Purpose/ Outcome:

The goal of this project is the development user-friendly software that will help standardize printing biological materials. This will allow users to design and print complex and viable mammalian tissue structures, thereby translating 3D shapes into a complex series of deposition commands.

A main component of this project is the use of the CellJet Cell Printer to generate viable 3D constructs comprised of living cells. Such constructs would be suitable for drug-discovery and pharmacological toxicity assays, scaffolds for bone and tissue regeneration in situ, and simple artificial structures to support tissue engineering research, for example, blood vessel, nerve fiber, skeletal and heart. The CellJet was donated to us by our collaborators at Digilab, who specialize in robotic fluid handling for scientific research. The CellJet is a fluidic control system that uses a stepper motor-driven syringe pump in conjunction with a micro-solenoid valve to dispense droplet volumes ranging from a few nanoliters to 4 microliters(*1*). The motorized syringe pump drives liquid through a system of tubing that delivers the pressurized liquid to the microsolenoid valve. A ceramic tip is positioned at the end of the microsolenoid valve, and is mounted onto a “print-head”, which controls and moves the tip across all three axes using high-resolution stepper motors. The valve opens and closes to deposit liquid from the ceramic tip, and the volume of the droplet is determined by the pressure applied in the tubing. The CellJet is controlled using G-Code, which is a coding language that is used to command cell printers. It allows the user to send instructions on where to move, and how fast to move to the printers. The CellJet has built-in software, but the current software is not adequate for the purposes of this project because the software does not allow for easy user input and generation of 3D models. Improvements that will allow the software to easily convert 3D CAD models to discrete printable points that the CellJet will then use to print biologic material layer by layer is necessary, and is the main focus of this project.

The objectives for this project are broken down into different milestones. The first milestone is the creation of a procedure to convert basic 3D structure to discrete, printable points that can be integrated with the current program. The next stage of this project will be integrating the software into the cell jet with common G-code software available. The last milestone of the project is the creation of a software package that integrates 3D modeling and accommodates for biological printing of live cells. We expect to be able to build software that is compatible with the software from Digilab that allows the user to easily build a 3D biological model using live cells.

Significance/ Originality:

There are many methods used for 3D printing biological materials. One 3D printing method, fused deposition modeling (FDM), deposits molten thermoplastic materials through extrusion heads (*2*). Although fused deposition modeling can create models with higher porosity, the types of materials comparable with the method is very limited because the materials are extruded at high temperatures (*3*). Another method is Three Dimensional Printing (3DP) that creates 3D structures by printing liquid solutions onto a powder bed (*4*). This method allows for a wider range of materials to be used because the process occurs at room temperature (*5*). However, one disadvantage of the method is the limited pore size in the final constructs due to powder used in this method (*3*). Because each tissue printing system has its own benefits and drawbacks, and because many tissue-printing systems are done on a lab-to-lab basis, there is no uniform system for designing and printing biologics, and this is slowing down the progress of the bio-printing field. We hope to work with Digilab and their cell jet tissue printing system to create a new standard in live tissue printing. In addition to the new

software that will be developed through this project, new methods of tissue engineering will be explored, and knowledge of viability of tissue engineering will be developed.

Methods/ Research Design:

We expect the first milestones of the project to be accomplished in three weeks. The first milestone sets the basis for the other milestones. We will develop a software method to go from a basic 3D CAD model to discrete printable points to be used in the current software. We expect the second milestone to also be accomplished within three weeks. The second milestone will integrate the 3D modeling software with the cell jet using G-Code software that is currently available. We expect the last milestone, which is the integration of the 3D modeling with live tissue cells, to be the most difficult to accomplish because it includes building a software that is compatible with the software from Digilab.

Some of the resources required for the completion of this project are:

- Cell jet from Digilab
- Software (Digilab Cell jet software, G-Code, Excel, Cura, Skeinforge)
- Tissue culture supplies
- Polymers

Due to the novel nature of the project and due to the fact that many systems are building their own custom software, a challenge is being able to build a custom package that is focused enough to meet the needs that the current lab is working on, but broad enough to meet the needs of many different laboratories. In order to address this problem, we would need to interact with other labs to see what their needs are, and to see how make my software applicable to their needs

Dissemination

I plan to present my project results at the Spring RISE Poster Session at Northeastern, and at the Northeast Bioengineering Conference (NEBEC) in Binghamton, NY. If possible, I would also like to present my project at the Biomedical Engineering Society (BMES) Conference in Minneapolis, Minnesota and at the Society for Biomaterials (SFB) Conference. In addition to attending these conferences, I also plan to write a peer review journal after my project is completed.

Evaluation:

The success of this project will mainly be dependent on the milestones previously established. I will also work with outside partners/collaborators such as Digilab, or other research labs to ensure that our software is flexible enough to meet their needs.

References:

1. Digilab. (2010).
2. C. L. Ventola, Medical Applications for 3D Printing: Current and Projected Uses. *P&T* **39**, 704-711 (2014).
3. H. N. Chia, B. M. Wu, Recent advances in 3D printing of biomaterials. *J Biol Eng* **9**, 4 (2015).
4. V. Mironov, T. Boland, T. Trusk, G. Forgacs, R. R. Markwald, Organ printing: computer-aided jet-based 3D tissue engineering. *Trends in Biotechnology* **21**, 157-161 (2003).
5. S. V. Murphy, A. Atala, 3D bioprinting of tissues and organs. *Nat Biotechnol* **32**, 773-785 (2014).