Thesis Project Portfolio

Development of a Robotic Lewis Rat Ankle & Foot for Advanced Testing and Evaluation of Regenerative Treatment Solutions

(Technical Report)

Innovative Impact of Regulatory Challenges Faced When Transitioning from Animal Testing to Human Clinical Trials

(STS Research Paper)

An Undergraduate Thesis

Presented to the Faculty of the School of Engineering and Applied Science

University of Virginia • Charlottesville, Virginia

In Fulfillment of the Requirements for the Degree

Bachelor of Science, School of Engineering

Maximus A. Cresti

Spring, 2025

Department of Biomedical Engineering

Table of Contents

Executive Summary

Today, the development of a single new drug is estimated to cost $2.6 billion and takes, on average, 10-15 years before reaching the market. To begin treating patients, these drugs must undergo rigorous preclinical and clinical trials, which traditionally succeed animal testing. My capstone project addresses this issue by developing a robotic rat hindlimb model that mimics the Lewis Rat walking motion. By replicating the walking motion, researchers will be able to assess how Volumetric Muscle Loss (VML) affects the normal walking motion of rats, and eventually, translate this work to human studies aimed at developing treatments for VML. My STS paper explores the ethical implications of animal testing and how it can be replaced with alternative, more effective, and ethical validation methods. It investigates various sources, including case studies that argue against the use of animal testing for new drug development. The model we are developing in our capstone project will reduce the need for animal testing in VML treatment development by allowing new methods to replicate VML alternative to rat testing. If successful, this model will offer scientists a promising advantage over animal testing commonly used in labs to not only perform similar experiments but also expand the capabilities of VML research.

Volumetric muscle loss (VML) refers to the irreversible damage to a significant portion of muscle tissue, usually resulting from significant trauma, surgical removal, or serious battlefield injury. Unlike smaller scale muscle injuries, VML surpasses the body's physiological capability to heal, leaving patients with substantial structural and functional damage including loss of strength, range of motion, and overall endurance. Current therapies primarily include muscle grafts, either autografts or allografts, where muscle tissue from another portion of the body or a donor is transplanted to fill the injured region. The intense nature of these procedures, however, lead to significant limitations in their efficacy such as donor site morbidity, immune

rejection, and failure to restore fully integrated muscle tissue that recovers functionality. Recent research around regenerative medicine, such as delivery of stem cell therapy, growth factors, and biomaterial scaffolds, has focused on addressing these shortcomings.

Throughout the development process, we developed and improved numerous parts of the model to create a fully actuated model that is capable of the full range of motion of the Lewis Rat. With full actuation achieved, our efforts shifted toward software development to replicate the biological rat's ankle motion. Specifically, we sought to quantify the relationship between the servo angle responsible for dorsiflexion and the resulting foot angle relative to the tibia. This provided us with a full array of angles to code for our servos. After collecting the motion capture data of our model, we were able to produce a graph of ankle dorsiflexion angle versus frame that showed a remarkable resemblance to the data capture from the actual rat motion capture. While we haven’t conducted any statistical comparisons, this will be the immediate next step in our capstone research.

The ethical critique of animal testing took a formal shape in 1959 through Russell and Burch’s “3Rs” framework. The ethical shortcomings of animal testing are mirrored by its scientific failures. While some drugs clear animal testing, only 8% succeed in human clinical trials, and the costs of these inefficiencies are borne in both human risk and economic loss. By analyzing diverse evidence concerning the efficacy of animal testing, the ethical implications of harvesting innocent lives, and the use of alternative methods to prove preclinical efficacy, this thesis paper will argue that animal testing is unethical, ineffective, and inefficient, suggesting a need for a more significant shift to new alternative approaches in the medical research community.

This research adopts a multidisciplinary methodology combining scientific literature, ethical analysis, and STS frameworks. A literature review was conducted, assessing failure rates, drug development costs, and ethical critiques. Case studies, such as the thalidomide tragedy and Ethiopian research institutions, illustrate the risks of extrapolating from animal models. STS frameworks will also be analyzed. Cultural lag helps explain resistance to NAMs. Despite superior alternatives, many scientists adhere to familiar animal models, constrained by institutional inertia and outdated regulatory frameworks. This delay highlights a gap between technological potential and societal adoption. SCOT reveals how technological systems are shaped by cultural norms and power dynamics. Continued dependence on animal testing reflects inherent biases, disregarding ethical considerations.