Development of Calcified Artery Model

Description of Project:
The aim of this project is to develop a physical model of artery calcification that mimics the characteristics of human arteries that have developed calcium deposits due to age, diabetes, and other confounding factors. Currently several models of healthy arteries are available for medical device testing and education purposes. However, none of the existing models mimic the unique properties of calcified arteries, resulting in unrealistic conditions for vascular repair device testing. Devices like intravascular lithotripsy, peripheral laser atherectomy, stents, and stent-grafts are commonly used in patients already suffering from arterial calcification, and their clinical performance is directly affected by the extent and structure of the arterial calcium which substantially increases the local arterial properties. To address this problem, I am proposing to develop and test a synthetic calcified artery model with controlled calcium structure, which can provide a realistic and consistent model for vascular device testing.

Significance:
While it is difficult to determine exactly how many people currently suffer from arterial calcification, arterial calcification is "present in 90% of men and 67% of women older than the age of 70" (Mohan et. al). This means that most people will develop arterial calcification later in life. Additionally, other diseases such as diabetes, which affects 11.3% of Americans and counting, causes arterial calcification and damage to arteries and veins (Diabetes Research Institute). Untreated arterial calcification can lead to heart attack, stroke, or major adverse cardiovascular events (MACE). According to a study performed by the Department of Health one fifth of deaths are a result of heart disease, showing that it is imperative we find a solution to these problems. While devices are being developed in an effort to break up and reduce calcium deposits, these devices are very difficult to test, as each artery is different and has different levels of calcium deposits. To determine the most effective means of removing calcium deposits, a synthetic arterial model with controlled and consistent calcification is needed. Additionally, both stents and stent-grafts are most commonly deployed in patients with existing vascular problems, such as vascular calcification, which is why this model would not only be useful when testing products designed for removing calcium build up in arteries, but for existing products that require use in calcified arteries.

Hypothesis: I hypothesize that calcium mineral rings in a synthetic elastomeric arterial model will increase the local stiffness similar to native calcified arteries. To test this hypothesis, I will develop calcified artery model prototypes with different calcium ring geometries and quantify their local stiffness through benchtop mechanical and pulsatile flow tests. The stiffness metrics from these tests will be compared to those of calcified and uncalcified regions of native human arteries.

Methods:
The development of this model will involve three steps. The first step is to research chemicals that will replicate effectively calcium build up in the arterial wall. To replicate calcium build up in the medial layer different calcium minerals/salts, including carbonates, phosphates, etc. will be used in initial testing, but further research may be necessary as many available chemicals are significantly more calcium by weight than calcium phosphate.

After completing the requisite preliminary research, the next step will be to start building models with varying geometrical parameters, and differing means of calcium application. These models will be made using a synthetic elastomeric material that mimics the mechanical properties of uncalcified arteries and then calcium will be incorporated in this material at specific locations. After completing several models, each will be put through extensive testing, including but not limited to SEM imaging, mechanical testing, benchtop pulsatile flow circuit characterization, solubility quantification. Radial stiffness, compliance, and compression strength of the model prototypes will be compared against native arteries exhibiting

signs of extensive vascular calcification. Based on the results, these steps will be repeated until the model exhibits the properties displayed by a calcified artery.

Project Timeline:
I will spend all of April doing research on effective ways to replicate calcium phosphate in an arterial model. I will then spend May-June making prototype models and testing using SEM imaging, mechanical testing, and other means to assess if the model possesses the same properties as a human artery. July-August I will spend testing currently available devices to see if my model is an effective means of testing other products.

April	May-June	June-August
Initial Research and Testing of different calcium deposits and their interactions with synthetic fibers used to replicate	Making and testing prototypes, SEM, mechanical testing, benchtop pulsatile flow circuit testing and comparison, solubility quantification, and deploying some devices such as stents.	Testing current devices for calcium removal, so an effective comparison can be made between efficacy in human arteries and in the model.

Student and Faculty Mentor Roles:
I will complete this project with aid from Dr. Maleckis, my faculty mentor.

The student researcher's role will include:
- Literature search and analysis
- Manufacture effective model prototypes.
- Test prototypes to be compared against known properties of calcified arteries.
- Results analysis

The faculty mentor's role will include:
- Provide feedback on general approach and manufacturing techniques used in model development.
- Provide training on testing, imaging, and development methods including but not limited to: SEM imaging, electrospinning, mechanical tests, and actual device deployment
- Provide help with results interpretation and report development

Previous Internal Funding:
A FUSE grant was awarded to Elizabeth Caldwell for the summer of 2023. This project has no relation to the previously submitted FUSE (Functional Outcomes of Noninvasive Sensory Feedback in Upper Limb Prostheses: A Meta-Analysis).This FUSE project provided funding for a full Meta-Anaylsis of upper limb prostheses feedback that will be published later this year.

Budget Justification:
I expect to work on this project for 3 hours a day from April 2024 to August 2024 (20 weeks of work), with majority of work occurring May-August. I request a stipend of $2,000 and $500 in project-related expenses totaling $2,500. Materials required will include items listed in the following table below.

Item:	Justification:	Estimated Cost:
Gloves	Many of the chemicals handled require proper use of gloves. Three to five pairs a day for 20 weeks is four to five boxes of gloves.	$94.95
Plaster of paris	Use of two types of plaster of paris dry mix and pre mixed to mimic calcium deposits.	$25.97
Needles and syringes	Necessary for electrospinning artery material.	$39.78
Rod removal materials:	In order to remove items from the electrospinning rod I will purchase aluminum foil to protect the rod, superglue to adhere foil to the rod, and tools including tweezers, exacto-knife and blades, scissors, etc. for proper removal.	$53.47
Chemical for electrospinning solution:	Dimethylformamide, tetrahydrofuran, polymers 55DE and 82A.	$283.00
	Total Estimated Cost:	$452.17

The remaining roughly 10% of the budget requested is to be reserved for unpredicted materials, taxes, shipping costs, etc.

References:

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University of Nebraska Omaha

DEPARTMENT OF BIOMECHANICS

September 15th, 2023

Dear FUSE Committee,

I am pleased to provide this letter of mentor support for Elizabeth (Libby) Caldwell's FUSE proposal entitled, "Development of Artery Calcification Model for Catheter-Based Device Testing." This project seeks to produce an effective model of a human artery affected by coronary calcification. This project is relevant as it enables currently developing devices of calcification removal to be effectively tested prior to their use in human and animal models, and would allow effective comparisons to be made between existing methods and currently developing methods.

This project will give Libby the opportunity to utilize novel equipment as well as new mechanical testing methods. These learning opportunities will grant Libby a more well-rounded set of skills in Biomechanical research. Libby is in her senior year of her undergraduate degree, and has consistently shown herself to be a dependable member of my team, with tremendous motivation to drive her work forward.

It will be my role in this project to supervise development of models created throughout this project, to continue to guide Libby's critical thinking skills as she tests her models and compares them to calcium deposits found in human arteries, and review and implement any changes I deem necessary to produce an accurate model. Progress on the study will be monitored through bi-weekly update meetings, as well as monthly reports that will reference the project timeline. I verify that the proposed budget of $2,000.00 is appropriate for Libby's stipend. This model will require new materials and chemicals to appropriately model calcium deposits. I also certify that a material budget of $500 is appropriate.

I believe that Libby would be an ideal recipient for the FUSE, based on her demonstrated character and the novelty and rigor of the proposed project. If you have any questions regarding her qualifications, please contact me via phone (402-554-3228) or by email (kmaleckis@unomaha.edu).

Sincerely,

Maleckis

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