 to 0.1536	No	ns	0.9988
7d vs. 28d	-0.04367	-0.2332 to 0.1459	No	ns	0.9959
7d vs. 35d	0.003333	-0.1862 to 0.1929	No	ns	>0.9999
7d vs. 42d	-0.09967	-0.2852 to 0.09389	No	ns	0.7548
7d vs. 49d	-0.081	-0.2706 to 0.1086	No	ns	0.8772
7d vs. 56d	-0.037	-0.2266 to 0.1526	No	ns	0.9985
14d vs. 21d	-0.2917	-0.4812 to -0.1021	Yes	***	0.0003
14d vs. 28d	-0.2993	-0.4889 to -0.1098	Yes	***	0.0002
14d vs. 35d	-0.2523	-0.4419 to -0.06275	Yes	**	0.0024
14d vs. 42d	-0.3513	-0.5409 to -0.1618	Yes	****	<0.0001
14d vs. 49d	-0.3367	-0.5262 to -0.1471	Yes	****	<0.0001
14d vs. 56d	-0.2927	-0.4822 to -0.1031	Yes	***	0.0003
21d vs. 28d	-0.007667	-0.1972 to 0.1819	No	ns	>0.9999
21d vs. 35d	0.03933	-0.1502 to 0.2289	No	ns	0.9978
21d vs. 42d	-0.05967	-0.2492 to 0.1299	No	ns	0.9739
21d vs. 49d	-0.045	-0.2346 to 0.1446	No	ns	0.995
21d vs. 56d	-0.001	-0.1906 to 0.1886	No	ns	>0.9999
28d vs. 35d	0.047	-0.1426 to 0.2366	No	ns	0.9935
28d vs. 42d	-0.052	-0.2416 to 0.1376	No	ns	0.9881
28d vs. 49d	-0.03733	-0.2269 to 0.1522	No	ns	0.9985
28d vs. 56d	0.006667	-0.1829 to 0.1962	No	ns	>0.9999
35d vs. 42d	-0.099	-0.2886 to 0.09056	No	ns	0.7218
35d vs. 49d	-0.08433	-0.2739 to 0.1052	No	ns	0.8531
35d vs. 56d	-0.04033	-0.2299 to 0.1492	No	ns	0.9975
42d vs. 49d	0.01467	-0.1749 to 0.2042	No	ns	>0.9999
42d vs. 56d	0.05867	-0.1309 to 0.2482	No	ns	0.9762
49d vs. 56d	0.044	-0.1456 to 0.2336	No	ns	0.9957

Baseline Paw Angle at Peak Stance (cm^2) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0916
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.917, df=8
How big is the difference?	
Mean of column A	0.7769
Mean of column B	0.6637
Difference between means (B - A) ± SEM	-0.1132 ± 0.05905
95% confidence interval	-0.2494 to 0.02298
R squared (eta squared)	0.3147
F test to compare variances	
F, DFn, Dfd	4.019, 4, 4
P value	0.2065
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Shared Stance FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	4.956	0.5792	ns	No	Mean of Male	0.7319
Time	12.4	0.0861	ns	No	Mean of Female	-3.902
Sex	8.491	0.1326	ns	No	Difference between means	4.634
Subject	24.22	0.0099	**	Yes	SE of difference	2.767
					95% CI of difference	-1.747 to 11.02

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	11.02	1.325 to 20.72	Yes	*	0.0266
21d					
Male vs. Female	0.004	-9.695 to 9.703	No	ns	0.9993
28d					
Male vs. Female	5.844	-3.855 to 15.54	No	ns	0.2325
35d					
Male vs. Female	5.471	-4.229 to 15.17	No	ns	0.2633
42d					
Male vs. Female	6.451	-3.249 to 16.15	No	ns	0.1882
49d					
Male vs. Female	0.374	-9.325 to 10.07	No	ns	0.9387
56d					
Male vs. Female	3.271	-6.429 to 12.97	No	ns	0.5021
Male					
7d vs. 21d	4.09	-9.113 to 17.29	No	ns	0.9614
7d vs. 28d	5.937	-7.267 to 19.14	No	ns	0.8078
7d vs. 35d	-2.99	-16.19 to 10.21	No	ns	0.9922
7d vs. 42d	0.37	-12.83 to 13.57	No	ns	>0.9999
7d vs. 49d	0.8667	-12.34 to 14.07	No	ns	>0.9999
7d vs. 56d	0.5567	-12.65 to 13.76	No	ns	>0.9999
21d vs. 28d	1.847	-11.36 to 15.05	No	ns	0.9995
21d vs. 35d	-7.08	-20.28 to 6.123	No	ns	0.6515
21d vs. 42d	-3.72	-16.92 to 9.483	No	ns	0.9758
21d vs. 49d	-3.223	-16.43 to 9.980	No	ns	0.9884
21d vs. 56d	-3.533	-16.74 to 9.670	No	ns	0.9813
28d vs. 35d	-8.927	-22.13 to 4.277	No	ns	0.3805
28d vs. 42d	-5.567	-18.77 to 7.637	No	ns	0.8499
28d vs. 49d	-5.07	-18.27 to 8.133	No	ns	0.8977
28d vs. 56d	-5.38	-18.58 to 7.823	No	ns	0.869
35d vs. 42d	3.36	-9.843 to 16.56	No	ns	0.9856
35d vs. 49d	3.857	-9.347 to 17.06	No	ns	0.971
35d vs. 56d	3.547	-9.657 to 16.75	No	ns	0.981
42d vs. 49d	0.4967	-12.71 to 13.70	No	ns	>0.9999
42d vs. 56d	0.1867	-13.02 to 13.39	No	ns	>0.9999
49d vs. 56d	-0.31	-13.51 to 12.89	No	ns	>0.9999
Female					
7d vs. 21d	-6.93	-20.13 to 6.273	No	ns	0.6736
7d vs. 28d	0.7567	-12.45 to 13.96	No	ns	>0.9999
7d vs. 35d	-8.543	-21.75 to 4.660	No	ns	0.4336
7d vs. 42d	-4.203	-17.41 to 9.000	No	ns	0.9561
7d vs. 49d	-9.783	-22.99 to 3.420	No	ns	0.2748
7d vs. 56d	-7.197	-20.40 to 6.007	No	ns	0.6341
21d vs. 28d	7.687	-5.517 to 20.89	No	ns	0.5603
21d vs. 35d	-1.613	-14.82 to 11.59	No	ns	0.9998
21d vs. 42d	2.727	-10.48 to 15.93	No	ns	0.9952
21d vs. 49d	-2.853	-16.06 to 10.35	No	ns	0.9939
21d vs. 56d	-0.2667	-13.47 to 12.94	No	ns	>0.9999
28d vs. 35d	-9.3	-22.50 to 3.903	No	ns	0.332
28d vs. 42d	-4.96	-18.16 to 8.243	No	ns	0.9069
28d vs. 49d	-10.54	-23.74 to 2.663	No	ns	0.1986
28d vs. 56d	-7.953	-21.16 to 5.250	No	ns	0.5201
35d vs. 42d	4.34	-8.863 to 17.54	No	ns	0.9489
35d vs. 49d	-1.24	-14.44 to 11.96	No	ns	>0.9999
35d vs. 56d	1.347	-11.86 to 14.55	No	ns	>0.9999
42d vs. 49d	-5.58	-18.78 to 7.623	No	ns	0.8484
42d vs. 56d	-2.993	-16.20 to 10.21	No	ns	0.9921
49d vs. 56d	2.587	-10.62 to 15.79	No	ns	0.9964

Baseline % Shared Stance FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.1504
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.591, df=8
How big is the difference?	
Mean of column A	17.39
Mean of column B	20.67
Difference between means (B - A) ± 2.063	
95% confidence interval	-1.476 to 8.037
R squared (eta squared)	0.2403
F test to compare variances	
F, DFn, Dfd	1.440, 4, 4
P value	0.7325
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Shared Stance 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	4.552	0.4302	ns	No	Mean of Male	0.4417
Time	5.709	0.2905	ns	No	Mean of Female	-5.45
Sex	9.842	0.217	ns	No	Difference between means	5.892
Subject	43.84	<0.0001	****	Yes	SE of difference	4.396
					95% CI of difference	-4.246 to 16.03

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	2.107	-9.783 to 14.00	No	ns	0.724
21d					
Male vs. Female	6.753	-5.137 to 18.64	No	ns	0.26
28d					
Male vs. Female	12.13	0.2367 to 24.02	Yes	*	0.0458
35d					
Male vs. Female	6.783	-5.107 to 18.67	No	ns	0.258
42d					
Male vs. Female	-0.73	-12.62 to 11.16	No	ns	0.9026
49d					
Male vs. Female	9.433	-2.457 to 21.32	No	ns	0.1176
56d					
Male vs. Female	4.77	-7.120 to 16.66	No	ns	0.425
Male					
7d vs. 21d	-3.677	-16.93 to 9.575	No	ns	0.9776
7d vs. 28d	-8.68	-21.93 to 4.571	No	ns	0.4188
7d vs. 35d	-7.667	-20.92 to 5.585	No	ns	0.5675
7d vs. 42d	2.067	-11.18 to 15.32	No	ns	0.999
7d vs. 49d	-7.083	-20.33 to 6.168	No	ns	0.6548
7d vs. 56d	-6	-19.85 to 6.651	No	ns	0.7242
21d vs. 28d	-5.003	-18.25 to 8.248	No	ns	0.9048
21d vs. 35d	-3.99	-17.24 to 9.261	No	ns	0.9664
21d vs. 42d	5.743	-7.508 to 18.99	No	ns	0.8328
21d vs. 49d	-3.407	-16.66 to 9.845	No	ns	0.9848
21d vs. 56d	-2.923	-16.17 to 10.33	No	ns	0.9932
28d vs. 35d	1.013	-12.24 to 14.26	No	>0.9999	
28d vs. 42d	10.75	-2.505 to 24.00	No	ns	0.184
28d vs. 49d	1.597	-11.65 to 14.85	No	ns	0.9998
28d vs. 56d	2.08	-11.17 to 15.33	No	ns	0.999
35d vs. 42d	9.733	-3.518 to 22.98	No	ns	0.2844
35d vs. 49d	0.5833	-12.67 to 13.83	No	ns	>0.9999
35d vs. 56d	1.067	-12.18 to 14.32	No	ns	>0.9999
42d vs. 49d	-9.15	-22.40 to 4.101	No	ns	0.3554
42d vs. 56d	-8.667	-21.92 to 4.585	No	ns	0.4206
49d vs. 56d	0.4833	-12.77 to 13.73	No	ns	>0.9999
Female					
7d vs. 21d	0.97	-12.28 to 14.22	No	ns	>0.9999
7d vs. 28d	1.34	-11.91 to 14.59	No	ns	>0.9999
7d vs. 35d	-2.99	-16.24 to 10.26	No	ns	0.9923
7d vs. 42d	-0.77	-14.02 to 12.48	No	ns	>0.9999
7d vs. 49d	0.2433	-13.01 to 13.49	No	ns	>0.9999
7d vs. 56d	-3.937	-17.19 to 9.315	No	ns	0.9685
21d vs. 28d	0.37	-12.88 to 13.62	No	ns	>0.9999
21d vs. 35d	-3.96	-17.21 to 9.291	No	ns	0.9676
21d vs. 42d	-1.74	-14.99 to 11.51	No	ns	0.9996
21d vs. 49d	-0.7267	-13.98 to 12.52	No	>0.9999	
21d vs. 56d	-4.907	-18.16 to 8.345	No	ns	0.9125
28d vs. 35d	-4.33	-17.58 to 8.921	No	ns	0.9503
28d vs. 42d	-2.11	-15.36 to 11.14	No	ns	0.9989
28d vs. 49d	-1.097	-14.35 to 12.15	No	>0.9999	
28d vs. 56d	-5.277	-18.53 to 7.975	No	ns	0.8809
35d vs. 42d	2.22	-11.03 to 15.47	No	ns	0.9985
35d vs. 49d	3.233	-10.02 to 16.48	No	ns	0.9884
35d vs. 56d	-0.9467	-14.20 to 12.30	No	>0.9999	
42d vs. 49d	1.013	-12.24 to 14.26	No	ns	>0.9999
42d vs. 56d	-3.167	-16.42 to 10.08	No	ns	0.9896

Baseline % Shared Stance 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.8654
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.1750, df=8
How big is the difference?	
Mean of column A	19.88
Mean of column B	20.8
Difference between means (B - A) ± 0.9233 ± 5.275	
95% confidence interval	-11.24 to 13.09
R squared (eta squared)	0.003815
F test to compare variances	
F, DFn, Dfd	2.460, 4, 4
P value	0.4046
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in % Shared Stance 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	10.24	0.0365	*	Yes	Mean of Male	-5.512
Time	2.918	0.6472	ns	No	Mean of Female	-5.182
Sex	0.03484	0.9443	ns	No	Difference between means	-0.3294
Subject	53.69	<0.0001	****	Yes	SE of difference	4.572
					95% CI of difference	-10.87 to 10.21

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	4.919	-6.728 to 16.57	No	ns	0.4011
21d					
Male vs. Female	1.605	-10.04 to 13.25	No	ns	0.7835
28d					
Male vs. Female	4.945	-6.701 to 16.59	No	ns	0.3986
35d					
Male vs. Female	5.345	-6.301 to 16.99	No	ns	0.3618
42d					
Male vs. Female	-10.21	-21.86 to 1.435	No	ns	0.0845
49d					
Male vs. Female	-4.781	-16.43 to 6.865	No	ns	0.4143
56d					
Male vs. Female	-4.128	-15.77 to 7.519	No	ns	0.4806
Male					
7d vs. 21d	4.98	-6.954 to 16.91	No	ns	0.8559
7d vs. 28d	4.463	-7.470 to 16.40	No	ns	0.9086
7d vs. 35d	3.977	-7.957 to 15.91	No	ns	0.9456
7d vs. 42d	9.59	-2.344 to 21.52	No	ns	0.1924
7d vs. 49d	5.957	-5.977 to 17.89	No	ns	0.7223
7d vs. 56d	6.807	-5.127 to 18.74	No	ns	0.5838
21d vs. 28d	-0.5167	-12.45 to 11.42	No	ns	>0.9999
21d vs. 35d	-1.003	-12.94 to 10.93	No	ns	>0.9999
21d vs. 42d	4.61	-7.324 to 16.54	No	ns	0.8951
21d vs. 49d	0.9767	-10.96 to 12.91	No	ns	>0.9999
21d vs. 56d	1.827	-10.11 to 13.76	No	ns	0.9991
28d vs. 35d	-0.4867	-12.42 to 11.45	No	ns	>0.9999
28d vs. 42d	5.127	-6.807 to 17.06	No	ns	0.8384
28d vs. 49d	1.493	-10.44 to 13.43	No	ns	0.9997
28d vs. 56d	2.343	-9.590 to 14.28	No	ns	0.9964
35d vs. 42d	5.613	-6.320 to 17.55	No	ns	0.7735
35d vs. 49d	1.98	-9.954 to 13.91	No	ns	0.9986
35d vs. 56d	2.83	-9.104 to 14.76	No	ns	0.99
42d vs. 49d	-3.633	-15.57 to 8.300	No	ns	0.9645
42d vs. 56d	-2.783	-14.72 to 9.150	No	ns	0.9909
49d vs. 56d	0.85	-11.08 to 12.78	No	ns	>0.9999
Female					
7d vs. 21d	1.667	-10.27 to 13.60	No	ns	0.9995
7d vs. 28d	4.49	-7.444 to 16.42	No	ns	0.9063
7d vs. 35d	4.403	-7.530 to 16.34	No	ns	0.9139
7d vs. 42d	-5.54	-17.47 to 6.394	No	ns	0.7839
7d vs. 49d	-3.743	-15.68 to 8.190	No	ns	0.9591
7d vs. 56d	-2.24	-14.17 to 9.694	No	ns	0.9972
21d vs. 28d	2.823	-9.110 to 14.76	No	ns	0.9901
21d vs. 35d	2.737	-9.197 to 14.67	No	ns	0.9916
21d vs. 42d	-7.207	-19.14 to 4.727	No	ns	0.5171
21d vs. 49d	-5.41	-17.34 to 6.524	No	ns	0.8019
21d vs. 56d	-3.907	-15.84 to 8.027	No	ns	0.9499
28d vs. 35d	-0.08667	-12.02 to 11.85	No	ns	>0.9999
28d vs. 42d	-10.03	-21.96 to 1.904	No	ns	0.1532
28d vs. 49d	-8.233	-20.17 to 3.700	No	ns	0.3564
28d vs. 56d	-6.73	-18.66 to 5.204	No	ns	0.5967
35d vs. 42d	-9.943	-21.88 to 1.990	No	ns	0.1604
35d vs. 49d	-8.147	-20.08 to 3.787	No	ns	0.369
35d vs. 56d	-6.643	-18.58 to 5.290	No	ns	0.6111
42d vs. 49d	1.797	-10.14 to 13.73	No	ns	0.9992
42d vs. 56d	3.3	-8.634 to 15.23	No	ns	0.9779
49d vs. 56d	1.503	-10.43 to 13.44	No	ns	0.9997

Baseline % Shared Stance 10DegDown

Column B vs. Column A	Female vs. Male
Unpaired t test	
P value	0.9886
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.01476, df=8
How big is the difference?	
Mean of column A	20.44
Mean of column B	20.51
Difference between means (B - A) ± SEM	0.06867 ± 4.652
95% confidence interval	-10.66 to 10.80
R squared (eta squared)	0.00002723
F test to compare variances	
F, DFn, Dfd	1.960, 4, 4
P value	0.5307
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Gait Symmetry FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	1.212	0.7573 ns	No	No	-0.02055
Time	4.277	0.0584 ns	No	No	-0.02026
Sex	0.0005207	0.9944 ns	No	No	-0.0002917
Subject	78.22	<0.0001	****	Yes	0.03997
					95% CI of difference
					-0.09246 to 0.09187
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.01	-0.07777 to 0.0977	No	ns	0.8207
14d					
Male vs. Female	0.016	-0.07177 to 0.1038	No	ns	0.7169
21d					
Male vs. Female	-0.01933	-0.1071 to 0.06843	No	ns	0.6614
28d					
Male vs. Female	0.023	-0.06477 to 0.1108	No	ns	0.6024
35d					
Male vs. Female	-0.005333	-0.09310 to 0.0824	No	ns	0.9038
42d					
Male vs. Female	-0.013	-0.1008 to 0.07477	No	ns	0.7683
49d					
Male vs. Female	-0.011	-0.09877 to 0.0767	No	ns	0.8031
56d					
Male vs. Female	-0.002667	-0.09043 to 0.0851	No	ns	0.9518
Male					
7d vs. 14d	0.03133	-0.03006 to 0.0927	No	ns	0.7442
7d vs. 21d	0.05633	-0.005057 to 0.117	No	ns	0.0944
7d vs. 28d	0.02667	-0.03472 to 0.0880	No	ns	0.8678
7d vs. 35d	0.03333	-0.02806 to 0.0947	No	ns	0.6812
7d vs. 42d	0.044	-0.01739 to 0.1054	No	ns	0.3355
7d vs. 49d	0.052	-0.009390 to 0.113	No	ns	0.1547
7d vs. 56d	0.05033	-0.01106 to 0.1117	No	ns	0.1846
14d vs. 21d	0.025	-0.03639 to 0.0863	No	ns	0.9017
14d vs. 28d	-0.004667	-0.06606 to 0.0567	No	ns	>0.9999
14d vs. 35d	0.002	-0.05939 to 0.0633	No	ns	>0.9999
14d vs. 42d	0.01267	-0.04872 to 0.0740	No	ns	0.9979
14d vs. 49d	0.02067	-0.04072 to 0.0820	No	ns	0.9624
14d vs. 56d	0.019	-0.04239 to 0.0803	No	ns	0.9762
21d vs. 28d	-0.02967	-0.09106 to 0.0317	No	ns	0.7927
21d vs. 35d	-0.023	-0.08439 to 0.0383	No	ns	0.9345
21d vs. 42d	-0.01233	-0.07372 to 0.0490	No	ns	0.9982
21d vs. 49d	-0.004333	-0.06572 to 0.0570	No	ns	>0.9999
21d vs. 56d	-0.006	-0.06739 to 0.0553	No	ns	>0.9999
28d vs. 35d	0.006667	-0.05472 to 0.0680	No	ns	>0.9999
28d vs. 42d	0.01733	-0.04406 to 0.0787	No	ns	0.9859
28d vs. 49d	0.02533	-0.03606 to 0.0867	No	ns	0.8954
28d vs. 56d	0.02367	-0.03772 to 0.0850	No	ns	0.9245
35d vs. 42d	0.01067	-0.05072 to 0.0720	No	ns	0.9993
35d vs. 49d	0.01867	-0.04272 to 0.0800	No	ns	0.9785
35d vs. 56d	0.017	-0.04439 to 0.0783	No	ns	0.9874
42d vs. 49d	0.008	-0.05339 to 0.0693	No	ns	0.9999
42d vs. 56d	0.006333	-0.05506 to 0.0677	No	ns	>0.9999
49d vs. 56d	-0.001667	-0.06306 to 0.0597	No	ns	>0.9999
Female					
7d vs. 14d	0.03733	-0.02406 to 0.0987	No	ns	0.5471
7d vs. 21d	0.027	-0.03439 to 0.0883	No	ns	0.8603
7d vs. 28d	0.03967	-0.02172 to 0.1011	No	ns	0.4691
7d vs. 35d	0.018	-0.04339 to 0.0793	No	ns	0.9625
7d vs. 42d	0.021	-0.04039 to 0.0823	No	ns	0.959
7d vs. 49d	0.031	-0.03039 to 0.0923	No	ns	0.7542
7d vs. 56d	0.03767	-0.02372 to 0.0990	No	ns	0.5358
14d vs. 21d	-0.01033	-0.07172 to 0.0510	No	ns	0.9994
14d vs. 28d	0.002333	-0.05906 to 0.0637	No	ns	>0.9999
14d vs. 35d	-0.01933	-0.08072 to 0.0420	No	ns	0.9738
14d vs. 42d	-0.01633	-0.07772 to 0.0450	No	ns	0.9901
14d vs. 49d	-0.006333	-0.06772 to 0.0550	No	ns	>0.9999
14d vs. 56d	0.0003333	-0.06106 to 0.0617	No	ns	>0.9999
21d vs. 28d	0.01267	-0.04872 to 0.0740	No	ns	0.9979
21d vs. 35d	-0.009	-0.07039 to 0.0523	No	ns	0.9998
21d vs. 42d	-0.006	-0.06739 to 0.0553	No	ns	>0.9999
21d vs. 49d	0.004	-0.05739 to 0.0653	No	ns	>0.9999
21d vs. 56d	0.01067	-0.05072 to 0.0720	No	ns	0.9993
28d vs. 35d	-0.02167	-0.08306 to 0.0397	No	ns	0.9517
28d vs. 42d	-0.01867	-0.08006 to 0.0427	No	ns	0.9785
28d vs. 49d	-0.008667	-0.07006 to 0.0527	No	ns	0.9998
28d vs. 56d	-0.002	-0.06339 to 0.0593	No	ns	>0.9999
35d vs. 42d	0.003	-0.05839 to 0.0643	No	ns	>0.9999
35d vs. 49d	0.013	-0.04639 to 0.0743	No	ns	0.9975
35d vs. 56d	0.01967	-0.04172 to 0.0810	No	ns	0.9712
42d vs. 49d	0.01	-0.05139 to 0.0713	No	ns	0.9995
42d vs. 56d	0.01667	-0.04472 to 0.0780	No	ns	0.9888
49d vs. 56d	0.006667	-0.05472 to 0.0680	No	ns	>0.9999

Baseline Gait Symmetry FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.9385
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.07958, df=8
How big is the difference?	
Mean of column A	1.026
Mean of column B	1.029
Difference between means (B - A)	$\pm 0.003000 \pm 0.03770$
95% confidence interval	-0.08393 to 0.08993
R squared (eta squared)	0.000791
F test to compare variances	
F, DFn, Dfd	3.683, 4, 4
P value	0.2346
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Gait Symmetry 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	2.431	0.707 ns	No	No	Mean of Male	-0.009625
Time	7.036	0.0864 ns	No	No	Mean of Female	-0.01209
Sex	0.1055	0.9092 ns	No	No	Difference between means	0.002467
Subject	60.83	<0.0001	****	Yes	SE of difference	0.02094
					95% CI of difference	-0.04583 to 0.05077
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	
7d						
Male vs. Female	0.0158	-0.03522 to 0.0668	No	ns	0.5383	
14d						
Male vs. Female	-0.0242	-0.07522 to 0.0268	No	ns	0.3469	
21d						
Male vs. Female	-0.002867	-0.05388 to 0.0481	No	ns	0.911	
28d						
Male vs. Female	0.0078	-0.04322 to 0.0588	No	ns	0.761	
35d						
Male vs. Female	0.008467	-0.04255 to 0.0594	No	ns	0.7413	
42d						
Male vs. Female	-0.003867	-0.05488 to 0.0471	No	ns	0.8801	
49d						
Male vs. Female	0.007467	-0.04355 to 0.0584	No	ns	0.7709	
56d						
Male vs. Female	0.01113	-0.03988 to 0.0621	No	ns	0.6643	
Male						
7d vs. 14d	0.043	-0.006171 to 0.092	No	ns	0.1284	
7d vs. 21d	0.032	-0.01717 to 0.0811	No	ns	0.4597	
7d vs. 28d	0.028	-0.02117 to 0.0771	No	ns	0.6274	
7d vs. 35d	0.02067	-0.02850 to 0.0698	No	ns	0.8861	
7d vs. 42d	0.039	-0.01017 to 0.0881	No	ns	0.2181	
7d vs. 49d	0.041	-0.008171 to 0.090	No	ns	0.1688	
7d vs. 56d	0.01867	-0.03050 to 0.0678	No	ns	0.93	
14d vs. 21d	-0.011	-0.06017 to 0.0381	No	ns	0.9965	
14d vs. 28d	-0.015	-0.06417 to 0.0341	No	ns	0.9781	
14d vs. 35d	-0.02233	-0.07150 to 0.0268	No	ns	0.8395	
14d vs. 42d	-0.004	-0.05317 to 0.0451	No	ns	>0.9999	
14d vs. 49d	-0.002	-0.05117 to 0.0471	No	ns	>0.9999	
14d vs. 56d	-0.02433	-0.07350 to 0.0248	No	ns	0.7725	
21d vs. 28d	-0.004	-0.05317 to 0.0451	No	ns	>0.9999	
21d vs. 35d	-0.01133	-0.06050 to 0.0378	No	ns	0.9958	
21d vs. 42d	0.007	-0.04217 to 0.0561	No	ns	0.9998	
21d vs. 49d	0.009	-0.04017 to 0.0581	No	ns	0.999	
21d vs. 56d	-0.01333	-0.06250 to 0.0358	No	ns	0.9889	
28d vs. 35d	-0.007333	-0.05650 to 0.0418	No	ns	0.9997	
28d vs. 42d	0.011	-0.03817 to 0.0601	No	ns	0.9965	
28d vs. 49d	0.013	-0.03617 to 0.0621	No	ns	0.9904	
28d vs. 56d	-0.009333	-0.05850 to 0.0398	No	ns	0.9988	
35d vs. 42d	0.01833	-0.03084 to 0.0675	No	ns	0.936	
35d vs. 49d	0.02033	-0.02884 to 0.0695	No	ns	0.8944	
35d vs. 56d	-0.002	-0.05117 to 0.0471	No	ns	>0.9999	
42d vs. 49d	0.002	-0.04717 to 0.0511	No	ns	>0.9999	
42d vs. 56d	-0.02033	-0.06950 to 0.0288	No	ns	0.8944	
49d vs. 56d	-0.02233	-0.07150 to 0.0268	No	ns	0.8395	
Female						
7d vs. 14d	0.003	-0.04617 to 0.0521	No	ns	>0.9999	
7d vs. 21d	0.01333	-0.03584 to 0.0625	No	ns	0.9889	
7d vs. 28d	0.02	-0.02917 to 0.0691	No	ns	0.9022	
7d vs. 35d	0.01333	-0.03584 to 0.0625	No	ns	0.9889	
7d vs. 42d	0.01933	-0.02984 to 0.0685	No	ns	0.9168	
7d vs. 49d	0.03267	-0.01650 to 0.0818	No	ns	0.4328	
7d vs. 56d	0.014	-0.03517 to 0.0631	No	ns	0.9852	
14d vs. 21d	0.01033	-0.03884 to 0.0595	No	ns	0.9977	
14d vs. 28d	0.017	-0.03217 to 0.0661	No	ns	0.9567	
14d vs. 35d	0.01033	-0.03884 to 0.0595	No	ns	0.9977	
14d vs. 42d	0.01633	-0.03284 to 0.0655	No	ns	0.965	
14d vs. 49d	0.02967	-0.01950 to 0.0788	No	ns	0.5571	
14d vs. 56d	0.011	-0.03817 to 0.0601	No	ns	0.9965	
21d vs. 28d	0.006667	-0.04250 to 0.0558	No	ns	0.9999	
21d vs. 35d	0.000000002	-0.04917 to 0.0491	No	ns	>0.9999	
21d vs. 42d	0.006	-0.04317 to 0.0551	No	ns	>0.9999	
21d vs. 49d	0.01933	-0.02984 to 0.0685	No	ns	0.9168	
21d vs. 56d	0.0006667	-0.04850 to 0.0498	No	ns	>0.9999	
28d vs. 35d	-0.006667	-0.05584 to 0.0425	No	ns	0.9999	
28d vs. 42d	-0.0006666	-0.04984 to 0.0485	No	ns	>0.9999	
28d vs. 49d	0.01267	-0.03650 to 0.0618	No	ns	0.9918	
28d vs. 56d	-0.006	-0.05517 to 0.0431	No	ns	>0.9999	
35d vs. 42d	0.006	-0.04317 to 0.0551	No	ns	>0.9999	
35d vs. 49d	0.01933	-0.02984 to 0.0685	No	ns	0.9168	
35d vs. 56d	0.0006667	-0.04850 to 0.0498	No	ns	>0.9999	
42d vs. 49d	0.01333	-0.03584 to 0.0625	No	ns	0.9889	
42d vs. 56d	-0.005333	-0.05450 to 0.0438	No	ns	>0.9999	
49d vs. 56d	-0.01867	-0.06784 to 0.0305	No	ns	0.93	

Baseline Gait Symmetry 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.91
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.1167, df=8
How big is the difference?	
Mean of column A	1.018
Mean of column B	1.021
Difference between means (B - A)	$\pm 0.002800 \pm 0.02400$
95% confidence interval	-0.05255 to 0.05815
R squared (eta squared)	0.001698
F test to compare variances	
F, DFn, Dfd	3.136, 4, 4
P value	0.2942
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Gait Symmetry 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	-0.003317
Time x Sex	19.94	0.0052	**	Yes	Mean of Male	-0.01789
Time	1.84	0.9625	ns	No	Mean of Female	0.01458
Sex	5.187	0.2327	ns	No	Difference between means	0.01129
Subject	24.89	0.0019	**	Yes	SE of difference	-0.01145 to 0.04060

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.04753	0.008853 to 0.0862	Yes	*	0.0168
14d					
Male vs. Female	-0.03447	-0.07315 to 0.0042	No	ns	0.0798
21d					
Male vs. Female	0.009533	-0.02915 to 0.0482	No	ns	0.6241
28d					
Male vs. Female	0.02287	-0.01581 to 0.0615	No	ns	0.242
35d					
Male vs. Female	0.0332	-0.005480 to 0.071	No	ns	0.0912
42d					
Male vs. Female	-0.0088	-0.04748 to 0.0298	No	ns	0.651
49d					
Male vs. Female	0.0542	0.01552 to 0.0928	Yes	**	0.0068
56d					
Male vs. Female	-0.007467	-0.04615 to 0.0312	No	ns	0.701
Male					
7d vs. 14d	0.03133	-0.02161 to 0.0842	No	ns	0.5811
7d vs. 21d	0.01833	-0.03461 to 0.0712	No	ns	0.9563
7d vs. 28d	0.01833	-0.03461 to 0.0712	No	ns	0.9563
7d vs. 35d	0.008667	-0.04428 to 0.0616	No	ns	0.9995
7d vs. 42d	0.02667	-0.02628 to 0.0796	No	ns	0.7567
7d vs. 49d	-0.003667	-0.05661 to 0.0492	No	ns	>0.9999
7d vs. 56d	0.025	-0.02795 to 0.0779	No	ns	0.8112
14d vs. 21d	-0.013	-0.06595 to 0.0399	No	ns	0.9939
14d vs. 28d	-0.013	-0.06595 to 0.0399	No	ns	0.9939
14d vs. 35d	-0.02267	-0.07561 to 0.0302	No	ns	0.8762
14d vs. 42d	-0.004667	-0.05761 to 0.0482	No	ns	>0.9999
14d vs. 49d	-0.035	-0.08795 to 0.0179	No	ns	0.4394
14d vs. 56d	-0.006333	-0.05928 to 0.0468	No	ns	>0.9999
21d vs. 28d	-0.00000018	-0.05295 to 0.0529	No	ns	>0.9999
21d vs. 35d	-0.009667	-0.06261 to 0.0432	No	ns	0.999
21d vs. 42d	0.008333	-0.04461 to 0.0612	No	ns	0.9996
21d vs. 49d	-0.022	-0.07495 to 0.0309	No	ns	0.892
21d vs. 56d	0.006667	-0.04628 to 0.0596	No	ns	>0.9999
28d vs. 35d	-0.009667	-0.06261 to 0.0432	No	ns	0.999
28d vs. 42d	0.008333	-0.04461 to 0.0612	No	ns	0.9996
28d vs. 49d	-0.022	-0.07495 to 0.0309	No	ns	0.892
28d vs. 56d	0.006667	-0.04628 to 0.0596	No	ns	>0.9999
35d vs. 42d	0.018	-0.03495 to 0.0709	No	ns	0.9604
35d vs. 49d	-0.01233	-0.06528 to 0.0408	No	ns	0.9956
35d vs. 56d	0.01633	-0.03661 to 0.0692	No	ns	0.9767
42d vs. 49d	-0.03033	-0.08328 to 0.0226	No	ns	0.6203
42d vs. 56d	-0.001667	-0.05461 to 0.0512	No	ns	>0.9999
49d vs. 56d	0.02867	-0.02428 to 0.0816	No	ns	0.6843
Female					
7d vs. 14d	-0.05067	-0.1036 to 0.00228	No	ns	0.0702
7d vs. 21d	-0.01967	-0.07261 to 0.0332	No	ns	0.9372
7d vs. 28d	-0.006333	-0.05928 to 0.0466	No	ns	>0.9999
7d vs. 35d	-0.005667	-0.05861 to 0.0472	No	ns	>0.9999
7d vs. 42d	-0.02967	-0.08261 to 0.0232	No	ns	0.6462
7d vs. 49d	0.003	-0.04995 to 0.0559	No	ns	>0.9999
7d vs. 56d	-0.03	-0.08295 to 0.0229	No	ns	0.6333
14d vs. 21d	0.031	-0.02195 to 0.0839	No	ns	0.5942
14d vs. 28d	0.04433	-0.008615 to 0.097	No	ns	0.165
14d vs. 35d	0.045	-0.007948 to 0.097	No	ns	0.1518
14d vs. 42d	0.021	-0.03195 to 0.0739	No	ns	0.9133
14d vs. 49d	0.05367	0.0007187 to 0.1066	Yes	*	0.0448
14d vs. 56d	0.02067	-0.03228 to 0.0736	No	ns	0.9197
21d vs. 28d	0.01333	-0.03961 to 0.0662	No	ns	0.9929
21d vs. 35d	0.014	-0.03895 to 0.0669	No	ns	0.9904
21d vs. 42d	-0.01	-0.06295 to 0.0429	No	ns	0.9988
21d vs. 49d	0.02267	-0.03028 to 0.0756	No	ns	0.8762
21d vs. 56d	-0.01033	-0.06328 to 0.0426	No	ns	0.9985
28d vs. 35d	0.0006667	-0.05228 to 0.0536	No	ns	>0.9999
28d vs. 42d	-0.02333	-0.07628 to 0.0296	No	ns	0.8591
28d vs. 49d	0.009333	-0.04361 to 0.0622	No	ns	0.9992
28d vs. 56d	-0.02367	-0.07661 to 0.0292	No	ns	0.8501
35d vs. 42d	-0.024	-0.07695 to 0.0289	No	ns	0.8408
35d vs. 49d	0.008667	-0.04428 to 0.0616	No	ns	0.9995
35d vs. 56d	-0.02433	-0.07728 to 0.0286	No	ns	0.8313
42d vs. 49d	0.03267	-0.02028 to 0.0856	No	ns	0.5288
42d vs. 56d	-0.0003333	-0.05328 to 0.0526	No	ns	>0.9999
49d vs. 56d	-0.033	-0.08595 to 0.0199	No	ns	0.5158

Baseline Gait Symmetry 10DegDown

Column B vs. Column A	Female vs. Male
Unpaired t test	
P value	0.3657
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.9590, df=8
How big is the difference?	
Mean of column A	1.014
Mean of column B	1.024
Difference between means (B - A) ± SEM	0.01020 ± 0.01064
95% confidence interval	-0.01433 to 0.03473
R squared (eta squared)	0.1031
F test to compare variances	
F, DFn, Dfd	3.371, 4, 4
P value	0.2661
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Max dA/dT (cm^2/s) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	23.84	<0.0001	****	Yes	Mean of Male	1.599
Time	18.35	<0.0001	****	Yes	Mean of Female	-1.069
Sex	1.477	0.5512	ns	No	Difference between means	2.668
Subject	30.52	<0.0001	****	Yes	SE of difference	4.288
					95% CI of difference	-7.221 to 12.56

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-1.505	-13.14 to 10.13	No	ns	0.797
14d					
Male vs. Female	29.97	18.33 to 41.61	Yes	****	<0.0001
21d					
Male vs. Female	-2.822	-14.46 to 8.817	No	ns	0.6298
28d					
Male vs. Female	-5.226	-16.86 to 6.413	No	ns	0.3731
35d					
Male vs. Female	4.724	-6.914 to 16.36	No	ns	0.4204
42d					
Male vs. Female	1.69	-9.948 to 13.33	No	ns	0.7726
49d					
Male vs. Female	-2.27	-13.91 to 9.369	No	ns	0.6982
56d					
Male vs. Female	-3.221	-14.86 to 8.418	No	ns	0.5823
Male					
7d vs. 14d	-13.24	-26.51 to 0.03677	No	ns	0.0511
7d vs. 21d	-6.556	-19.83 to 6.717	No	ns	0.7741
7d vs. 28d	-5.053	-18.33 to 8.220	No	ns	0.929
7d vs. 35d	-16.43	-29.71 to -3.162	Yes	**	0.006
7d vs. 42d	-10.81	-24.08 to 2.468	No	ns	0.1916
7d vs. 49d	-5.639	-18.91 to 7.634	No	ns	0.8804
7d vs. 56d	-6.712	-19.99 to 6.561	No	ns	0.7529
14d vs. 21d	6.68	-6.593 to 19.95	No	ns	0.7573
14d vs. 28d	8.184	-5.089 to 21.46	No	ns	0.5296
14d vs. 35d	-3.198	-16.47 to 10.07	No	ns	0.9945
14d vs. 42d	2.431	-10.84 to 15.70	No	ns	0.999
14d vs. 49d	7.598	-5.675 to 20.87	No	ns	0.6213
14d vs. 56d	6.524	-6.749 to 19.80	No	ns	0.7784
21d vs. 28d	1.504	-11.77 to 14.78	No	ns	>0.9999
21d vs. 35d	-9.878	-23.15 to 3.395	No	ns	0.2896
21d vs. 42d	-4.249	-17.52 to 9.024	No	ns	0.9714
21d vs. 49d	0.9177	-12.36 to 14.19	No	ns	>0.9999
21d vs. 56d	-0.1557	-13.43 to 13.12	No	ns	>0.9999
28d vs. 35d	-11.38	-24.66 to 1.891	No	ns	0.1442
28d vs. 42d	-5.753	-19.03 to 7.520	No	ns	0.8691
28d vs. 49d	-0.586	-13.86 to 12.69	No	ns	>0.9999
28d vs. 56d	-1.659	-14.93 to 11.61	No	ns	>0.9999
35d vs. 42d	5.629	-7.644 to 18.90	No	ns	0.8813
35d vs. 49d	10.8	-2.477 to 24.07	No	ns	0.1924
35d vs. 56d	9.723	-3.550 to 23.00	No	ns	0.3087
42d vs. 49d	5.167	-8.106 to 18.44	No	ns	0.9208
42d vs. 56d	4.093	-9.180 to 17.37	No	ns	0.9767
49d vs. 56d	-1.073	-14.35 to 12.20	No	ns	>0.9999
Female					
7d vs. 14d	18.24	4.966 to 31.51	Yes	**	0.0015
7d vs. 21d	-7.873	-21.15 to 5.400	No	ns	0.5782
7d vs. 28d	-8.774	-22.05 to 4.499	No	ns	0.4393
7d vs. 35d	-10.21	-23.48 to 3.067	No	ns	0.2518
7d vs. 42d	-7.61	-20.88 to 5.663	No	ns	0.6193
7d vs. 49d	-6.404	-19.68 to 6.869	No	ns	0.7941
7d vs. 56d	-8.428	-21.70 to 4.845	No	ns	0.4917
14d vs. 21d	-26.11	-39.39 to -12.84	Yes	****	<0.0001
14d vs. 28d	-27.01	-40.29 to -13.74	Yes	****	<0.0001
14d vs. 35d	-28.44	-41.72 to -15.17	Yes	****	<0.0001
14d vs. 42d	-25.85	-39.12 to -12.58	Yes	****	<0.0001
14d vs. 49d	-24.64	-37.92 to -11.37	Yes	****	<0.0001
14d vs. 56d	-26.67	-39.94 to -13.39	Yes	****	<0.0001
21d vs. 28d	-0.9007	-14.17 to 12.37	No	ns	>0.9999
21d vs. 35d	-2.332	-15.61 to 10.94	No	ns	0.9993
21d vs. 42d	0.263	-13.01 to 13.54	No	ns	>0.9999
21d vs. 49d	1.47	-11.80 to 14.74	No	ns	>0.9999
21d vs. 56d	-0.555	-13.83 to 12.72	No	ns	>0.9999
28d vs. 35d	-1.432	-14.70 to 11.84	No	ns	>0.9999
28d vs. 42d	1.164	-12.11 to 14.44	No	ns	>0.9999
28d vs. 49d	2.37	-10.90 to 15.64	No	ns	0.9992
28d vs. 56d	0.3457	-12.93 to 13.62	No	ns	>0.9999
35d vs. 42d	2.595	-10.68 to 15.87	No	ns	0.9985
35d vs. 49d	3.802	-9.471 to 17.08	No	ns	0.9847
35d vs. 56d	1.777	-11.50 to 15.05	No	ns	0.9999
42d vs. 49d	1.207	-12.07 to 14.48	No	ns	>0.9999
42d vs. 56d	-0.818	-14.09 to 12.46	No	ns	>0.9999
49d vs. 56d	-2.025	-15.30 to 11.25	No	ns	0.9997

Baseline Max dA/dT (cm^2/s) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.1857
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.448, df=8
How big is the difference?	
Mean of column A	53.81
Mean of column B	45.14
Difference between means (B - A) ±	-8.672 ± 5.990
95% confidence interval	-22.48 to 5.141
R squared (eta squared)	0.2076
F test to compare variances	
F, DFn, Dfd	6.155, 4, 4
P value	0.1063
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Max dA/dT (cm^2/s) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	15.35	<0.0001	****	Yes	Mean of Male	0.2857
Time	26.5	<0.0001	****	Yes	Mean of Female	2.177
Sex	0.392	0.7723	ns	No	Difference between means	-1.892
Subject	35	<0.0001	****	Yes	SE of difference	6.32
					95% CI of difference	-16.47 to 12.68

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	5.084	-11.14 to 21.30	No	ns	0.5334
14d					
Male vs. Female	24.01	7.793 to 40.23	Yes	**	0.0043
21d					
Male vs. Female	-5.279	-21.50 to 10.94	No	ns	0.5179
28d					
Male vs. Female	-8.158	-24.38 to 8.062	No	ns	0.3188
35d					
Male vs. Female	3.145	-13.07 to 19.37	No	ns	0.6997
42d					
Male vs. Female	-16.62	-32.84 to -0.4023	Yes	*	0.0447
49d					
Male vs. Female	-5.777	-22.00 to 10.44	No	ns	0.4793
56d					
Male vs. Female	-11.54	-27.76 to 4.680	No	ns	0.1601
Male					
7d vs. 14d	4.6	-12.55 to 21.75	No	ns	0.9896
7d vs. 21d	-7.098	-24.25 to 10.05	No	ns	0.894
7d vs. 28d	2.522	-14.63 to 19.67	No	ns	0.9998
7d vs. 35d	-5.666	-22.82 to 11.49	No	ns	0.966
7d vs. 42d	-0.9563	-18.11 to 16.20	No	ns	>0.9999
7d vs. 49d	3.868	-13.28 to 21.02	No	ns	0.9964
7d vs. 56d	7.196	-9.956 to 24.35	No	ns	0.8871
14d vs. 21d	-11.7	-28.85 to 5.454	No	ns	0.3987
14d vs. 28d	-2.078	-19.23 to 15.07	No	ns	>0.9999
14d vs. 35d	-10.27	-27.42 to 6.885	No	ns	0.567
14d vs. 42d	-5.557	-22.71 to 11.60	No	ns	0.9694
14d vs. 49d	-0.7327	-17.88 to 16.42	No	ns	>0.9999
14d vs. 56d	2.595	-14.56 to 19.75	No	ns	0.9997
21d vs. 28d	9.62	-7.532 to 26.77	No	ns	0.645
21d vs. 35d	1.432	-15.72 to 18.58	No	ns	>0.9999
21d vs. 42d	6.142	-11.01 to 23.29	No	ns	0.9479
21d vs. 49d	10.97	-6.186 to 28.12	No	ns	0.4829
21d vs. 56d	14.29	-2.858 to 31.45	No	ns	0.1693
28d vs. 35d	-8.189	-25.34 to 8.963	No	ns	0.8026
28d vs. 42d	-3.479	-20.63 to 13.67	No	ns	0.9981
28d vs. 49d	1.345	-15.81 to 18.50	No	ns	>0.9999
28d vs. 56d	4.673	-12.48 to 21.83	No	ns	0.9886
35d vs. 42d	4.71	-12.44 to 21.86	No	ns	0.988
35d vs. 49d	9.534	-7.618 to 26.69	No	ns	0.6553
35d vs. 56d	12.86	-4.290 to 30.01	No	ns	0.2807
42d vs. 49d	4.824	-12.33 to 21.98	No	ns	0.9862
42d vs. 56d	8.152	-9.000 to 25.30	No	ns	0.8061
49d vs. 56d	3.328	-13.82 to 20.48	No	ns	0.9986
Female					
7d vs. 14d	23.53	6.377 to 40.68	Yes	**	0.0016
7d vs. 21d	-17.46	-34.61 to -0.3092	Yes	*	0.0432
7d vs. 28d	-10.72	-27.87 to 6.432	No	ns	0.5122
7d vs. 35d	-7.605	-24.76 to 9.547	No	ns	0.8553
7d vs. 42d	-22.66	-39.81 to -5.511	Yes	**	0.0026
7d vs. 49d	-6.994	-24.15 to 10.16	No	ns	0.9011
7d vs. 56d	-9.429	-26.58 to 7.723	No	ns	0.6677
14d vs. 21d	-40.99	-58.14 to -23.84	Yes	****	<0.0001
14d vs. 28d	-34.25	-51.40 to -17.10	Yes	****	<0.0001
14d vs. 35d	-31.13	-48.29 to -13.98	Yes	****	<0.0001
14d vs. 42d	-46.19	-63.34 to -29.04	Yes	****	<0.0001
14d vs. 49d	-30.52	-47.67 to -13.37	Yes	****	<0.0001
14d vs. 56d	-32.96	-50.11 to -15.81	Yes	****	<0.0001
21d vs. 28d	6.741	-10.41 to 23.89	No	ns	0.917
21d vs. 35d	9.856	-7.296 to 27.01	No	ns	0.6167
21d vs. 42d	-5.201	-22.35 to 11.95	No	ns	0.9788
21d vs. 49d	10.47	-6.685 to 27.62	No	ns	0.5427
21d vs. 56d	8.033	-9.119 to 25.18	No	ns	0.8175
28d vs. 35d	3.115	-14.04 to 20.27	No	ns	0.9991
28d vs. 42d	-11.94	-29.09 to 5.209	No	ns	0.3721
28d vs. 49d	3.726	-13.43 to 20.88	No	ns	0.9971
28d vs. 56d	1.291	-15.86 to 18.44	No	ns	>0.9999
35d vs. 42d	-15.06	-32.21 to 2.095	No	ns	0.1254
35d vs. 49d	0.6113	-16.54 to 17.76	No	ns	>0.9999
35d vs. 56d	-1.823	-18.98 to 15.33	No	ns	>0.9999
42d vs. 49d	15.67	-1.483 to 32.82	No	ns	0.0972
42d vs. 56d	13.23	-3.918 to 30.39	No	ns	0.248
49d vs. 56d	-2.435	-19.59 to 14.72	No	ns	0.9998

Baseline Max dA/dT (cm^2/s) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.1723
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.499, df=8
How big is the difference?	
Mean of column A	53.59
Mean of column B	43.28
Difference between means (B - A) ±	-10.30 ± 6.873
95% confidence interval	-26.15 to 5.547
R squared (eta squared)	0.2193
F test to compare variances	
F, DFn, Dfd	6.860, 4, 4
P value	0.0889
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Max dA/dT (cm^2/s) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	14.08	0.0011	**	Yes	Mean of Male	-2.506
Time	15.85	0.0004	***	Yes	Mean of Female	-1.337
Sex	0.2415	0.8359	ns	No	Difference between means	-1.169
Subject	42.21	<0.0001	****	Yes	SE of difference	5.465
					95% CI of difference	-13.77 to 11.43

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	1.434	-12.61 to 15.48	No	ns	0.839
14d					
Male vs. Female	19.54	5.495 to 33.58	Yes	**	0.0071
21d					
Male vs. Female	-9.434	-23.48 to 4.608	No	ns	0.1843
28d					
Male vs. Female	-8.176	-22.22 to 5.867	No	ns	0.2491
35d					
Male vs. Female	3.926	-10.12 to 17.97	No	ns	0.5784
42d					
Male vs. Female	-5.391	-19.43 to 8.651	No	ns	0.4459
49d					
Male vs. Female	-4.91	-18.95 to 9.133	No	ns	0.4874
56d					
Male vs. Female	-6.341	-20.38 to 7.701	No	ns	0.3704
Male					
7d vs. 14d	3.341	-11.54 to 18.22	No	ns	0.9965
7d vs. 21d	6.32	-8.559 to 21.20	No	ns	0.8805
7d vs. 28d	2.289	-12.59 to 17.17	No	ns	0.9997
7d vs. 35d	-3.006	-17.89 to 11.87	No	ns	0.9982
7d vs. 42d	-0.1097	-14.99 to 14.77	No	ns	>0.9999
7d vs. 49d	1.282	-13.60 to 16.16	No	ns	>0.9999
7d vs. 56d	5.695	-9.184 to 20.57	No	ns	0.9271
14d vs. 21d	2.979	-11.90 to 17.86	No	ns	0.9983
14d vs. 28d	-1.052	-15.93 to 13.83	No	ns	>0.9999
14d vs. 35d	-6.348	-21.23 to 8.531	No	ns	0.8781
14d vs. 42d	-3.451	-18.33 to 11.43	No	ns	0.9957
14d vs. 49d	-2.06	-16.94 to 12.82	No	ns	0.9998
14d vs. 56d	2.354	-12.53 to 17.23	No	ns	0.9996
21d vs. 28d	-4.031	-18.91 to 10.85	No	ns	0.9889
21d vs. 35d	-9.328	-24.21 to 5.553	No	ns	0.5084
21d vs. 42d	-6.43	-21.31 to 8.449	No	ns	0.8708
21d vs. 49d	-5.038	-19.92 to 9.841	No	ns	0.9612
21d vs. 56d	-0.625	-15.50 to 14.25	No	ns	>0.9999
28d vs. 35d	-5.295	-20.17 to 9.584	No	ns	0.9496
28d vs. 42d	-2.399	-17.28 to 12.48	No	ns	0.9996
28d vs. 49d	-1.007	-15.89 to 13.87	No	ns	>0.9999
28d vs. 56d	3.406	-11.47 to 18.28	No	ns	0.996
35d vs. 42d	2.897	-11.98 to 17.78	No	ns	0.9986
35d vs. 49d	4.288	-10.59 to 19.17	No	ns	0.9842
35d vs. 56d	8.701	-6.178 to 23.58	No	ns	0.5956
42d vs. 49d	1.391	-13.49 to 16.27	No	ns	>0.9999
42d vs. 56d	5.805	-9.074 to 20.68	No	ns	0.9199
49d vs. 56d	4.413	-10.47 to 19.29	No	ns	0.9813
Female					
7d vs. 14d	21.44	6.566 to 36.32	Yes	***	0.0008
7d vs. 21d	-4.549	-19.43 to 10.33	No	ns	0.9778
7d vs. 28d	-7.321	-22.20 to 7.558	No	ns	0.7775
7d vs. 35d	-0.5147	-15.39 to 14.36	No	ns	>0.9999
7d vs. 42d	-6.935	-21.81 to 7.944	No	ns	0.821
7d vs. 49d	-5.063	-19.94 to 9.816	No	ns	0.9602
7d vs. 56d	-2.081	-16.96 to 12.80	No	ns	0.9998
14d vs. 21d	-25.99	-40.87 to -11.11	Yes	****	<0.0001
14d vs. 28d	-28.77	-43.64 to -13.89	Yes	****	<0.0001
14d vs. 35d	-21.96	-36.84 to -7.080	Yes	***	0.0005
14d vs. 42d	-28.38	-43.26 to -13.50	Yes	****	<0.0001
14d vs. 49d	-26.51	-41.39 to -11.63	Yes	****	<0.0001
14d vs. 56d	-23.53	-38.40 to -8.646	Yes	***	0.0002
21d vs. 28d	-2.772	-17.65 to 12.11	No	ns	0.9989
21d vs. 35d	4.034	-10.84 to 18.91	No	ns	0.9889
21d vs. 42d	-2.387	-17.27 to 12.49	No	ns	0.9996
21d vs. 49d	-0.514	-15.39 to 14.36	No	ns	>0.9999
21d vs. 56d	2.468	-12.41 to 17.35	No	ns	0.9995
28d vs. 35d	6.806	-8.073 to 21.69	No	ns	0.8345
28d vs. 42d	0.3857	-14.49 to 15.26	No	ns	>0.9999
28d vs. 49d	2.258	-12.62 to 17.14	No	ns	0.9997
28d vs. 56d	5.24	-9.639 to 20.12	No	ns	0.9522
35d vs. 42d	-6.421	-21.30 to 8.458	No	ns	0.8717
35d vs. 49d	-4.548	-19.43 to 10.33	No	ns	0.9778
35d vs. 56d	-1.566	-16.44 to 13.31	No	ns	>0.9999
42d vs. 49d	1.873	-13.01 to 16.75	No	ns	>0.9999
42d vs. 56d	4.855	-10.02 to 19.73	No	ns	0.9682
49d vs. 56d	2.982	-11.90 to 17.86	No	ns	0.9983

Baseline Max dA/dT (cm^2/s) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.0858
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.959, df=8
How big is the difference?	
Mean of column A	55.09
Mean of column B	46.15
Difference between means (B - A) ± SEM	-8.933 ± 4.559
95% confidence interval	-19.45 to 1.581
R squared (eta squared)	0.3243
F test to compare variances	
F, DFn, Dfd	3.573, 4, 4
P value	0.245
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Min dA/dT (cm^2/s) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	9.687	0.0004	***	Yes	Mean of Male	1.397
Time	9.603	0.0004	***	Yes	Mean of Female	0.3665
Sex	1.748	0.6481	ns	No	Difference between means	1.03
Subject	62.18	<0.0001	****	Yes	SE of difference	2.173
					95% CI of difference	-3.980 to 6.040

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	1.578	-3.313 to 6.469	No	ns	0.5216
14d					
Male vs. Female	-5.137	-10.03 to -0.2456	Yes	*	0.0399
21d					
Male vs. Female	3.119	-1.772 to 8.010	No	ns	0.2073
28d					
Male vs. Female	1.591	-3.299 to 6.482	No	ns	0.518
35d					
Male vs. Female	1.491	-3.400 to 6.382	No	ns	0.5447
42d					
Male vs. Female	1.149	-3.742 to 6.040	No	ns	0.6405
49d					
Male vs. Female	2.923	-1.968 to 7.814	No	ns	0.2369
56d					
Male vs. Female	1.527	-3.364 to 6.418	No	ns	0.535
Male					
7d vs. 14d	0.45	-3.348 to 4.248	No	ns	>0.9999
7d vs. 21d	-0.5413	-4.340 to 3.257	No	ns	0.9998
7d vs. 28d	-0.7767	-4.575 to 3.022	No	ns	0.998
7d vs. 35d	1.556	-2.242 to 5.354	No	ns	0.8989
7d vs. 42d	0.486	-3.312 to 4.284	No	ns	>0.9999
7d vs. 49d	-1.181	-4.980 to 2.617	No	ns	0.9756
7d vs. 56d	0.5573	-3.241 to 4.356	No	ns	0.9998
14d vs. 21d	-0.9913	-4.790 to 2.807	No	ns	0.9911
14d vs. 28d	-1.227	-5.025 to 2.572	No	ns	0.97
14d vs. 35d	1.106	-2.692 to 4.904	No	ns	0.9832
14d vs. 42d	0.036	-3.762 to 3.834	No	ns	>0.9999
14d vs. 49d	-1.631	-5.430 to 2.167	No	ns	0.8744
14d vs. 56d	0.1073	-3.691 to 3.906	No	ns	>0.9999
21d vs. 28d	-0.2353	-4.034 to 3.563	No	ns	>0.9999
21d vs. 35d	2.097	-1.701 to 5.896	No	ns	0.6627
21d vs. 42d	1.027	-2.771 to 4.826	No	ns	0.9891
21d vs. 49d	-0.64	-4.438 to 3.158	No	ns	0.9994
21d vs. 56d	1.099	-2.700 to 4.897	No	ns	0.9838
28d vs. 35d	2.333	-1.466 to 6.131	No	ns	0.5347
28d vs. 42d	1.263	-2.536 to 5.061	No	ns	0.9648
28d vs. 49d	-0.4047	-4.203 to 3.394	No	ns	>0.9999
28d vs. 56d	1.334	-2.464 to 5.132	No	ns	0.9529
35d vs. 42d	-1.07	-4.868 to 2.728	No	ns	0.9861
35d vs. 49d	-2.737	-6.536 to 1.061	No	ns	0.3287
35d vs. 56d	-0.9987	-4.797 to 2.800	No	ns	0.9907
42d vs. 49d	-1.667	-5.466 to 2.131	No	ns	0.8615
42d vs. 56d	0.07133	-3.727 to 3.870	No	ns	>0.9999
49d vs. 56d	1.739	-2.060 to 5.537	No	ns	0.8341
Female					
7d vs. 14d	-6.264	-10.06 to -2.466	Yes	****	<0.0001
7d vs. 21d	0.9997	-2.799 to 4.798	No	ns	0.9907
7d vs. 28d	-0.763	-4.561 to 3.035	No	ns	0.9982
7d vs. 35d	1.469	-2.329 to 5.267	No	ns	0.9233
7d vs. 42d	0.057	-3.741 to 3.855	No	ns	>0.9999
7d vs. 49d	0.164	-3.634 to 3.962	No	ns	>0.9999
7d vs. 56d	0.5067	-3.292 to 4.305	No	ns	0.9999
14d vs. 21d	7.264	3.466 to 11.06	Yes	****	<0.0001
14d vs. 28d	5.501	1.703 to 9.300	Yes	***	0.0007
14d vs. 35d	7.733	3.935 to 11.53	Yes	****	<0.0001
14d vs. 42d	6.321	2.523 to 10.12	Yes	****	<0.0001
14d vs. 49d	6.428	2.630 to 10.23	Yes	****	<0.0001
14d vs. 56d	6.771	2.973 to 10.57	Yes	****	<0.0001
21d vs. 28d	-1.763	-5.561 to 2.036	No	ns	0.8243
21d vs. 35d	0.4693	-3.329 to 4.268	No	ns	>0.9999
21d vs. 42d	-0.9427	-4.741 to 2.856	No	ns	0.9935
21d vs. 49d	-0.8357	-4.634 to 2.963	No	ns	0.9969
21d vs. 56d	-0.493	-4.291 to 3.305	No	ns	>0.9999
28d vs. 35d	2.232	-1.566 to 6.030	No	ns	0.5898
28d vs. 42d	0.82	-2.978 to 4.618	No	ns	0.9972
28d vs. 49d	0.927	-2.871 to 4.725	No	ns	0.9941
28d vs. 56d	1.27	-2.529 to 5.068	No	ns	0.9638
35d vs. 42d	-1.412	-5.210 to 2.386	No	ns	0.937
35d vs. 49d	-1.305	-5.103 to 2.493	No	ns	0.9581
35d vs. 56d	-0.9623	-4.761 to 2.836	No	ns	0.9926
42d vs. 49d	0.107	-3.691 to 3.905	No	ns	>0.9999
42d vs. 56d	0.4497	-3.349 to 4.248	No	ns	>0.9999
49d vs. 56d	0.3427	-3.456 to 4.141	No	ns	>0.9999

Baseline Min dA/dT (cm^2/s) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.4856
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.7311, df=8
How big is the difference?	
Mean of column A	-13.02
Mean of column B	-11.2
Difference between means (B - A) ± 1.825 ± 2.497	
95% confidence interval	-3.933 to 7.584
R squared (eta squared)	0.06262
F test to compare variances	
F, DFn, Dfd	11.86, 4, 4
P value	0.0344
P value summary	*
Significantly different (P < 0.05)?	Yes
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Min dA/dT (cm^2/s) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	14.58	<0.0001	****	Yes	Mean of Male	0.2264
Time	19.27	<0.0001	****	Yes	Mean of Female	0.04106
Sex	0.05564	0.9254	ns	No	Difference between means	0.1854
Subject	47.69	<0.0001	****	Yes	SE of difference	1.919
					95% CI of difference	-4.239 to 4.610

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-1.134	-5.647 to 3.378	No	ns	0.6173
14d					
Male vs. Female	-6.706	-11.22 to -2.194	Yes	**	0.0042
21d					
Male vs. Female	1.704	-2.808 to 6.216	No	ns	0.4534
28d					
Male vs. Female	-0.4666	-4.979 to 4.046	No	ns	0.837
35d					
Male vs. Female	0.4551	-4.057 to 4.967	No	ns	0.841
42d					
Male vs. Female	3.88	-0.6326 to 8.392	No	ns	0.0907
49d					
Male vs. Female	1.321	-3.192 to 5.833	No	ns	0.5608
56d					
Male vs. Female	2.43	-2.082 to 6.943	No	ns	0.286
Male					
7d vs. 14d	-2.433	-6.444 to 1.579	No	ns	0.5506
7d vs. 21d	-1.421	-5.432 to 2.591	No	ns	0.9508
7d vs. 28d	-2.587	-6.598 to 1.424	No	ns	0.4715
7d vs. 35d	-1.399	-5.411 to 2.612	No	ns	0.9546
7d vs. 42d	-2.096	-6.107 to 1.915	No	ns	0.7213
7d vs. 49d	-3.424	-7.436 to 0.5871	No	ns	0.148
7d vs. 56d	-3.003	-7.015 to 1.008	No	ns	0.2825
14d vs. 21d	1.012	-2.999 to 5.023	No	ns	0.9928
14d vs. 28d	-0.1543	-4.166 to 3.857	No	ns	>0.9999
14d vs. 35d	1.033	-2.978 to 5.045	No	ns	0.9918
14d vs. 42d	0.3367	-3.675 to 4.348	No	ns	>0.9999
14d vs. 49d	-0.9917	-5.003 to 3.020	No	ns	0.9936
14d vs. 56d	-0.5707	-4.582 to 3.441	No	ns	0.9998
21d vs. 28d	-1.166	-5.178 to 2.845	No	ns	0.9833
21d vs. 35d	0.02133	-3.990 to 4.033	No	ns	>0.9999
21d vs. 42d	-0.6753	-4.687 to 3.336	No	ns	0.9994
21d vs. 49d	-2.004	-6.015 to 2.008	No	ns	0.7642
21d vs. 56d	-1.583	-5.594 to 2.429	No	ns	0.9155
28d vs. 35d	1.188	-2.824 to 5.199	No	ns	0.9815
28d vs. 42d	0.491	-3.520 to 4.502	No	ns	>0.9999
28d vs. 49d	-0.8373	-4.849 to 3.174	No	ns	0.9978
28d vs. 56d	-0.4163	-4.428 to 3.595	No	ns	>0.9999
35d vs. 42d	-0.6967	-4.708 to 3.315	No	ns	0.9993
35d vs. 49d	-2.025	-6.036 to 1.986	No	ns	0.7545
35d vs. 56d	-1.604	-5.615 to 2.407	No	ns	0.9098
42d vs. 49d	-1.328	-5.340 to 2.683	No	ns	0.9656
42d vs. 56d	-0.9073	-4.919 to 3.104	No	ns	0.9963
49d vs. 56d	0.421	-3.590 to 4.432	No	ns	>0.9999
Female					
7d vs. 14d	-8.005	-12.02 to -3.993	Yes	****	<0.0001
7d vs. 21d	1.418	-2.594 to 5.429	No	ns	0.9514
7d vs. 28d	-1.919	-5.931 to 2.092	No	ns	0.8008
7d vs. 35d	0.19	-3.821 to 4.201	No	ns	>0.9999
7d vs. 42d	2.918	-1.093 to 6.929	No	ns	0.3172
7d vs. 49d	-0.9693	-4.981 to 3.042	No	ns	0.9944
7d vs. 56d	0.5613	-3.450 to 4.573	No	ns	0.9998
14d vs. 21d	9.422	5.411 to 13.43	Yes	****	<0.0001
14d vs. 28d	6.085	2.074 to 10.10	Yes	***	0.0003
14d vs. 35d	8.195	4.183 to 12.21	Yes	****	<0.0001
14d vs. 42d	10.92	6.911 to 14.93	Yes	****	<0.0001
14d vs. 49d	7.035	3.024 to 11.05	Yes	****	<0.0001
14d vs. 56d	8.566	4.555 to 12.58	Yes	****	<0.0001
21d vs. 28d	-3.337	-7.348 to 0.6744	No	ns	0.1709
21d vs. 35d	-1.228	-5.239 to 2.784	No	ns	0.9777
21d vs. 42d	1.5	-2.511 to 5.512	No	ns	0.935
21d vs. 49d	-2.387	-6.398 to 1.624	No	ns	0.5743
21d vs. 56d	-0.8563	-4.868 to 3.155	No	ns	0.9974
28d vs. 35d	2.109	-1.902 to 6.121	No	ns	0.7149
28d vs. 42d	4.837	0.8259 to 8.849	Yes	**	0.0081
28d vs. 49d	0.95	-3.061 to 4.961	No	ns	0.9951
28d vs. 56d	2.481	-1.531 to 6.492	No	ns	0.5258
35d vs. 42d	2.728	-1.283 to 6.739	No	ns	0.4025
35d vs. 49d	-1.159	-5.171 to 2.852	No	ns	0.9839
35d vs. 56d	0.3713	-3.640 to 4.383	No	ns	>0.9999
42d vs. 49d	-3.887	-7.899 to 0.1241	No	ns	0.0639
42d vs. 56d	-2.357	-6.368 to 1.655	No	ns	0.5901
49d vs. 56d	1.531	-2.481 to 5.542	No	ns	0.9282

Baseline Min dA/dT (cm^2/s) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.7908
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.2743, df=8
How big is the difference?	
Mean of column A	-11.3
Mean of column B	-10.78
Difference between means (B - A) ± 0.5164 ± 1.882	
95% confidence interval	-3.825 to 4.857
R squared (eta squared)	0.009319
F test to compare variances	
F, DFn, Dfd	3.472, 4, 4
P value	0.2553
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Min dA/dT (cm^2/s) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	15.51	0.0008	***	Yes	Mean of Male 0.9285
Time	17.8	0.0003	***	Yes	Mean of Female 0.8535
Sex	0.01427	0.9572	ns	No	Difference between means 0.07503
Subject	37.26	<0.0001	****	Yes	SE of difference 1.355
					95% CI of difference -3.051 to 3.201
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-1.912	-5.535 to 1.710	No	ns	0.2955
14d					
Male vs. Female	-3.192	-6.814 to 0.4300	No	ns	0.0831
21d					
Male vs. Female	1.278	-2.344 to 4.900	No	ns	0.4835
28d					
Male vs. Female	0.2585	-3.364 to 3.881	No	ns	0.8871
35d					
Male vs. Female	-3.537	-7.159 to 0.08501	No	ns	0.0555
42d					
Male vs. Female	2.78	-0.8423 to 6.402	No	ns	0.1302
49d					
Male vs. Female	3.194	-0.4279 to 6.816	No	ns	0.0829
56d					
Male vs. Female	1.732	-1.891 to 5.354	No	ns	0.3432
Male					
7d vs. 14d	-2.887	-6.940 to 1.166	No	ns	0.3434
7d vs. 21d	-2.245	-6.298 to 1.808	No	ns	0.6591
7d vs. 28d	-1.35	-5.403 to 2.703	No	ns	0.9645
7d vs. 35d	1.788	-2.265 to 5.841	No	ns	0.8586
7d vs. 42d	-1.825	-5.878 to 2.228	No	ns	0.8452
7d vs. 49d	-1.842	-5.895 to 2.211	No	ns	0.8389
7d vs. 56d	-2.468	-6.521 to 1.585	No	ns	0.5453
14d vs. 21d	0.6413	-3.412 to 4.694	No	ns	0.9996
14d vs. 28d	1.537	-2.516 to 5.590	No	ns	0.9305
14d vs. 35d	4.674	0.6212 to 8.727	Yes	*	0.0133
14d vs. 42d	1.061	-2.992 to 5.114	No	ns	0.991
14d vs. 49d	1.044	-3.009 to 5.097	No	ns	0.9918
14d vs. 56d	0.4183	-3.635 to 4.471	No	ns	>0.9999
21d vs. 28d	0.8953	-3.158 to 4.948	No	ns	0.9968
21d vs. 35d	4.033	-0.02013 to 8.086	No	ns	0.052
21d vs. 42d	0.42	-3.633 to 4.473	No	ns	>0.9999
21d vs. 49d	0.403	-3.650 to 4.456	No	ns	>0.9999
21d vs. 56d	-0.223	-4.276 to 3.830	No	ns	>0.9999
28d vs. 35d	3.138	-0.9155 to 7.191	No	ns	0.2443
28d vs. 42d	-0.4753	-4.528 to 3.578	No	ns	>0.9999
28d vs. 49d	-0.4923	-4.545 to 3.561	No	ns	>0.9999
28d vs. 56d	-1.118	-5.171 to 2.935	No	ns	0.9877
35d vs. 42d	-3.613	-7.666 to 0.4401	No	ns	0.114
35d vs. 49d	-3.63	-7.683 to 0.4231	No	ns	0.1107
35d vs. 56d	-4.256	-8.309 to -0.2029	Yes	*	0.0331
42d vs. 49d	-0.017	-4.070 to 4.036	No	ns	>0.9999
42d vs. 56d	-0.643	-4.696 to 3.410	No	ns	0.9996
49d vs. 56d	-0.626	-4.679 to 3.427	No	ns	0.9997
Female					
7d vs. 14d	-4.166	-8.219 to -0.1132	Yes	*	0.0398
7d vs. 21d	0.945	-3.108 to 4.998	No	ns	0.9955
7d vs. 28d	0.821	-3.232 to 4.874	No	ns	0.9981
7d vs. 35d	0.163	-3.890 to 4.216	No	ns	>0.9999
7d vs. 42d	2.867	-1.186 to 6.920	No	ns	0.352
7d vs. 49d	3.284	-0.7888 to 7.317	No	ns	0.2023
7d vs. 56d	1.176	-2.877 to 5.229	No	ns	0.9836
14d vs. 21d	5.111	1.058 to 9.164	Yes	**	0.0048
14d vs. 28d	4.987	0.9342 to 9.040	Yes	**	0.0064
14d vs. 35d	4.329	0.2762 to 8.382	Yes	*	0.0283
14d vs. 42d	7.033	2.980 to 11.09	Yes	****	<0.0001
14d vs. 49d	7.431	3.378 to 11.48	Yes	****	<0.0001
14d vs. 56d	5.342	1.289 to 9.395	Yes	**	0.0027
21d vs. 28d	-0.124	-4.177 to 3.929	No	ns	>0.9999
21d vs. 35d	-0.782	-4.835 to 3.271	No	ns	0.9986
21d vs. 42d	1.922	-2.131 to 5.975	No	ns	0.8079
21d vs. 49d	2.319	-1.734 to 6.372	No	ns	0.6217
21d vs. 56d	0.2307	-3.822 to 4.284	No	ns	>0.9999
28d vs. 35d	-0.658	-4.711 to 3.395	No	ns	0.9996
28d vs. 42d	2.046	-2.007 to 6.099	No	ns	0.7546
28d vs. 49d	2.443	-1.610 to 6.496	No	ns	0.5581
28d vs. 56d	0.3547	-3.698 to 4.408	No	ns	>0.9999
35d vs. 42d	2.704	-1.349 to 6.757	No	ns	0.4274
35d vs. 49d	3.101	-0.9518 to 7.154	No	ns	0.2573
35d vs. 56d	1.013	-3.040 to 5.066	No	ns	0.9932
42d vs. 49d	0.3973	-3.656 to 4.450	No	ns	>0.9999
42d vs. 56d	-1.691	-5.744 to 2.362	No	ns	0.8898
49d vs. 56d	-2.089	-6.142 to 1.964	No	ns	0.735

Baseline Min dA/dT (cm^2/s) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.7039
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.3939, df=8
How big is the difference?	
Mean of column A	-12.35
Mean of column B	-11.77
Difference between means (B - A) ± SEM	0.5755 ± 1.461
95% confidence interval	-2.794 to 3.945
R squared (eta squared)	0.01903
F test to compare variances	
F, DFn, Dfd	3.593, 4, 4
P value	0.2431
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Placement (cm) FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	-0.003233
Time x Sex	2.016	0.3602	ns	No	Mean of Male	-0.015
Time	5.474	0.0085	**	Yes	Mean of Female	0.01177
Sex	0.04156	0.9496	ns	No	Difference between means	0.1804
Subject	78.14	<0.0001	****	Yes	SE of difference	-0.4042 to 0.4278

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.0486	-0.3434 to 0.4406	No	ns	0.8052
14d					
Male vs. Female	0.08693	-0.3051 to 0.4790	No	ns	0.6593
21d					
Male vs. Female	-0.0414	-0.4334 to 0.3506	No	ns	0.8336
28d					
Male vs. Female	0.0006	-0.3914 to 0.3926	No	ns	0.9976
35d					
Male vs. Female	0.08527	-0.3068 to 0.4773	No	ns	0.6654
42d					
Male vs. Female	0.1153	-0.2768 to 0.5073	No	ns	0.559
49d					
Male vs. Female	-0.06573	-0.4578 to 0.3263	No	ns	0.7387
56d					
Male vs. Female	-0.1354	-0.5274 to 0.2566	No	ns	0.4927
Male					
7d vs. 14d	-0.094	-0.3540 to 0.1660	No	ns	0.9452
7d vs. 21d	0.01133	-0.2486 to 0.2713	No	ns	>0.9999
7d vs. 28d	-0.016	-0.2760 to 0.2440	No	ns	>0.9999
7d vs. 35d	-0.1983	-0.4583 to 0.06162	No	ns	0.2606
7d vs. 42d	-0.08267	-0.3426 to 0.1773	No	ns	0.9724
7d vs. 49d	-0.1197	-0.3796 to 0.1403	No	ns	0.8301
7d vs. 56d	-0.07	-0.3300 to 0.1900	No	ns	0.9893
14d vs. 21d	0.1053	-0.1546 to 0.3653	No	ns	0.904
14d vs. 28d	0.078	-0.1820 to 0.3380	No	ns	0.98
14d vs. 35d	-0.1043	-0.3643 to 0.1556	No	ns	0.9082
14d vs. 42d	0.01133	-0.2486 to 0.2713	No	ns	>0.9999
14d vs. 49d	-0.02567	-0.2856 to 0.2343	No	ns	>0.9999
14d vs. 56d	0.024	-0.2360 to 0.2840	No	ns	>0.9999
21d vs. 28d	-0.02733	-0.2873 to 0.2326	No	ns	>0.9999
21d vs. 35d	-0.2097	-0.4696 to 0.05029	No	ns	0.2008
21d vs. 42d	-0.094	-0.3540 to 0.1660	No	ns	0.9452
21d vs. 49d	-0.131	-0.3910 to 0.1290	No	ns	0.7561
21d vs. 56d	-0.08133	-0.3413 to 0.1786	No	ns	0.9748
28d vs. 35d	-0.1823	-0.4423 to 0.07762	No	ns	0.3627
28d vs. 42d	-0.06667	-0.3266 to 0.1933	No	ns	0.992
28d vs. 49d	-0.1037	-0.3636 to 0.1563	No	ns	0.911
28d vs. 56d	-0.054	-0.3140 to 0.2060	No	ns	0.9978
35d vs. 42d	0.1157	-0.1443 to 0.3756	No	ns	0.8531
35d vs. 49d	0.07867	-0.1813 to 0.3386	No	ns	0.9791
35d vs. 56d	0.1283	-0.1316 to 0.3883	No	ns	0.7746
42d vs. 49d	-0.037	-0.2970 to 0.2230	No	ns	0.9998
42d vs. 56d	0.01267	-0.2473 to 0.2726	No	ns	>0.9999
49d vs. 56d	0.04967	-0.2103 to 0.3096	No	ns	0.9987
Female					
7d vs. 14d	-0.05567	-0.3156 to 0.2043	No	ns	0.9974
7d vs. 21d	-0.07867	-0.3386 to 0.1813	No	ns	0.9791
7d vs. 28d	-0.064	-0.3240 to 0.1960	No	ns	0.9938
7d vs. 35d	-0.1617	-0.4216 to 0.09829	No	ns	0.5186
7d vs. 42d	-0.016	-0.2760 to 0.2440	No	ns	>0.9999
7d vs. 49d	-0.234	-0.4940 to 0.02595	No	ns	0.1071
7d vs. 56d	-0.254	-0.5140 to 0.00595	No	ns	0.06
14d vs. 21d	-0.023	-0.2830 to 0.2370	No	ns	>0.9999
14d vs. 28d	-0.008333	-0.2683 to 0.2516	No	ns	>0.9999
14d vs. 35d	-0.106	-0.3660 to 0.1540	No	ns	0.9011
14d vs. 42d	0.03967	-0.2203 to 0.2996	No	ns	0.9997
14d vs. 49d	-0.1783	-0.4383 to 0.08162	No	ns	0.3912
14d vs. 56d	-0.1983	-0.4583 to 0.06162	No	ns	0.2606
21d vs. 28d	0.01467	-0.2453 to 0.2746	No	ns	>0.9999
21d vs. 35d	-0.083	-0.3430 to 0.1770	No	ns	0.9718
21d vs. 42d	0.06267	-0.1973 to 0.3226	No	ns	0.9945
21d vs. 49d	-0.1553	-0.4153 to 0.1046	No	ns	0.5691
21d vs. 56d	-0.1753	-0.4353 to 0.08462	No	ns	0.4131
28d vs. 35d	-0.09767	-0.3576 to 0.1623	No	ns	0.9335
28d vs. 42d	0.048	-0.2120 to 0.3080	No	ns	0.999
28d vs. 49d	-0.17	-0.4300 to 0.08995	No	ns	0.4534
28d vs. 56d	-0.19	-0.4500 to 0.06995	No	ns	0.3114
35d vs. 42d	0.1457	-0.1143 to 0.4056	No	ns	0.6461
35d vs. 49d	-0.07233	-0.3323 to 0.1876	No	ns	0.9871
35d vs. 56d	-0.09233	-0.3523 to 0.1676	No	ns	0.9501
42d vs. 49d	-0.218	-0.4780 to 0.04195	No	ns	0.1636
42d vs. 56d	-0.238	-0.4980 to 0.02195	No	ns	0.0958
49d vs. 56d	-0.02	-0.2800 to 0.2400	No	ns	>0.9999

Baseline Paw Placement (cm) FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.8651
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.1754, df=8
How big is the difference?	
Mean of column A	0.3871
Mean of column B	0.351
Difference between means (B - A) ±	±0.03607 ± 0.2056
95% confidence interval	-0.5102 to 0.4381
R squared (eta squared)	0.003831
F test to compare variances	
F, DFn, Dfd	14.27, 4, 4
P value	0.0246
P value summary	*
Significantly different (P < 0.05)?	Yes
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Placement (cm) 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	7.922	0.012	*	Yes	-0.09429
Time	17.53	<0.0001	****	Yes	0.03687
Sex	5.672	0.3541	ns	No	-0.1312
Subject	46.91	<0.0001	****	Yes	0.1334
					95% CI of difference
					-0.4387 to 0.1764
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	-0.3067	-0.6295 to 0.01617	No	ns	0.0623
14d					
Male vs. Female	-0.1577	-0.4805 to 0.1652	No	ns	0.3329
21d					
Male vs. Female	-0.1367	-0.4595 to 0.1862	No	ns	0.4009
28d					
Male vs. Female	0.1183	-0.2045 to 0.4412	No	ns	0.4667
35d					
Male vs. Female	-0.03667	-0.3595 to 0.2862	No	ns	0.8212
42d					
Male vs. Female	-0.022	-0.3448 to 0.3008	No	ns	0.8921
49d					
Male vs. Female	-0.1	-0.4228 to 0.2228	No	ns	0.5382
56d					
Male vs. Female	-0.408	-0.7308 to -0.0851	Yes	*	0.0141
Male					
7d vs. 14d	-0.1523	-0.4595 to 0.1548	No	ns	0.7706
7d vs. 21d	-0.02667	-0.3338 to 0.2805	No	ns	>0.9999
7d vs. 28d	-0.3073	-0.6145 to -0.0001	Yes	*	0.0498
7d vs. 35d	-0.324	-0.6312 to -0.0168	Yes	*	0.0318
7d vs. 42d	-0.279	-0.5862 to 0.02817	No	ns	0.101
7d vs. 49d	-0.3627	-0.6698 to -0.0554	Yes	*	0.0103
7d vs. 56d	-0.2523	-0.5595 to 0.05484	No	ns	0.1828
14d vs. 21d	0.1257	-0.1815 to 0.4328	No	ns	0.8995
14d vs. 28d	-0.155	-0.4622 to 0.1522	No	ns	0.7549
14d vs. 35d	-0.1717	-0.4788 to 0.1355	No	ns	0.6491
14d vs. 42d	-0.1267	-0.4338 to 0.1805	No	ns	0.8957
14d vs. 49d	-0.2103	-0.5175 to 0.09684	No	ns	0.3936
14d vs. 56d	-0.1	-0.4072 to 0.2072	No	ns	0.9686
21d vs. 28d	-0.2807	-0.5878 to 0.02651	No	ns	0.0971
21d vs. 35d	-0.2973	-0.6045 to 0.00984	No	ns	0.0645
21d vs. 42d	-0.2523	-0.5595 to 0.05484	No	ns	0.1828
21d vs. 49d	-0.336	-0.6432 to -0.0288	Yes	*	0.0227
21d vs. 56d	-0.2257	-0.5328 to 0.08151	No	ns	0.3051
28d vs. 35d	-0.01667	-0.3238 to 0.2905	No	ns	>0.9999
28d vs. 42d	0.02833	-0.2788 to 0.3355	No	ns	>0.9999
28d vs. 49d	-0.05533	-0.3625 to 0.2518	No	ns	0.9991
28d vs. 56d	0.055	-0.2522 to 0.3622	No	ns	0.9992
35d vs. 42d	0.045	-0.2622 to 0.3522	No	ns	0.9998
35d vs. 49d	-0.03867	-0.3458 to 0.2685	No	ns	>0.9999
35d vs. 56d	0.07167	-0.2355 to 0.3788	No	ns	0.9955
42d vs. 49d	-0.08367	-0.3908 to 0.2235	No	ns	0.9886
42d vs. 56d	0.02667	-0.2805 to 0.3338	No	ns	>0.9999
49d vs. 56d	0.1103	-0.1968 to 0.4175	No	ns	0.9471
Female					
7d vs. 14d	-0.003333	-0.3105 to 0.3038	No	ns	>0.9999
7d vs. 21d	0.1433	-0.1638 to 0.4505	No	ns	0.8202
7d vs. 28d	0.1177	-0.1895 to 0.4248	No	ns	0.9268
7d vs. 35d	-0.054	-0.3612 to 0.2532	No	ns	0.9993
7d vs. 42d	0.005667	-0.3015 to 0.3128	No	ns	>0.9999
7d vs. 49d	-0.156	-0.4632 to 0.1512	No	ns	0.7489
7d vs. 56d	-0.3537	-0.6608 to -0.0464	Yes	*	0.0135
14d vs. 21d	0.1467	-0.1605 to 0.4538	No	ns	0.8025
14d vs. 28d	0.121	-0.1862 to 0.4282	No	ns	0.9161
14d vs. 35d	-0.05067	-0.3578 to 0.2565	No	ns	0.9995
14d vs. 42d	0.009	-0.2982 to 0.3162	No	ns	>0.9999
14d vs. 49d	-0.1527	-0.4598 to 0.1545	No	ns	0.7687
14d vs. 56d	-0.3503	-0.6575 to -0.0431	Yes	*	0.015
21d vs. 28d	-0.02567	-0.3328 to 0.2815	No	ns	>0.9999
21d vs. 35d	-0.1973	-0.5045 to 0.1098	No	ns	0.4766
21d vs. 42d	-0.1377	-0.4448 to 0.1695	No	ns	0.8484
21d vs. 49d	-0.2993	-0.6065 to 0.00784	No	ns	0.0613
21d vs. 56d	-0.497	-0.8042 to -0.1898	Yes	***	0.0001
28d vs. 35d	-0.1717	-0.4788 to 0.1355	No	ns	0.6491
28d vs. 42d	-0.112	-0.4192 to 0.1952	No	ns	0.9429
28d vs. 49d	-0.2737	-0.5808 to 0.03351	No	ns	0.1144
28d vs. 56d	-0.4713	-0.7785 to -0.1642	Yes	***	0.0003
35d vs. 42d	0.05967	-0.2475 to 0.3668	No	ns	0.9986
35d vs. 49d	-0.102	-0.4092 to 0.2052	No	ns	0.965
35d vs. 56d	-0.2997	-0.6068 to 0.00750	No	ns	0.0607
42d vs. 49d	-0.1617	-0.4688 to 0.1455	No	ns	0.714
42d vs. 56d	-0.3593	-0.6665 to -0.0521	Yes	*	0.0114
49d vs. 56d	-0.1977	-0.5048 to 0.1095	No	ns	0.4744

Baseline Paw Placement (cm) 10DegUp

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2723
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.179, df=8
How big is the difference?	
Mean of column A	0.348
Mean of column B	0.1733
Difference between means (B - A) ±	-0.1747 ± 0.1482
95% confidence interval	-0.5163 to 0.1670
R squared (eta squared)	0.148
F test to compare variances	
F, DFn, Dfd	6.810, 4, 4
P value	0.09
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Placement (cm) 10DegDown

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	2.454	0.4306	ns	No	Mean of Male	0.02754
Time	10.63	0.0006	***	Yes	Mean of Female	0.08403
Sex	1.395	0.6921	ns	No	Difference between means	-0.05649
Subject	66.19	<0.0001	****	Yes	SE of difference	0.1376
					95% CI of difference	-0.3737 to 0.2607

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
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7d					
Male vs. Female	-0.06053	-0.3729 to 0.2518	No	ns	0.6999
14d					
Male vs. Female	-0.08453	-0.3969 to 0.2278	No	ns	0.5906
21d					
Male vs. Female	0.0338	-0.2786 to 0.3462	No	ns	0.8295
28d					
Male vs. Female	0.01147	-0.3009 to 0.3238	No	ns	0.9418
35d					
Male vs. Female	0.01547	-0.2969 to 0.3278	No	ns	0.9215
42d					
Male vs. Female	-0.1439	-0.4562 to 0.1685	No	ns	0.361
49d					
Male vs. Female	-0.0332	-0.3456 to 0.2792	No	ns	0.8325
56d					
Male vs. Female	-0.1905	-0.5029 to 0.1218	No	ns	0.2275
Male					
7d vs. 14d	-0.14	-0.3902 to 0.1102	No	ns	0.6478
7d vs. 21d	-0.194	-0.4442 to 0.05622	No	ns	0.2426
7d vs. 28d	-0.2027	-0.4529 to 0.04755	No	ns	0.1966
7d vs. 35d	-0.21	-0.4602 to 0.04022	No	ns	0.1629
7d vs. 42d	-0.1477	-0.3979 to 0.1026	No	ns	0.5845
7d vs. 49d	-0.248	-0.4982 to 0.00221	No	ns	0.0537
7d vs. 56d	-0.2247	-0.4749 to 0.02555	No	ns	0.1089
14d vs. 21d	-0.054	-0.3042 to 0.1962	No	ns	0.9972
14d vs. 28d	-0.06267	-0.3129 to 0.1876	No	ns	0.9931
14d vs. 35d	-0.07	-0.3202 to 0.1802	No	ns	0.9867
14d vs. 42d	-0.007667	-0.2579 to 0.2426	No	ns	>0.9999
14d vs. 49d	-0.108	-0.3582 to 0.1422	No	ns	0.8715
14d vs. 56d	-0.08467	-0.3349 to 0.1656	No	ns	0.9613
21d vs. 28d	-0.008667	-0.2589 to 0.2416	No	ns	>0.9999
21d vs. 35d	-0.016	-0.2662 to 0.2342	No	ns	>0.9999
21d vs. 42d	0.04833	-0.2039 to 0.2966	No	ns	0.999
21d vs. 49d	-0.054	-0.3042 to 0.1962	No	ns	0.9972
21d vs. 56d	-0.03067	-0.2809 to 0.2196	No	ns	>0.9999
28d vs. 35d	-0.007333	-0.2576 to 0.2429	No	ns	>0.9999
28d vs. 42d	0.055	-0.1952 to 0.3052	No	ns	0.9969
28d vs. 49d	-0.04533	-0.2956 to 0.2049	No	ns	0.9991
28d vs. 56d	-0.022	-0.2722 to 0.2282	No	ns	>0.9999
35d vs. 42d	0.06233	-0.1879 to 0.3126	No	ns	0.9933
35d vs. 49d	-0.038	-0.2882 to 0.2122	No	ns	0.9997
35d vs. 56d	-0.01467	-0.2649 to 0.2356	No	ns	>0.9999
42d vs. 49d	-0.1003	-0.3506 to 0.1499	No	ns	0.9086
42d vs. 56d	-0.077	-0.3272 to 0.1732	No	ns	0.977
49d vs. 56d	0.02333	-0.2269 to 0.2736	No	ns	>0.9999
Female					
7d vs. 14d	-0.164	-0.4142 to 0.08622	No	ns	0.4504
7d vs. 21d	-0.09967	-0.3499 to 0.1506	No	ns	0.9115
7d vs. 28d	-0.1307	-0.3809 to 0.1196	No	ns	0.7219
7d vs. 35d	-0.134	-0.3842 to 0.1162	No	ns	0.696
7d vs. 42d	-0.231	-0.4812 to 0.01922	No	ns	0.0906
7d vs. 49d	-0.2207	-0.4709 to 0.02955	No	ns	0.1219
7d vs. 56d	-0.3547	-0.6049 to -0.1044	Yes	***	0.001
14d vs. 21d	0.06433	-0.1859 to 0.3146	No	ns	0.9919
14d vs. 28d	0.03333	-0.2169 to 0.2836	No	ns	0.9999
14d vs. 35d	0.03	-0.2202 to 0.2802	No	ns	>0.9999
14d vs. 42d	-0.067	-0.3172 to 0.1832	No	ns	0.9897
14d vs. 49d	-0.05667	-0.3069 to 0.1936	No	ns	0.9963
14d vs. 56d	-0.1907	-0.4409 to 0.05955	No	ns	0.2621
21d vs. 28d	-0.031	-0.2812 to 0.2192	No	ns	>0.9999
21d vs. 35d	-0.03433	-0.2846 to 0.2159	No	ns	0.9999
21d vs. 42d	-0.1313	-0.3816 to 0.1189	No	ns	0.7168
21d vs. 49d	-0.121	-0.3712 to 0.1292	No	ns	0.7922
21d vs. 56d	-0.255	-0.5052 to -0.0047	Yes	*	0.0428
28d vs. 35d	-0.003333	-0.2536 to 0.2469	No	ns	>0.9999
28d vs. 42d	-0.1003	-0.3506 to 0.1499	No	ns	0.9086
28d vs. 49d	-0.09	-0.3402 to 0.1602	No	ns	0.9467
28d vs. 56d	-0.224	-0.4742 to 0.02622	No	ns	0.111
35d vs. 42d	-0.097	-0.3472 to 0.1532	No	ns	0.9224
35d vs. 49d	-0.08667	-0.3369 to 0.1636	No	ns	0.9562
35d vs. 56d	-0.2207	-0.4709 to 0.02955	No	ns	0.1219
42d vs. 49d	0.01033	-0.2399 to 0.2606	No	ns	>0.9999
42d vs. 56d	-0.1237	-0.3739 to 0.1266	No	ns	0.7736
49d vs. 56d	-0.134	-0.3842 to 0.1162	No	ns	0.696

Baseline Paw Placement (cm) 10DegDown

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.399
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.8908, df=8
How big is the difference?	
Mean of column A	0.4463
Mean of column B	0.3301
Difference between means (B - A) ± SEM	-0.1162 ± 0.1304
95% confidence interval	-0.4170 to 0.1846
R squared (eta squared)	0.09025
F test to compare variances	
F, DFn, Dfd	1.941, 4, 4
P value	0.5364
P value summary	ns
Significantly different (P < 0.05)?	No
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Drag FLAT

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	1.656	0.7272	ns	No	Mean of Male	0.05121
Time	7.216	0.0279	*	Yes	Mean of Female	0.4386
Sex	0.4876	0.8176	ns	No	Difference between means	-0.3874
Subject	68.64	<0.0001	****	Yes	SE of difference	1.625
					95% CI of difference	-4.135 to 3.360
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	
7d						
Male vs. Female	-0.1095	-3.850 to 3.631	No	ns	0.9534	
21d						
Male vs. Female	1.099	-2.641 to 4.840	No	ns	0.5584	
28d						
Male vs. Female	-0.543	-4.284 to 3.198	No	ns	0.7723	
35d						
Male vs. Female	-1.043	-4.784 to 2.697	No	ns	0.5786	
42d						
Male vs. Female	-1.29	-5.030 to 2.451	No	ns	0.4927	
49d						
Male vs. Female	-0.483	-4.224 to 3.258	No	ns	0.7969	
56d						
Male vs. Female	-0.3426	-4.083 to 3.398	No	ns	0.8551	
Male						
7d vs. 21d	-0.9273	-3.984 to 2.130	No	ns	0.9651	
7d vs. 28d	-1.768	-4.824 to 1.289	No	ns	0.5682	
7d vs. 35d	0.8575	-2.199 to 3.914	No	ns	0.9763	
7d vs. 42d	0.4397	-2.617 to 3.497	No	ns	0.9994	
7d vs. 49d	-0.9502	-4.007 to 2.107	No	ns	0.9608	
7d vs. 56d	-0.09847	-3.155 to 2.959	No	ns	>0.9999	
21d vs. 28d	-0.8402	-3.897 to 2.217	No	ns	0.9786	
21d vs. 35d	1.785	-1.272 to 4.842	No	ns	0.5569	
21d vs. 42d	1.367	-1.690 to 4.424	No	ns	0.8117	
21d vs. 49d	-0.02287	-3.080 to 3.034	No	ns	>0.9999	
21d vs. 56d	0.8289	-2.228 to 3.886	No	ns	0.98	
28d vs. 35d	2.625	-0.4320 to 5.682	No	ns	0.1363	
28d vs. 42d	2.207	-0.8498 to 5.264	No	ns	0.3036	
28d vs. 49d	0.8173	-2.240 to 3.874	No	ns	0.9814	
28d vs. 56d	1.669	-1.388 to 4.726	No	ns	0.6323	
35d vs. 42d	-0.4178	-3.475 to 2.639	No	ns	0.9995	
35d vs. 49d	-1.808	-4.865 to 1.249	No	ns	0.542	
35d vs. 56d	-0.956	-4.013 to 2.101	No	ns	0.9597	
42d vs. 49d	-1.39	-4.447 to 1.667	No	ns	0.7997	
42d vs. 56d	-0.5381	-3.595 to 2.519	No	ns	0.998	
49d vs. 56d	0.8517	-2.205 to 3.909	No	ns	0.9771	
Female						
7d vs. 21d	0.2815	-2.776 to 3.338	No	ns	>0.9999	
7d vs. 28d	-2.201	-5.258 to 0.8560	No	ns	0.3068	
7d vs. 35d	-0.07617	-3.133 to 2.981	No	ns	>0.9999	
7d vs. 42d	-0.7403	-3.797 to 2.317	No	ns	0.9888	
7d vs. 49d	-1.324	-4.381 to 1.733	No	ns	0.8334	
7d vs. 56d	-0.3315	-3.388 to 2.725	No	ns	0.9999	
21d vs. 28d	-2.482	-5.539 to 0.5745	No	ns	0.1828	
21d vs. 35d	-0.3576	-3.415 to 2.699	No	ns	0.9998	
21d vs. 42d	-1.022	-4.079 to 2.035	No	ns	0.9448	
21d vs. 49d	-1.605	-4.662 to 1.452	No	ns	0.6732	
21d vs. 56d	-0.613	-3.670 to 2.444	No	ns	0.9959	
28d vs. 35d	2.125	-0.9321 to 5.182	No	ns	0.3476	
28d vs. 42d	1.461	-1.596 to 4.518	No	ns	0.7606	
28d vs. 49d	0.8774	-2.180 to 3.934	No	ns	0.9734	
28d vs. 56d	1.87	-1.187 to 4.926	No	ns	0.502	
35d vs. 42d	-0.6641	-3.721 to 2.393	No	ns	0.9937	
35d vs. 49d	-1.247	-4.304 to 1.810	No	ns	0.8683	
35d vs. 56d	-0.2553	-3.312 to 2.802	No	ns	>0.9999	
42d vs. 49d	-0.5833	-3.640 to 2.474	No	ns	0.9969	
42d vs. 56d	0.4088	-2.648 to 3.466	No	ns	0.9996	
49d vs. 56d	0.9921	-2.065 to 4.049	No	ns	0.9519	

Baseline Paw Drag FLAT

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.6456
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.4778, df=8
How big is the difference?	
Mean of column A	-11.25
Mean of column B	-10.36
Difference between means (B - A) ± 0.8923 ± 1.868	
95% confidence interval	-3.414 to 5.199
R squared (eta squared)	0.02774
F test to compare variances	
F, DFn, Dfd	10.52, 4, 4
P value	0.0426
P value summary	*
Significantly different (P < 0.05)?	Yes
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Drag 10DegUp

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means
Time x Sex	4.883	0.0805	ns	No	Mean of Male Mean of Female Difference between means
Time	5.39	0.0555	ns	No	SE of difference
Sex	0.01938	0.9637	ns	No	95% CI of difference
Subject	70.42	<0.0001	****	Yes	-0.1972 -0.3001 0.1029 2.192 -4.952 to 5.158

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
7d					
Male vs. Female	0.5385	-4.418 to 5.495	No	ns	0.8285
21d					
Male vs. Female	-0.1142	-5.071 to 4.842	No	ns	0.9633
28d					
Male vs. Female	-1.946	-6.903 to 3.010	No	ns	0.4349
35d					
Male vs. Female	-2.155	-7.111 to 2.802	No	ns	0.3876
42d					
Male vs. Female	3.004	-1.952 to 7.961	No	ns	0.2297
49d					
Male vs. Female	0.746	-4.210 to 5.702	No	ns	0.7642
56d					
Male vs. Female	0.6463	-4.310 to 5.603	No	ns	0.7949
Male					
7d vs. 21d	0.1611	-3.652 to 3.974	No	ns	>0.9999
7d vs. 28d	-1.132	-4.945 to 2.681	No	ns	0.9686
7d vs. 35d	0.4789	-3.334 to 4.292	No	ns	0.9997
7d vs. 42d	-0.9903	-4.803 to 2.823	No	ns	0.984
7d vs. 49d	-1.49	-5.303 to 2.323	No	ns	0.8899
7d vs. 56d	-1.299	-5.112 to 2.514	No	ns	0.9397
21d vs. 28d	-1.293	-5.106 to 2.520	No	ns	0.941
21d vs. 35d	0.3178	-3.495 to 4.131	No	ns	>0.9999
21d vs. 42d	-1.151	-4.964 to 2.661	No	ns	0.9659
21d vs. 49d	-1.651	-5.464 to 2.162	No	ns	0.8334
21d vs. 56d	-1.46	-5.273 to 2.352	No	ns	0.8988
28d vs. 35d	1.611	-2.202 to 5.424	No	ns	0.8486
28d vs. 42d	0.1417	-3.671 to 3.955	No	ns	>0.9999
28d vs. 49d	-0.358	-4.171 to 3.455	No	ns	>0.9999
28d vs. 56d	-0.1674	-3.980 to 3.645	No	ns	>0.9999
35d vs. 42d	-1.469	-5.282 to 2.344	No	ns	0.8962
35d vs. 49d	-1.969	-5.782 to 1.844	No	ns	0.6899
35d vs. 56d	-1.778	-5.591 to 2.035	No	ns	0.7803
42d vs. 49d	-0.4996	-4.312 to 3.313	No	ns	0.9996
42d vs. 56d	-0.309	-4.122 to 3.504	No	ns	>0.9999
49d vs. 56d	0.1906	-3.622 to 4.003	No	ns	>0.9999
Female					
7d vs. 21d	-0.4916	-4.304 to 3.321	No	ns	0.9997
7d vs. 28d	-3.616	-7.429 to 0.1964	No	ns	0.0734
7d vs. 35d	-2.214	-6.027 to 1.599	No	ns	0.5632
7d vs. 42d	1.476	-2.337 to 5.288	No	ns	0.8943
7d vs. 49d	-1.282	-5.095 to 2.530	No	ns	0.9432
7d vs. 56d	-1.192	-5.004 to 2.621	No	ns	0.9598
21d vs. 28d	-3.125	-6.938 to 0.6879	No	ns	0.1746
21d vs. 35d	-1.723	-5.536 to 2.090	No	ns	0.8043
21d vs. 42d	1.967	-1.846 to 5.780	No	ns	0.6908
21d vs. 49d	-0.7909	-4.604 to 3.022	No	ns	0.9951
21d vs. 56d	-0.7	-4.513 to 3.113	No	ns	0.9975
28d vs. 35d	1.402	-2.411 to 5.215	No	ns	0.9151
28d vs. 42d	5.092	1.279 to 8.905	Yes	**	0.0028
28d vs. 49d	2.334	-1.479 to 6.147	No	ns	0.5008
28d vs. 56d	2.425	-1.388 to 6.238	No	ns	0.4546
35d vs. 42d	3.69	-0.1230 to 7.503	No	ns	0.0637
35d vs. 49d	0.9318	-2.881 to 4.745	No	ns	0.9883
35d vs. 56d	1.023	-2.790 to 4.836	No	ns	0.9811
42d vs. 49d	-2.758	-6.571 to 1.055	No	ns	0.3015
42d vs. 56d	-2.667	-6.480 to 1.146	No	ns	0.3401
49d vs. 56d	0.0909	-3.722 to 3.904	No	ns	>0.9999

Baseline Paw Drag 10DegUp

Column B vs. Column A	Female vs. Male
Unpaired t test	
P value	0.6145
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.5240, df=8
How big is the difference?	
Mean of column A	-10.62
Mean of column B	-9.584
Difference between means (B - A) ± 1.971	
95% confidence interval	-3.512 to 5.577
R squared (eta squared)	0.03318
F test to compare variances	
F, DFn, Dfd	12.69, 4, 4
P value	0.0305
P value summary	*
Significantly different (P < 0.05)?	Yes
Data analyzed	
Sample size, column A	5
Sample size, column B	5

Change in Paw Drag 10DegDown						Baseline Paw Drag 10DegDown		
Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means		Column B vs. Column A	Female vs. Male
Time x Sex	3.282	0.5533	ns	No	Mean of Male	1.273		
Time	6.272	0.1721	ns	No	Mean of Female	0.4502		
Sex	2.272	0.5862	ns	No	Difference between means	0.8231		
Subject	56.51	<0.0001	****	Yes	SE of difference	1.451		
					95% CI of difference	-2.524 to 4.170	Unpaired t test	
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		P value	0.1766
7d							P value summary	ns
Male vs. Female	-0.7358	-4.368 to 2.896	No	ns	0.6864		Significantly different (P < 0.05)?	No
21d							One- or two-tailed P value?	Two-tailed
Male vs. Female	0.8988	-2.733 to 4.531	No	ns	0.622		t, df	t=1.482, df=8
28d							How big is the difference?	
Male vs. Female	0.4759	-3.156 to 4.108	No	ns	0.7939		Mean of column A	-11.93
35d							Mean of column B	-9.892
Male vs. Female	-0.01895	-3.651 to 3.613	No	ns	0.9917		Difference between means (B - A) ± SEM	2.043 ± 1.378
42d							95% confidence interval	-1.135 to 5.221
Male vs. Female	0.877	-2.755 to 4.509	No	ns	0.6305		R squared (eta squared)	0.2155
49d							F test to compare variances	
Male vs. Female	2.41	-1.222 to 6.042	No	ns	0.1891		F, DFn, Dfd	3.627, 4, 4
56d							P value	0.2399
Male vs. Female	1.855	-1.777 to 5.487	No	ns	0.3107		P value summary	ns
Male							Significantly different (P < 0.05)?	No
7d vs. 21d	-2.293	-5.903 to 1.318	No	ns	0.4566		Data analyzed	
7d vs. 28d	-1.814	-5.425 to 1.796	No	ns	0.716		Sample size, column A	5
7d vs. 35d	-2.605	-6.216 to 1.006	No	ns	0.3045		Sample size, column B	5
7d vs. 42d	-1.557	-5.168 to 2.053	No	ns	0.8359			
7d vs. 49d	-2.194	-5.804 to 1.417	No	ns	0.5099			
7d vs. 56d	-2.896	-6.507 to 0.7147	No	ns	0.1942			
21d vs. 28d	0.4781	-3.132 to 4.089	No	ns	0.9996			
21d vs. 35d	-0.3124	-3.923 to 3.298	No	ns	>0.9999			
21d vs. 42d	0.7353	-2.875 to 4.346	No	ns	0.9956			
21d vs. 49d	0.0989	-3.512 to 3.710	No	ns	>0.9999			
21d vs. 56d	-0.6034	-4.214 to 3.007	No	ns	0.9985			
28d vs. 35d	-0.7905	-4.401 to 2.820	No	ns	0.9935			
28d vs. 42d	0.2571	-3.353 to 3.868	No	ns	>0.9999			
28d vs. 49d	-0.3792	-3.990 to 3.231	No	ns	0.9999			
28d vs. 56d	-1.082	-4.692 to 2.529	No	ns	0.9672			
35d vs. 42d	1.048	-2.563 to 4.658	No	ns	0.972			
35d vs. 49d	0.4113	-3.199 to 4.022	No	ns	0.9998			
35d vs. 56d	-0.291	-3.902 to 3.320	No	ns	>0.9999			
42d vs. 49d	-0.6364	-4.247 to 2.974	No	ns	0.998			
42d vs. 56d	-1.339	-4.949 to 2.272	No	ns	0.912			
49d vs. 56d	-0.7023	-4.313 to 2.908	No	ns	0.9966			
Female								
7d vs. 21d	-0.6579	-4.269 to 2.953	No	ns	0.9976			
7d vs. 28d	-0.6027	-4.213 to 3.008	No	ns	0.9985			
7d vs. 35d	-1.888	-5.499 to 1.723	No	ns	0.6773			
7d vs. 42d	0.05553	-3.555 to 3.666	No	ns	>0.9999			
7d vs. 49d	0.9521	-2.658 to 4.563	No	ns	0.9827			
7d vs. 56d	-0.3055	-3.916 to 3.305	No	ns	>0.9999			
21d vs. 28d	0.0552	-3.555 to 3.666	No	ns	>0.9999			
21d vs. 35d	-1.23	-4.841 to 2.380	No	ns	0.9397			
21d vs. 42d	0.7135	-2.897 to 4.324	No	ns	0.9963			
21d vs. 49d	1.61	-2.001 to 5.221	No	ns	0.8136			
21d vs. 56d	0.3524	-3.258 to 3.963	No	ns	>0.9999			
28d vs. 35d	-1.285	-4.896 to 2.325	No	ns	0.9265			
28d vs. 42d	0.6583	-2.952 to 4.269	No	ns	0.9976			
28d vs. 49d	1.555	-2.056 to 5.165	No	ns	0.8369			
28d vs. 56d	0.2972	-3.313 to 3.908	No	ns	>0.9999			
35d vs. 42d	1.944	-1.667 to 5.554	No	ns	0.6474			
35d vs. 49d	2.84	-0.7704 to 6.451	No	ns	0.2127			
35d vs. 56d	1.583	-2.028 to 5.193	No	ns	0.8254			
42d vs. 49d	0.8966	-2.714 to 4.507	No	ns	0.9873			
42d vs. 56d	-0.3611	-3.972 to 3.250	No	ns	>0.9999			
49d vs. 56d	-1.258	-4.868 to 2.353	No	ns	0.9333			

Appendix I.10. Statistical report of all Digigait parameters, comparing values prior to injury and over time following ACL rupture, including p-values and 95% confidence intervals for all analyses. This file also contains Digigait variable definitions for all parameters analyzed.

Change in R/L Ratio Normalized to Bodyweight						Baseline R/L Ratio Normalized to Bodyweight		
Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means		Column B vs. Column A	Female vs. Male
Time x Sex	12.33	0.0195 *		Yes	Mean of Female -0.1447			
Time	31.8 <0.0001	***		Yes	Mean of Male -0.3529			
Sex	20.71	0.0048 **		Yes	Difference between means 0.2082			
Subject	6.57	0.1114 ns		No	SE of difference 0.04786			
					95% CI of difference 0.09105 to 0.3253			
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		Unpaired t test P value	0.3939
3d							P value summary	ns
Female vs. Male	-0.01772	-0.2397 to 0.2043	No	ns	0.8734		Significantly different (P < 0.05)?	No
7d							One- or two-tailed P value?	Two-tailed
Female vs. Male	0.05095	-0.1710 to 0.2729	No	ns	0.6473		t, df	t=0.9182, df=6
14d							Mean of column A	1.02
Female vs. Male	0.1782	-0.04380 to 0.4002	No	ns	0.1134		Mean of column B	0.9824
21d							Difference between means (B - A) ± SEM	-0.03746 ± 0.04080
Female vs. Male	0.06252	-0.1595 to 0.2845	No	ns	0.5747		95% confidence interval	-0.1373 to 0.06236
28d							R squared (eta squared)	0.1232
Female vs. Male	0.22	-0.001963 to 0.442	No	ns	0.052			
35d								
Female vs. Male	0.3731	0.1511 to 0.5951	Yes	**	0.0014			
42d								
Female vs. Male	0.1834	-0.03862 to 0.4053	No	ns	0.1035			
49d								
Female vs. Male	0.5203	0.2983 to 0.7423	Yes	****	<0.0001			
56d								
Female vs. Male	0.3028	0.08079 to 0.5247	Yes	**	0.0084			
Female								
3d vs. 7d	-0.1534	-0.4972 to 0.1905	No	ns	0.8729			
3d vs. 14d	-0.3732	-0.7170 to -0.0293	Yes	*	0.0242			
3d vs. 21d	-0.3393	-0.6832 to 0.00455	No	ns	0.0557			
3d vs. 28d	-0.5642	-0.9081 to -0.2204	Yes	****	<0.0001			
3d vs. 35d	-0.5291		Yes	***	0.0003			
3d vs. 42d	-0.4147	-0.7586 to -0.0708	Yes	***	0.008			
3d vs. 49d	-0.6535	-0.9974 to -0.3097	Yes	***	<0.0001			
3d vs. 56d	-0.492	-0.8359 to -0.1481	Yes	***	0.0008			
7d vs. 14d	-0.2198	-0.5637 to 0.1241	No	ns	0.5011			
7d vs. 21d	-0.1859	-0.5298 to 0.1579	No	ns	0.7095			
7d vs. 28d	-0.4109	-0.7548 to -0.0670	Yes	**	0.0089			
7d vs. 35d	-0.3757	-0.7196 to -0.0318	Yes	*	0.0227			
7d vs. 42d	-0.2614	-0.6052 to 0.0825	No	ns	0.2729			
7d vs. 49d	-0.5002	-0.8441 to -0.1563	Yes	***	0.0006			
7d vs. 56d	-0.3387	-0.6825 to 0.0052	No	ns	0.0566			
14d vs. 21d	0.03386	-0.3100 to 0.3777	No	ns	>0.9999			
14d vs. 28d	-0.1911	-0.5349 to 0.1528	No	ns	0.6791			
14d vs. 35d	-0.1559	-0.4998 to 0.1880	No	ns	0.8626			
14d vs. 42d	-0.04156	-0.3854 to 0.3023	No	ns	>0.9999			
14d vs. 49d	-0.2804	-0.6242 to 0.0634	No	ns	0.1946			
14d vs. 56d	-0.1188	-0.4627 to 0.2250	No	ns	0.9678			
21d vs. 28d	-0.2249	-0.5688 to 0.1189	No	ns	0.4698			
21d vs. 35d	-0.1898	-0.5336 to 0.1541	No	ns	0.687			
21d vs. 42d	-0.07542	-0.4193 to 0.2684	No	ns	0.9984			
21d vs. 49d	-0.3142	-0.6581 to 0.02963	No	ns	0.0981			
21d vs. 56d	-0.1527	-0.4966 to 0.1912	No	ns	0.8755			
28d vs. 35d	0.03518	-0.3087 to 0.3791	No	ns	>0.9999			
28d vs. 42d	0.1495	-0.1944 to 0.4934	No	ns	0.8877			
28d vs. 49d	-0.0893	-0.4332 to 0.2546	No	ns	0.9948			
28d vs. 56d	0.07223	-0.2716 to 0.4161	No	ns	0.9988			
35d vs. 42d	0.1143	-0.2295 to 0.4582	No	ns	0.9745			
35d vs. 49d	-0.1245	-0.4684 to 0.2194	No	ns	0.9579			
35d vs. 56d	0.03705	-0.3068 to 0.3809	No	ns	>0.9999			
42d vs. 49d	-0.2388	-0.5827 to 0.1051	No	ns	0.3886			
42d vs. 56d	-0.07728	-0.4211 to 0.2666	No	ns	0.9981			
49d vs. 56d	0.1615	-0.1823 to 0.5054	No	ns	0.838			
Male								
3d vs. 7d	-0.08469	-0.4286 to 0.2592	No	ns	0.9964			
3d vs. 14d	-0.1773	-0.5211 to 0.1666	No	ns	0.7587			
3d vs. 21d	-0.2591	-0.6029 to 0.08479	No	ns	0.2836			
3d vs. 28d	-0.3265	-0.6704 to 0.01736	No	ns	0.0748			
3d vs. 35d	-0.1382	-0.4821 to 0.2056	No	ns	0.9249			
3d vs. 42d	-0.2137	-0.5575 to 0.1302	No	ns	0.5393			
3d vs. 49d	-0.1155	-0.4594 to 0.2284	No	ns	0.9729			
3d vs. 56d	-0.1715	-0.5154 to 0.1723	No	ns	0.7893			
7d vs. 14d	-0.09257	-0.4364 to 0.2513	No	ns	0.9934			
7d vs. 21d	-0.1744	-0.5182 to 0.1695	No	ns	0.7744			
7d vs. 28d	-0.2418	-0.5857 to 0.1020	No	ns	0.372			
7d vs. 35d	-0.05354	-0.3974 to 0.2903	No	ns	0.9899			
7d vs. 42d	-0.129	-0.4728 to 0.2149	No	ns	0.9485			
7d vs. 49d	-0.03081	-0.3747 to 0.3131	No	ns	>0.9999			
7d vs. 56d	-0.08683	-0.4307 to 0.2570	No	ns	0.9957			
14d vs. 21d	-0.0818	-0.4257 to 0.2621	No	ns	0.9971			
14d vs. 28d	-0.1492	-0.4931 to 0.1946	No	ns	0.8887			
14d vs. 35d	0.03904	-0.3048 to 0.3829	No	ns	>0.9999			
14d vs. 42d	-0.03638	-0.3803 to 0.3075	No	ns	>0.9999			
14d vs. 49d	0.06177	-0.2821 to 0.4056	No	ns	0.9996			
14d vs. 56d	0.005742	-0.3381 to 0.3496	No	ns	>0.9999			
21d vs. 28d	-0.06744	-0.4113 to 0.2764	No	ns	0.9993			
21d vs. 35d	0.1208	-0.2230 to 0.4647	No	ns	0.9645			
21d vs. 42d	0.04542	-0.2984 to 0.3893	No	ns	>0.9999			
21d vs. 49d	0.1436	-0.2003 to 0.4874	No	ns	0.9084			
21d vs. 56d	0.08755	-0.2563 to 0.4314	No	ns	0.9954			
28d vs. 35d	0.1883	-0.1556 to 0.5321	No	ns	0.6958			
28d vs. 42d	0.1129	-0.2310 to 0.4567	No	ns	0.9764			
28d vs. 49d	0.211	-0.1329 to 0.5549	No	ns	0.5558			
28d vs. 56d	0.155	-0.1889 to 0.4989	No	ns	0.8664			
35d vs. 42d	-0.07542	-0.4193 to 0.2684	No	ns	0.9984			
35d vs. 49d	0.02273	-0.3211 to 0.3666	No	ns	>0.9999			
35d vs. 56d	-0.03329	-0.3772 to 0.3106	No	ns	>0.9999			
42d vs. 49d	0.09815	-0.2457 to 0.4420	No	ns	0.9902			
42d vs. 56d	0.04213	-0.3017 to 0.3860	No	ns	>0.9999			
49d vs. 56d	-0.05603	-0.3999 to 0.2878	No	ns	0.9998			

Appendix I.11. Statistical report of all Bioseb parameters, comparing values prior to injury and over time following ACL rupture, including p-values and 95% confidence intervals for all analyses.

Change in Radiograph Total Score

Source of Variation	% of total variation	P value	P value summary	Significant?	Difference between column means	
Time x Sex	1.556	0.6488	ns	No	Mean of Female	9.444
Time	79.31	<0.0001	****	Yes	Mean of Male	9.444
Sex	0	>0.9999	ns	No	Difference between means	0
Subject	6.662	0.0016	**	Yes	SE of difference	1.526
					95% CI of difference	-3.734 to 3.734

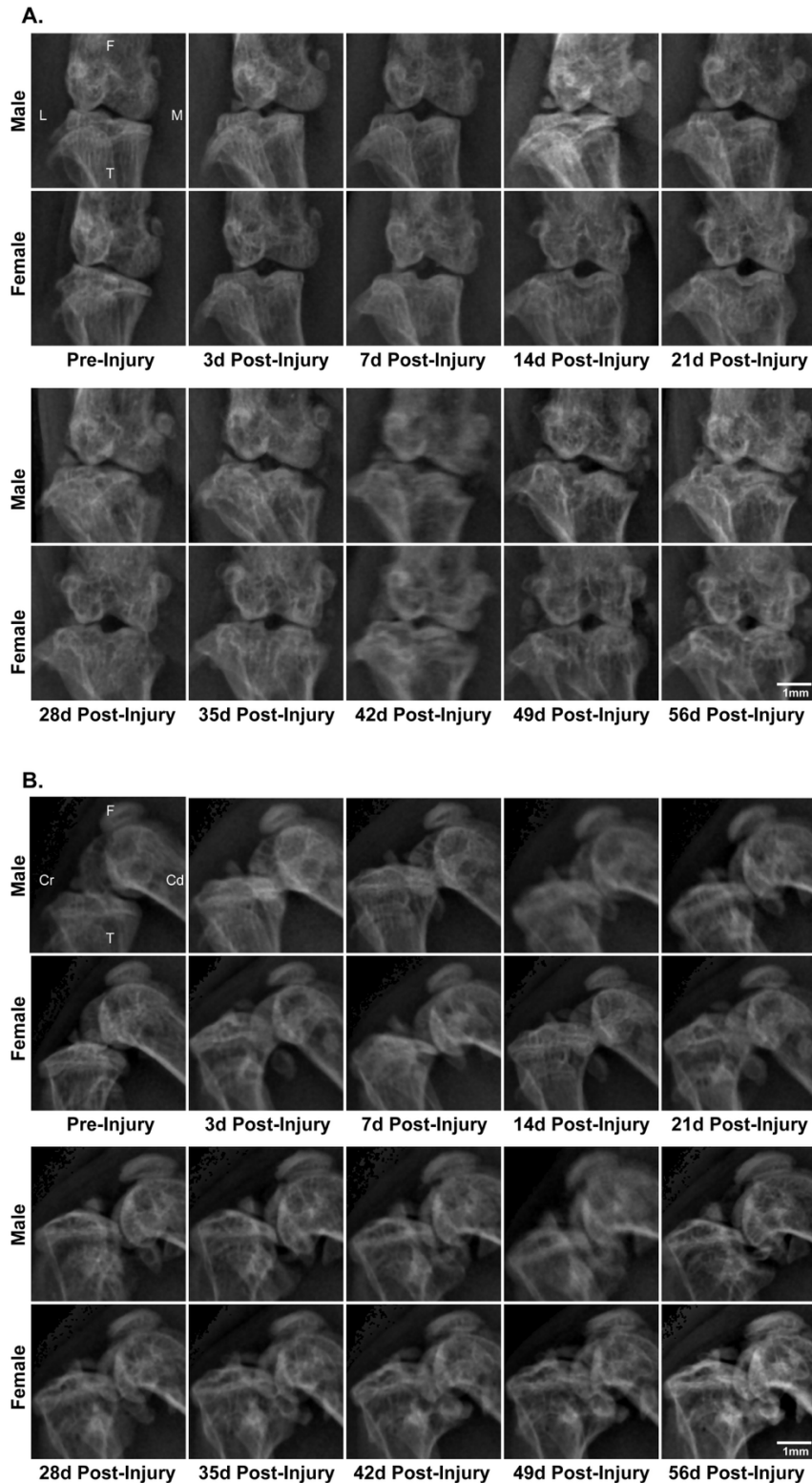
Baseline Total Radiograph Score

Column B	Female
vs.	vs.
Column A	Male
Unpaired t test	
P value	0.2316
P value summary	ns
Significantly different (P < 0.05)?	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.331, df=6

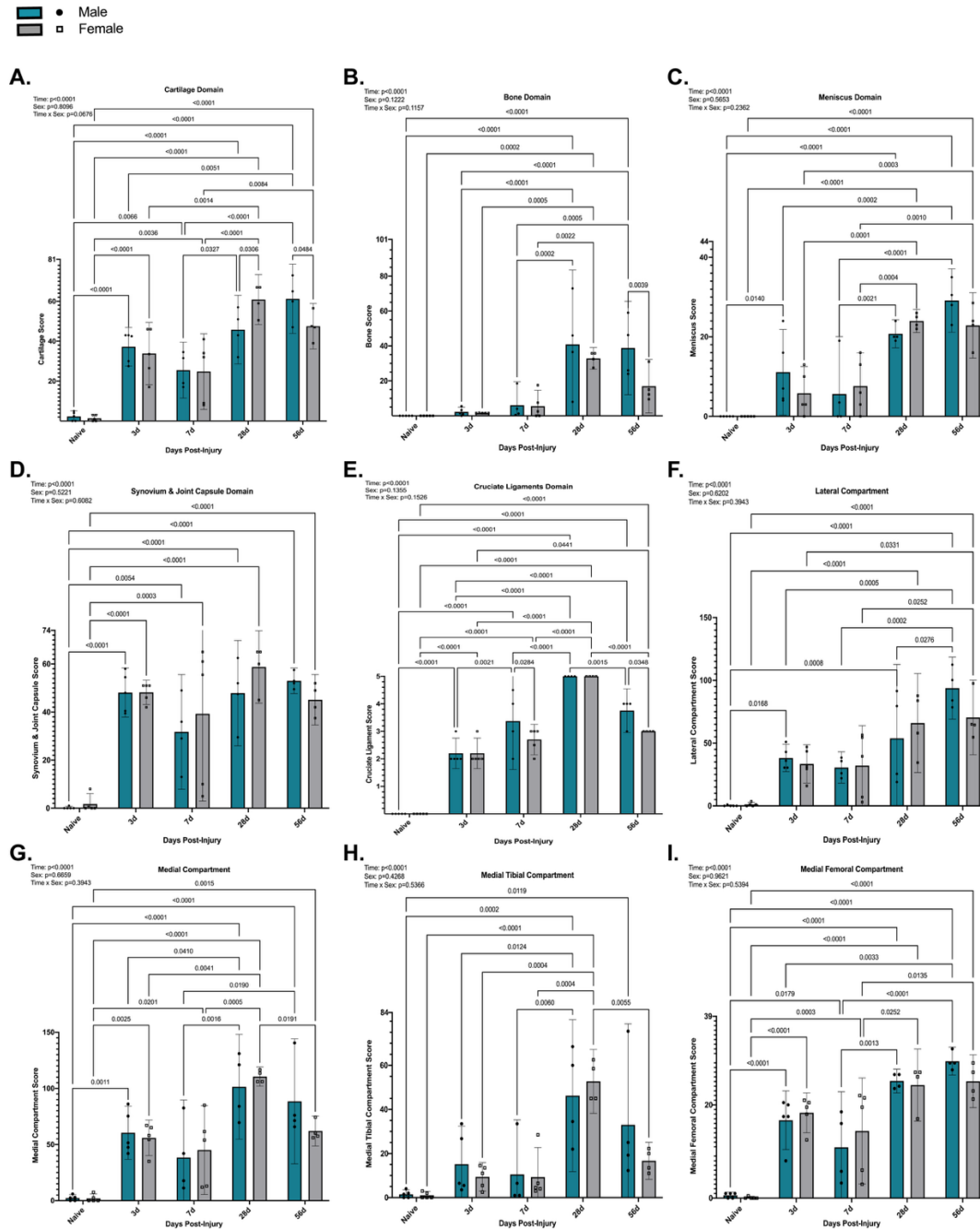
Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	
3d						
Female vs. Male	-0.25	-4.780 to 4.280	No	ns	0.8933	
7d						
Female vs. Male	-3	-10.88 to 4.881	No	ns	0.3769	
14d						
Female vs. Male	-0.25	-3.915 to 3.415	No	ns	0.8706	
21d						
Female vs. Male	1	-3.484 to 5.484	No	ns	0.5702	
28d						
Female vs. Male	0	-10.56 to 10.56	No	ns	>0.9999	
35d						
Female vs. Male	1.5	-5.395 to 8.395	No	ns	0.6051	
42d						
Female vs. Male	2	-2.238 to 6.238	No	ns	0.2903	
49d						
Female vs. Male	2	-2.796 to 6.796	No	ns	0.3248	
56d						
Female vs. Male	-3	-13.03 to 7.026	No	ns	0.4886	
Female						
3d vs. 7d	0.25	-13.61 to 14.11	No	ns	>0.9999	
3d vs. 14d	0	-3.746 to 3.746	No	ns	>0.9999	
3d vs. 21d	-5	-13.38 to 3.377	No	ns		0.1859
3d vs. 28d	-9	-14.92 to -3.077	Yes	**		0.0154
3d vs. 35d	-14	-21.01 to -6.991	Yes	**		0.0007
3d vs. 42d	-14	-29.89 to 1.894	No	ns		0.0703
3d vs. 49d	-16	-25.55 to -6.449	Yes	*		0.0117
3d vs. 56d	-16	-26.92 to -5.078	Yes	*		0.0171
7d vs. 14d	-0.25	-14.85 to 14.35	No	ns	>0.9999	
7d vs. 21d	-5.25	-18.33 to 7.829	No	ns		0.4169
7d vs. 28d	-9.25	-23.85 to 5.350	No	ns		0.1616
7d vs. 35d	-14.25	-21.92 to -6.584	Yes	**		0.0086
7d vs. 42d	-14.25	-32.09 to 3.594	No	ns		0.0909
7d vs. 49d	-16.25	-38.31 to 5.814	No	ns		0.1118
7d vs. 56d	-16.25	-32.45 to -0.05494	Yes	*		0.0495
14d vs. 21d	-5	-12.49 to 2.493	No	ns		0.1427
14d vs. 28d	-9	-11.65 to -6.351	Yes	**		0.0017
14d vs. 35d	-14	-21.01 to -6.991	Yes	**		0.0007
14d vs. 42d	-14	-27.51 to -0.4924	Yes	*		0.0453
14d vs. 49d	-16	-26.26 to -5.740	Yes	*		0.0143
14d vs. 56d	-16	-29.25 to -2.755	Yes	*		0.0296
21d vs. 28d	-4	-9.923 to 1.923	No	ns		0.1386
21d vs. 35d	-9	-16.01 to -1.991	Yes	*		0.0249
21d vs. 42d	-9	-17.38 to -0.6229	Yes	*		0.0411
21d vs. 49d	-11	-22.55 to 0.5470	No	ns		0.057
21d vs. 56d	-11	-29.54 to 7.543	No	ns		0.1885
28d vs. 35d	-5	-12.01 to 2.009	No	ns		0.1211
28d vs. 42d	-5	-15.92 to 5.922	No	ns		0.3275
28d vs. 49d	-7	-17.92 to 3.922	No	ns		0.1573
28d vs. 56d	-7	-22.67 to 8.672	No	ns		0.3434
35d vs. 42d	0	-13.25 to 13.25	No	ns	>0.9999	
35d vs. 49d	-2	-17.22 to 13.22	No	ns		0.9819
35d vs. 56d	-2	-15.51 to 11.51	No	ns		0.9671
42d vs. 49d	-2	-19.37 to 15.37	No	ns		0.9912
42d vs. 56d	-2	-27.82 to 23.82	No	ns		0.9993
49d vs. 56d	0	-18.54 to 18.54	No	ns	>0.9999	
Male						
3d vs. 7d	-2.5	-10.66 to 5.665	No	ns		0.6217
3d vs. 14d	0	-7.009 to 7.009	No	ns	>0.9999	
3d vs. 21d	-3.75	-15.41 to 7.910	No	ns		0.5843
3d vs. 28d	-8.75	-25.16 to 7.660	No	ns		0.2393
3d vs. 35d	-12.25	-21.94 to -2.562	Yes	*		0.0261
3d vs. 42d	-11.75	-25.35 to 1.855	No	ns		0.0741
3d vs. 49d	-13.75	-22.28 to -5.217	Yes	*		0.013
3d vs. 56d	-18.75	-34.05 to -3.446	Yes	*		0.0285
7d vs. 14d	2.5	-4.254 to 9.254	No	ns		0.4767
7d vs. 21d	-1.25	-9.783 to 7.283	No	ns		0.9687
7d vs. 28d	-6.25	-25.96 to 13.46	No	ns		0.5952
7d vs. 35d	-9.75	-17.86 to -1.639	Yes	*		0.03
7d vs. 42d	-9.25	-26.70 to 8.197	No	ns		0.2422
7d vs. 49d	-11.25	-27.01 to 4.508	No	ns		0.1208
7d vs. 56d	-16.25	-30.85 to -1.650	Yes	*		0.0372
14d vs. 21d	-3.75	-8.617 to 1.117	No	ns		0.0997
14d vs. 28d	-8.75	-31.60 to 14.10	No	ns		0.4512
14d vs. 35d	-12.25	-24.50 to -0.00257	Yes	*		0.05
14d vs. 42d	-11.75	-23.11 to -0.3945	Yes	*		0.0455
14d vs. 49d	-13.75	-24.79 to -2.708	Yes	*		0.0272
14d vs. 56d	-18.75	-33.59 to -3.912	Yes	*		0.0281
21d vs. 28d	-5	-31.75 to 21.75	No	ns		0.9097
21d vs. 35d	-8.5	-22.89 to 5.888	No	ns		0.1903
21d vs. 42d	-8	-20.43 to 4.425	No	ns		0.1555
21d vs. 49d	-10	-25.22 to 5.218	No	ns		0.1481
21d vs. 56d	-15	-29.75 to -0.2507	Yes	*		0.0478
28d vs. 35d	-3.5	-17.69 to 10.89	No	ns		0.7922
28d vs. 42d	-3	-31.04 to 25.04	No	ns		0.5943
28d vs. 49d	-5	-26.68 to 16.68	No	ns		0.8138
28d vs. 56d	-10	-32.63 to 12.63	No	ns		0.3506
35d vs. 42d	0.5	-18.88 to 19.88	No	ns	>0.9999	
35d vs. 49d	-1.5	-19.17 to 16.17	No	ns		0.9986
35d vs. 56d	-6.5	-17.26 to 4.261	No	ns		0.1808
42d vs. 49d	-2	-12.26 to 8.260	No	ns		0.8941
42d vs. 56d	-7	-23.11 to 9.114	No	ns		0.3618
49d vs. 56d	-5	-25.00 to 15.00	No	ns		0.7651
Row Effect - Time						
3d vs. 7d	-1.125	-6.467 to 4.217	No	ns		0.9861
3d vs. 14d	0	-2.404 to 2.404	No	ns	>0.9999	
3d vs. 21d	-4.375	-8.833 to 0.08264	No	ns		0.0546
3d vs. 28d	-8.875	-14.16 to -3.593	Yes	***		0.0029
3d vs. 35d	-13.13	-17.00 to -9.245	Yes	****	<0.0001	
3d vs. 42d	-12.88	-19.46 to -6.294	Yes	**		0.0011
3d vs. 49d	-14.88	-19.15 to -10.60	Yes	****	<0.0001	
3d vs. 56d	-17.38	-23.48 to -11.27	Yes	****		0.0001
7d vs. 14d	1.125	-4.217 to 6.467	No	ns		0.9861
7d vs. 21d	-3.25	-8.959 to 2.459	No	ns		0.3934
7d vs. 28d	-7.75	-15.55 to 0.05103	No	ns		0.0516
7d vs. 35d	-12	-16.94 to -7.060	Yes	***		0.0003
7d vs. 42d	-11.75	-20.30 to -3.203	Yes	**		0.0095

7d vs. 49d	-13.75 -22.88 to -4.621	Yes	**		0.0056
7d vs. 56d	-16.25 -22.85 to -9.653	Yes	***		0.0003
14d vs. 21d	-4.375 -7.258 to -1.492	Yes	***		0.0054
14d vs. 28d	-8.875 -15.84 to -1.914	Yes	*		0.0144
14d vs. 35d	-13.13 -17.62 to -8.631	Yes	****	<0.0001	
14d vs. 42d	-12.88 -18.51 to -7.240	Yes	***		0.0004
14d vs. 49d	-14.88 -19.78 to -9.971	Yes	****	<0.0001	
14d vs. 56d	-17.38 -23.78 to -10.97	Yes	***		0.0001
21d vs. 28d	-4.5 -12.83 to 3.829	No	ns		0.4453
21d vs. 35d	-8.75 -13.61 to -3.892	Yes	**		0.0019
21d vs. 42d	-8.5 -13.10 to -3.896	Yes	**		0.0016
21d vs. 49d	-10.5 -16.33 to -4.666	Yes	**		0.0019
21d vs. 56d	-13 -20.85 to -5.148	Yes	**		0.0032
28d vs. 35d	-4.25 -9.239 to 0.7388	No	ns		0.1023
28d vs. 42d	-4 -13.24 to 5.242	No	ns		0.6664
28d vs. 49d	-6 -13.52 to 1.518	No	ns		0.1332
28d vs. 56d	-8.5 -17.17 to 0.1687	No	ns		0.0549
35d vs. 42d	0.25 -6.862 to 7.362	No	ns	>0.9999	
35d vs. 49d	-1.75 -8.817 to 5.317	No	ns		0.9657
35d vs. 56d	-4.25 -10.60 to 2.098	No	ns		0.2486
42d vs. 49d	-2 -8.103 to 4.103	No	ns		0.8719
42d vs. 56d	-4.5 -14.54 to 5.542	No	ns		0.6334
49d vs. 56d	-2.5 -11.67 to 6.673	No	ns		0.9441

Appendix I.12. Statistical report of total radiograph scorings, comparing values prior to injury and over time following ACL rupture, including p-values and 95% confidence intervals for all analyses. Radiographic evidence of PTOA progression was observed by 21-days post-injury (14d vs 21d, $p=0.0054$) with radiographic score increasing significantly at 35-days post-injury (3d vs 35d, $p<0.0001$). After 35-days post-injury, radiographic scores continued to trend higher until study completion at 56-days post-injury.



Appendix I.13. Representative longitudinal **(A)** craniocaudal and **(B)** mediolateral stifle radiographs of all timepoints for the same male and female animal throughout the study timeline. F = Femur, T = Tibia, L = Lateral, M = Medial, Cr = Cranial, Cd = Caudal.



Appendix I.14. Analysis of additional histology parameters. Scores for (A) cartilage, (B) bone, (C) meniscus, (D) synovium and joint capsule, and (E) cruciate ligament domains are displayed. The overall scores for the (F) lateral and (G) medial compartments, as well as the scores for the (H) medial tibial and (I) medial femoral compartments are also presented. Two-way models were fit for each histology parameter and p -values calculated for sex, time, and sex/time interaction factors. Due to unequal animal numbers across groups (see exclusion statement in Figure 2.1 and Appendix I.2.), a mixed-effects model with multiple comparisons was utilized (no repeated measures). For all group comparisons, p -values of less than 0.05 are shown. Bars represent mean $\pm$ 95% confidence interval with individual animals marked. The maximum value on each y-axis represents the highest possible histology score for each category.

Total Score

Fixed effects (type III)		P value	P value summary	Statistically significant (P < 0.05)?	F (DFn, DFd)	Difference between column means	
Time		<0.0001	****	Yes	F (4, 27) = 47.40	Predicted mean of Male	104.6
Sex		0.5663	ns	No	F (1, 8) = 0.3577	Predicted mean of Female	98.48
Time x Sex		0.1961	ns	No	F (4, 27) = 1.628	Difference between predicted means	6.143
Tukey's multiple comparisons test		Predicted (LS) mean diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	95% CI of difference
Naïve							
Male vs. Female		-0.6	-40.17 to 38.97	No	ns	0.9756	-17.54 to 29.83
3d							
Male vs. Female		9.3	-30.27 to 48.87	No	ns	0.6362	
7d							
Male vs. Female		-6.919	-48.86 to 35.02	No	ns	0.7397	
28d							
Male vs. Female		-21.03	-65.22 to 23.16	No	ns	0.3406	
56d							
Male vs. Female		49.97	5.784 to 94.15	Yes	*	0.0278	
Male							
Naïve vs. 3d		-98.35	-153.4 to -43.31	Yes	***	0.0002	
Naïve vs. 7d		-70.48	-129.0 to -11.92	Yes	*	0.0125	
Naïve vs. 28d		-158.4	-217.0 to -99.86	Yes	****	<0.0001	
Naïve vs. 56d		-183.4	-241.9 to -124.8	Yes	****	<0.0001	
3d vs. 7d		27.87	-30.69 to 86.43	No	ns	0.6391	
3d vs. 28d		-60.07	-118.6 to -1.505	Yes	*	0.0423	
3d vs. 56d		-85.01	-143.6 to -26.45	Yes	**	0.002	
7d vs. 28d		-87.94	-149.5 to -26.40	Yes	**	0.0024	
7d vs. 56d		-112.9	-174.8 to -50.90	Yes	***	0.0001	
28d vs. 56d		-24.94	-86.91 to 37.04	No	ns	0.7651	
Female							
Naïve vs. 3d		-88.45	-143.5 to -33.41	Yes	***	0.0006	
Naïve vs. 7d		-76.8	-131.8 to -21.76	Yes	**	0.0031	
Naïve vs. 28d		-178.9	-237.4 to -120.3	Yes	****	<0.0001	
Naïve vs. 56d		-132.8	-191.4 to -74.23	Yes	****	<0.0001	
3d vs. 7d		11.65	-43.39 to 66.69	No	ns	0.9709	
3d vs. 28d		-90.4	-149.0 to -31.84	Yes	***	0.001	
3d vs. 56d		-44.34	-102.9 to 14.22	No	ns	0.2061	
7d vs. 28d		-102.1	-160.6 to -43.49	Yes	***	0.0002	
7d vs. 56d		-55.99	-114.6 to 2.574	No	ns	0.0661	
28d vs. 56d		46.06	-15.47 to 107.6	No	ns	0.2152	

Cartilage

Fixed effects (type III)	P value	P value summary	Statistically significant (P < 0.05)?	F (DFn, DFd)	Difference between column means		
Time	<0.0001	****	Yes	F (4, 27) = 50.75	Predicted mean of Male		34.47
Sex		0.8096 ns	No	F (1, 8) = 0.06205	Predicted mean of Female		33.71
Time x Sex		0.0676 ns	No	F (4, 27) = 2.482	Difference between predicted means		0.7612
					SE of difference		3.056
					95% CI of difference		-6.286 to 7.808
Tukey's multiple comparisons test	Predicted (LS) mean diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		
Naive							
Male vs. Female		0.9 -11.21 to 13.01	No	ns	0.8809		
3d							
Male vs. Female		3.4 -8.709 to 15.51	No	ns	0.5723		
7d							
Male vs. Female		0.8884 -11.95 to 13.73	No	ns	0.8891		
28d							
Male vs. Female		-15.02 -28.55 to -1.486	Yes	*	0.0306		
56d							
Male vs. Female		13.63 0.1043 to 27.16	Yes	*	0.0484		
Male							
Naive vs. 3d		-34.9 -51.91 to -17.89	Yes	****	<0.0001		
Naive vs. 7d		-23.39 -41.48 to -5.301	Yes	**		0.0066	
Naive vs. 28d		-43.64 -61.73 to -25.55	Yes	****	<0.0001		
Naive vs. 56d		-58.91 -77.00 to -40.83	Yes	****	<0.0001		
3d vs. 7d		11.51 -6.576 to 29.60	No	ns		0.3627	
3d vs. 28d		-8.738 -26.83 to 9.349	No	ns		0.6261	
3d vs. 56d		-24.01 -42.10 to -5.927	Yes	**		0.0051	
7d vs. 28d		-20.25 -39.27 to -1.229	Yes	*		0.0327	
7d vs. 56d		-35.52 -54.65 to -16.40	Yes	****	<0.0001		
28d vs. 56d		-15.27 -34.40 to 3.846	No	ns		0.1655	
Female							
Naive vs. 3d		-32.4 -49.41 to -15.39	Yes	****	<0.0001		
Naive vs. 7d		-23.4 -40.41 to -6.387	Yes	**		0.0036	
Naive vs. 28d		-59.55 -77.64 to -41.47	Yes	****	<0.0001		
Naive vs. 56d		-46.18 -64.27 to -28.09	Yes	****	<0.0001		
3d vs. 7d		9 -8.013 to 26.01	No	ns		0.5436	
3d vs. 28d		-27.15 -45.24 to -9.067	Yes	**		0.0014	
3d vs. 56d		-13.78 -31.87 to 4.308	No	ns		0.2011	
7d vs. 28d		-36.15 -54.24 to -18.07	Yes	****	<0.0001		
7d vs. 56d		-22.78 -40.87 to -4.692	Yes	**		0.0084	
28d vs. 56d		13.38 -5.646 to 32.40	No	ns		0.2689	

Bone

Fixed effects (type III)	P value	P value summary	Statistically significant (P < 0.05)?	F (DFn, DFd)	Difference between column means		
					Predicted mean of Male	Predicted mean of Female	Difference between predicted means
Time	<0.0001	****	Yes	F (4, 27) = 26.03			17.92
Sex		0.1222 ns	No	F (1, 8) = 2.987			11.34
Time x Sex		0.1157 ns	No	F (4, 27) = 2.048			6.574
						SE of difference	3.804
						95% CI of difference	-2.197 to 15.35
Tukey's multiple comparisons test	Predicted (LS) mean diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		
Naive							
Male vs. Female		0 -13.33 to 13.33	No	ns	>0.9999		
3d							
Male vs. Female		0.7 -12.63 to 14.03	No	ns	0.9157		
7d							
Male vs. Female		1.059 -13.04 to 15.16	No	ns	0.8797		
28d							
Male vs. Female		8.572 -6.260 to 23.41	No	ns	0.2486		
56d							
Male vs. Female		22.54 7.712 to 37.37	Yes	**	0.0039		
Male							
Naive vs. 3d		-2.25 -20.05 to 15.55	No	ns	0.9958		
Naive vs. 7d		-6.559 -25.55 to 12.43	No	ns	0.8491		
Naive vs. 28d		-41.37 -60.36 to -22.38	Yes	****	<0.0001		
Naive vs. 56d		-39.4 -58.38 to -20.42	Yes	****	<0.0001		
3d vs. 7d		-4.309 -23.30 to 14.68	No	ns	0.9627		
3d vs. 28d		-39.12 -58.11 to -20.13	Yes	****	<0.0001		
3d vs. 56d		-37.15 -56.13 to -18.17	Yes	****	<0.0001		
7d vs. 28d		-34.81 -54.71 to -14.91	Yes	***	0.0002		
7d vs. 56d		-32.84 -53.00 to -12.68	Yes	***	0.0005		
28d vs. 56d		1.971 -18.19 to 22.14	No	ns	0.9985		
Female							
Naive vs. 3d		-1.55 -19.35 to 16.25	No	ns	0.999		
Naive vs. 7d		-5.5 -23.30 to 12.30	No	ns	0.8934		
Naive vs. 28d		-32.8 -51.79 to -13.81	Yes	***	0.0002		
Naive vs. 56d		-16.86 -35.85 to 2.129	No	ns	0.1		
3d vs. 7d		-3.95 -21.75 to 13.85	No	ns	0.9655		
3d vs. 28d		-31.25 -50.24 to -12.26	Yes	***	0.0005		
3d vs. 56d		-15.31 -34.30 to 3.679	No	ns	0.159		
7d vs. 28d		-27.3 -46.29 to -8.308	Yes	**	0.0022		
7d vs. 56d		-11.36 -30.35 to 7.629	No	ns	0.4235		
28d vs. 56d		15.94 -3.962 to 35.84	No	ns	0.1636		

Meniscus

Fixed effects (type III)					Difference between column means	
Time	P value	P value summary	Statistically significant (P < 0.05)?	F (DFn, DFd)	Predicted mean of Male	13.25
Sex	<0.0001	0.5653 ns	Yes	F (4, 27) = 40.71	Predicted mean of Female	12.08
Time x Sex		0.2363 ns	No	F (1, 8) = 0.3597	Difference between predicted means	1.171
			No	F (4, 27) = 1.479	SE of difference	1.952
					95% CI of difference	-3.331 to 5.672
Tukey's multiple comparisons test		Predicted (LS) mean diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
Naive						
Male vs. Female		0	-6.946 to 6.946	No	ns	>0.9999
3d						
Male vs. Female		5.3	-1.646 to 12.25	No	ns	0.1304
7d						
Male vs. Female		-1.998	-9.350 to 5.354	No	ns	0.5846
28d						
Male vs. Female		-3.338	-11.07 to 4.398	No	ns	0.387
56d						
Male vs. Female		5.891	-1.843 to 13.62	No	ns	0.131
Male						
Naive vs. 3d		-11.1	-20.45 to -1.754	Yes	*	0.014
Naive vs. 7d		-5.602	-15.57 to 4.367	No	ns	0.4853
Naive vs. 28d		-20.73	-30.69 to -10.76	Yes	****	<0.0001
Naive vs. 56d		-28.83	-38.79 to -18.87	Yes	****	<0.0001
3d vs. 7d		5.498	-4.470 to 15.47	No	ns	0.5035
3d vs. 28d		-9.627	-19.59 to 0.3416	No	ns	0.0622
3d vs. 56d		-17.73	-27.69 to -7.767	Yes	***	0.0002
7d vs. 28d		-15.13	-25.57 to -4.676	Yes	**	0.0021
7d vs. 56d		-23.23	-33.81 to -12.65	Yes	****	<0.0001
28d vs. 56d		-8.104	-18.68 to 2.474	No	ns	0.1967
Female						
Naive vs. 3d		-5.8	-15.15 to 3.546	No	ns	0.3874
Naive vs. 7d		-7.6	-16.95 to 1.746	No	ns	0.153
Naive vs. 28d		-24.07	-34.03 to -14.10	Yes	****	<0.0001
Naive vs. 56d		-22.94	-32.91 to -12.97	Yes	****	<0.0001
3d vs. 7d		-1.8	-11.15 to 7.546	No	ns	0.9794
3d vs. 28d		-18.27	-28.23 to -8.297	Yes	***	0.0001
3d vs. 56d		-17.14	-27.11 to -7.172	Yes	***	0.0003
7d vs. 28d		-16.47	-26.43 to -6.497	Yes	***	0.0004
7d vs. 56d		-15.34	-25.31 to -5.372	Yes	**	0.001
28d vs. 56d		1.125	-9.324 to 11.57	No	ns	0.9977

Synovium & Joint Capsule

Fixed effects (type III)		P value	P value summary	Statistically significant (P < 0.05)?	F (DFn, DFd)	Difference between column means	
Time		<0.0001	****	Yes	F (4, 35) = 27.92	Predicted mean of Male	36.19
Sex		0.5221 ns	No	No	F (1, 35) = 0.4181	Predicted mean of Female	38.62
Time x Sex		0.6082 ns	No	No	F (4, 35) = 0.6834	Difference between predicted means	-2.43
						SE of difference	3.758
						95% CI of difference	-10.06 to 5.200
Tukey's multiple comparisons test		Predicted (LS) mean diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	
Naive							
Male vs. Female		-1.5	-17.58 to 14.58	No	ns	0.8509	
3d							
Male vs. Female		-0.1	-16.18 to 15.98	No	ns	0.99	
7d							
Male vs. Female		-7.55	-24.61 to 9.510	No	ns	0.3751	
28d							
Male vs. Female		-10.88	-28.86 to 7.108	No	ns	0.2278	
56d							
Male vs. Female		7.875	-10.11 to 25.86	No	ns	0.3801	
Male							
Naive vs. 3d		-47.9	-70.68 to -25.12	Yes	****	<0.0001	
Naive vs. 7d		-31.55	-55.71 to -7.389	Yes	**		0.0054
Naive vs. 28d		-47.68	-71.84 to -23.51	Yes	****	<0.0001	
Naive vs. 56d		-52.8	-76.96 to -28.64	Yes	****	<0.0001	
3d vs. 7d		16.35	-7.811 to 40.51	No	ns		0.3132
3d vs. 28d		0.225	-23.94 to 24.39	No	ns	>0.9999	
3d vs. 56d		-4.9	-29.06 to 19.26	No	ns		0.9767
7d vs. 28d		-16.13	-41.59 to 9.343	No	ns		0.3785
7d vs. 56d		-21.25	-46.72 to 4.218	No	ns		0.1395
28d vs. 56d		-5.125	-30.59 to 20.34	No	ns		0.9774
Female							
Naive vs. 3d		-46.5	-69.28 to -23.72	Yes	****	<0.0001	
Naive vs. 7d		-37.6	-60.38 to -14.82	Yes	***		0.0003
Naive vs. 28d		-57.05	-81.21 to -32.89	Yes	****	<0.0001	
Naive vs. 56d		-43.43	-67.59 to -19.26	Yes	****	<0.0001	
3d vs. 7d		8.9	-13.88 to 31.68	No	ns		0.7932
3d vs. 28d		-10.55	-34.71 to 13.61	No	ns		0.7194
3d vs. 56d		3.075	-21.09 to 27.24	No	ns		0.996
7d vs. 28d		-19.45	-43.61 to 4.711	No	ns		0.1644
7d vs. 56d		-5.825	-29.99 to 18.34	No	ns		0.9566
28d vs. 56d		13.63	-11.84 to 39.09	No	ns		0.5456

Cruciate Ligaments

Fixed effects (type III)	P value	P value summary	Statistically significant (P < 0.05)?	F (DFn, DFd)	Difference between column means		
Time	<0.0001	****	Yes	F (4, 27) = 177.5	Predicted mean of Male		2.858
Sex	0.1355 ns		No	F (1, 8) = 2.755	Predicted mean of Female		2.591
Time x Sex	0.1526 ns		No	F (4, 27) = 1.828	Difference between predicted means		0.267
					SE of difference		0.1609
					95% CI of difference		-0.1040 to 0.6380
Tukey's multiple comparisons test	Predicted (LS) mean diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		
Naive							
Male vs. Female	0	-0.5683 to 0.5683	No	ns	>0.9999		
3d							
Male vs. Female	0	-0.5683 to 0.5683	No	ns	>0.9999		
7d							
Male vs. Female	0.6773	0.07585 to 1.279	Yes	*	0.0284		
28d							
Male vs. Female	-0.02633	-0.6591 to 0.6065	No	ns	0.9332		
56d							
Male vs. Female	0.6842	0.05168 to 1.317	Yes	*	0.0348		
Male							
Naive vs. 3d	-2.2	-2.962 to -1.438	Yes	****	<0.0001		
Naive vs. 7d	-3.377	-4.190 to -2.564	Yes	****	<0.0001		
Naive vs. 28d	-5.002	-5.815 to -4.189	Yes	****	<0.0001		
Naive vs. 56d	-3.713	-4.525 to -2.900	Yes	****	<0.0001		
3d vs. 7d	-1.177	-1.990 to -0.3643	Yes	**	0.0021		
3d vs. 28d	-2.802	-3.615 to -1.989	Yes	****	<0.0001		
3d vs. 56d	-1.513	-2.325 to -0.7003	Yes	****	<0.0001		
7d vs. 28d	-1.625	-2.477 to -0.7730	Yes	****	<0.0001		
7d vs. 56d	-0.3355	-1.198 to 0.5273	No	ns	0.7864		
28d vs. 56d	1.289	0.4266 to 2.152	Yes	**	0.0015		
Female							
Naive vs. 3d	-2.2	-2.962 to -1.438	Yes	****	<0.0001		
Naive vs. 7d	-2.7	-3.462 to -1.938	Yes	****	<0.0001		
Naive vs. 28d	-5.029	-5.842 to -4.216	Yes	****	<0.0001		
Naive vs. 56d	-3.029	-3.842 to -2.216	Yes	****	<0.0001		
3d vs. 7d	-0.5	-1.262 to 0.2620	No	ns	0.3332		
3d vs. 28d	-2.829	-3.642 to -2.016	Yes	****	<0.0001		
3d vs. 56d	-0.8286	-1.642 to -0.01567	Yes	*	0.0441		
7d vs. 28d	-2.329	-3.142 to -1.516	Yes	****	<0.0001		
7d vs. 56d	-0.3286	-1.142 to 0.4843	No	ns	0.7621		
28d vs. 56d	2	1.148 to 2.852	Yes	****	<0.0001		

Lateral Compartment

Fixed effects (type III)		P value	P value summary	Statistically significant (P < 0.05)?	F (DFn, DFd)	Difference between column means	
Time		<0.0001	****	Yes	F (4, 35) = 25.76	Predicted mean of Male	43.33
Sex		0.6202	ns	No	F (1, 35) = 0.2500	Predicted mean of Female	40.62
Time x Sex		0.3943	ns	No	F (4, 35) = 1.053	Difference between predicted means	2.713
Tukey's multiple comparisons test		Predicted (LS) mean diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	SE of difference
							95% CI of difference
							-8.300 to 13.73
Naive							
Male vs. Female		-0.9	-24.12 to 22.32	No	ns	0.9377	
3d							
Male vs. Female		4.75	-18.47 to 27.97	No	ns	0.6804	
7d							
Male vs. Female		-1.538	-26.16 to 23.09	No	ns	0.8999	
28d							
Male vs. Female		-12.13	-38.08 to 13.83	No	ns	0.3495	
56d							
Male vs. Female		23.38	-2.583 to 49.33	No	ns	0.0761	
Male							
Naive vs. 3d		-38	-70.88 to -5.119	Yes	*	0.0168	
Naive vs. 7d		-30.36	-65.24 to 4.513	No	ns	0.113	
Naive vs. 28d		-53.68	-88.55 to -18.80	Yes	***	0.0008	
Naive vs. 56d		-93.61	-128.5 to -58.74	Yes	****	<0.0001	
3d vs. 7d		7.638	-27.24 to 42.51	No	ns	0.9692	
3d vs. 28d		-15.68	-50.55 to 19.20	No	ns	0.6976	
3d vs. 56d		-55.61	-90.49 to -20.74	Yes	***	0.0005	
7d vs. 28d		-23.31	-60.07 to 13.45	No	ns	0.3769	
7d vs. 56d		-63.25	-100.0 to -26.49	Yes	***	0.0002	
28d vs. 56d		-39.94	-76.70 to -3.176	Yes	*	0.0276	
Female							
Naive vs. 3d		-32.35	-65.23 to 0.5305	No	ns	0.0556	
Naive vs. 7d		-31	-63.88 to 1.881	No	ns	0.0725	
Naive vs. 28d		-64.9	-99.78 to -30.02	Yes	****	<0.0001	
Naive vs. 56d		-69.34	-104.2 to -34.46	Yes	****	<0.0001	
3d vs. 7d		1.35	-31.53 to 34.23	No	ns	>0.9999	
3d vs. 28d		-32.55	-67.43 to 2.325	No	ns	0.077	
3d vs. 56d		-36.99	-71.86 to -2.112	Yes	*	0.0331	
7d vs. 28d		-33.9	-68.78 to 0.9751	No	ns	0.0601	
7d vs. 56d		-38.34	-73.21 to -3.462	Yes	*	0.0252	
28d vs. 56d		-4.438	-41.20 to 32.32	No	ns	0.9967	

Medial Compartment

Fixed effects (type III)		P value	P value summary	Statistically significant (P < 0.05)?	F (DFn, DFd)	Difference between column means	
Time		<0.0001	****	Yes	F (4, 27) = 31.69	Predicted mean of Male	58.37
Sex		0.6659	ns	No	F (1, 8) = 0.2009	Predicted mean of Female	55.16
Time x Sex		0.4837	ns	No	F (4, 27) = 0.8893	Difference between predicted means	3.215
Tukey's multiple comparisons test		Predicted (LS) mean diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value	95% CI of difference
Naive							
Male vs. Female		0.3	-27.07 to 27.67	No	ns	0.9824	-13.33 to 19.76
3d							
Male vs. Female		4.55	-22.82 to 31.92	No	ns	0.7378	
7d							
Male vs. Female		-6.037	-35.05 to 22.97	No	ns	0.6753	
28d							
Male vs. Female		-8.578	-39.14 to 21.98	No	ns	0.5724	
56d							
Male vs. Female		25.84	-4.716 to 56.40	No	ns	0.0949	
Male							
Naive vs. 3d		-58.15	-96.09 to -20.21	Yes	**	0.0011	
Naive vs. 7d		-36.76	-77.14 to 3.614	No	ns	0.0874	
Naive vs. 28d		-99.76	-140.1 to -59.39	Yes	****	<0.0001	
Naive vs. 56d		-85.68	-126.1 to -45.31	Yes	****	<0.0001	
3d vs. 7d		21.39	-18.99 to 61.76	No	ns	0.5424	
3d vs. 28d		-41.61	-81.99 to -1.236	Yes	*	0.041	
3d vs. 56d		-27.53	-67.90 to 12.84	No	ns	0.2968	
7d vs. 28d		-63	-105.4 to -20.59	Yes	**	0.0016	
7d vs. 56d		-48.92	-91.66 to -6.175	Yes	*	0.019	
28d vs. 56d		14.08	-28.66 to 56.83	No	ns	0.8695	
Female							
Naive vs. 3d		-53.9	-91.84 to -15.96	Yes	**	0.0025	
Naive vs. 7d		-43.1	-81.04 to -5.165	Yes	*	0.0201	
Naive vs. 28d		-108.6	-149.0 to -68.26	Yes	****	<0.0001	
Naive vs. 56d		-60.14	-100.5 to -19.76	Yes	**	0.0015	
3d vs. 7d		10.8	-27.14 to 48.74	No	ns	0.9184	
3d vs. 28d		-54.74	-95.12 to -14.36	Yes	**	0.0041	
3d vs. 56d		-6.242	-46.62 to 34.14	No	ns	0.9909	
7d vs. 28d		-65.54	-105.9 to -25.16	Yes	***	0.0005	
7d vs. 56d		-17.04	-57.42 to 23.34	No	ns	0.7328	
28d vs. 56d		48.5	6.087 to 90.91	Yes	*	0.0191	

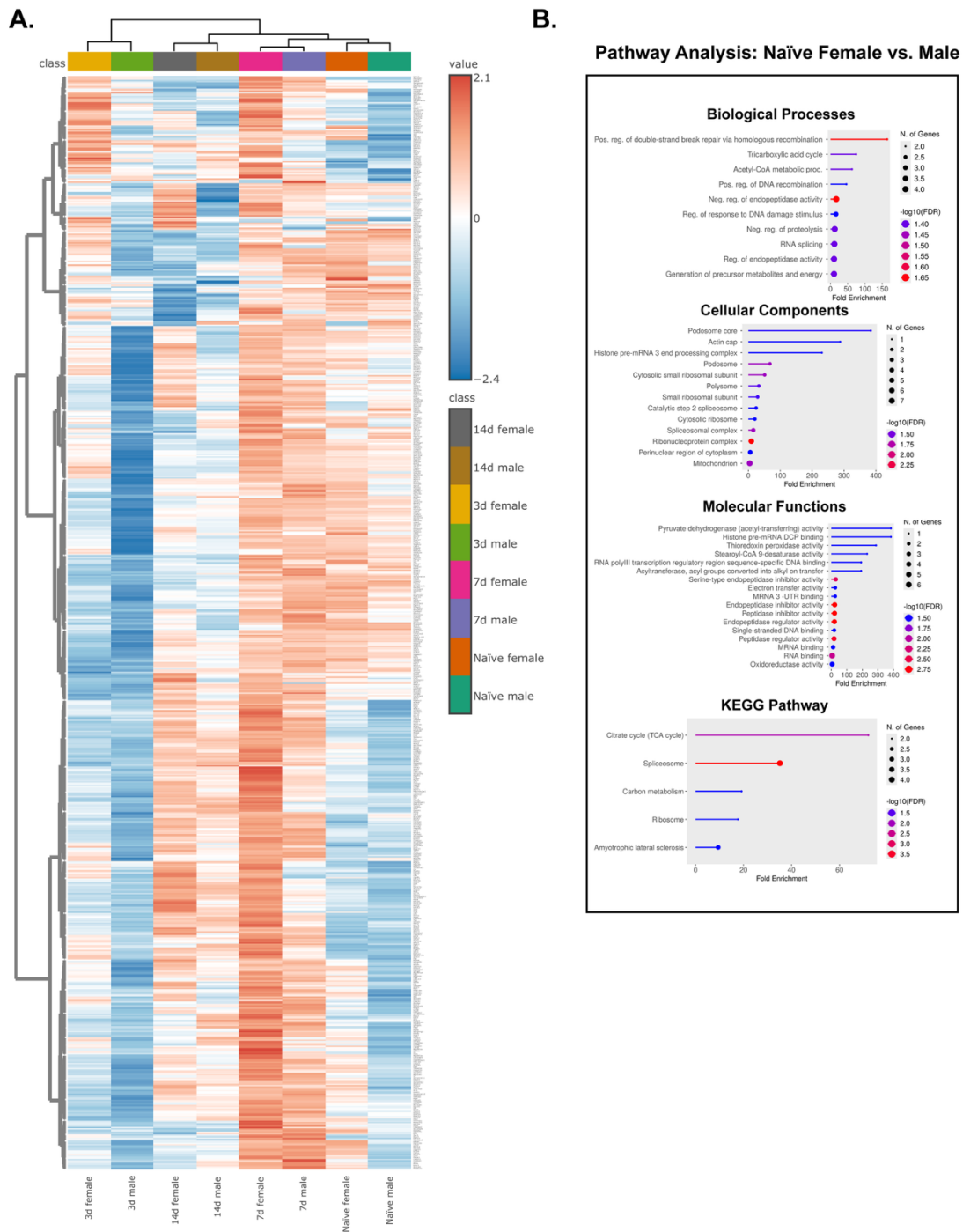
Medial Tibial Compartment

Fixed effects (type III)					P value	P value summary	Statistically significant (P < 0.05)?	F (DFn, DFd)	Difference between column means	
Time					<0.0001	****	Yes	F (4, 27) = 17.11	Predicted mean of Male	21.36
Sex					0.4268	ns	No	F (1, 8) = 0.7009	Predicted mean of Female	17.82
Time x Sex					0.5366	ns	No	F (4, 27) = 0.7986	Difference between predicted means	3.547
									SE of difference	4.237
									95% CI of difference	-6.223 to 13.32
Tukey's multiple comparisons test		Predicted (LS) mean diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value				
Naive										
Male vs. Female		0.5	-16.76 to 17.76	No	ns	0.9534				
3d										
Male vs. Female		5.75	-11.51 to 23.01	No	ns	0.5034				
7d										
Male vs. Female		1.423	-16.89 to 19.73	No	ns	0.8756				
28d										
Male vs. Female		-6.249	-25.55 to 13.05	No	ns	0.5152				
56d										
Male vs. Female		16.31	-2.984 to 35.61	No	ns	0.095				
Male										
Naive vs. 3d		-13.65	-38.13 to 10.83	No	ns	0.4929				
Naive vs. 7d		-9.223	-35.23 to 16.78	No	ns	0.8365				
Naive vs. 28d		-44.97	-70.98 to -18.97	Yes	***	0.0002				
Naive vs. 56d		-31.47	-57.47 to -5.470	Yes	*	0.0119				
3d vs. 7d		4.427	-21.58 to 30.43	No	ns	0.9869				
3d vs. 28d		-31.32	-57.33 to -5.320	Yes	*	0.0124				
3d vs. 56d		-17.82	-43.82 to 8.180	No	ns	0.2921				
7d vs. 28d		-35.75	-63.12 to -8.382	Yes	**	0.006				
7d vs. 56d		-22.25	-49.71 to 5.212	No	ns	0.1556				
28d vs. 56d		13.5	-13.96 to 40.96	No	ns	0.6108				
Female										
Naive vs. 3d		-8.4	-32.88 to 16.08	No	ns	0.852				
Naive vs. 7d		-8.3	-32.78 to 16.18	No	ns	0.8573				
Naive vs. 28d		-51.72	-77.72 to -25.72	Yes	****	<0.0001				
Naive vs. 56d		-15.66	-41.66 to 10.34	No	ns	0.417				
3d vs. 7d		0.1	-24.38 to 24.58	No	ns	>0.9999				
3d vs. 28d		-43.32	-69.32 to -17.32	Yes	***	0.0004				
3d vs. 56d		-7.259	-33.26 to 18.74	No	ns	0.9236				
7d vs. 28d		-43.42	-69.42 to -17.42	Yes	***	0.0004				
7d vs. 56d		-7.359	-33.36 to 18.64	No	ns	0.92				
28d vs. 56d		36.06	8.694 to 63.43	Yes	**	0.0055				

Medial Femoral Compartment

Fixed effects (type III)	P value	P value summary	Statistically significant (P < 0.05)?	F (DFn, DFd)	Difference between column means		
Time	<0.0001	****	Yes	F (4, 27) = 49.58	Predicted mean of Male		16.53
Sex	0.9621 ns		No	F (1, 8) = 0.002401	Predicted mean of Female		16.45
Time x Sex	0.5394 ns		No	F (4, 27) = 0.7941	Difference between predicted means		0.07699
					SE of difference		1.571
					95% CI of difference		-3.547 to 3.701
Tukey's multiple comparisons test	Predicted (LS) mean diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value		
Naive							
Male vs. Female	0.5	-5.569 to 6.569	No	ns	0.8681		
3d							
Male vs. Female	-1.6	-7.669 to 4.469	No	ns	0.5959		
7d							
Male vs. Female	-3.433	-9.866 to 3.001	No	ns	0.2861		
28d							
Male vs. Female	0.9011	-5.877 to 7.679	No	ns	0.7888		
56d							
Male vs. Female	4.017	-2.761 to 10.79	No	ns	0.237		
Male							
Naive vs. 3d	-16.1	-24.55 to -7.650	Yes	****	<0.0001		
Naive vs. 7d	-10.37	-19.36 to -1.377	Yes	*		0.0179	
Naive vs. 28d	-24.62	-33.61 to -15.63	Yes	****	<0.0001		
Naive vs. 56d	-28.55	-37.53 to -19.56	Yes	****	<0.0001		
3d vs. 7d	5.733	-3.258 to 14.72	No	ns		0.3608	
3d vs. 28d	-8.517	-17.51 to 0.4731	No	ns		0.0697	
3d vs. 56d	-12.45	-21.43 to -3.456	Yes	**		0.0033	
7d vs. 28d	-14.25	-23.70 to -4.803	Yes	**		0.0013	
7d vs. 56d	-18.18	-27.69 to -8.665	Yes	****	<0.0001		
28d vs. 56d	-3.928	-13.44 to 5.585	No	ns		0.748	
Female							
Naive vs. 3d	-18.2	-26.65 to -9.750	Yes	****	<0.0001		
Naive vs. 7d	-14.3	-22.75 to -5.850	Yes	***		0.0003	
Naive vs. 28d	-24.22	-33.21 to -15.23	Yes	****	<0.0001		
Naive vs. 56d	-25.03	-34.02 to -16.04	Yes	****	<0.0001		
3d vs. 7d	3.9	-4.550 to 12.35	No	ns		0.6646	
3d vs. 28d	-6.016	-15.01 to 2.974	No	ns		0.3145	
3d vs. 56d	-6.829	-15.82 to 2.162	No	ns		0.2035	
7d vs. 28d	-9.916	-18.91 to -0.9259	Yes	*		0.0252	
7d vs. 56d	-10.73	-19.72 to -1.738	Yes	*		0.0135	
28d vs. 56d	-0.8125	-10.26 to 8.635	No	ns		0.9991	

Appendix I.15. Statistical report of relevant histology scoring comparisons, including p-values and 95% confidence intervals for all analyses.



Appendix I.16. Additional findings from untargeted proteomic analyses. **(A)** Heatmap clustering analysis demonstrated global sex and time dependent ACL proteome profiles following injury. Each row represents a distinct protein, with all proteins displayed. Each column denotes an average of the $n=10$ mouse samples for that group. **(B)** Pathway analyses were performed for naïve female vs. male mice for all proteins that were significantly differentially abundant. The figure displays the top 20 pathways with the highest Fold Enrichment, or all pathways identified if fewer than 20. Circle size indicates the number of genes associated with a pathway and color represents the FDR.

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Male 3d vs Male 14d					significant_male_3d_vs_male_14d					significant_male_3d_vs_male_14d					significant_male_3d_vs_male_14d					significant_male_3d_vs_male_14d					significant_male_3d_vs_male_14d					significant_male_3d_vs_male_14d				
Thesis	yes	no	yes	no	Thesis	yes	no	yes	no	Thesis	yes	no	yes	no	Thesis	yes	no	yes	no	Thesis	yes	no	yes	no	Thesis	yes	no	yes	no	Thesis	yes	no	yes	no
Adna3	yes	-6.015	0.01524	0.01524	Cd3b3	no	0.01524	0.01524	0.01524	Jun2	no	0.01524	0.01524	0.01524	Jun5	no	0.01524	0.01524	0.01524	Pha1	no	0.01524	0.01524	0.01524	Pha1	no	0.01524	0.01524	0.01524	0.01524	0.01524	0.01524	0.01524	
Cd4a3	yes	-6.015	0.01524	0.01524	Cd3b3	no	0.01524	0.01524	0.01524	Jun2	no	0.01524	0.01524	0.01524	Jun5	no	0.01524	0.01524	0.01524	Pha1	no	0.01524	0.01524	0.01524	Pha1	no	0.01524	0.01524	0.01524	0.01524	0.01524	0.01524	0.01524	
Adna4	yes	-6.0174	0.00779	0.00779	Upa1	no	0.00779	0.00779	0.00779	Jun2	no	0.00779	0.00779	0.00779	Jun2	no	0.00779	0.00779	0.00779	Pha1	no	0.00779	0.00779	0.00779	Pha1	no	0.00779	0.00779	0.00779	0.00779	0.00779	0.00779	0.00779	
Agp	yes	-6.0473	0.0346	0.0346	Upa4	no	0.0346	0.0346	0.0346	Jun2	no	0.0346	0.0346	0.0346	Jun2	no	0.0346	0.0346	0.0346	Pha1	no	0.0346	0.0346	0.0346	Pha1	no	0.0346	0.0346	0.0346	0.0346	0.0346	0.0346	0.0346	
S10a10	yes	-5.928	0.0477	0.0477	Hmnpab	no	0.0477	0.0477	0.0477	Jun2	no	0.0477	0.0477	0.0477	Jun2	no	0.0477	0.0477	0.0477	Pha1	no	0.0477	0.0477	0.0477	Pha1	no	0.0477	0.0477	0.0477	0.0477	0.0477	0.0477	0.0477	
Cd4b3	yes	-6.013	0.01513	0.01513	Tn	no	0.01513	0.01513	0.01513	Jun2	no	0.01513	0.01513	0.01513	Jun2	no	0.01513	0.01513	0.01513	Pha1	no	0.01513	0.01513	0.01513	Pha1	no	0.01513	0.01513	0.01513	0.01513	0.01513	0.01513	0.01513	
Rp12	yes	-7.004	0.01132	0.01132	Rp11	no	0.01132	0.01132	0.01132	Jun2	no	0.01132	0.01132	0.01132	Jun2	no	0.01132	0.01132	0.01132	Pha1	no	0.01132	0.01132	0.01132	Pha1	no	0.01132	0.01132	0.01132	0.01132	0.01132	0.01132	0.01132	
Calu	yes	-5.927	0.04075	0.04075	Rp25	no	0.04075	0.04075	0.04075	Jun2	no	0.04075	0.04075	0.04075	Jun2	no	0.04075	0.04075	0.04075	Pha1	no	0.04075	0.04075	0.04075	Pha1	no	0.04075	0.04075	0.04075	0.04075	0.04075	0.04075	0.04075	
Baur1	yes	-6.7025	0.02027	0.02027	Cd11a1	no	0.02027	0.02027	0.02027	Jun2	no	0.02027	0.02027	0.02027	Jun2	no	0.02027	0.02027	0.02027	Pha1	no	0.02027	0.02027	0.02027	Pha1	no	0.02027	0.02027	0.02027	0.02027	0.02027	0.02027	0.02027	
Sepn7	yes	-6.0725	0.02847	0.02847	Cd2	no	0.02847	0.02847	0.02847	Jun2	no	0.02847	0.02847	0.02847	Jun2	no	0.02847	0.02847	0.02847	Pha1	no	0.02847	0.02847	0.02847	Pha1	no	0.02847	0.02847	0.02847	0.02847	0.02847	0.02847	0.02847	
Ed13	yes	-6.1040	0.02719	0.02719	Cd11a1	no	0.02719	0.02719	0.02719	Jun2	no	0.02719	0.02719	0.02719	Jun2	no	0.02719	0.02719	0.02719	Pha1	no	0.02719	0.02719	0.02719	Pha1	no	0.02719	0.02719	0.02719	0.02719	0.02719	0.02719	0.02719	
Pd1n1	yes	-7.0309	0.01129	0.01129	Hdnc	no	0.01129	0.01129	0.01129	Jun2	no	0.01129	0.01129	0.01129	Jun2	no	0.01129	0.01129	0.01129	Pha1	no	0.01129	0.01129	0.01129	Pha1	no	0.01129	0.01129	0.01129	0.01129	0.01129	0.01129	0.01129	
Rp11	yes	-6.074	0.0387	0.0387	Hdnc	no	0.0387	0.0387	0.0387	Jun2	no	0.0387	0.0387	0.0387	Jun2	no	0.0387	0.0387	0.0387	Pha1	no	0.0387	0.0387	0.0387	Pha1	no	0.0387	0.0387	0.0387	0.0387	0.0387	0.0387	0.0387	
Rp10	yes	-6.036	0.03306	0.03306	Hdnc	no	0.03306	0.03306	0.03306	Jun2	no	0.03306	0.03306	0.03306	Jun2	no	0.03306	0.03306	0.03306	Pha1	no	0.03306	0.03306	0.03306	Pha1	no	0.03306	0.03306	0.03306	0.03306	0.03306	0.03306	0.03306	
Sepn1	yes	-6.088	0.02207	0.02207	Upa2	no	0.02207	0.02207	0.02207	Jun2	no	0.02207	0.02207	0.02207	Jun2	no	0.02207	0.02207	0.02207	Pha1	no	0.02207	0.02207	0.02207	Pha1	no	0.02207	0.02207	0.02207	0.02207	0.02207	0.02207	0.02207	
Dn	yes	-6.1001	0.003381	0.003381	Upa3	no	0.003381	0.003381	0.003381	Jun2	no	0.003381	0.003381	0.003381	Jun2	no	0.003381	0.003381	0.003381	Pha1	no	0.003381	0.003381	0.003381	Pha1	no	0.003381	0.003381	0.003381	0.003381	0.003381	0.003381	0.003381	
PRn1	yes	-5.9495	0.0421	0.0421	Cd4b3	no	0.0421	0.0421	0.0421	Jun2	no	0.0421	0.0421	0.0421	Jun2	no	0.0421	0.0421	0.0421	Pha1	no	0.0421	0.0421	0.0421	Pha1	no	0.0421	0.0421	0.0421	0.0421	0.0421	0.0421	0.0421	
Cd4c	yes	-6.0155	0.03305	0.03305	Rp17	no	0.03305	0.03305	0.03305	Jun2	no	0.03305	0.03305	0.03305	Jun2	no	0.03305	0.03305	0.03305	Pha1	no	0.03305	0.03305	0.03305	Pha1	no	0.03305	0.03305	0.03305	0.03305	0.03305	0.03305	0.03305	
H1-3	yes	-6.1388	0.0264	0.0264	Rp18	no	0.0264	0.0264	0.0264	Jun2	no	0.0264	0.0264	0.0264	Jun2	no	0.0264	0.0264	0.0264	Pha1	no	0.0264	0.0264	0.0264	Pha1	no	0.0264	0.0264	0.0264	0.0264	0.0264	0.0264	0.0264	
Cu1	yes	-6.0237	0.02771	0.02771	Hmnp1	no	0.02771	0.02771	0.02771	Jun2	no	0.02771	0.02771	0.02771	Jun2	no	0.02771	0.02771	0.02771	Pha1	no	0.02771	0.02771	0.02771	Pha1	no	0.02771	0.02771	0.02771	0.02771	0.02771	0.02771	0.02771	
Cu1	yes	-5.9705	0.03265	0.03265	Hmnp1	no	0.03265	0.03265	0.03265	Jun2	no	0.03265	0.03265	0.03265	Jun2	no	0.03265	0.03265	0.03265	Pha1	no	0.03265	0.03265	0.03265	Pha1	no	0.03265	0.03265	0.03265	0.03265	0.03265	0.03265	0.03265	
Rp9	yes	-5.9203	0.04364	0.04364	Ser1	no	0.04364	0.04364	0.04364	Jun2	no	0.04364	0.04364	0.04364	Jun2	no	0.04364	0.04364	0.04364	Pha1	no	0.04364	0.04364	0.04364	Pha1	no	0.04364	0.04364	0.04364	0.04364	0.04364	0.04364	0.04364	
Rp2a	yes	-7.0348	0.01112	0.01112	Hdnc	no	0.01112	0.01112	0.01112	Jun2	no	0.01112	0.01112	0.01112	Jun2	no	0.01112	0.01112	0.01112	Pha1	no	0.01112	0.01112	0.01112	Pha1	no	0.01112	0.01112	0.01112	0.01112	0.01112	0.01112	0.01112	
Ad	yes	-6.082	0.00331	0.00331	Upa2	no	0.00331	0.00331	0.00331	Jun2	no	0.00331	0.00331	0.00331	Jun2	no	0.00331	0.00331	0.00331	Pha1	no	0.00331	0.00331	0.00331	Pha1	no	0.00331	0.00331	0.00331	0.00331	0.00331	0.00331	0.00331	
Cy5a	yes	-6.0821	0.03995	0.03995	Upa3	no	0.03995	0.03995	0.03995	Jun2	no	0.03995	0.03995	0.03995	Jun2	no	0.03995	0.03995	0.03995	Pha1	no	0.03995	0.03995	0.03995	Pha1	no	0.03995	0.03995	0.03995	0.03995	0.03995	0.03995	0.03995	
Apr4	yes	-6.0445	0.02595	0.02595	Rp24	no	0.02595	0.02595	0.02595	Jun2	no	0.02595	0.02595	0.02595	Jun2	no	0.02595	0.02595	0.02595	Pha1	no	0.02595	0.02595	0.02595	Pha1	no	0.02595	0.02595	0.02595	0.02595	0.02595	0.02595	0.02595	
Ad5	yes	-6.0528	0.01111	0.01111	Pd2	no	0.01111	0.01111	0.01111	Jun2	no	0.01111	0.01111	0.01111	Jun2	no	0.01111	0.01111	0.01111	Pha1	no	0.01111	0.01111	0.01111	Pha1	no	0.01111	0.01111	0.01111	0.01111	0.01111	0.01111	0.01111	
Ad5	yes	-6.0528	0.01111	0.01111	Pd2	no	0.01111	0.01111	0.01111	Jun2	no	0.01111	0.01111	0.01111	Jun2	no	0.01111	0.01111	0.01111	Pha1	no	0.01111	0.01111	0.01111	Pha1	no	0.01111	0.01111	0.01111	0.01111	0.01111	0.01111	0.01111	
Dad1	yes	-5.909	0.02454	0.02454	Upa2	no	0.02454	0.02454	0.02454	Jun2	no	0.02454	0.02454	0.02454	Jun2	no	0.02454	0.02454	0.02454	Pha1	no	0.02454	0.02454	0.02454	Pha1	no	0.02454	0.02454	0.02454	0.02454	0.02454	0.02454	0.02454	
Rp14	yes	-6.0741	0.00471	0.00471	Upa3	no	0.00471	0.00471	0.00471	Jun2	no	0.00471	0.00471	0.00471	Jun2	no	0.00471	0.00471	0.00471	Pha1	no	0.00471	0.00471	0.00471	Pha1	no	0.00471	0.00471	0.00471	0.00471	0.00471	0.00471	0.00471	

Male 7d vs Male 14d					significant_male_7d_vs_male_14d					logFC_male_7d_vs_male_14d					PValue_male_7d_vs_male_14d					significant_male_7d_vs_male_14d					logFC_male_7d_vs_male_14d					PValue_male_7d_vs_male_14d					significant_male_7d_vs_male_14d					logFC_male_7d_vs_male_14d					PValue_male_7d_vs_male_14d				
ColA3	yes	6.1865	0.00028	0.00028	Igk1	no	2.0404	0.1719	0.3081	Pha2	no	2.5442	0.0042	0.1301	Rp21	yes	1.3081	0.1774	0.6326																														
ColA3	yes	5.2007	0.00726	0.00726	Hme1	no	2.8795	0.1732	0.3088	Loa	no	1.7612	0.4729	0.1722	App5	no	1.2223	0.6328																															
Acta1	yes	4.1755	0.00142	0.00142	Tat1	no	2.7869	0.1746	0.3079	ColA2	yes	1.2647	0.4761	0.1432	Rp11	yes	0.7461	0.5242																															
Angpt1	yes	6.2803	0.00058	0.00058	Gtf1	no	1.0004	0.1747	0.3093	Clb1b	no	1.6552	0.4741	0.1286	Phn2	no	1.2766	0.6384																															
Prph1	yes	5.5261	0.00227	0.00227	Hme3	no	2.7974	0.18	0.3129	Ldb1	no	1.3329	0.4772	0.1472	Rp27a	no	1.0031	0.6438																															
Wdr1	yes	6.208	0.0008	0.0008	Tdp	no	2.4645	0.1825	0.318	Rp3	no	1.4279	0.4787	0.1507	Ser3d5	no	1.2087	0.6442																															
Cyp19	yes	5.1665	0.0048	0.0048	Hadhb	no	1.5388	0.185	0.3184	Chf1	no	1.2153	0.479	0.1513	Chaf1	no	0.7016	0.6448																															
Myo9b	yes	5.1036	0.00009	0.00009	Hsf1	no	2.7052	0.1852	0.3195	Cyc	no	1.2902	0.479	0.1508	Myo9b	no	1.0033	0.645																															
Sprn1	yes	5.6447	0.00209	0.00209	Ubc1	no	2.7581	0.188	0.3186	Hmp1	no	1.3062	0.4811	0.1502	Atg5f1c	no	1.2188	0.6536																															
ColA2	yes	5.2954	0.00084	0.00084	Rp18a	no	1.7876	0.1882	0.3204	Hsp14	no	1.3045	0.4827	0.1504	Rp13a	no	0.8627	0.6564																															
Murks	yes	4.9672	0.04602	0.04602	Hsp5	no	2.8729	0.1893	0.3216	Sfparc	no	1.8566	0.4837	0.1493	Rp17a	no	1.4003	0.657																															
Dh	yes	4.4402	0.0414	0.0414	Fat2	no	2.45	0.19	0.3207	Rp1b	no	1.2895	0.486	0.148	Rp28	no	1.1747	0.6586																															
Pp2a1	yes	5.4329	0.00787	0.00787	Hmra9b	no	2.7092	0.1944	0.3206	ColA3	no	1.2555	0.4861	0.1483	ColA3b	no	0.6837	0.6592																															
Gp3	yes	5.1249	0.02123	0.02123	Prace	no	2.7173	0.196	0.3207	Hsp1	no	1.2938	0.487	0.15	Cic	no	1.0103	0.6605																															
Car1	yes	5.3119	0.03491	0.03491	Hm2	no	2.3359	0.1967	0.3201	Hsp12	no	1.3071	0.4882	0.1493	Hsp1	no	1.0403	0.6613																															
Ac4f1	yes	4.4071	0.0001785	0.0001785	Vcl	no	1.7749	0.199	0.3202	Tat	no	1.2751	0.4892	0.1493	Hsp1	no	0.9005	0.6696																															
Cyp19	yes	5.7111	0.0001	0.0001	Hsp2	no	1.3975	0.1995	0.3203	ColA1	no	1.4842	0.4897	0.1487	Agp1	no	0.8873	0.671																															
Fat1	yes	5.1611	0.02774	0.02774	Hsp1	no	2.7129	0.2001	0.3208	Cuiv1	no	1.2718	0.4905	0.1483	Rp19	no	0.748	0.6751																															
Ube2n	yes	5.1364	0.03137	0.03137	Hsp2	no	2.6096	0.2008	0.3222	Nfse	no	1.6028	0.4907	0.1503	Katlg	no	0.8639	0.678																															
Hmra9	yes	5.4284	0.00078	0.00078	Hsp1	no	2.6079	0.2071	0.3228	Rp1a	no	1.2335	0.4946	0.1504	Rp13a	no	1.0384	0.6792																															
Sr5	yes	5.0823	0.0414	0.0414	Ser3f2	no	2.6381	0.2075	0.3233	Ser3f2	no	1.2548	0.4963	0.1504	Rp1a	no	0.8812	0.6817																															
Atg9	yes	5.0952	0.01493	0.01493	Hsp1	no	2.598	0.2089	0.3237	Hsp1	no	1.2693	0.4976	0.1507	Rp411	no	1.3172	0.685																															
Hmra9	yes	5.4296	0.00417	0.00417	Hsp1	no	2.5927	0.2091	0.3249	Hsp1	no	1.5367	0.4994	0.1507	Rp1a	no	1.128	0.6865																															
Shap3	yes	4.4452	0.0442	0.0442	Ctcf	no	2.462	0.2087	0.3249	Ser3f1b	no	1.2242	0.5023	0.1504	Rp1a	no	0.826	0.687																															
Act1	yes	5.1797	0.0283	0.0283	Rp1	no	2.2468	0.2097	0.3258	ColA3	no	1.4846	0.5034	0.1504	Cyp1	no	1.1397	0.6886																															
Shn3	yes	5.4291	0.0245	0.0245	Myo9	no	2.6336	0.2109	0.3277	Myo12a	no	1.3355	0.5044	0.1512	Apoe	no	0.9132	0.6966																															
Act2	yes	6.1881	0.0147	0.0147	Rp1	no	2.6375	0.2115	0.328	Act1	no	1.6932	0.505	0.1505	Ser3f1	no	0.7729	0.6986																															
Est	yes	8.1676	0.0000001	0.0000001	Ak	no	1.9984	0.2118	0.3282	Ak	no	1.4559	0.5087	0.1507	Agp21	no	0.9692	0.7033																															
Ucp2	yes	4.4772	0.04123	0.04123	Rp1	no	2.7152	0.2122	0.3287	Pp2a2	no	1.7745	0.509	0.1504	Cyp4	no	0.9644	0.7037																															
Entb	yes	5.2699	0.02727	0.02727	Ncl	no	2.5581	0.2148	0.3288	Pp1p	no	1.7808	0.5096	0.1512	Ser3f1	no	0.8971	0.7063																															
Gna2	yes	6.7778	0.000151	0.000151	Hm1b	no	2.5379	0.2168	0.3288	Sr3g1	no	1.4967	0.512	0.1508	Rp1	no	0.8892	0.7117																															
Macrotub1	yes	6.213	0.00227	0.00227	Rp1b	no	2.2644	0.2168	0.3288	Prph1	no	1.7524	0.5124	0.1508	Cyp1	no	0.8867	0.7127																															
Ucp2b	yes	5.5596	0.04209	0.04209	Hmra1	no	2.4422	0.2208	0.3288	Rp1	no	1.729	0.5127	0.1511	Rp1	no	0.8636	0.7149																															
Ucp2b	yes	7.0027	0.0004122	0.0004122	Hmra1	no	2.6655	0.2217	0.3288	Rp1	no	1.6607	0.5127	0.1504	Rp1	no	0.8636	0.7149																															
Ser1a	yes	5.2081	0.03928	0.03928	Caln1	no	2.6681	0.2236	0.3288	Hsp1	no	1.4785	0.5144	0.1504	C1a	no	0.8636	0.7227																															
Sprn1	yes	5.264	0.0261	0.0261	C1a	no	2.5344	0.2237	0.3288	Rp1	no	1.4647	0.5144	0.1504	C1a	no	0.8636	0.7227																															
Gna2	no	2.2619	0.09961	0.09961	Prn1	no	2.5653	0.227	0.3288	ColA3	no	1.716	0.5176	0.1507	Ucp1	no	0.9208	0.7374																															
Cav1	no	4.2791	0.00844	0.00844	Hmra1	no	2.6884	0.2271	0.3288	Rp27	no	1.2305	0.5179	0.1507	Agp1a	no	0.9203	0.7389																															
Atg9f1	yes	3.9861	0.07562	0.07562	Tpna1	no	2.5589	0.2284	0.3288	Rp1	no	1.4261	0.5179	0.1507	Agp1a	no	0.9203	0.7389																															
Hmra1	no	4.0129	0.04126	0.04126	Hmra1	no	2.7355	0.2299	0.3288	Hsp21	no	1.4345	0.5179	0.1507	Prph1	no	0.7478	0.7478																															
ColA3	no	4.1455	0.0415	0.0415	Cav1	no	2.2341	0.2341	0.3288	Cav1	no	1.8761	0.5179	0.1507	Prph1	no	0.7478	0.7478																															
Atg9f1	no	4.2053	0.0448	0.0448	Hmra1	no	2.5386	0.2353	0.3288	Rp1	no	1.3848	0.5179	0.1507	Rp1a	no	0.7521	0.7501																															
Tpna1	yes	4.0958	0.0448	0.0448	Hmra1	no	2.5386	0.2353	0.3288	Rp1	no	1.3848	0.5179	0.1507	Rp1a	no	0.7521	0.7501																															
Air1a	no	3.9171	0.07049	0.07049	Rp2																																												

APPENDIX II

CHAPTER 3 SUPPLEMENTARY FIGURES

Appendix II.1.

ER α and ER β Fluorescent IHC

By: Emily Van Zeeland and Lindsey Burton 06/22/2024

Sample Preparation: Fixation with 10% neutral buffered formalin, decalcification with 5% EDTA/PBS, paraffin embedded, sectioned at 5 μ m.

Samples: Mouse Stifles

Materials:

- 1) **Xylene**
- 2) **EtOH: 100%, 95%, 70%, 50%, 30%**
- 3) **MiliQ H₂O**
- 4) **Citric Acid**
- 5) **PBS**
- 6) **Tween20**
- 7) **Normal Goat Serum (NGS)** (ThermoFisher, 31873)
- 8) **Goat anti-Mouse IgG (H+L) Secondary Antibody** (ThermoFisher, 31160)
- 9) **Mouse isotype control** (ThermoFisher, 14-4714-81)
- 10) **Rabbit isotype control** (ThermoFisher, 31235)
- 11) **Goat anti-Mouse IgG AlexaFluor488** (ThermoFisher, A32723)
- 12) **Goat anti-Rabbit IgG AlexaFluor 647** (ThermoFisher, A32733)
- 13) **VECTASHIELD Vibrance Antifade Mounting Medium with DAPI** (Vector Laboratories, H-1800)

Solutions to Prepare:

1. Citrate Buffer
 - a. 10.01M Citric Acid in H₂O
 - b. Adjust pH to 6 using 12M NaOH
2. PBST
 - a. 0.1% Tween20 in PBS
 - b. Use stir plate to dissolve Tween20 into PBS
3. Blocking serum
 - a. 10% NGS in PBST
4. Permeabilization buffer
 - a. 0.2% Tween20/1.5% NGS in PBS
5. Blocking endogenous mouse IgG: Goat anti-Mouse IgG
 - a. 50ug/mL in PBST
6. Primary antibodies
 - a. 1:75 ER α primary antibody

Appendix II.1.

- b. 1:150 ER β primary antibody
 - c. In permeabilization buffer
- 7. Isotype control primary antibodies
 - a. 1:50 Mouse isotype control
 - b. 1:50 Rabbit isotype control
 - c. In permeabilization buffer
- 8. Secondary antibodies
 - a. 1:200 AlexaFluor488
 - b. 1:200 AlexaFluor 647
 - c. In permeabilization buffer

ER α and ER β Fluorescent IHC

Day 1

1. Bake slides overnight in blue heat-resistant slide container at 55°C.

Day 2

1. Fill blue heat-resistant slide container with citrate buffer and place in oven at 55°C to heat buffer for step 4.
2. Place slides in the designated solutions in the following order:
 - a. 5 minutes Xylene
 - b. 5 minutes Xylene
 - c. 5 minutes Xylene
 - d. 3 minutes 100% EtOH
 - e. 3 minutes 100% EtOH
 - f. 3 minutes 100% EtOH
 - g. 3 minutes 95% EtOH
 - h. 3 minutes 95% EtOH
 - i. 3 minutes 70% EtOH
 - j. 3 minutes 50% EtOH
 - k. 3 minutes 30% EtOH
 - l. 5 minutes MiliQ H₂O
 - m. 5 minutes MiliQ H₂O
 - n. 5 minutes MiliQ H₂O
 - o. 5 minutes 1X PBS
 - p. 5 minutes 1X PBS

Appendix II.1.

- q. 5 minutes 1X PBS
3. Incubate slides in prewarmed citrate buffer for 4 hours at 55°C
4. Wash slides in:
 - a. 5 minutes 1X PBS
 - b. 5 minutes 1X PBS
 - c. 5 minutes 1X PBS
5. Outline sections with PAP pen
6. Permeabilize for 15 minutes with 0.2% tween20/1.5% goat serum in PBS in humidified chamber
7. Tap permeabilization buffer off slide using a KimWipe
8. Block slides with 10% goat serum in PBST for 1 hour at room temperature in humidified chamber
9. After 1 hour incubation, remove block by tapping onto KimWipe
10. Wash slides in:
 - a. 5 minutes 1X PBS
 - b. 5 minutes 1X PBS
 - c. 5 minutes 1X PBS
11. Block endogenous mouse IgG with Goat anti-Mouse IgG (H+L) Secondary Antibody at 50ug/mL in PBST for 1 hour at room temperature in humidified chamber
12. After 1 hour incubation, remove block by tapping slides onto KimWipe
13. Incubate slides with primary antibody in permeabilization buffer (0.2% tween20/1.5%goat serum in PBS) for 16 hours at 4°C in humidified chamber
 - a. Include IgG control at same concentration
 - b. Include secondary antibody control (permeabilization buffer only)

Day 3

1. After overnight incubation, remove primary antibody by tapping slides on KimWipe.
2. Wash slides in:
 - a. 5 minutes 1X PBST
 - b. 5 minutes 1X PBST
 - c. 5 minutes 1X PBST
 - d. 5 minutes 1X PBS
 - e. 5 minutes 1X PBS

Appendix II.1.

- f. 5 minutes 1X PBS

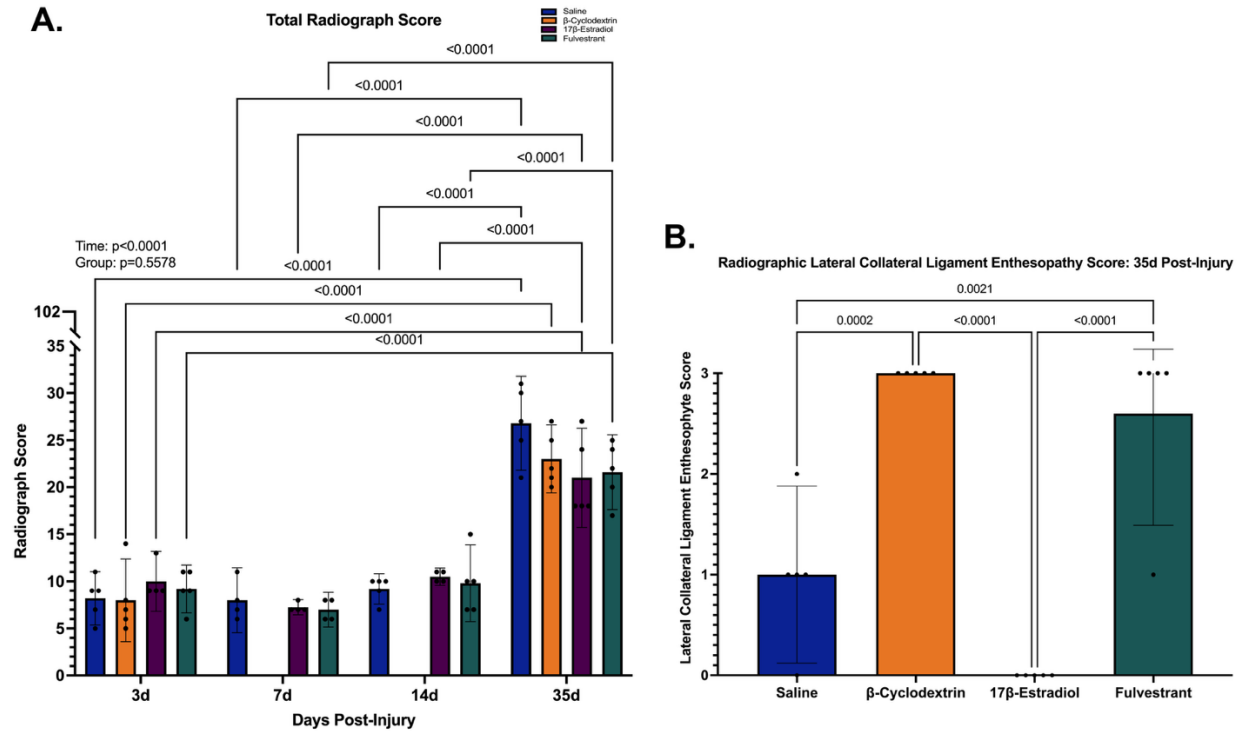
PERFORM THE FOLLOWING STEPS IN THE DARK

3. Incubate slides with secondary antibody in permeabilization buffer (0.2% tween20/1.5%goat serum in PBS) 1 hour at room temperature in humidified chamber
4. After 1 hour incubation, remove secondary antibody by tapping slides onto a KimWipe
5. Wash slides in:
 - a. 5 minutes 1X PBST
 - b. 5 minutes 1X PBST
 - c. 5 minutes 1X PBST
 - d. 5 minutes 1X PBS
 - e. 5 minutes 1X PBS
 - f. 5 minutes 1X PBS
6. Add 40µL of DAPI to each slide and cover with coverslip.
 - a. If using wet-mount DAPI, image immediately
 - b. If using hard-set DAPI, allow slides to dry for 1 hour in the dark and then image

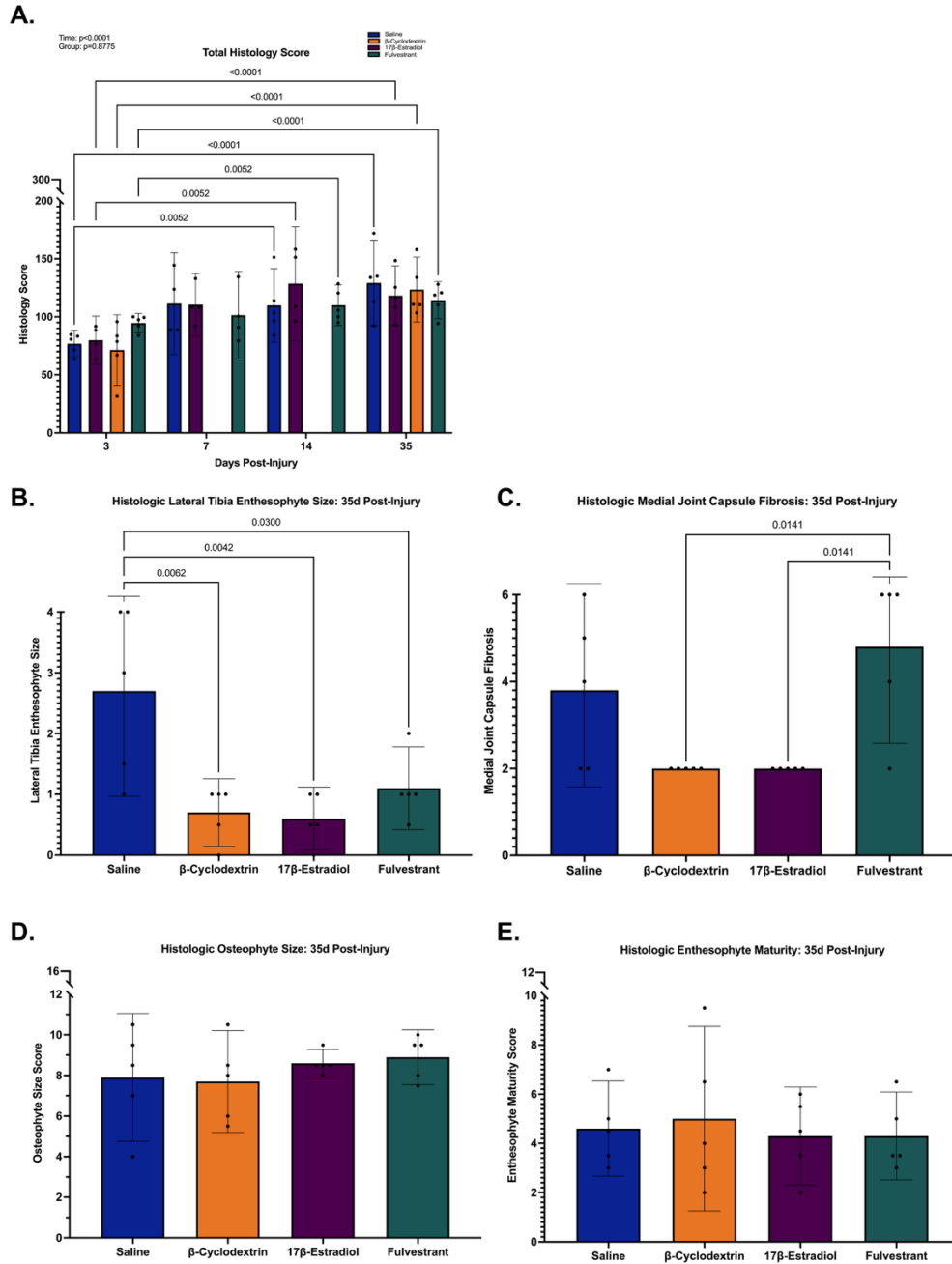
Notes:

- For permeabilization, blocking, and incubating with antibodies, it depends on the size of the section, but typically 250-350 µL is a good amount to add to each slide
- If there are multiple sections per slide, outline one section with the PAP pen and only stain that section to conserve reagents
- PAP pen can be reapplied as needed throughout the protocol. It is much better to reapply the PAP pen than to let your sections dry out. Sections should never be dry once they have been rehydrated.
- A positive control, negative control, and isotype control should be included with every batch of slides.
- The Vectashield Mounting Media is very viscous. Ensure enough time for the full volume to be aspirated before applying it to the slide.

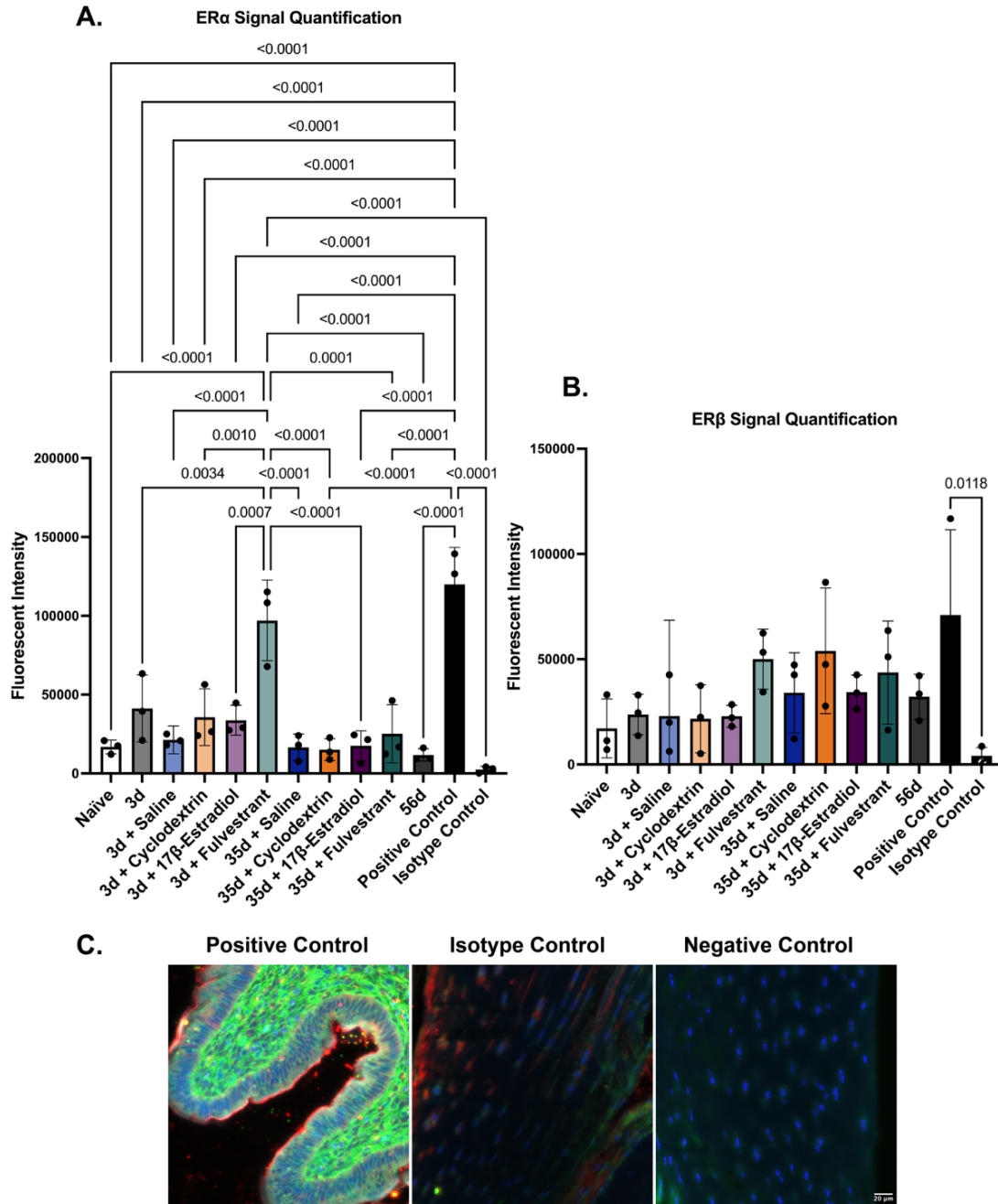
Appendix II.1. Detailed protocol for fluorescent IHC for $ER\alpha$ and $ER\beta$ in mouse stifles.



Appendix II.2. Additional analyses of radiographic scoring. **(A)** Complete statistical analysis of time-based differences in total radiographic scores within each group. Between-group comparisons across timepoints are not shown. **(B)** At 35 days post-injury, the β -cyclodextrin and Fulvestrant groups exhibited greater enthesopathy of the lateral collateral ligament compared to the saline group. p -values < 0.05 are indicated. Bars represent mean $\pm$ 95% confidence interval, with individual animals shown.



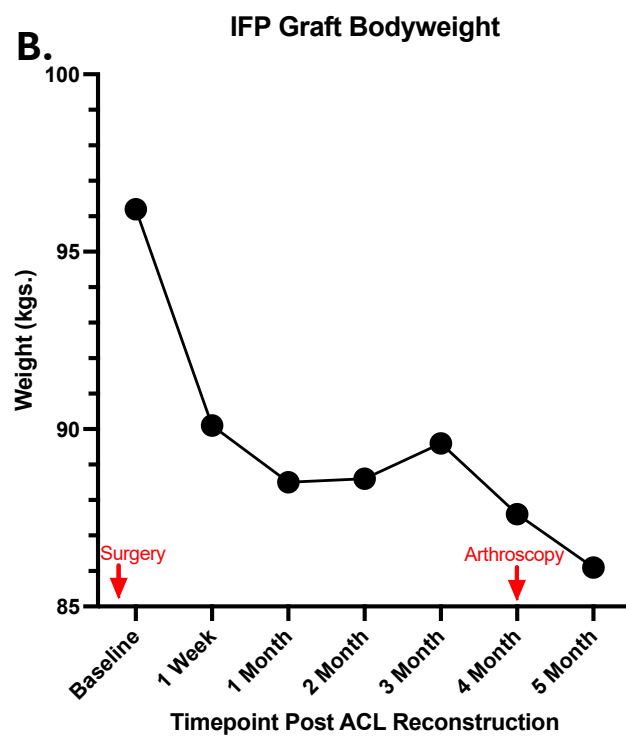
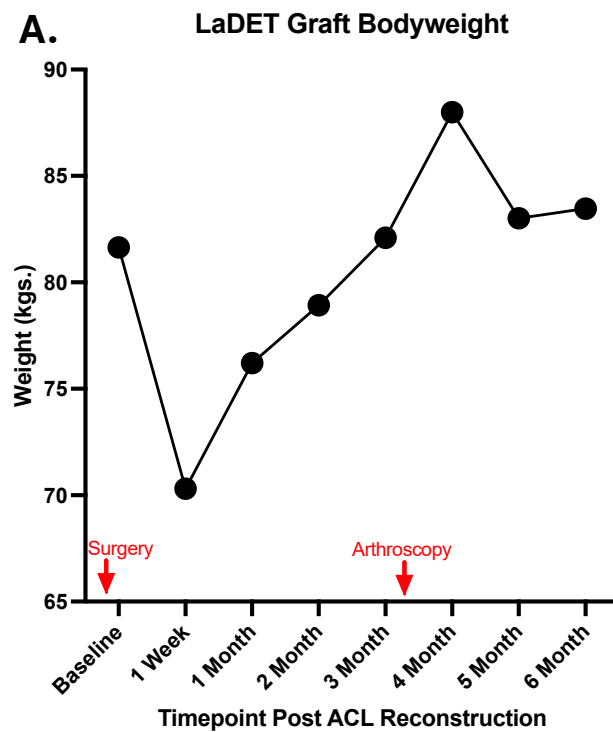
Appendix II.3. Additional analyses of histologic scoring parameters. **(A)** Complete statistical analysis of time-based differences in total histology scores within each group. Between-group comparisons across timepoints are not shown. **(B)** At 35 days post-injury, the saline group exhibited larger enthesophytes on the lateral tibia compared to all other groups. **(C)** The Fulvestrant group showed increased fibrosis of the medial joint capsule at 35 days compared to both the β -cyclodextrin and 17β -estradiol groups, though it was not significantly different from the saline group. **(D)** No group differences were observed in overall osteophyte size at 35 days. **(E)** Similarly, there were no differences in enthesophyte maturity among groups at this timepoint. p -values < 0.05 are indicated. Bars represent mean $\pm$ 95% confidence interval, with individual animals shown.



Appendix II.4. Validation of ER α and ER β Fluorescent IHC Controls. (A) The positive control for ER α showed increased signal intensity compared to all other groups, including the isotype control. (B) The positive control for ER β showed greater signal intensity than the isotype control but not compared to any other groups. Signal intensity was normalized using the negative control to account for background fluorescence. Prior to normalization, the negative control exhibited significantly lower signal intensity than the positive controls for both ER α and ER β but did not differ significantly from the isotype controls (not shown). (C) Representative 40X dual-stained fluorescent IHC images of female mouse ovary (positive control) and mouse ACL remnants (isotype and negative controls). Fluorescent channels show DAPI (blue), ER α (green), and ER β (red).

APPENDIX III

CHAPTER 4 SUPPLEMENTARY FIGURES



Appendix III.1. Individual animal bodyweights measured throughout study duration.

<i>Lameness score</i>	<i>Score</i>
<i>Normal ambulation, full weight bearing</i>	<i>0</i>
<i>Slight lameness on operated limb (partial weight bearing on all steps)</i>	<i>1</i>
<i>Moderate lameness on operated limb (partial weight bearing on some but not all steps)</i>	<i>2</i>
<i>Marked lameness on operated limb (non-weight bearing on all steps when walking voluntarily, but will partially bear weight when herded)</i>	<i>3</i>
<i>Non-weight bearing on the operative limb during all ambulation</i>	<i>4</i>

Appendix III.2. Lameness scoring system used to assess animal mobility.

Lachman's Assessment Form

Instructions: *Animals are evaluated for joint stability by qualified PSRL personnel, and scores will be recorded on a Lachman's Assessment Form. All study animals will be evaluated for Lachman's pre-operatively, post-operatively, and immediately post-euthanasia for all animals.*

<u>Lachman's Score</u>	<u>Score</u>
<i>Negative</i>	<i>0</i>
<i>0-5mm of anterior displacement</i>	<i>1+</i>
<i>5-10mm of anterior displacement - with no end point</i>	<i>2+</i>
<i>10mm of anterior displacement – with no end point</i>	<i>3+</i>

Appendix III.3. *Lachman's scoring system for evaluation of joint stability.*

Table of contents

\\USER

SHEEP 12.1.23

Stifle

SRL 2341 VAN ZEELAND STIFLE

localizer_sag+cor+tra	*
localizer_sag+cor+tra	*
SAG T1W	*
SAG PDFS	*
SAG T2W	*
DORSAL PDFS	*
DORSAL T2W	*
TRANS T2W	*
TRANS T2W LOWER DISTALLY	*

\\USER\SHEEP 12.1.23\stifle\SRL 2341 VAN ZEELAND STIFLE\localizer_sag+cor+tra *

TA: 20 sec Coil Selection: Auto Voxel Size: 0.5×0.5×6.0 mm³ Acc.: None Rel. SNR: 1.00

Properties

Start measurement without further preparation	On
Wait for User to Start	Off
Start measurements	Single Measurement
Prio Recon	Off
Auto Open Inline Display	Off
Auto Close Inline Display	Off
Load Images to MR View&GO	On
Auto Store Images	On
Load Images to Stamp Segments	On
Load Images to Graphic Segments	On
Graphic segment	All Segments
Inline Movie	Off

Resolution - Common

FoV Read	280 mm
FoV Phase	100.0 %
Slice Thickness	6.0 mm
Base Resolution	256
Phase Resolution	80 %
Interpolation	On

Resolution - Acceleration

Acceleration mode	None
Advanced Reconstruction	Off
Phase Partial Fourier	Off
Asymmetric Echo	Allowed

Routine

Slice Group	1
Slices	3
Distance Factor	50 %
Position	R59.2 P3.4 H0.6 mm
Orientation	S > C-0.3
Phase Encoding Dir.	A >> P
Slice Group	2
Slices	3
Distance Factor	50 %
Position	R59.2 P3.4 H0.6 mm
Orientation	S > C-0.3
Phase Encoding Dir.	A >> P
Slice Group	3
Slices	3
Distance Factor	50 %
Position	R59.2 P3.4 H0.6 mm
Orientation	S > C-0.3
Phase Encoding Dir.	A >> P
Phase Oversampling	38 %
FoV Read	280 mm
FoV Phase	100.0 %
Slice Thickness	6.0 mm
TR	7.3 ms
TE	3.60 ms
Averages	1
Concatenations	9
AutoAlign	---

Resolution - Filter

Raw Filter	Off
Elliptical Filter	On
Distortion Correction	2D
Normalize	Off
Image Filter	Off

Geometry - Common

Slice Group	1
Slices	3
Distance Factor	50 %
Position	R59.2 P3.4 H0.6 mm
Orientation	S > C-0.3
Phase Encoding Dir.	A >> P
Slice Group	2
Slices	3
Distance Factor	50 %
Position	R59.2 P3.4 H0.6 mm
Orientation	S > C-0.3
Phase Encoding Dir.	A >> P
Slice Group	3
Slices	3
Distance Factor	50 %
Position	R59.2 P3.4 H0.6 mm
Orientation	S > C-0.3
Phase Encoding Dir.	A >> P
Phase Oversampling	38 %
FoV Read	280 mm
FoV Phase	100.0 %
Slice Thickness	6.0 mm
TR	7.3 ms
Multi-Slice Mode	Sequential
Series	Interleaved
Concatenations	9

Contrast - Common

TR	7.3 ms
TE	3.60 ms
TD	0.00 ms
MTC	Off
Magn. Preparation	None
Flip Angle	20 deg
Fat-Water Contrast	Standard
Dark Blood	Off
Contrasts	1
Reconstruction	Magnitude

Contrast - Dynamic

Dynamic Mode	Standard
Measurements	1
Multiple Series	Each Measurement

Geometry - AutoAlign

Slice Group	1
Position	R59.2 P3.4 H0.6 mm
Orientation	S > C-0.3
Phase Encoding Dir.	A >> P
Slice Group	2
Position	R59.2 P3.4 H0.6 mm
Orientation	S > C-0.3
Phase Encoding Dir.	A >> P
Slice Group	3
Position	R59.2 P3.4 H0.6 mm
Orientation	S > C-0.3

Geometry - AutoAlign

Phase Encoding Dir.	A >> P
AutoAlign	---
Initial Position	R59.2 P3.4 H0.6
R	59.2 mm
P	3.4 mm
H	0.6 mm
Initial Orientation	S > C
S > C	-0.30
> T	0.00
Initial Rotation	0.00 deg

Geometry - Saturation

Saturation Mode	Standard
Special Saturation	None

Geometry - Tim Planning Suite

Set-n-Go Protocol	Off
Table Position	1 mm
Table Position	H
Inline Composing	Off

System - Miscellaneous

Coil Selection	ACS All but spine
MSMA	S - C - T
Sagittal	R >> L
Coronal	A >> P
Transversal	H >> F
Coil Combination	Adaptive Combine
Matrix Optimization	Off
Coil Focus	Flat

System - Adjustments

Adjustment Strategy	Standard
B0 Shim	Tune up
B1 Shim	TrueForm
CoilShim	Off
Adjustment Tolerance	Auto
Adjust with Body Coil	Off
Confirm Frequency	Never
Assume Silicone	Off

System - Adjust Volume

Position	Isocenter
Orientation	Transversal
Rotation	0.00 deg
A >> P	263 mm
R >> L	350 mm
F >> H	350 mm
Reset	Off

System - pTx

B1 Shim	TrueForm
Excitation	Slice-sel.
LR Balancing	Off

System - Tx/Rx

Frequency 1H	123.243725 MHz
? Ref. Amplitude 1H	0.000 V
Reset	Off
Image Scaling	1.000

Physio - Signal

1st Signal/Mode	None
-----------------	------

Physio - Signal

TR	7.3 ms
Segments	1
Concatenations	9

Physio - Cardiac

Fat-Water Contrast	Standard
Magn. Preparation	None
Dark Blood	Off
FoV Read	280 mm
FoV Phase	100.0 %
Phase Resolution	80 %
Dynamic Mode	Standard

Physio - PACE

Resp. Control	Off
Concatenations	9

Inline - Liver

Liver Registration	Off
Save Original Images	On

Inline - Subtraction

Subtract	Off
Measurements	1
StdDev	Off
Save Original Images	On

Inline - Cardiac

Magn. Preparation	None
Save Original Images	On
Contrasts	1
TE	3.60 ms
TR	7.3 ms

Inline - MIP

MIP Sag	Off
MIP Cor	Off
MIP Tra	Off
MIP Time	Off
Radial MIP	Off
Save Original Images	On
MPR Sag	Off
MPR Cor	Off
MPR Tra	Off

Inline - Soft Tissue

Wash-in	Off
Wash-out	Off
TTP	Off
PEI	Off
MIP Time	Off
Measurements	1

Inline - Composing

Inline Composing	Off
------------------	-----

Inline - MapIt

MapIt	None
Flip Angle	20 deg
Measurements	1
Contrasts	1
TE	3.60 ms
TR	7.3 ms

Inline - MapIt

Save Original Images	On
----------------------	----

Sequence - Part 1

Sequence Name	fl
Dimension	2D
Excitation	Slice-sel.
RF Pulse Type	Fast
Gradient Mode	Fast
Flow Compensation	None
Bandwidth	330 Hz/Px
Asymmetric Echo	Allowed
Segments	1

Sequence - Part 2

Introduction	On
RF Spoiling	On
Acoustic noise reduction	Off

Sequence - Assistant

SAR Assistant	Off
Allowed Delay	0 s

\\USER\SHEEP 12.1.23\stifle\SRL 2341 VAN ZEELAND STIFLE\localizer_sag+cor+tra *

TA: 35 sec Coil Selection: Auto Voxel Size: 0.5×0.5×6.0 mm³ Acc.: None Rel. SNR: 1.00**Properties**

Start measurement without further preparation	On
Wait for User to Start	Off
Start measurements	Single Measurement
Prio Recon	Off
Auto Open Inline Display	Off
Auto Close Inline Display	Off
Load Images to MR View&GO	On
Auto Store Images	On
Load Images to Stamp Segments	On
Load Images to Graphic Segments	On
Graphic segment	All Segments
Inline Movie	Off

Resolution - Common

FoV Read	280 mm
FoV Phase	100.0 %
Slice Thickness	6.0 mm
Base Resolution	256
Phase Resolution	80 %
Interpolation	On

Resolution - Acceleration

Acceleration mode	None
Advanced Reconstruction	Off
Phase Partial Fourier	Off
Asymmetric Echo	Allowed

Routine

Slice Group	1
Slices	5
Distance Factor	50 %
Position	R65.8 P23.7 H67.6 mm
Orientation	S > T-1.4 > C-0.6
Phase Encoding Dir.	A >> P
Slice Group	2
Slices	5
Distance Factor	50 %
Position	R65.8 P23.7 H67.6 mm
Orientation	S > T-1.4 > C-0.6
Phase Encoding Dir.	A >> P
Slice Group	3
Slices	5
Distance Factor	50 %
Position	R65.8 P23.7 H67.6 mm
Orientation	S > T-1.4 > C-0.6
Phase Encoding Dir.	A >> P
Phase Oversampling	38 %
FoV Read	280 mm
FoV Phase	100.0 %
Slice Thickness	6.0 mm
TR	7.3 ms
TE	3.60 ms
Averages	1
Concatenations	16
AutoAlign	---

Resolution - Filter

Raw Filter	Off
Elliptical Filter	On
Distortion Correction	2D
Normalize	Off
Image Filter	Off

Geometry - Common

Slice Group	1
Slices	5
Distance Factor	50 %
Position	R65.8 P23.7 H67.6 mm
Orientation	S > T-1.4 > C-0.6
Phase Encoding Dir.	A >> P
Slice Group	2
Slices	5
Distance Factor	50 %
Position	R65.8 P23.7 H67.6 mm
Orientation	S > T-1.4 > C-0.6
Phase Encoding Dir.	A >> P
Slice Group	3
Slices	5
Distance Factor	50 %
Position	R65.8 P23.7 H67.6 mm
Orientation	S > T-1.4 > C-0.6
Phase Encoding Dir.	A >> P
Phase Oversampling	38 %
FoV Read	280 mm
FoV Phase	100.0 %
Slice Thickness	6.0 mm
TR	7.3 ms
Multi-Slice Mode	Sequential
Series	Interleaved
Concatenations	16

Contrast - Common

TR	7.3 ms
TE	3.60 ms
TD	0.00 ms
MTC	Off
Magn. Preparation	None
Flip Angle	20 deg
Fat-Water Contrast	Standard
Dark Blood	Off
Contrasts	1
Reconstruction	Magnitude

Contrast - Dynamic

Dynamic Mode	Standard
Measurements	1
Multiple Series	Each Measurement

Geometry - AutoAlign

Slice Group	1
Position	R65.8 P23.7 H67.6 mm
Orientation	S > T-1.4 > C-0.6
Phase Encoding Dir.	A >> P
Slice Group	2
Position	R65.8 P23.7 H67.6 mm
Orientation	S > T-1.4 > C-0.6
Phase Encoding Dir.	A >> P
Slice Group	3
Position	R65.8 P23.7 H67.6 mm
Orientation	S > T-1.4 > C-0.6

Geometry - AutoAlign

Phase Encoding Dir.	A >> P
AutoAlign	---
Initial Position	R65.8 P23.7 H67.6
R	65.8 mm
P	23.7 mm
H	67.6 mm
Initial Orientation	S > T
S > T	-1.40
> C	-0.60
Initial Rotation	22.13 deg

Geometry - Saturation

Saturation Mode	Standard
Special Saturation	None

Geometry - Tim Planning Suite

Set-n-Go Protocol	Off
Table Position	68 mm
Table Position	H
Inline Composing	Off

System - Miscellaneous

Coil Selection	ACS All but spine
MSMA	S - C - T
Sagittal	R >> L
Coronal	A >> P
Transversal	H >> F
Coil Combination	Adaptive Combine
Matrix Optimization	Off
Coil Focus	Flat

System - Adjustments

Adjustment Strategy	Standard
B0 Shim	Tune up
B1 Shim	TrueForm
CoilShim	Off
Adjustment Tolerance	Auto
Adjust with Body Coil	Off
Confirm Frequency	Never
Assume Silicone	Off

System - Adjust Volume

Position	Isocenter
Orientation	Transversal
Rotation	0.00 deg
A >> P	263 mm
R >> L	350 mm
F >> H	350 mm
Reset	Off

System - pTx

B1 Shim	TrueForm
Excitation	Slice-sel.
LR Balancing	Off

System - Tx/Rx

Frequency 1H	123.243725 MHz
? Ref. Amplitude 1H	0.000 V
Reset	Off
Image Scaling	1.000

Physio - Signal

1st Signal/Mode	None
-----------------	------

Physio - Signal

TR	7.3 ms
Segments	1
Concatenations	16

Physio - Cardiac

Fat-Water Contrast	Standard
Magn. Preparation	None
Dark Blood	Off
FoV Read	280 mm
FoV Phase	100.0 %
Phase Resolution	80 %
Dynamic Mode	Standard

Physio - PACE

Resp. Control	Off
Concatenations	16

Inline - Liver

Liver Registration	Off
Save Original Images	On

Inline - Subtraction

Subtract	Off
Measurements	1
StdDev	Off
Save Original Images	On

Inline - Cardiac

Magn. Preparation	None
Save Original Images	On
Contrasts	1
TE	3.60 ms
TR	7.3 ms

Inline - MIP

MIP Sag	Off
MIP Cor	Off
MIP Tra	Off
MIP Time	Off
Radial MIP	Off
Save Original Images	On
MPR Sag	Off
MPR Cor	Off
MPR Tra	Off

Inline - Soft Tissue

Wash-in	Off
Wash-out	Off
TTP	Off
PEI	Off
MIP Time	Off
Measurements	1

Inline - Composing

Inline Composing	Off
------------------	-----

Inline - MapIt

MapIt	None
Flip Angle	20 deg
Measurements	1
Contrasts	1
TE	3.60 ms
TR	7.3 ms

Inline - MapIt

Save Original Images	On
----------------------	----

Sequence - Part 1

Sequence Name	fl
Dimension	2D
Excitation	Slice-sel.
RF Pulse Type	Fast
Gradient Mode	Fast
Flow Compensation	None
Bandwidth	330 Hz/Px
Asymmetric Echo	Allowed
Segments	1

Sequence - Part 2

Introduction	On
RF Spoiling	On
Acoustic noise reduction	Off

Sequence - Assistant

SAR Assistant	Off
Allowed Delay	0 s

\\USER\SHEEP 12.1.23\Stifle\SRL 2341 VAN ZEELAND STIFLE\SAG T1W *

TA: 4:02 min Coil Selection: Auto Voxel Size: 0.4×0.4×2.0 mm³ Acc.: 2 Rel. SNR: 1.00**Properties**

Start measurement without further preparation	On
Wait for User to Start	Off
Start measurements	Single Measurement
Prio Recon	Off
Auto Open Inline Display	Off
Auto Close Inline Display	Off
Load Images to MR View&GO	On
Auto Store Images	On
Load Images to Stamp Segments	On
Load Images to Graphic Segments	On
Graphic segment	1st Segment
Inline Movie	Off

Resolution - Acceleration

Reference Scans	Self-calibration
Acceleration Factor PE	2
Reference Lines PE	32
Advanced Reconstruction	Off
Phase Partial Fourier	Off

Resolution - Filter

Raw Filter	Off
Elliptical Filter	On
Distortion Correction	2D
Normalize	Prescan
Image Filter	Off

Routine

Slice Group	1
Slices	32
Distance Factor	10 %
Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Phase Encoding Dir.	H >> F
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	828.0 ms
TE	8.70 ms
Averages	2
Concatenations	2
AutoAlign	---

Geometry - Common

Slice Group	1
Slices	32
Distance Factor	10 %
Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Phase Encoding Dir.	H >> F
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	828.0 ms
Multi-Slice Mode	Interleaved
Series	Interleaved
Concatenations	2

Contrast - Common

TR	828.0 ms
TE	8.70 ms
TD	0.00 ms
MTC	Off
Magn. Preparation	None
Flip Angle	122 deg
Fat-Water Contrast	Standard
Dark Blood	Off
Contrasts	1
Wrap-up Magn.	None
Reconstruction	Magnitude

Geometry - AutoAlign

Slice Group	1
Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Phase Encoding Dir.	H >> F
AutoAlign	---
Initial Position	R70.9 P31.3 H77.9
R	70.9 mm
P	31.3 mm
H	77.9 mm
Initial Orientation	S > T
S > T	-3.00
> C	0.00
Initial Rotation	90.00 deg

Contrast - Dynamic

Dynamic Mode	Standard
Measurements	1
Multiple Series	Each Measurement

Geometry - Navigator**Geometry - Saturation**

Special Saturation	None
--------------------	------

Resolution - Common

FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
Base Resolution	384
Phase Resolution	75 %
Trajectory	Cartesian
Interpolation	Off

Geometry - Tim Planning Suite

Set-n-Go Protocol	Off
Table Position	78 mm
Table Position	H
Inline Composing	Off

Resolution - Acceleration

Acceleration mode	GRAPPA
-------------------	--------

System - Miscellaneous

Coil Selection	Auto Coil Select
MSMA	S - C - T
Sagittal	R >> L
Coronal	A >> P

System - Miscellaneous

Transversal	F >> H
Coil Combination	Adaptive Combine
Matrix Optimization	Off
Coil Focus	Flat

System - Adjustments

Adjustment Strategy	Standard
B0 Shim	Tune up
B1 Shim	TrueForm
CoilShim	Off
Adjustment Tolerance	Auto
Adjust with Body Coil	Off
Confirm Frequency	Never
Assume Silicone	Off

System - Adjust Volume

Position	Isocenter
Orientation	Transversal
Rotation	0.00 deg
A >> P	263 mm
R >> L	350 mm
F >> H	350 mm
Reset	Off

System - pTx

B1 Shim	TrueForm
LR Balancing	Off

System - Tx/Rx

Frequency 1H	123.243725 MHz
? Ref. Amplitude 1H	0.000 V
Reset	Off
Image Scaling	1.000

Physio - Signal

1st Signal/Mode	None
TR	828.0 ms
Concatenations	2

Physio - Cardiac

Fat-Water Contrast	Standard
Magn. Preparation	None
Dark Blood	Off
FoV Read	140 mm
FoV Phase	100.0 %
Phase Resolution	75 %
Trajectory	Cartesian
Dynamic Mode	Standard

Physio - PACE

Resp. Control	Off
Concatenations	2

Inline - Subtraction

Subtract	Off
Measurements	1
StdDev	Off
Save Original Images	On

Inline - Cardiac

Magn. Preparation	None
Save Original Images	On
Contrasts	1

Inline - Cardiac

TE	8.70 ms
TR	828.0 ms

Inline - MIP

MIP Sag	Off
MIP Cor	Off
MIP Tra	Off
MIP Time	Off
Radial MIP	Off
Save Original Images	On
MPR Sag	Off
MPR Cor	Off
MPR Tra	Off

Inline - Composing

Inline Composing	Off
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Sequence - Part 1

Sequence Name	tse
Dimension	2D
RF Pulse Type	Fast
Gradient Mode	Fast
Flow Compensation	None
Bandwidth	241 Hz/Px
Echo Spacing	8.65 ms
Free Echo Spacing	Off
Define	Turbo Factor
Turbo Factor	4
Echo Trains per Slice	72

Sequence - Part 2

Introduction	On
Phase Correction	Automatic
Compensate T2 Decay	Off
Hyperecho	Off
WARP	Off
Red. EC Sensitivity	Off
Acoustic noise reduction	Off
Reduce Motion Sens.	Off

Sequence - Assistant

SAR Assistant	Off
Allowed Delay	20 s

\\USER\SHEEP 12.1.23\Stifle\SRL 2341 VAN ZEELAND STIFLE\SAG PDFS *

TA: 3:40 min Coil Selection: Auto Voxel Size: 0.4×0.4×2.0 mm³ Acc.: 2 Rel. SNR: 1.00**Properties**

Start measurement without further preparation	On
Wait for User to Start	Off
Start measurements	Single Measurement
Prio Recon	Off
Auto Open Inline Display	Off
Auto Close Inline Display	Off
Load Images to MR View&GO	On
Auto Store Images	On
Load Images to Stamp Segments	On
Load Images to Graphic Segments	On
Graphic segment	1st Segment
Inline Movie	Off

Resolution - Acceleration

Reference Scans	Self-calibration
Acceleration Factor PE	2
Reference Lines PE	32
Advanced Reconstruction	Off
Phase Partial Fourier	Off

Resolution - Filter

Raw Filter	Off
Elliptical Filter	On
Distortion Correction	2D
Normalize	Prescan
Image Filter	Off

Routine

Slice Group	1
Slices	32
Distance Factor	10 %
Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Phase Encoding Dir.	H >> F
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	3030.0 ms
TE	50.00 ms
Averages	2
Concatenations	1
AutoAlign	---

Geometry - Common

Slice Group	1
Slices	32
Distance Factor	10 %
Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Phase Encoding Dir.	H >> F
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	3030.0 ms
Multi-Slice Mode	Interleaved
Series	Interleaved
Concatenations	1

Contrast - Common

TR	3030.0 ms
TE	50.00 ms
MTC	Off
Magn. Preparation	None
Flip Angle	132 deg
Fat-Water Contrast	Fat Saturation
Fat Saturation	Strong
Dark Blood	Off
Contrasts	1
Wrap-up Magn.	None
Reconstruction	Magnitude

Geometry - AutoAlign

Slice Group	1
Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Phase Encoding Dir.	H >> F
AutoAlign	---
Initial Position	R70.9 P31.3 H77.9
R	70.9 mm
P	31.3 mm
H	77.9 mm
Initial Orientation	S > T
S > T	-3.00
> C	0.00
Initial Rotation	90.00 deg

Contrast - Dynamic

Dynamic Mode	Standard
Measurements	1
Multiple Series	Each Measurement

Geometry - Navigator**Geometry - Saturation**

Special Saturation	None
--------------------	------

Resolution - Common

FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
Base Resolution	320
Phase Resolution	75 %
Trajectory	Cartesian
Interpolation	Off

Geometry - Tim Planning Suite

Set-n-Go Protocol	Off
Table Position	78 mm
Table Position	H
Inline Composing	Off

Resolution - Acceleration

Acceleration mode	GRAPPA
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System - Miscellaneous

Coil Selection	Auto Coil Select
MSMA	S - C - T
Sagittal	R >> L
Coronal	A >> P

System - Miscellaneous

Transversal	F >> H
Coil Combination	Adaptive Combine
Matrix Optimization	Off
Coil Focus	Flat

System - Adjustments

Adjustment Strategy	Standard
B0 Shim	Standard
B1 Shim	TrueForm
CoilShim	Off
Adjustment Tolerance	Auto
Adjust with Body Coil	Off
Confirm Frequency	Never
Assume Silicone	Off

System - Adjust Volume

Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Rotation	90.00 deg
F >> H	140 mm
A >> P	140 mm
R >> L	71 mm
Reset	Off

System - pTx

B1 Shim	TrueForm
LR Balancing	Off

System - Tx/Rx

Frequency 1H	123.243725 MHz
? Ref. Amplitude 1H	0.000 V
Reset	Off
Image Scaling	1.000

Physio - Signal

1st Signal/Mode	None
TR	3030.0 ms
Concatenations	1

Physio - Cardiac

Fat-Water Contrast	Fat Saturation
Magn. Preparation	None
Dark Blood	Off
FoV Read	140 mm
FoV Phase	100.0 %
Phase Resolution	75 %
Trajectory	Cartesian
Dynamic Mode	Standard

Physio - PACE

Resp. Control	Off
Concatenations	1

Inline - Subtraction

Subtract	Off
Measurements	1
StdDev	Off
Save Original Images	On

Inline - Cardiac

Magn. Preparation	None
Save Original Images	On
Contrasts	1

Inline - Cardiac

TE	50.00 ms
TR	3030.0 ms

Inline - MIP

MIP Sag	Off
MIP Cor	Off
MIP Tra	Off
MIP Time	Off
Radial MIP	Off
Save Original Images	On
MPR Sag	Off
MPR Cor	Off
MPR Tra	Off

Inline - Composing

Inline Composing	Off
------------------	-----

Sequence - Part 1

Sequence Name	tse
Dimension	2D
RF Pulse Type	Fast
Gradient Mode	Fast
Flow Compensation	None
Bandwidth	240 Hz/Px
Echo Spacing	8.29 ms
Free Echo Spacing	Off
Define	Turbo Factor
Turbo Factor	7
Echo Trains per Slice	35

Sequence - Part 2

Introduction	On
Phase Correction	Automatic
Compensate T2 Decay	Off
Hyperecho	Off
WARP	Off
Red. EC Sensitivity	Off
Acoustic noise reduction	Off
Reduce Motion Sens.	Off

Sequence - Assistant

SAR Assistant	Off
Allowed Delay	20 s

\\USER\SHEEP 12.1.23\Stifle\SRL 2341 VAN ZEELAND STIFLE\SAG T2W *

TA: 6:49 min Coil Selection: Auto Voxel Size: 0.4×0.4×2.0 mm³ Acc.: 2 Rel. SNR: 1.00**Properties**

Start measurement without further preparation	On
Wait for User to Start	Off
Start measurements	Single Measurement
Prio Recon	Off
Auto Open Inline Display	Off
Auto Close Inline Display	Off
Load Images to MR View&GO	On
Auto Store Images	On
Load Images to Stamp Segments	On
Load Images to Graphic Segments	On
Graphic segment	1st Segment
Inline Movie	Off

Resolution - Acceleration

Reference Scans	Self-calibration
Acceleration Factor PE	2
Reference Lines PE	32
Advanced Reconstruction	Off
Phase Partial Fourier	Off

Resolution - Filter

Raw Filter	Off
Elliptical Filter	On
Distortion Correction	2D
Normalize	Prescan
Image Filter	Off

Routine

Slice Group	1
Slices	32
Distance Factor	10 %
Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Phase Encoding Dir.	H >> F
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	2950.0 ms
TE	99.00 ms
Averages	3
Concatenations	3
AutoAlign	---

Geometry - Common

Slice Group	1
Slices	32
Distance Factor	10 %
Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Phase Encoding Dir.	H >> F
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	2950.0 ms
Multi-Slice Mode	Interleaved
Series	Interleaved
Concatenations	3

Contrast - Common

TR	2950.0 ms
TE	99.00 ms
TD	0.00 ms
MTC	Off
Magn. Preparation	None
Flip Angle	150 deg
Fat-Water Contrast	Standard
Dark Blood	Off
Contrasts	1
Wrap-up Magn.	None
Reconstruction	Magnitude

Geometry - AutoAlign

Slice Group	1
Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Phase Encoding Dir.	H >> F
AutoAlign	---
Initial Position	R70.9 P31.3 H77.9
R	70.9 mm
P	31.3 mm
H	77.9 mm
Initial Orientation	S > T
S > T	-3.00
> C	0.00
Initial Rotation	90.00 deg

Contrast - Dynamic

Dynamic Mode	Standard
Measurements	1
Multiple Series	Each Measurement

Geometry - Navigator**Geometry - Saturation**

Special Saturation	None
--------------------	------

Resolution - Common

FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
Base Resolution	320
Phase Resolution	75 %
Trajectory	Cartesian
Interpolation	Off

Geometry - Tim Planning Suite

Set-n-Go Protocol	Off
Table Position	78 mm
Table Position	H
Inline Composing	Off

Resolution - Acceleration

Acceleration mode	GRAPPA
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System - Miscellaneous

Coil Selection	Auto Coil Select
MSMA	S - C - T
Sagittal	R >> L
Coronal	A >> P

System - Miscellaneous

Transversal	F >> H
Coil Combination	Adaptive Combine
Matrix Optimization	Off
Coil Focus	Flat

System - Adjustments

Adjustment Strategy	Standard
B0 Shim	Standard
B1 Shim	TrueForm
CoilShim	Off
Adjustment Tolerance	Auto
Adjust with Body Coil	Off
Confirm Frequency	Never
Assume Silicone	Off

System - Adjust Volume

Position	R70.9 P31.3 H77.9 mm
Orientation	S > T-3.0
Rotation	90.00 deg
F >> H	140 mm
A >> P	140 mm
R >> L	71 mm
Reset	Off

System - pTx

B1 Shim	TrueForm
LR Balancing	Off

System - Tx/Rx

Frequency 1H	123.243725 MHz
? Ref. Amplitude 1H	0.000 V
Reset	Off
Image Scaling	1.000

Physio - Signal

1st Signal/Mode	None
TR	2950.0 ms
Concatenations	3

Physio - Cardiac

Fat-Water Contrast	Standard
Magn. Preparation	None
Dark Blood	Off
FoV Read	140 mm
FoV Phase	100.0 %
Phase Resolution	75 %
Trajectory	Cartesian
Dynamic Mode	Standard

Physio - PACE

Resp. Control	Off
Concatenations	3

Inline - Subtraction

Subtract	Off
Measurements	1
StdDev	Off
Save Original Images	On

Inline - Cardiac

Magn. Preparation	None
Save Original Images	On
Contrasts	1

Inline - Cardiac

TE	99.00 ms
TR	2950.0 ms

Inline - MIP

MIP Sag	Off
MIP Cor	Off
MIP Tra	Off
MIP Time	Off
Radial MIP	Off
Save Original Images	On
MPR Sag	Off
MPR Cor	Off
MPR Tra	Off

Inline - Composing

Inline Composing	Off
------------------	-----

Sequence - Part 1

Sequence Name	tse
Dimension	2D
RF Pulse Type	Fast
Gradient Mode	Fast
Flow Compensation	None
Bandwidth	240 Hz/Px
Echo Spacing	8.29 ms
Free Echo Spacing	Off
Define	Turbo Factor
Turbo Factor	17
Echo Trains per Slice	15

Sequence - Part 2

Introduction	On
Phase Correction	Automatic
Compensate T2 Decay	Off
Hyperecho	Off
WARP	Off
Red. EC Sensitivity	Off
Acoustic noise reduction	Off
Reduce Motion Sens.	Off

Sequence - Assistant

SAR Assistant	Off
Allowed Delay	20 s

\\USER\SHEEP 12.1.23\Stifle\SRL 2341 VAN ZEELAND STIFLE\DORSAL PDFS *

TA: 6:03 min Coil Selection: Auto Voxel Size: 0.4×0.4×2.0 mm³ Acc.: 2 Rel. SNR: 1.00**Properties**

Start measurement without further preparation	On
Wait for User to Start	Off
Start measurements	Single Measurement
Prio Recon	Off
Auto Open Inline Display	Off
Auto Close Inline Display	Off
Load Images to MR View&GO	On
Auto Store Images	On
Load Images to Stamp Segments	On
Load Images to Graphic Segments	On
Graphic segment	1st Segment
Inline Movie	Off

Resolution - Acceleration

Reference Scans	Self-calibration
Acceleration Factor PE	2
Reference Lines PE	32
Advanced Reconstruction	Off
Phase Partial Fourier	Off

Resolution - Filter

Raw Filter	Off
Elliptical Filter	On
Distortion Correction	2D
Normalize	Prescan
Image Filter	Off

Routine

Slice Group	1
Slices	40
Distance Factor	10 %
Position	R74.1 P21.0 H75.7 mm
Orientation	C > T14.9 > S-4.1
Phase Encoding Dir.	R >> L
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	5020.0 ms
TE	50.00 ms
Averages	2
Concatenations	1
AutoAlign	---

Geometry - Common

Slice Group	1
Slices	40
Distance Factor	10 %
Position	R74.1 P21.0 H75.7 mm
Orientation	C > T14.9 > S-4.1
Phase Encoding Dir.	R >> L
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	5020.0 ms
Multi-Slice Mode	Interleaved
Series	Interleaved
Concatenations	1

Contrast - Common

TR	5020.0 ms
TE	50.00 ms
MTC	Off
Magn. Preparation	None
Flip Angle	150 deg
Fat-Water Contrast	Fat Saturation
Fat Saturation	Strong
Dark Blood	Off
Contrasts	1
Wrap-up Magn.	None
Reconstruction	Magnitude

Geometry - AutoAlign

Slice Group	1
Position	R74.1 P21.0 H75.7 mm
Orientation	C > T14.9 > S-4.1
Phase Encoding Dir.	R >> L
AutoAlign	---
Initial Position	R74.1 P21.0 H75.7
R	74.1 mm
P	21.0 mm
H	75.7 mm
Initial Orientation	C > T
C > T	14.90
> S	-4.10
Initial Rotation	0.00 deg

Contrast - Dynamic

Dynamic Mode	Standard
Measurements	1
Multiple Series	Each Measurement

Geometry - Navigator**Geometry - Saturation**

Special Saturation	None
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Resolution - Common

FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
Base Resolution	320
Phase Resolution	75 %
Trajectory	Cartesian
Interpolation	Off

Geometry - Tim Planning Suite

Set-n-Go Protocol	Off
Table Position	76 mm
Table Position	H
Inline Composing	Off

Resolution - Acceleration

Acceleration mode	GRAPPA
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System - Miscellaneous

Coil Selection	Auto Coil Select
MSMA	S - C - T
Sagittal	R >> L
Coronal	A >> P

System - Miscellaneous

Transversal	F >> H
Coil Combination	Adaptive Combine
Matrix Optimization	Off
Coil Focus	Flat

System - Adjustments

Adjustment Strategy	Standard
B0 Shim	Standard
B1 Shim	TrueForm
CoilShim	Off
Adjustment Tolerance	Auto
Adjust with Body Coil	Off
Confirm Frequency	Never
Assume Silicone	Off

System - Adjust Volume

Position	R74.1 P21.0 H75.7 mm
Orientation	C > T14.9 > S-4.1
Rotation	0.00 deg
R >> L	140 mm
F >> H	140 mm
A >> P	88 mm
Reset	Off

System - pTx

B1 Shim	TrueForm
LR Balancing	Off

System - Tx/Rx

Frequency 1H	123.243725 MHz
? Ref. Amplitude 1H	0.000 V
Reset	Off
Image Scaling	1.000

Physio - Signal

1st Signal/Mode	None
TR	5020.0 ms
Concatenations	1

Physio - Cardiac

Fat-Water Contrast	Fat Saturation
Magn. Preparation	None
Dark Blood	Off
FoV Read	140 mm
FoV Phase	100.0 %
Phase Resolution	75 %
Trajectory	Cartesian
Dynamic Mode	Standard

Physio - PACE

Resp. Control	Off
Concatenations	1

Inline - Subtraction

Subtract	Off
Measurements	1
StdDev	Off
Save Original Images	On

Inline - Cardiac

Magn. Preparation	None
Save Original Images	On
Contrasts	1

Inline - Cardiac

TE	50.00 ms
TR	5020.0 ms

Inline - MIP

MIP Sag	Off
MIP Cor	Off
MIP Tra	Off
MIP Time	Off
Radial MIP	Off
Save Original Images	On
MPR Sag	Off
MPR Cor	Off
MPR Tra	Off

Inline - Composing

Inline Composing	Off
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Sequence - Part 1

Sequence Name	tse
Dimension	2D
RF Pulse Type	Fast
Gradient Mode	Fast
Flow Compensation	None
Bandwidth	240 Hz/Px
Echo Spacing	8.29 ms
Free Echo Spacing	Off
Define	Turbo Factor
Turbo Factor	7
Echo Trains per Slice	35

Sequence - Part 2

Introduction	On
Phase Correction	Automatic
Compensate T2 Decay	Off
Hyperecho	Off
WARP	Off
Red. EC Sensitivity	Off
Acoustic noise reduction	Off
Reduce Motion Sens.	Off

Sequence - Assistant

SAR Assistant	Off
Allowed Delay	20 s

\\USER\SHEEP 12.1.23\Stifle\SRL 2341 VAN ZEELAND STIFLE\DORSAL T2W *

TA: 8:20 min Coil Selection: Auto Voxel Size: 0.4×0.4×2.0 mm³ Acc:: 2 Rel. SNR: 1.00**Properties**

Start measurement without further preparation	On
Wait for User to Start	Off
Start measurements	Single Measurement
Prio Recon	Off
Auto Open Inline Display	Off
Auto Close Inline Display	Off
Load Images to MR View&GO	On
Auto Store Images	On
Load Images to Stamp Segments	On
Load Images to Graphic Segments	On
Graphic segment	1st Segment
Inline Movie	Off

Resolution - Acceleration

Reference Scans	Self-calibration
Acceleration Factor PE	2
Reference Lines PE	32
Advanced Reconstruction	Off
Phase Partial Fourier	Off

Resolution - Filter

Raw Filter	Off
Elliptical Filter	On
Distortion Correction	2D
Normalize	Prescan
Image Filter	Off

Routine

Slice Group	1
Slices	40
Distance Factor	10 %
Position	R74.1 P21.0 H75.7 mm
Orientation	C > T14.9 > S-4.1
Phase Encoding Dir.	R >> L
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	5800.0 ms
TE	99.00 ms
Averages	3
Concatenations	2
AutoAlign	---

Geometry - Common

Slice Group	1
Slices	40
Distance Factor	10 %
Position	R74.1 P21.0 H75.7 mm
Orientation	C > T14.9 > S-4.1
Phase Encoding Dir.	R >> L
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	5800.0 ms
Multi-Slice Mode	Interleaved
Series	Interleaved
Concatenations	2

Contrast - Common

TR	5800.0 ms
TE	99.00 ms
TD	0.00 ms
MTC	Off
Magn. Preparation	None
Flip Angle	150 deg
Fat-Water Contrast	Standard
Dark Blood	Off
Contrasts	1
Wrap-up Magn.	None
Reconstruction	Magnitude

Geometry - AutoAlign

Slice Group	1
Position	R74.1 P21.0 H75.7 mm
Orientation	C > T14.9 > S-4.1
Phase Encoding Dir.	R >> L
AutoAlign	---
Initial Position	R74.1 P21.0 H75.7
R	74.1 mm
P	21.0 mm
H	75.7 mm
Initial Orientation	C > T
C > T	14.90
> S	-4.10
Initial Rotation	0.00 deg

Contrast - Dynamic

Dynamic Mode	Standard
Measurements	1
Multiple Series	Each Measurement

Geometry - Navigator**Geometry - Saturation**

Special Saturation	None
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Resolution - Common

FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
Base Resolution	320
Phase Resolution	75 %
Trajectory	Cartesian
Interpolation	Off

Geometry - Tim Planning Suite

Set-n-Go Protocol	Off
Table Position	76 mm
Table Position	H
Inline Composing	Off

Resolution - Acceleration

Acceleration mode	GRAPPA
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System - Miscellaneous

Coil Selection	Auto Coil Select
MSMA	S - C - T
Sagittal	R >> L
Coronal	A >> P

System - Miscellaneous

Transversal	F >> H
Coil Combination	Adaptive Combine
Matrix Optimization	Off
Coil Focus	Flat

System - Adjustments

Adjustment Strategy	Standard
B0 Shim	Standard
B1 Shim	TrueForm
CoilShim	Off
Adjustment Tolerance	Auto
Adjust with Body Coil	Off
Confirm Frequency	Never
Assume Silicone	Off

System - Adjust Volume

Position	R74.1 P21.0 H75.7 mm
Orientation	C > T14.9 > S-4.1
Rotation	0.00 deg
R >> L	140 mm
F >> H	140 mm
A >> P	88 mm
Reset	Off

System - pTx

B1 Shim	TrueForm
LR Balancing	Off

System - Tx/Rx

Frequency 1H	123.243725 MHz
? Ref. Amplitude 1H	0.000 V
Reset	Off
Image Scaling	1.000

Physio - Signal

1st Signal/Mode	None
TR	5800.0 ms
Concatenations	2

Physio - Cardiac

Fat-Water Contrast	Standard
Magn. Preparation	None
Dark Blood	Off
FoV Read	140 mm
FoV Phase	100.0 %
Phase Resolution	75 %
Trajectory	Cartesian
Dynamic Mode	Standard

Physio - PACE

Resp. Control	Off
Concatenations	2

Inline - Subtraction

Subtract	Off
Measurements	1
StdDev	Off
Save Original Images	On

Inline - Cardiac

Magn. Preparation	None
Save Original Images	On
Contrasts	1

Inline - Cardiac

TE	99.00 ms
TR	5800.0 ms

Inline - MIP

MIP Sag	Off
MIP Cor	Off
MIP Tra	Off
MIP Time	Off
Radial MIP	Off
Save Original Images	On
MPR Sag	Off
MPR Cor	Off
MPR Tra	Off

Inline - Composing

Inline Composing	Off
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Sequence - Part 1

Sequence Name	tse
Dimension	2D
RF Pulse Type	Fast
Gradient Mode	Fast
Flow Compensation	None
Bandwidth	240 Hz/Px
Echo Spacing	8.29 ms
Free Echo Spacing	Off
Define	Turbo Factor
Turbo Factor	18
Echo Trains per Slice	14

Sequence - Part 2

Introduction	On
Phase Correction	Automatic
Compensate T2 Decay	Off
Hyperecho	Off
WARP	Off
Red. EC Sensitivity	Off
Acoustic noise reduction	Off
Reduce Motion Sens.	Off

Sequence - Assistant

SAR Assistant	Off
Allowed Delay	20 s

\\USER\SHEEP 12.1.23\Stifle\SRL 2341 VAN ZEELAND STIFLE\TRANS T2W *

TA: 8:20 min Coil Selection: Auto Voxel Size: 0.4×0.4×2.0 mm³ Acc.: 2 Rel. SNR: 1.00**Properties**

Start measurement without further preparation	On
Wait for User to Start	Off
Start measurements	Single Measurement
Prio Recon	Off
Auto Open Inline Display	Off
Auto Close Inline Display	Off
Load Images to MR View&GO	On
Auto Store Images	On
Load Images to Stamp Segments	On
Load Images to Graphic Segments	On
Graphic segment	1st Segment
Inline Movie	Off

Resolution - Acceleration

Reference Scans	Self-calibration
Acceleration Factor PE	2
Reference Lines PE	32
Advanced Reconstruction	Off
Phase Partial Fourier	Off

Resolution - Filter

Raw Filter	Off
Elliptical Filter	On
Distortion Correction	2D
Normalize	Prescan
Image Filter	Off

Routine

Slice Group	1
Slices	40
Distance Factor	10 %
Position	R61.4 P22.4 H74.1 mm
Orientation	T > C-15.3 > S2.9
Phase Encoding Dir.	A >> P
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	5800.0 ms
TE	99.00 ms
Averages	3
Concatenations	2
AutoAlign	---

Geometry - Common

Slice Group	1
Slices	40
Distance Factor	10 %
Position	R61.4 P22.4 H74.1 mm
Orientation	T > C-15.3 > S2.9
Phase Encoding Dir.	A >> P
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	5800.0 ms
Multi-Slice Mode	Interleaved
Series	Interleaved
Concatenations	2

Contrast - Common

TR	5800.0 ms
TE	99.00 ms
TD	0.00 ms
MTC	Off
Magn. Preparation	None
Flip Angle	150 deg
Fat-Water Contrast	Standard
Dark Blood	Off
Contrasts	1
Wrap-up Magn.	None
Reconstruction	Magnitude

Geometry - AutoAlign

Slice Group	1
Position	R61.4 P22.4 H74.1 mm
Orientation	T > C-15.3 > S2.9
Phase Encoding Dir.	A >> P
AutoAlign	---
Initial Position	R61.4 P22.4 H74.1
R	61.4 mm
P	22.4 mm
H	74.1 mm
Initial Orientation	T > C
T > C	-15.30
> S	2.90
Initial Rotation	0.00 deg

Contrast - Dynamic

Dynamic Mode	Standard
Measurements	1
Multiple Series	Each Measurement

Geometry - Navigator**Geometry - Saturation**

Special Saturation	None
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Resolution - Common

FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
Base Resolution	320
Phase Resolution	75 %
Trajectory	Cartesian
Interpolation	Off

Geometry - Tim Planning Suite

Set-n-Go Protocol	Off
Table Position	74 mm
Table Position	H
Inline Composing	Off

Resolution - Acceleration

Acceleration mode	GRAPPA
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System - Miscellaneous

Coil Selection	Auto Coil Select
MSMA	S - C - T
Sagittal	R >> L
Coronal	A >> P

System - Miscellaneous

Transversal	F >> H
Coil Combination	Adaptive Combine
Matrix Optimization	Off
Coil Focus	Flat

System - Adjustments

Adjustment Strategy	Standard
B0 Shim	Standard
B1 Shim	TrueForm
CoilShim	Off
Adjustment Tolerance	Auto
Adjust with Body Coil	Off
Confirm Frequency	Never
Assume Silicone	Off

System - Adjust Volume

Position	R61.4 P22.4 H74.1 mm
Orientation	T > C-15.3 > S2.9
Rotation	0.00 deg
A >> P	140 mm
R >> L	140 mm
F >> H	88 mm
Reset	Off

System - pTx

B1 Shim	TrueForm
LR Balancing	Off

System - Tx/Rx

Frequency 1H	123.243725 MHz
? Ref. Amplitude 1H	0.000 V
Reset	Off
Image Scaling	1.000

Physio - Signal

1st Signal/Mode	None
TR	5800.0 ms
Concatenations	2

Physio - Cardiac

Fat-Water Contrast	Standard
Magn. Preparation	None
Dark Blood	Off
FoV Read	140 mm
FoV Phase	100.0 %
Phase Resolution	75 %
Trajectory	Cartesian
Dynamic Mode	Standard

Physio - PACE

Resp. Control	Off
Concatenations	2

Inline - Subtraction

Subtract	Off
Measurements	1
StdDev	Off
Save Original Images	On

Inline - Cardiac

Magn. Preparation	None
Save Original Images	On
Contrasts	1

Inline - Cardiac

TE	99.00 ms
TR	5800.0 ms

Inline - MIP

MIP Sag	Off
MIP Cor	Off
MIP Tra	Off
MIP Time	Off
Radial MIP	Off
Save Original Images	On
MPR Sag	Off
MPR Cor	Off
MPR Tra	Off

Inline - Composing

Inline Composing	Off
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Sequence - Part 1

Sequence Name	tse
Dimension	2D
RF Pulse Type	Fast
Gradient Mode	Fast
Flow Compensation	None
Bandwidth	240 Hz/Px
Echo Spacing	8.29 ms
Free Echo Spacing	Off
Define	Turbo Factor
Turbo Factor	18
Echo Trains per Slice	14

Sequence - Part 2

Introduction	On
Phase Correction	Automatic
Compensate T2 Decay	Off
Hyperecho	Off
WARP	Off
Red. EC Sensitivity	Off
Acoustic noise reduction	Off
Reduce Motion Sens.	Off

Sequence - Assistant

SAR Assistant	Off
Allowed Delay	20 s

\\USER\SHEEP 12.1.23\Stifle\SRL 2341 VAN ZEELAND STIFLE\TRANS T2W LOWER DISTALLY *

TA: 5:38 min Coil Selection: Auto Voxel Size: 0.4×0.4×2.0 mm³ Acc.: 2 Rel. SNR: 1.00**Properties**

Start measurement without further preparation	On
Wait for User to Start	Off
Start measurements	Single Measurement
Prio Recon	Off
Auto Open Inline Display	Off
Auto Close Inline Display	Off
Load Images to MR View&GO	On
Auto Store Images	On
Load Images to Stamp Segments	On
Load Images to Graphic Segments	On
Graphic segment	1st Segment
Inline Movie	Off

Resolution - Acceleration

Reference Scans	Self-calibration
Acceleration Factor PE	2
Reference Lines PE	32
Advanced Reconstruction	Off
Phase Partial Fourier	Off

Resolution - Filter

Raw Filter	Off
Elliptical Filter	On
Distortion Correction	2D
Normalize	Prescan
Image Filter	Off

Routine

Slice Group	1
Slices	40
Distance Factor	10 %
Position	R59.5 P13.4 H38.4 mm
Orientation	T > C-15.3 > S2.9
Phase Encoding Dir.	A >> P
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	5800.0 ms
TE	99.00 ms
Averages	2
Concatenations	2
AutoAlign	---

Geometry - Common

Slice Group	1
Slices	40
Distance Factor	10 %
Position	R59.5 P13.4 H38.4 mm
Orientation	T > C-15.3 > S2.9
Phase Encoding Dir.	A >> P
Phase Oversampling	100 %
FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
TR	5800.0 ms
Multi-Slice Mode	Interleaved
Series	Interleaved
Concatenations	2

Contrast - Common

TR	5800.0 ms
TE	99.00 ms
TD	0.00 ms
MTC	Off
Magn. Preparation	None
Flip Angle	150 deg
Fat-Water Contrast	Standard
Dark Blood	Off
Contrasts	1
Wrap-up Magn.	None
Reconstruction	Magnitude

Geometry - AutoAlign

Slice Group	1
Position	R59.5 P13.4 H38.4 mm
Orientation	T > C-15.3 > S2.9
Phase Encoding Dir.	A >> P
AutoAlign	---
Initial Position	R59.5 P13.4 H38.4
R	59.5 mm
P	13.4 mm
H	38.4 mm
Initial Orientation	T > C
T > C	-15.30
> S	2.90
Initial Rotation	0.00 deg

Contrast - Dynamic

Dynamic Mode	Standard
Measurements	1
Multiple Series	Each Measurement

Geometry - Navigator**Geometry - Saturation**

Special Saturation	None
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Resolution - Common

FoV Read	140 mm
FoV Phase	100.0 %
Slice Thickness	2.0 mm
Base Resolution	320
Phase Resolution	75 %
Trajectory	Cartesian
Interpolation	Off

Geometry - Tim Planning Suite

Set-n-Go Protocol	Off
Table Position	38 mm
Table Position	H
Inline Composing	Off

Resolution - Acceleration

Acceleration mode	GRAPPA
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System - Miscellaneous

Coil Selection	Auto Coil Select
MSMA	S - C - T
Sagittal	R >> L
Coronal	A >> P

System - Miscellaneous

Transversal	F >> H
Coil Combination	Adaptive Combine
Matrix Optimization	Off
Coil Focus	Flat

System - Adjustments

Adjustment Strategy	Standard
B0 Shim	Standard
B1 Shim	TrueForm
CoilShim	Off
Adjustment Tolerance	Auto
Adjust with Body Coil	Off
Confirm Frequency	Never
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Physio - Cardiac

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Magn. Preparation	None
Dark Blood	Off
FoV Read	140 mm
FoV Phase	100.0 %
Phase Resolution	75 %
Trajectory	Cartesian
Dynamic Mode	Standard

Physio - PACE

Resp. Control	Off
Concatenations	2

Inline - Subtraction

Subtract	Off
Measurements	1
StdDev	Off
Save Original Images	On

Inline - Cardiac

Magn. Preparation	None
Save Original Images	On
Contrasts	1

Inline - Cardiac

TE	99.00 ms
TR	5800.0 ms

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MIP Cor	Off
MIP Tra	Off
MIP Time	Off
Radial MIP	Off
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MPR Cor	Off
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Inline - Composing

Inline Composing	Off
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