



**Biomedical
Engineering**

FLORIDA INTERNATIONAL UNIVERSITY

6th Annual Undergraduate Research Day

Friday, February 19th, 2016

EC 2300

Event Itinerary:

8:30 - 9:00 am	Breakfast
9:00 - 10:00 am	Keynote Speaker: Dr. David Vorp
10:00 - 12:30 pm	Poster Presentations
12:30 - 2:30 pm	Award Ceremony and Lunch Reception

Key Note Speaker:

David A. Vorp, Ph.D.
Vascular Bioengineering: Clinical Applications and Needs
William K. Whiteford Professor of Bioengineering,
and Professor of Cardiothoracic Surgery, Surgery,
and the Clinical & Translational Sciences Institute
University of Pittsburgh, Pittsburgh, PA



Presented by:

Department of Biomedical Engineering
Wallace H. Coulter Biomedical Engineering Distinguished Lecture Series

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P1: Endothelial Cell Responses to Flow Profiles after Balloon Aortic Valvuloplasty

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Abstract

Every year, more than 35,000 newborns in the U.S. suffer from congenital heart defects. Critical neonatal aortic valve stenosis (NAVS) in particular is a medical emergency. Typically, balloon aortic valvuloplasty (BAV) is performed to ease the flow of blood. However, restenosis is very common, and it is therefore of interest to identify valve tissue remodeling responses to its hemodynamic environment after balloon intervention. At the cellular scale, valve endothelial cells (VECs) are the first to sense mechanical signals which leads to a cascade of autocrine and paracrine signaling to valve interstitial cells (VICs). To understand VEC response to flow profiles following balloon intervention, we will expose side-specific (ventricular and aortic) VECs to a clinically representative flow waveform depicting both post-balloon and normal states. From these experiments we will evaluate the changes in VEC intracellular structural protein structure and resulting gene expression. Subsequent comparisons between normal and post-balloon groups will delineate potentially abnormal VEC responses which could then be linked to the underlying causes for rapid restenosis following BAV.

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P2: Native to Engineered Valvular Tissue Integration under Flex-Flow States

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Abstract

Introduction: At least five million Americans are diagnosed with heart valve disease each year. Current replacement techniques involve the utilization of manufactured mechanical and bio-prosthetic valves. While a mature technology in adults, these prosthetics cannot accommodate somatic growth; as a result, multiple surgeries and treatments are needed to treat pediatric patients with critical congenital valve disease with high morbidity and mortality rates. We propose that rather than using synthetic materials, that living, autologous tissue substitutes can be engineered for repair purposes. Previous studies in our laboratories have shown that bone marrow derived mesenchymal stem cells (BMSCs) subjected to a physiological combination of steady fluid-induced shear stress (≈ 4.73 dynes/cm²) and cyclic flexure (1 Hz frequency), i.e., Flex-Flow supports their effective differentiation to heterogeneous valve cell types (endothelial and myofibroblast cells). Here, we investigated the effectiveness in integration of native valve tissue to engineered tissue under flex-flow conditions, with particular focus on the transition zone between the two structures.

Materials and Methods: A density of 2×10^6 cells/cm² of BMSCs were seeded into a PGA: PLLA scaffolds (17 x 6 x 1 [mm]) in rotatory culture (8 rpm) at 37 °C and 5% CO₂ for 8 days. Twenty ml of Dulbecco's modified Eagle's medium (DMEM), 10% fetal bovine serum, 1% streptomycin/penicillin solution, 50 μ g/ml L ascorbic acid and 50ng/ml bFGF were added to each tube during the cell seeding procedure. At 8 days, each BMSC seeded scaffold was sutured to a freshly harvested porcine valve tissue section and then subsequently placed in a bioreactor chamber filled with the culture medium to impart Flex-Flow conditions as previously to the growing constructs for 2 weeks, with media changes once a week during this timeframe. At the end of the mechanical conditioning period, samples were analyzed via histology using, Movat Pentachrome, Hematoxylin and Eosin, and Verhoeff-Van Gieson (VVG) stains.

Results and Discussion: Using Movat Pentachrome histological staining (Fig. 1), it was observed that valve extracellular matrix components were present in the engineered tissues, including collagen and GAGs. Meanwhile the porcine native valves not surprisingly exhibited the characteristic tri-layer heart valve structure. Previous work in our laboratory demonstrated that flex-flow conditions directed differentiated BMSCs that were CD 31+ (i.e., endothelial phenotype), to the surface of the engineered tissue specimens whereas α -SMA positive expressing cells (i.e., myofibroblast phenotype) were found predominantly within the interstitial layers.

Conclusions: Physiologically-relevant flex-flow conditions utilizing BMSCs support valve tissue formation, the valve phenotype and may potentially enhance longitudinal integration of native to engineered valve tissue integration. Such integration may play a critical role in subsequent heart valve repair procedures involving engineered valvular tissues.

P3: Design and Development of a Vibrotactile Sensory Feedback System for upper Limb Prostheses

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Abstract

Currently, upper limb prostheses lack the capacity to provide sensory feedback to the user. Not being able to feel the objects manipulated by the user makes it much more difficult to perform simple daily life tasks. This reduces the usefulness of the prosthesis and its value to the user, who could ultimately decide to abandon the prosthesis. The purpose of this project is to develop a system to provide a prosthesis user with a non-invasive substitution to the sensory feedback lost after amputation, and unavailable in current prostheses. Different stimulation methods can be used to provide sensory feedback: mechanical, electrical or vibrotactile stimulation. Vibrotactile stimulation uses vibration motors to stimulate tactile receptors in the skin. We have chosen to implement two different types of vibrotactors to provide sensory feedback: one C2 vibrotactor to provide force information and an array of coin vibrotactors to provide hand opening information. Both tactors will be attached to the residual arm and connected to sensors in the prosthesis. An Arduino microcontroller was programmed to analyze signals from two sensors on the prosthetic hand: a grasping force sensor and a hand position sensor. The microcontroller then generates signals for the vibrotactors providing direction of force and hand opening simultaneously. Force feedback is provided by pulses produced by the C2 vibrotactor, the input of the grasping force sensor initiates a pulsating vibration that varies in frequency with respect to the force applied. Position is provided by a longitudinal array of coin motors that are activated one by one with respect to the input of the position sensor. Several technical challenges arose during the design of the device and were resolved as they presented. First, choosing the right vibrotactor from a wide market selection to assemble an array that could deliver appropriate vibrations while not overheating or desensitizing the skin. Second, neither of the two vibrotactors could be driven directly with the output generated by the Arduino. The C2 vibrotactor required an audio amplifier to function, and a transistor array was needed to coordinate the coin tactor activation. The last challenge encountered in the project consisted in programming the Arduino to control both vibrotactors independently and implementing and debugging stimulus timing commands. The next steps in the project will be to build a working prototype by connecting the assembled feedback device to an upper limb prosthesis, run pilot studies in non-amputee subjects to determine the best paradigm and patterns to be used as feedback, and debug the remaining deficiencies in the Arduino code. This device could then be used to run studies on amputee subjects to determine whether it can help improve their overall performance using an upper limb prosthesis and ultimately recover the practical value that is so lacking in current prostheses.

P4: Structural Changes in Bone Marrow Stem Cells to Oscillatory Flow: Relevance to Valve Development

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Abstract

Valvular heart disease and valve replacement is a cardiovascular complication in which many people in the United States undergo yearly. Heart valves play a vital role in regulating blood flow through the heart. Tissue engineering heart valves (TEHV), based on bone marrow stem cells (BMSCs) and biodegradable scaffolds have been investigated as the next step to current prosthesis limitations particularly to address somatic growth. Recent studies have shown that shear stress can regulate the proliferation and differentiation of BMSCs through a variety of signaling pathways. This study proved that coupled flexure and flow environments augmented tissue formation using PGA: PLLA scaffolds seeded with BMSCs. At the intracellular scale, changes in BMSC cytoskeleton have been observed when BMSCs were exposed to fluid induced shear stress. Alterations in F-actin structure may thus be closely linked to gene expression and protein synthesis in the mechanobiology of stem cells. Therefore, in this investigation, we applied OSS to growing BMSCs to understand their structural changes to this environment, which would subsequently have implications to the fine tuning on heart valve tissue engineering protocols. Transient transfection of BMSCs was performed using an electroporation protocol already established (pTAGGFP-actin DNA) and (pTAGRFP-viculin DNA). Cell viability was assessed using FITC AnnexinV apoptosis detection and analyzed under flow cytometry. A square wave was used in order to create a pulsatile flow environment.

On fixed cells, there were alterations in the filament structure. Subsequently transfected cells were subject to OSS conditions and compared to no flow controls. Our early observations indicate that there were distinct changes to the cellular structure, particularly actin filaments, which displays alignment to the flow direction, similar to ECs. These findings demonstrate that these cells are positive the surface proteins marker CD31. We believe that the current study reports on the first steps needed to delineate how structural cytoskeletal changes in BMSCs after OSS exposure leads to favorable gene expression changes which supports the valvular phenotype.

P5: Lower Extremity Wound Imaging Using a Hand-held Near-infrared Optical Scanner

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Abstract

Lower extremity ulcers are devastating complications that are still un-recognized. To date, clinicians employ visual inspection of the wound site during its standard 4-week of healing process via monitoring of surface granulation. A novel ultra-portable near-infrared optical scanner (NIROS) has been developed at the Optical Imaging Laboratory that can perform non-contact 2D area imaging of the wound site. From preliminary studies it was observed that the non-healing wounds had a greater absorption contrast with respect to the normal site, unlike in the healing wounds. Currently, non-contact near-infrared (NIR) imaging studies were carried out on 22 lower extremity wounds at two podiatric clinics, and the sensitivity and specificity of the scanner evaluated. A quantitative optical biometric was developed that differentiates healing from non-healing wounds, based on the threshold values obtained during ROC analysis. In addition, optical images of the wound obtained from weekly imaging studies are also assessed to determine the ability of the device to predict wound healing consistently on a periodic basis. This can potentially impact early intervention in the treatment of lower extremity ulcers when an objective and quantitative wound healing approach is developed. Lastly, the incorporation of MATLAB graphical user interface (GUI) to automate the process of image acquisition, image processing and image analysis realizes the potential of NIROS to perform non-contact and real-time imaging on lower extremity wounds.

P6: Physiologically Relevant Effects of Fluid Pulsatility on Engineered Tissue Growth

Manuel Perez, Alex Williams, Arash Moshkforoush, Omkar Mankame, Manuel Salinas, Nikolaos Tsoukias, Sharan Ramaswamy
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Abstract

Fluid-flow induced shear stress has been shown to influence collagen formation in the growth of engineered tissues. Previous studies examined collagen formation in engineered tissue under static flow, steady-state flow, pulsatile square-wave flow, cyclic flexure as well as combined cyclic flexure and steady-state flow simulations. These conditions, however, do not fully represent cardiac pulses experienced by native cardiovascular tissues. This study examined collagen development in engineered tissue by subjecting samples to flow regimes that more closely mimic pulsatile physiological conditions. A bioreactor was used to simulate in-vivo conditions experienced by engineered tissue using rectangular strips of specimens immersed in flow media. Computational fluid dynamics (CFD) software was used to analyze flow physics and flow characteristics around the specimens. Computational findings were compared to previous tissue engineering studies conducted in our own laboratory. ANSYS computational fluid dynamics software was utilized in performing CFD simulations and modelling flow parameters and flow physics under viscous laminar flow within the chamber. Such CFD simulations applied both steady state flow and flow from the physiologically relevant waveform while utilizing the bioreactor geometry, which consisted of a U-shaped tubular conditioning chamber that houses the tissue samples and through which flow media was pumped across the face of the tissue samples.

P7: Porcine Small Intestinal Submucosal Valve Functionality in the Aortic Position

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Abstract

Congenital heart defects are a relatively common problem in our society. One of the more challenging subsets of these patients are young and physically small children presenting with critical heart valve deformities. For these patients, valve replacement procedures are fraught with difficulties and complications since available prosthetic valves have major limitations in terms of growth potential and longevity. The concept of tissue engineered heart valves (TEHVs) which can provide for growth, self-repair, infection resistance, and a permanent approach for replacing defective heart valves¹ is thought to be a potentially ideal solution. Our recent experience suggests that porcine small intestinal submucosa (PSIS) would be especially attractive for use as a bioscaffold for TEHVs. PSIS may possess the ability to recruit endogenous cardiovascular cells, leading to phenotypically-matched replacement tissue when the scaffold has completely degraded. As a first step, the aim of this study was to assess the functional effectiveness of tri-leaflet PSIS bioscaffolds in the aortic position using a left heart simulator in our laboratory².

Our clinical collaborators have thus far implanted acellular PSIS bioscaffolds in the mitral (n =2), aortic (n =1), and tricuspid (n =1) positions. All valves worked flawlessly, with the longest follow-up being over a year (mitral valve). Hydrodynamic evaluation in our lab subsequently revealed that flow and pressure waveforms derived from PSIS-valve testing were physiologically-shaped. Preliminary evidence suggests that PSIS-valves function by exhibiting physiologically normal flow and pressure waveforms. However, additional quantification of hydrodynamic parameters and additional testing are necessary in order to determine the efficiency of PSIS bioscaffolds for valvular application.

P8: Creating a Platform for Combining Wireless Electrophysiological Signals and Physiological Responses

Tommaso Benigni, Celine Wassaf, Jorge Riera Diaz
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Abstract

Electroencephalographic (EEG) and electro-dermal activity (EDA) techniques are useful to measure electrophysiological and physiological signals from the body (ref 1). EEG amplifiers and EDA sensors continue to get progressively more sophisticated. However, the problem is that in the majority of situations these devices require large and heavy parts which impede their use in behavioral studies, as movements are hard and discouraged. In addition, wireless versions of these devices have not been synchronized in order to obtain these biological signals while the body is moving. This project will combine wireless EEG and EDA sensors into a Python program in order to synchronize data recorded simultaneously by these devices.

The project used the Cognionics EEG dry headband, an EDA sensor created from Arduino components. Python was used to program the data-acquisition platform due to the simplicity to receive wireless signals. The lab streaming Layer (LSL) was then used to interface the headband to the python program. A code was written in Arduino to obtain EDA data. This data was sent wirelessly to a recording computer and synchronized using python, where it was inputted into a GUI using the Tkinter library. The program includes a save button that allows the user to save selected data into an excel file, from which the data can be imported into MATLAB for further analyzes.

This software will be used in our lab to studying how children with Autism Spectrum Disorder (ASD) perform during video-game-based therapies. Biofeedback is necessary to understand whether or not the child is stressed or relaxed, the level of attention and to obtain valuable information about the physiological state of the child and not only the mental state. This coupling does not have to be limited to just EEG and EDA sensors. In fact, the program is simple enough that any number of wireless sensors can be integrated to measure different types of physiological changes simultaneously to accommodate a wide variety of experiments.

P9: NIROS for Non-contact Hemodynamic Imaging: Instrument Development

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University

Abstract

A near-infrared optical scanner (NIROS) has been developed for non-contact sub-surface imaging of wounds. The current device, NIROS employs two LEDs of different wavelengths to image the same region during diabetic foot imaging studies. However, the illumination region by the two LEDs had minimal overlap, limiting the extraction of oxy- and deoxy-hemoglobin signals from the region of interest using the multi-wavelength NIR signals. Herein, the source system of NIROS was modified to a single multi-wavelength LED to assess the changes in blood flow, in terms of changes in HbO and HbR, with maximum overlap between the illuminated regions. Appropriate LED drivers were developed and an external trigger switch was incorporated to multiplex the light source and automate the image acquisition process in real-time. In addition, a diffuser has been incorporated to the source system (via a custom holder), such that the area of illumination is uniform apart from allowing maximal overlap across the multi-wavelengths during imaging. Studies are currently carried out to assess the performance of the modified near-infrared optical scanner from phantom studies.