Thesis Project Portfolio

Electromechanical Bioreactor for Volumetric Muscle Loss Treatment

(Technical Report)

Reassessing the Use of Race Based Correction Factors in Clinical Calculations

(STS Research Paper)

An Undergraduate Thesis

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Table of Contents

Sociotechnical Synthesis

Precision medicine (PM) is a clinical methodology which applies patient genomic and proteomic information to develop targeted treatment strategies for diseases. Recently, PM practices have been continuously integrated into treatment methods given they improve patient outcomes by decreasing return rates of disease/injury and reduce the time, cost and failure of clinical trials. The technical thesis applies the principles of PM to a tissue engineering approach to stimulate skeletal muscle constructs while the STS thesis explores correction factors used in clinical calculations of PM models, specifically assessing the use of race adjustment values.

The technical thesis sought to design and fabricate a bioreactor system to electromechanically stimulate a tissue engineered scaffold in a novel approach to treat volumetric muscle loss (VML). VML is the permanent injury to muscle tissue resulting in decreased function. Since muscle function is dependent on innervation and a mature connection at the musculotendinous junction (MTJ), the Caliari lab has developed a scaffold for regenerating skeletal muscle to address these requirements. The collagen-glycosaminoglycan polypyrrole scaffold is 3D, anisotropically aligned, and electrically conductive. The goal of this scaffold is to drive maturation and proliferation of myogenic cells according to these spatial and environmental cues to treat VML/MTJ injuries. The bioreactor developed by our team will assist in myogenic growth by providing electrical pulsation immediately succeeded by mechanical actuation to mimic natural muscle contraction.

To achieve a functioning prototype, our team worked in pairs to concurrently develop hardware and software components of the system. The hardware, consisting of a mechanical rod system and electrode network, were optimized for function, sterility, and tunability. From a software standpoint, we constructed an electromechanical circuit to control uniaxial strain and electrical pulsing. This includes LCD touchscreens for an enhanced graphical user interface. Future work will further validate bioreactor stimulation by examining myogenic cell alignment and organization within the scaffold. It is the hope that mature scaffolds following stimulation can eventually be utilized in an *in vivo* rodent model to address induced VML/MTJ injury.

The STS thesis assesses the use of race based correction coefficients in clinical calculations for PM strategies. This thesis first explores how race adjustment values are legitimated, specifically through (i) policy to diversify participants in clinical research, (ii) the alliance of researchers and medical organizations, and (iii) historical factors rooting race in genetics. The impacts of these factors are then described, highlighting that race coefficients lead to negative health outcomes and increased patient-provider distrust particularly for minoritized populations. Throughout, the use of race in the calculation of estimated glomerular filtration rate, a model used to determine urgency of transplantation or dialysis in patients with chronic kidney disease, is applied as an exemplary case study. Looking forward, experts in the PM space have already advocated for a revision of race in clinical calculations. Further, it is acknowledged by clinicians that the advancement of genomic technologies will allow for treatment to be advised in a more individualized manner, largely reducing the need for categorical data such as race.