The College of New Jersey
Application for Mentored Undergraduate Summer Experience (MUSE)
Summer 2010

Name: Karen Chang Yan

Title: Assistant Professor

Years at TCNJ: 4

Department: Mechanical Engineering

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Title of Research Project:

Study of Heart Tissue Damage via Dynamic Heart Phantom and MRI and Biopolymer Tissue Scaffold Degradation

Number of student collaborators: 2

IACUC or IRB approval: N/A

Date: 02/12/2010

Project and Learning Plan

Intellectual Merit

Project 1: Heart Tissue Damage via Dynamic Heart Phantom and MRI

Coronary artery disease is the leading cause of death in the United States. With the advent of the technology in medical imaging, improved diagnostic medical imaging procedure can reduce the mortality. Among them, the application of cardiac Magnetic Resonance Imaging (MRI), a non-invasive procedure, has been expanded to determine diagnostic information on cardiac function. Given the inherent difficulty in imaging the heart in motion, many efforts have been made to improve cardiac motion tracking and eliminate motion related artifacts. A dynamic heart phantom (DHP) capable of simulating true physiological motions is a valuable research tool for improving quality of MR images and determining critical diagnostic information.

Our research focuses on charactering the stiffness change of the heart tissue due to a heart attack (myocardial infarction). We have developed a prototype of a dynamic heart phantom through a senior design project and collaboration with the cardiac research group at University of Pennsylvania. The DHP is designed to produce cyclic compression, twisting and translation motions with the rate of 60-80 cycles per minute, the range of normal heart rates. A hollow cylindrical gel structure filled with fluid is used to simulate the left ventricle. During the MUSE program, we plan to conduct a set of tests to establish a performance baseline for the developed DHP utilizing silicon gel as the phantom material. We will then modify the phantom material properties via reinforcing the simulated left ventricle at selected locations to mimic infarcted tissue. Modified specimens will then be tested for deformation under prescribed conditions, and we will also go to UPenn MRI facility to obtain the corresponding MR images. Comparisons will be made between the deformations measured and those obtained from the MR images to correlate the deformation change with underlying stiffness change. The results will be used to derive a quantitative index based on the stiffness change for characterizing the damage of infarcted heart tissue, which in turn can be used for early diagnosis and monitoring the progress of diseases. The finding from this work will be disseminated at 2010 ASME IMECE Conference.

Project 2: Biopolymer tissue scaffold degradation

Tissue Engineering, integrating science and engineering to engineer functional tissues and organs for repair and replacement of damaged tissues/organs, has been evolving into one of the most promising therapies in regenerative medicine. One important approach towards creating engineered tissue is *Scaffold-Guided Tissue Engineering* (SGTE). SGTE uses biodegradable polymers as three-dimensional (3D) tissue scaffold to direct cell development. Specifically, a 3D porous tissue scaffold is designed and fabricated using biodegradable materials. The next step is to plant and encapsulate live cells in the scaffold. The complete system is then implanted to provide temporary support and guide tissue growth in a controlled manner. The scaffolds degrade away harmlessly in the body after providing the desired functions. Hence, it is vital to control the degradation of tissue scaffolds in order to provide adequate environment for cell growth.

The objective of this research is to understand effects of scaffold design parameters and environments on scaffold degradation. The project consists of both experimental study and development of a predictive mathematic model. The experimental work entails systematic studies of scaffold degradation in a simulated physiological environment and focus on characterizing physical behaviors of 3D polymer tissue scaffolds as a functional of degradation. This is an on-going project, which began in the 2008 summer with the MUSE program support. Up to date, we have developed experimental protocol and investigated the effects of material composition, pore size and cellular activities, and fluid flow applied in a dynamic environment via a bioreactor. Initial results from the dynamic testing (with one flow rate, 6ml/min) show significant effects of the fluid flow. During the 2010 MUSE program, we plan to further examine the effects of fluid flow with flow rate at 2ml/min, 4ml/min, 8ml/min and 10ml/min. Specifically, a set of controlled 6-week *in vitro* degradation tests will be conducted for scaffold specimens. Specimens will be prepared and submerged in phosphate buffered saline solution (PBS) in the bioreactor with adjusted flow rate. Each week, a subset of samples is removed and evaluated. Polymer degradation will be characterized by mass loss, porosity change, mechanical property change, and molecular weight loss. We also plan to formulate a mathematical model to link the scaffold overall mechanical and degradation behavior based on the obtained experimental data; corresponding simulation models will generated in ANSYS, engineering analysis software. I plan to submit a journal paper based on the results of this work.

Role of Students and Mentor

The proposed research consists of two separate projects; two students will be necessary so that each student can fully engage in a specific project. I plan to involve two junior students, Mary Kate McDonough and Erin McMullin. Based on the students' background and familiarity to the projects, Mary Kate will be focusing on the first project (heart phantom study) and Erin will be working on the second project (degradation study). In the heart phantom study, the student will learn how to design test plans for the experimental study, prepare test samples, perform tests, collect and analyze experimental data under my guidance. In the degradation study, the student will conduct experiment, collect and analyze experimental data. She will also learn how to use the engineering analysis software and perform analysis to correlate with the experimental data. I will provide simulation strategies and develop the underlying mathematic model.

Although the nature of the proposed research presents an opportunity for the participating students to focus on experimental and/or analytic skills, the students will have exposure to all aspects of the projects. Unlike learning experience in a classroom or an internship work, the students will work with the faculty in a collaborative fashion, tackle open-ended problems, engage in a research project in an emerging interdisciplinary field, expose to various aspects of scientific research, and learn from fellow students. Furthermore, as the proposed projects are on-going research, participation of junior students presents an opportunity for continuing the collaborative research in the following academic year.

Broader Impacts

Participating in the MUSE program will be a pivotal experience for both students and faculty mentors. As a pre-tenure faculty member, the summer program will provide a great opportunity to advance my on-going scholarly work as a mentor to junior collaborators. The participating students are interested in pursuing advance degrees in the field of biomedical engineering; the MUSE program will provide a unique learning experience and enhance their interests in scientific research. Furthermore, as a female faculty in engineering, I have been actively involving in mentoring students from underrepresented group, especially female students. Both participating students for the proposed research are female students.

Curriculum Vitae (N/A)
Budget
Past MUSE Report
Student Statement (N/A)

Budget:

i. Student stipend: $5,000 (2 students, $2500 per student)
ii. Student housing: $2,714 (2 students, $1357 per student)
iii. Faculty stipend: $1,000
iv. Project-related expenses (supplies, equipment, books, travel etc.): $482
    Materials:
        Scaffold samples -- $250
        Gel material -- $100
        Travel to UPenn -- $132 (3 planned trips, $44/trip for miles reimbursement)

Report for 2009 Mentored Undergraduate Summer Experience (MUSE)

Karen C. Yan

Project Title: Study of Biopolymer Tissue Scaffold Degradation and Mechanical Force-Induced Cell Damage

My research is in the field of scaffold guided tissue engineering. The objective of this field is to engineer tissue constructs at laboratory as an alternative to millions of traditional devices implanted into the human body every year to replace diseased and /or damaged tissue due to disease, or trauma. During the 2009 MUSE program, my students and I have worked on two projects: biopolymer tissue scaffold degradation and mechanical force induced cell damage.

(a) Biopolymer Tissue Scaffold Degradation
Student: Maria Swift, Biomedical Engineering

During the 2009 MUSE program, I had an opportunity to collaborate with a sophomore student, Maria Swift, in this research. The objective of this project is to characterize and model the degradation rates of biodegradable polymers and corresponding scaffold behaviors, with emphasis on environmental effects including solution types and static versus dynamic conditions. We began with conducting a 6-week *in vitro* degradation test for scaffolds with two solution types. The progress of scaffold degradation was characterized by micrography and measuring changes in weight, water uptake, molecular weight and mechanical testing. Clear trends were observed from the initial data. In addition, we designed a bioreactor capable of producing adjustable fluid flow rate for the dynamic test. Two prototypes were fabricated and tested for their functionality.

The student presented the results of this work at the end of MUSE program. Furthermore, we obtained additional data by performing the degradation test under a dynamic condition in the fall semester. The results of this work were reported in a conference paper at the 2009 ASME International Mechanical Engineering Congress and Exposition (IMECE). A journal paper is in preparation to be submitted to the Journal of Engineering Materials and Technology.

(b) Mechanical Force-Induced Cell Damage
Student: Kamila Paluch, Biomedical Engineering

In this project, my student collaborator and I examined the cell damage due to mechanical force during a fabrication process, in particular, a 3D cell printing process. We generated both 2D and 3D simulation models, and performed Computational Fluid Dynamics analyses to determine the magnitude and duration of shear stress that cells experience during the printing process as a function of process parameters. We further formulated a mathematical model for estimating the resulting cell damage, and performed stochastic simulations in corresponding to the experimental test conditions. The obtained predictions match well with the experimental data.

The student presented the results of this work at the end of MUSE program. She plans to go to graduate school in the fall 2010, and has completed her applications. The results of this work were also reported in a conference paper at the 2009 ASME International Mechanical Engineering Congress and Exposition (IMECE). A journal paper is in preparation to be submitted to Biofabrication.

Conference Publications

1. ***K.C. Yan***, C. Roros, M. Swift, and W. Sun, "Effects of Process Parameters on Cell Damage in a 3D Alginate Tissue Construct with Cell Encapsulated", In the Proceeding of the 2009 ASME International Mechanical Engineering Congress & Exposition, Lake Buena Vista, FL, USA, Nov. 13-19, 2009
   C. Roros and M. Swift, student co-authors, participated in the 2008 and 2009 MUSE programs respectively.

2. ***K.C. Yan***, K. Paluch, K. Nair, and W. Sun, "Effects of Scaffold Design Parameters and Local Environment on Biopolymer Scaffold Degradation", In the Proceeding of the 2009 ASME International Mechanical Engineering Congress & Exposition, Lake Buena Vista, FL, USA, Nov. 13-19, 2009
   K. Paluch, a student co-author, participated in the 2009 MUSE program.

Technical Presentation:

1. "Effects of Process Parameters on Cell Damage in a 3D Alginate Tissue Construct with Cell Encapsulated", 2009 ASME International Mechanical Engineering Congress & Exposition, Lake Buena Vista, FL, USA, Nov. 13-19, 2009

2. "Effects of Scaffold Design Parameters and Local Environment on Biopolymer Scaffold Degradation", 2009 ASME International Mechanical Engineering Congress & Exposition, Lake Buena Vista, FL, USA, Nov. 13-19, 2009

Manuscript under preparation

1. ***K.C. Yan***, M. Swift, C. Roros, E., McMullin and W. Sun, "Controlling Biopolymer Scaffold Degradation via Design Variables and Local Conditions", to be submitted to *ASME Transaction: Journal of Engineering Materials and Technology*

2. ***K.C. Yan***, K. Paluch, K. Nair, and W. Sun, "Computational Fluid Dynamics Analysis of Bio-printing Induced Cell Damage", to be submitted to *Biofabrication*

Report for 2008 Mentored Undergraduate Summer Experience (MUSE)

Karen C. Yan

Project Title: Modeling and Characterization of Biopolymer Tissue Scaffold Degradation
Student: Christina Roros, Biomedical Engineering

My research is in the field of scaffold guided tissue engineering. The objective of this field is to engineer tissue constructs at laboratory as an alternative to millions of traditional devices implanted into the human body every year to replace diseased and /or damaged tissue due to disease, or trauma. One of projects that I have been working on is Degradation of Biopolymer Tissue Scaffolds. Scaffolds, 3D interconnected porous structures, are seeded with cells first, and then implanted into body to provide temporary support and guidance for tissue growth. While the scaffold degrades/erodes away over time, new tissue forms and replaces the scaffold. Therefore, it is important to understand the degradation rates and mechanisms of these polymers and resulting changes in scaffold behaviors.

During the 2008 MUSE program, I had an opportunity to collaborate with a rising sophomore student, Christina Roros, in this research. The objective of the MUSE project is to characterize and model the degradation rates of biodegradable polymers and corresponding scaffold behaviors, with emphasis on material composition and scaffold design parameters. Experimental study was our main focus. We began with developing experimental protocol and making test samples which are made of poly(ε-caprolactone) (PCL), a biocompatible, biodegradable polymer and PCL/Hydroxyapatite (HA) composites. We then conducted a 6-week *in vitro* degradation test for scaffolds with varying material compositions and internal structures. The progress of scaffold degradation was characterized by micrography and measuring changes in weight, water uptake and molecular weight. Clear trends were observed from the initial data. In addition, we also explored possible mathematical modeling approaches to predict changes of scaffold behaviors during the degradation process.

The student presented the results of this work at the end of MUSE program and the Engineering Scholar's Reception in the fall of 2008. Furthermore, this collaborative work facilitated by 2008 MUSE program has provided preliminary data, for a research proposal submitted to NSF-CMMI on Oct.1, 2008. This project is an on-going project; we have obtained additional data by introducing live cells to the scaffolds in the fall semester, and additional parameters will be considered. We plan to submit and present a paper at 2009 ASME International Mechanical Engineering Congress and Exposition (IMECE).