Engineering a UV Illumination Device for Decentralized Autologous Cancer Immunotherapy

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Table of Contents

Abstract *3*

Introduction *4*

Background and Literature Integration *4*

Scientific Basis of UV and Riboflavin Inactivation 4

Need for Decentralized Engineering Solutions 5

Verification Strategies for UV-Based Systems 5

Material Constraints Under UV Exposure 6

Summary 7

Design Project Description *7*

Individual Contributions *7*

Proposed Validation Testing and Expected Outcomes *8*

Burst Testing for Seal Integrity 8

Sterility Testing 9

Computational Fluid Dynamics (CFD) Analysis 9

Summary of Validation Approach 10

Lessons Learned *10*

Technical Skills Development 10

Engineering Process and Design Iteration 11

Professional and Personal Growth 11

Connection to Future Career Goals 11

Broader Context *12*

Conclusion *12*

References *13*

Abstract

Autologous cancer immunotherapy offers a promising approach to treatment by utilizing a patient's own tumor cells to stimulate an immune response; however, current implementations rely on cleanroom dependent transfer steps that limit accessibility and scalability. The Innocell process, developed by PhotonPharma, employs riboflavin and ultraviolet (UV) light to inactivate tumor cells while preserving their antigenic structure for personalized therapeutic use.

This senior design project focused on the design and development of a benchtop UV illumination device incorporating a closed, single-use containment system to enable tumor cell inactivation within a sealed environment and eliminate open aseptic handling. Ultimately, the device will incorporate all steps of the Innocell process, including tissue dissociation, UV illumination, and final dose aliquoting. The system currently integrates controlled UV exposure and agitation while minimizing operator interaction to a single operational step, addressing risks associated with manual processing and contamination.

The engineering approach emphasized iterative prototyping of containment systems, evaluation of material compatibility under UV exposure, and development of standard operating procedures (SOPs) for device operation, cell culturing, and analytical assays. A primary design challenge was achieving consistent and reliable sealing of the containment system, which limited the ability to produce a fully functional prototype and prevented completion of experimental validation.

Despite this limitation, a comprehensive validation framework was established, including proposed burst testing for seal integrity, sterilization validation using biological indicators to confirm autoclave effectiveness, and computational fluid dynamics (CFD) analysis to assess mixing behavior and uniformity of UV exposure. These strategies were designed to quantify mechanical performance, sterility assurance, and treatment consistency within the system.

Overall, this work demonstrates both the feasibility and key engineering challenges associated with developing a closed-system, decentralized immunotherapy device, highlighting the critical roles of manufacturability, material behavior, and seal reliability in advancing accessible autologous cancer treatment technologies.

Introduction

Autologous cancer immunotherapy represents a rapidly developing area of oncology that leverages a patient's own tumor cells to generate a targeted immune response. Despite its potential, current implementations are constrained by reliance on cleanroom environments, which increases cost, complexity, and limits accessibility. These requirements create barriers to adoption in hospital laboratory settings where rapid, patient-specific treatment is needed.

The Innocell process utilizes riboflavin and ultraviolet (UV) light to inactivate tumor cells while preserving antigenic structures necessary for immune activation. In this senior design project, a benchtop UV illumination device was developed to integrate a closed, single-use containment system capable of eliminating cleanroom-dependent transfer steps. My contributions focused on standard operating procedures (SOPs) development, experimental preparation, validation of containment system, and design iteration of the containment system.

To inform the design of this system, relevant literature on UV-based inactivation, validation methods, and material constraints were analyzed.

Background and Literature Integration

Scientific Basis of UV and Riboflavin Inactivation

Riboflavin and UV light-based inactivation relies on photochemical reactions that damage nucleic acids, preventing cellular replication while preserving surface antigens necessary for immune recognition. This mechanism is critical for autologous cancer immunotherapy, as it allows tumor cells to retain their antigenic profile while eliminating their ability to proliferate.

Preclinical evidence supporting this mechanism is demonstrated in murine tumor model study, where riboflavin and UV (RF+UV) treated tumor cells showed complete loss of proliferative capacity while maintaining antigen integrity and enhancing immune activation [1]. In this study, treated tumor cells reduced metastasis and improved survival outcomes compared to untreated controls, indicating that antigen preservation plays a key role in eliciting an immune response.

Further support is provided by a canine safety study, which evaluated the Innocell process in dogs with naturally occurring tumors [2]. This study reported minimal adverse effects, including only mildly transient symptoms such as fever and lethargy, while also showing measurable immune-related cytokine responses. The use of a large animal model with spontaneous tumors strengthens the translational relevance of this approach.

Together, these studies demonstrate both the biological effectiveness and safety of RF+UV inactivation, establishing a strong foundation for its implementation in a clinical device.

Need for Decentralized Engineering Solutions

Despite promising results in both preclinical and translational models, current implementations of autologous immunotherapy remain limited by process complexity and infrastructure requirements. A process and workflow analysis study describing autologous cancer therapies highlights that existing systems often rely on centralized manufacturing environments, specialized equipment, and highly trained personnel [3].

These requirements introduce significant barriers to scalability, particularly in hospital settings where rapid, patient-specific treatment is needed. The reliance on cleanroom environments further increases cost and operational complexity.

This limitation directly informed the primary engineering objective of this project: to develop a closed, single-use containment system capable of eliminating cleanroom-dependent steps. By enabling decentralized operation in standard laboratory environments, the device addresses a key gap identified in the literature.

A large-scale clinical implementation of RF+UV pathogen reduction technology was demonstrated in the African Investigation of Mirasol System (AIMS), a randomized controlled trial evaluating prevention of transfusion-transmitted malaria in endemic regions [4]. In this study, RF+UV treatment was applied to whole blood products to reduce transmission of Plasmodium species during transfusion. The trial demonstrated that the Mirasol system could be successfully implemented in resource-limited healthcare environments while maintaining operational feasibility and biological effectiveness.

The significance of the study extends beyond pathogen reduction alone, as it demonstrated the practicality of RF+UV technologies in decentralized clinical settings outside highly specialized manufacturing facilities. This directly supports the engineering motivation of the current project, which aims to reduce reliance on centralized cleanroom infrastructure by developing a closed-system device capable of operation within hospital laboratory environments.

Verification Strategies for UV-Based Systems

Verification of RF+UV systems requires a quantitative assessment of biological activity and sterility. A controlled experimental study on platelet products demonstrated that RF+UV treatment achieved greater than 4-6 log reduction in bacterial contamination across both Gram-positive and Gram-negative species utilizing the Mirasol Pathogen Reduction Technology (PRT) [5]. This study provides rigorous benchmark for inactivation effectiveness detailed methodologies for UV exposure and validation protocols.

These verification strategies informed experimental design for this project, particularly in the selection of proliferation assays such as EdU incorporation and cytotoxicity assays such as Lactate Dehydrogenase (LDH) release to evaluate HeLa cell inactivation.

A comprehensive review of RF+UV pathogen reduction technology evaluated the application of the Mirasol PRT system across platelets, plasma, and whole blood products [6]. The review describes the underlying photochemical mechanism in which riboflavin interacts with nucleic acids under UV illumination, resulting in irreversible damage that prevents replication of pathogens and leukocytes while minimizing damage to functional blood components. Importantly, the study highlights that riboflavin, and its photoproducts are naturally occurring and non-toxic, eliminating the need for compound removal following treatment.

The review also summarizes the broad-spectrum effectiveness of RF+UV treatment against viruses, bacteria, parasites, and white blood cells across multiple blood products, demonstrating the versatility and scalability of the technology [6]. In addition, to biological effectiveness, the authors discuss engineering considerations associated with UV exposure, including illumination geometry, UV penetration, treatment consistency, and preservation of component functionality. These considerations directly relate to the design challenges addressed in the current project, particularly the need to achieve uniform UV exposure and reliable fluid mixing within a closed containment system.

Furthermore, the review supports the feasibility of adapting RF+UV technologies into integrated closed-system platforms for broader clinical implementation. This aligns closely with the engineering objective of the current project, which seeks to develop a decentralized UV illumination device capable of performing tumor cell inactivation within a sealed, single-use environment.

Additional support is provided by a review of in-vitro pathogen reduction technology study on the Mirasol PRT, which demonstrated that riboflavin-based UV systems effectively inactivate viruses, bacteria, and parasites in blood products without compromising cellular function [7]. This work highlights the reliability and safety of RF+UV systems in real-world healthcare applications and supports adaptation for therapeutic device development.

Material Constraints Under UV Exposure

Material compatibility is a critical design consideration for systems exposed to UV radiation. A scoping literature review on UV-C material degradation found that commonly used medical polymers, including polycarbonate and polyethylene, are susceptible to yellowing, embrittlement, and loss of mechanical strength under prolonged UV exposure [8].

These degradation mechanisms present significant risks for containment systems, particularly those requiring both optical clarity for UV transmission and structural integrity for maintaining sterility.

As a result, this project required careful material selection and iterative prototyping to identify material capable of maintaining performance under UV exposure. The findings from this review directly informed testing strategies and design constraints for the containment system [8].

Summary

The literature reviewed spans multiple levels of evidence, including murine tumor studies, canine safety evaluations, controlled laboratory validation studies, in-vitro studies, and clinical pathogen reduction systems. Together, these sources establish the biological mechanism, safety profile, validation of benchmarks, and material constraints associated with RF+UV inactivation.

These insights were directly translated into the engineering design of the UV illumination device, guiding decisions related to system functionality, validation planning, and material selection.

Design Project Description

The Innocell process consists of several key steps: tissue dissociation, UV illumination, and final dose aliquoting. This project focused on improving the UV illumination step through a closed system design.

The UV illumination device was developed as a benchtop system capable of inactivating HeLa cells within a sealed, single-use containment environment. The system integrates controlled UV exposure and mechanical agitation while minimizing user interaction to a single activation step.

HeLa cells were used as they are a cancer cell line that is widely used in biomedical research. Using HeLa cells, a biological material required training in blood pathogens, how to use a biosafety cabinet, hazardous waste disposal and general laboratory training.

The engineering process involved iterative prototyping of containment bags, material selection, and development of SOPs. Although a fully functional sealed system was not achieved, preventing completion of full validation testing, the project established a structured framework for evaluating system performance.

Individual Contributions

My contributions to this project focused on standardization, experimental preparation, and iterative design of the containment system and validation of the containment system. A primary component of my work was the development of SOPs, including protocols for cell culturing, device operation, EdU assays, and LDH assays [9,10,11,12]. These SOPs were designed to ensure repeatability and consistency in both biological testing and device use, aligning with practices commonly used in biopharmaceutical manufacturing. Writing these procedures required translating complex experimental steps into clear, reproducible workflows, reinforcing the importance of documentation in regulated environments.

In addition to documentation, I contributed to laboratory-based work, including performing cell culture and preparing samples for downstream analysis. This experience provided a practical understanding of how biological systems interface with engineered devices, particularly in

maintaining sterile technique and ensuring sample integrity. Working with cell culture also highlighted the sensitivity of biological materials to environmental conditions, reinforcing the need for a closed-system design.

I also played a role in the design and fabrication of the single-use containment bags. This included assisting in the manufacturing process and evaluating the effectiveness of sealing methods. Through post-mortem analysis of failed bag designs, I identified key limitations in the mold and sealing approach, particularly related to inconsistent pressure distribution and incomplete sealing around tubing interfaces [13]. These observations were critical in understanding why a fully functional containment system was not achieved and informed potential design improvements.

Due to the lack of a fully sealed and operational containment system, formal validation experiments including burst testing for seal integrity, sterility testing, and computational fluid dynamics (CFD) analysis were not completed. However, I contributed to the planning and design of these validation approaches. This included defining testing methods for evaluating seal strength, outlining sterility testing strategies to assess contamination risk, and developing CFD modeling concepts to analyze agitation and fluid behavior within the system. These efforts demonstrate an understanding of validation requirements necessary for translating a prototype into a functional biopharmaceutical device.

Overall, my contributions reflect involvement across multiple stages of the engineering process, including documentation, experimental preparation, design iteration, and validation planning. This experience emphasized the interconnected nature of design, testing, and manufacturability in the development of biomedical devices.

Proposed Validation Testing and Expected Outcomes

Due to the lack of a fully functional and sealed containment system, formal validation experiments were not completed. However, validation strategies were developed to assess performance, focusing on seal integrity, sterility assurance, and fluid behavior within the containment system. These testing approaches were designed to align with standard practices in biopharmaceutical device development.

Burst Testing for Seal Integrity

Burst testing was proposed to evaluate the mechanical strength and reliability of the containment system seals. This test would involve pressurizing the sealed bag with fluid at a controlled rate until failure occurs. The pressure at failure, as well as the mode and location of failure, would be recorded.

The expected outcome of burst testing would be that the containment system consistently withstands pressures exceeding its intended operating conditions without leakage or rupture.

Ideally, failure, if it occurs, would be observed in the bulk material rather than at seal interfaces, indicating that the sealing process is stronger than the base material.

This testing would provide critical insight into seal uniformity, material compatibility, and manufacturing consistency. Observations of premature failure at tubing interfaces or along seal lines would indicate areas requiring redesign, such as improved pressure distribution during sealing or modification of mold geometry. Overall, burst testing would inform whether the containment system is capable of maintaining structural integrity during handling, operation, and transport.

Sterility Testing

Sterilization validation was proposed to assess the effectiveness of autoclaving the single-use containment system prior to use. This testing would utilize biological indicators containing heat-resistant bacterial spores to verify that sterilization conditions are sufficient to achieve microbial inactivation.

The proposed method would involve placing biological indicators within the containment system. The assembled system would then be subjected to standard autoclaving conditions (i.e. 121 °C for a defined exposure time). Following sterilization, the biological indicators would be incubated under growth-promoting conditions to determine whether any viable organisms remain.

The expected outcome would be no observable growth from the biological indicators, confirming that the sterilization cycle is effective in achieving the required level of microbial inactivation. Any observed growth would indicate insufficient sterilization, potentially due to incomplete steam penetration, material shielding effects, or inadequate cycle parameters.

This testing would provide critical validation that the containment system can be reliably sterilized prior to use, which is essential for maintaining aseptic conditions during cell processing. Additionally, results would inform design considerations such as material selection, bag geometry, and seal configuration to ensure compatibility with autoclave sterilization and effective steam penetration throughout the system.

Computational Fluid Dynamics (CFD) Analysis

Computational fluid dynamics (CFD) analysis was proposed to evaluate fluid motion and mixing behavior within the containment system during UV illumination. The model would simulate fluid flow under expected operating conditions, including agitation induced by the device.

The primary objective of CFD analysis would be to determine whether uniform mixing is achieved throughout the sample volume. Uniform mixing is critical to ensure consistent exposure of all cells to UV light and riboflavin, directly impacting the effectiveness of inactivation.

Expected results would include identification of flow patterns, velocity distributions, and potential dead zones where fluid motion is limited. The presence of stagnant regions would indicate insufficient mixing, which could lead to uneven UV exposure and incomplete inactivation of cells.

CFD results would inform design modifications such as adjusting agitation speed, modifying bag geometry, or incorporating internal features to promote mixing. Additionally, the analysis would optimize operating parameters to balance effective mixing with minimal mechanical stress on the containment system.

Summary of Validation Approach

Together, these validation methods: burst testing, sterility testing, and CFD analysis, represent a comprehensive approach to evaluating the mechanical, biological, and functional performance of the device. While not completed, the development of these testing strategies demonstrates an understanding of the critical requirements for translating a prototype into a reliable and scalable biopharmaceutical system.

These proposed evaluations also highlight the importance of early-stage design robustness, as limitations in seal integrity prevent progression to full validation. Future work will focus on resolving these design challenges to enable completion of these validation steps.

Lessons Learned

Technical Skills Development

This project provided significant hands-on experience in both biological and mechanical aspects of engineering. I developed practical skills in cell culturing, including aseptic techniques and maintaining viable cell populations for experimental use. Prior to this project, I had limited experience working with live cells, and this work improved my ability to operate in a laboratory environment where contamination control and precision are critical.

I also gained experience using a CNC machine for fabrication of mold components. This included learning how to properly zero tools, align materials in the x,y, and z-planes, and use parallels to ensure consistent positioning within the vice. Understanding these machining fundamentals was essential for producing repeatable parts and highlighted the importance of precision in manufacturing processes.

Additionally, I developed skills in bag manufacturing and material handling. This included evaluating different sealing approaches and understanding how temperature, pressure, and material properties affect bond formation. Working through these challenges provided insight into the complexity of designing single-use systems that must maintain both structural integrity and sterility.

Engineering Process and Design Iteration

One of the most important lessons from this project was the role of iterative design in engineering development. Initial prototypes of the containment system revealed significant challenges related to sealing and material performance, which prevented the creation of a fully functional system. These failures required reevaluation of design assumptions and highlighted the need for early-stage testing focused on manufacturability and reliability.

This experience reinforced the idea that design is not a linear process, but rather a cycle of prototyping, testing, and refinement. It also demonstrated that small issues, such as incomplete seals, can have large downstream impacts by preventing validation and system integration. As a result, I gained a greater appreciation for designing with testing in mind and ensuring that foundational components are robust before advancing to more complex validation steps.

Professional and Personal Growth

Working on this project required collaboration across a multidisciplinary team, combining elements of mechanical design, biological testing, and process development. This experience improved my ability to communicate technical information clearly and work effectively with team members who had different areas of expertise.

I also learned how to adapt to project constraints and unexpected challenges. Th inability to achieve a fully functional containment system required shifting focus from execution to analysis and planning, which helped me develop problem-solving skills and maintain progress despite limitations. This adaptability is critical in real-world engineering environments, where projects often face constraints related to time, resources, and technical feasibility.

Connection to Future Career Goals

This project reinforced my interest in pursuing a career in pharmaceutical manufacturing by demonstrating how engineering decisions directly impact product quality, safety, and accessibility. The emphasis on SOP development, validation planning, and process reliability closely aligns with practices used in regulated biopharmaceutical environments.

Through this experience, I developed a better understanding of how early-stage design decisions influence downstream manufacturing and validation processes. This perspective will be valuable in future roles where ensuring consistency, scalability, and compliance are critical to delivering effective medical products.

Broader Context

The device has the potential to improve access to autologous cancer immunotherapy by eliminating cleanroom-based processing. By enabling use in a hospital laboratory setting, the system reduces infrastructure requirements and training complexity.

Additionally, minimizing user interaction reduces the potential of operator error, supporting consistent and scalable implementation of personalized therapies.

Conclusion

The development of a closed-system UV illumination device demonstrates the potential to decentralize autologous cancer immunotherapy. While challenges in containment design prevented full validation, the project established a strong foundation for future development.

Future work will focus on improving seal integrity, completing validation testing, and integrating additional process steps into a fully functional system.

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