VIRGINIA TECH WAKE FOREST UNIVERSITY
School of Biomedical Engineering and Sciences
NEWS
Fall 2009

Our New Buildings COME TO LIFE

Virginia Tech, School of Biomedical Engineering and Sciences, Home Building (ICTAS)
Primary and Core Faculty in All Research Areas
50,000 sq ft Dedicated Space

Wake Forest University Health Sciences, School of Biomedical Engineering and Sciences, Home Building (MRI)
Primary and Core Faculty in All Research Areas
18,000 sq ft Dedicated Space

Virginia Tech, High-rate Impact and Imaging Laboratory, VCOM II Building
Impact Biomechanics and High-speed Bi-planar X-ray System
12,000 sq ft Dedicated Space

IN THIS ISSUE:

Dr. Stefan Duma is the new Head of the Virginia Tech –Wake Forest University School of Biomedical Engineering and Sciences.

A Great Time to Grow

In direct contrast to the global economic downturn, our biomedical research and educational programs continue to grow and expand at a dramatic rate. As shown on the cover of this publication, we have taken ownership of 3 new facilities. Of which, 2 are new buildings, and one is renovated and expanded to better accomodate our research. The School now has a total of over 80,000 square feet of dedicated biomedical engineering research and teaching space at both campuses. More information about the groundbreaking research in each of these buildings is provided on the next three pages. For those who are reading about our program for the first time, we are a joint degree partnership between Virginia Tech and Wake Forest University that is called the School of Biomedical Engineering and Sciences. We offer MS and PhD degrees in biomedical engineering as well as a joint DVM-PhD degree in collaboration with the Virginia – Maryland Regional College of Veterinary Medicine. I hope that you will take a few minutes and read about the exciting research in all of our biomedical programs.

Our rapid growth is fueled by strong and sustained commitments from both Virginia Tech and Wake Forest University. Currently we have 39 tenure track faculty (16 primary and 23 joint) as well as an additional 68 affiliate faculty appointments in our biomedical program. We have an ambitious growth plan to add an additional 10 primary faculty and 10 affiliate faculty over the next 10 years. You can learn more about our faculty throughout this Newsletter and in summary form on pages 8 and 9. Over the past academic year, our biomedical engineering faculty listed on these pages published 184 journal papers (an average of 4.7 for our 39 faculty) and an additional 206 conference papers. This newsletter highlights many of these research accomplishments in more detail.

Allow me to draw your attention toward two articles in particular. First, the Wake Forest Institute for Regenerative Medicine is a thriving example of the collaboration between the two schools. Second, this year we announced the new Childress Institute for Pediatric Trauma which was made possible through the generosity of Richard and Judy Childress. Researchers at Virginia Tech and Wake Forest University are combining to make these two Institutes world leaders in tissue engineering and pediatric trauma.

Finally, the back cover of this newsletter outlines our program's historical contributions to the Biomedical Engineering Society (BMES). Our involvement started in 1978 and was highlighted in 1990 when Virginia Tech hosted the first BMES conference in Blacksburg, Virginia. Prior to this conference, BMES had always held joint conferences with other groups, so 1990 was the first stand-alone BMES conference. For the 2009 BMES conference in Pittsburgh, we have over 50 faculty and graduate students presenting over 50 papers and posters. I hope you will have the opportunity to see one of these presentations as I strongly believe that research excellence is the best demonstration of successful growth in any academic field.

Thank you for taking the time to read our newsletter, and please let me know if you are ever in the Virginia/North Carolina area as I would be happy to show you around our new buildings.

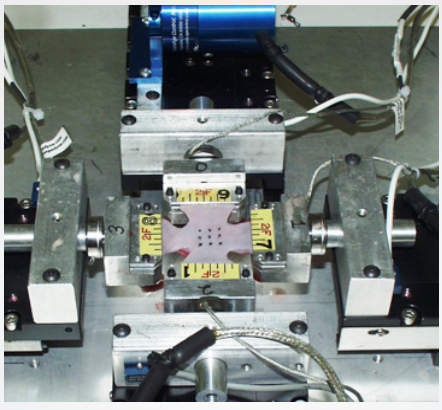
Sincerely,

Stefan Duma

Stefan Duma, PhD

Professor and Head

Sports Biomechanics: *Ph.D. Student Steve Rowson assembles one of the custom football helmet acceleration sensors, Dr. Duma's project.*



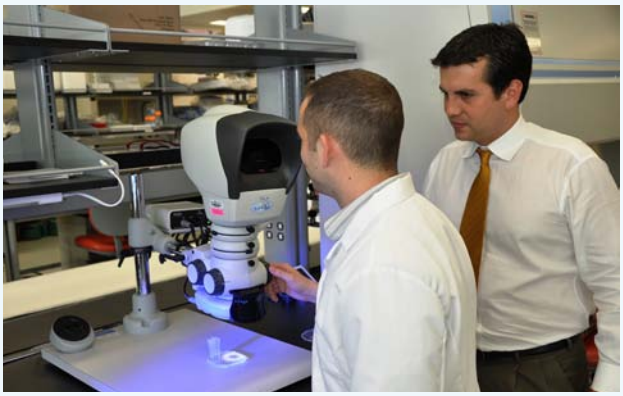
Pregnant Occupants: *Dynamic bi-axial tissue testing is shown for a pregnant uterine tissue sample, fundamental to Dr. Duma's research.*

Bone Material Properties: *Research Scientist Andrew Kemper prepares a cortical bone sample using the custom mini-CNC machine.*

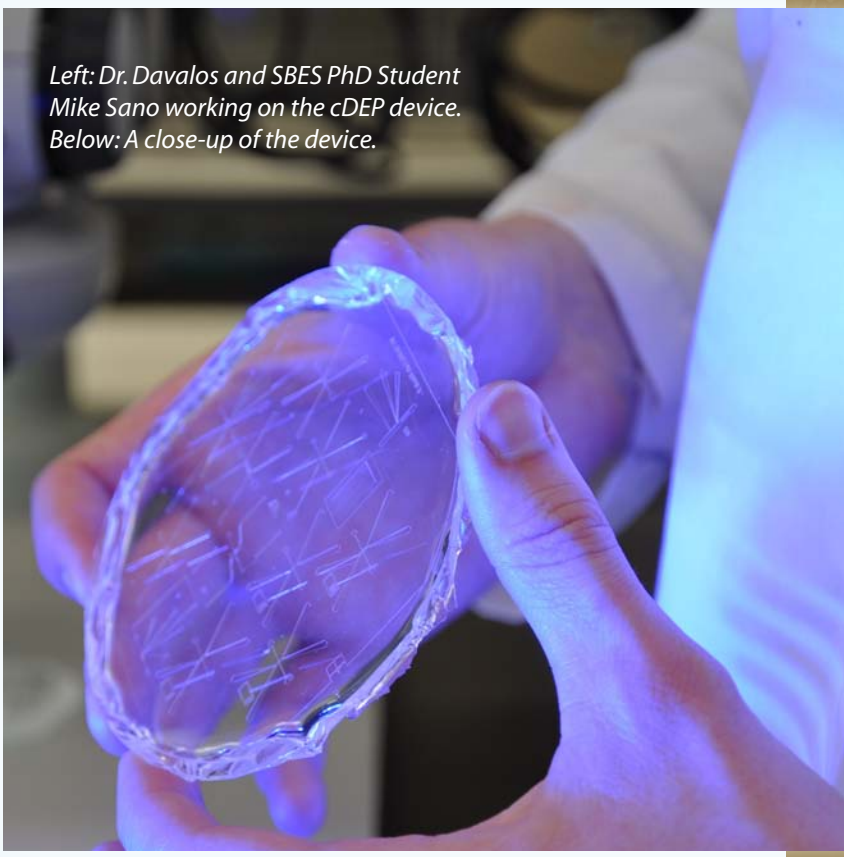
Research in the New ICTAS Building

Rafael Davalos

Dr. Rafael V. Davalos, Director of the Bioelectromechanical Systems Laboratory, along with his graduate students, Hadi Shafiee, John Caldwell, and Michael Sano, have developed a new technique to separate and manipulate cells based on their unique electrical properties. The ability to separate cells by their physical properties is incredibly useful in research and medical settings. In these settings, the investigation of a specific type of cell is often hindered by the presence of many dissimilar cells in the same sample. Numerous methods exist to perform separation, however Davalos' technique relies upon dielectrophoresis (DEP) or the motion of a particle due to its polarization in the presence of a non-uniform electric field. The major advantages of DEP over other methods of cell sorting include its ability to perform separation without extensive sample preparation and the



relatively high speed at which cells can be separated. This rapid turnaround is extremely important when evaluating gene expression. Conventional techniques employing DEP require direct contact between electrodes and the sample fluid, which inhibits clinical translation since the electrodes can induce fouling, bubble formation and unwanted electrochemical effects. Similar to conventional DEP, the newly developed method uses an electric field that is created in a channel of a microfluidic device to apply a force on cells flowing through the channel. However, what is unconventional about this new technique is that the electrodes, which create the field, are inserted into two conductive microchambers separated from the sample channel by thin insulating barriers. By separating the electrodes from the sample channel with insulating barriers, all of the problems arising from direct contact can be avoided and the required electric field can still be generated in the device using an AC field. Furthermore, this new technique, appropriately called "contactless dielectrophoresis (cDEP)" allows the use of a simplified and inexpensive fabrication process and reduces joule heating in the sample. The researchers have filed a provisional patent on their new technique and have fabricated microfluidic devices to observe the cDEP response (trapping and cell chaining) of multiple cancer cells, including human leukemia, breast, and prostate cancer cells. The preliminary results of their invention are now concluded in a paper that appeared in Biomedical Microdevices in May of 2009 titled: "Contactless dielectrophoresis: a new technique for cell manipulation". They believe their work improves upon existing techniques to separate and identify cells suspended in a medium and Dr. Davalos has been invited to give a talk on these results at the 2009 FACSS Conference, in Louisville, KY. The preliminary results of the cDEP technique were also presented by Hadi Shafiee in a summer workshop on cellular and molecular mechanics at the University of Illinois Urbana-Champagne in 2009 where he received the award for best poster.



Left: Dr. Davalos and SBES PhD Student Mike Sano working on the cDEP device. Below: A close-up of the device.

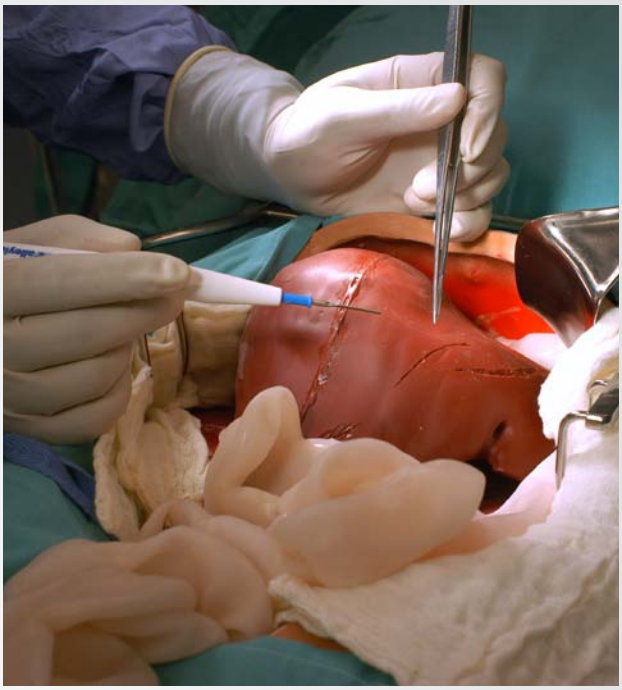
Jessica Sparks

Research in New Lab Facilities

Communication errors are the number one cause of preventable injuries in hospitalized patients. Patient simulators (mannequins) are a promising tool for improving communication within operating room teams. However, current mannequin simulators are not designed to simulate surgical tasks, thereby limiting the ability of surgeons to participate fully in surgical team training scenarios. Dr. Jessica Sparks, director of the Tissue Mechanics Lab, and students Smitha Raghunathan, Jill LeBlanc, and Garrett Bowman, have developed a mannequin abdomen that simulates open surgical procedures for blunt force abdominal trauma. The research was conducted in collaboration with Dr. Carl Westcott, Dr. Jeff Carter, Ian Saunders, and Serene Mirkis of the Patient Simulation Lab at Wake Forest University Health Sciences and Dr. Joel Stitzel of the Virginia Tech – Wake Forest Center for Injury Biomechanics (CIB). The new abdomen can be combined with commercially available mannequin simulators to create a "trauma patient simulator" useful for training full operating room teams in emergency scenarios.

In the trauma patient simulator, both the liver and spleen are injured, as they are the most commonly injured abdominal organs. Hollow polyurethane organs were created using organ geometry from CT scans. Organ size, material durometer, and color were selected to simulate the approximate size, texture and coloring of the actual organ. Bleeding from the lacerations was simulated by pumping red-colored water through plumbing leading to the hollow organs. During the scenario, when proper action is taken against the liver and spleen damage (packing with gauze) the pump can be turned off remotely, halting the bleeding.

Dr. Sparks working with SBES students in the patient simulation lab.



By developing enhanced patient simulators that incorporate specific surgical tasks, the Tissue Mechanics Lab, in conjunction with the Patient Simulation Lab and the CIB, hopes to create better opportunities for trauma teams to work on communication skills in a safe training environment, to enhance patient safety.

As part of the VT-WFU Center for Injury Biomechanics, the Tissue Mechanics Lab also has ongoing research to tackle the problem of blunt abdominal trauma from a different perspective: injury mitigation in motor vehicle crashes. Understanding the biomechanical aspects of abdominal trauma is a daunting task due to the numerous modes of injury that can be encountered, the variety of shapes and sizes of people, and variation in impact location and direction. Characterizing all these scenarios would require a tremendous amount of money, time, and manpower; therefore, modeling is a more viable alternative. Mechanical loading on crash test dummies during a crash can then be applied to "virtual" crash test dummies (computer models), where organ, skeletal, and overall body response can be monitored. Once a model has been validated for a range of scenarios, it can be used to predict organ response to better understand injury severity. In this vein, the Tissue Mechanics Lab currently is developing a computer model of liver tissue that integrates the fluid and solid components of the organ. This can be used to better understand the relationship between solid matrix pressure, fluid pressure, and injury.

Research in New High-Rate Impact and Imaging Lab

Warren Hardy

The Virginia Tech – Wake Forest University Center for Injury Biomechanics (CIB) has instituted a new state-of-the-art impact laboratory and crash sled facility. This facility supports the research efforts of Drs. Duma, Gabler, Hardy, Sparks, and Stitzel, who study trauma and try to prevent it. The jewel in this showcase is a 1.4-MN ServoSled system (commonly known as a "crash sled") manufactured by Seattle Safety. This sled is used primarily in the study of transportation-related trauma, with its chief applications found in the automotive environment. Although the sled is often used for basic research, more applied studies are conducted using reinforced vehicle structures, or "bucks", fastened to the deck of the sled, which can accommodate up to a 2500-kg payload. The bucks are used to evaluate vehicle interior components and restraint systems. The sled starts from rest and is pneumatically driven (20 MPa maximum) to the desired speed while following a prescribed acceleration pulse. The pulse is shaped using a hydraulic braking system, and high-frequency (500 Hz), closed-loop control of acceleration and brake pressure. The acceleration pulse is selected to mimic the crash performance of a specific vehicle or other impact event, and the pulse is quickly and easily modified and programmed to suit. Frontal, rear, and side-impact car crashes can be simulated using human surrogates, including crash dummies. Nearly 200 transducer channels can be collected using onboard signal conditioning and data acquisition hardware. Multiple high-speed video cameras positioned both off and on the sled are used to capture event kinematics. The ServoSled System is capable of delivering 475,000 N-m, which translates to a maximum 90 kph and 93 g (20 g/ms) within a 2-m driving stroke. At full payload the sled can achieve 57 kph and 37 g. This system is designed to provide late-event and negative acceleration, both of which are typically unattainable by other systems. This crash sled is helping the CIB better understand the mechanisms of injury, and to develop better mitigation schemes and protection systems. One of the primary funding agencies to make use of the sled is the National Highway Traffic Safety Administration.

Adjacent to the crash sled is the high-speed, biplane (3D) x-ray suite. This 500-square foot installation is used in the study of impact event kinematics that cannot be imaged by conventional means. For example, this type of system is used to examine brain deformation, mediastinal motion and strain in the aorta, relative interactions of organ systems within the abdomen, and cervical spine kinematics in the cadaver. Skeletal structures can be imaged directly, but soft tissues are targeted using radiopaque neutral-density markers. A high-frequency, dual-axis x-ray generator provides the exposure energy (80 kW), up to 150 kV or 1,000 mA. State-of-the art, 40-cm diameter image intensifiers provide the largest possible field of view, and highest available frequency response (> 3 kHz). The output of these intensifiers is imaged using high-resolution monochrome CMOS video cameras, which are normally operated above 1000 fps. This system is accurate to within 0.1 mm in 3D space, typically. For the second consecutive year, Dr. Hardy's research using high-speed biplane x-ray received the John Paul Stapp Award for the best paper published in the Stapp Car Crash Journal, which is the premier international forum for research in impact biomechanics and human injury tolerance.

Ph.D. students Nick White and Meghan Howes adjust a high-speed, biaxial tissue testing apparatus.

Dr. Hardy discusses the capabilities of the new VTTI/CIB ServoSled system with Craig McNally, Andrew Kemper, Nick White, and Meghan Howes.

The impact laboratory is outfitted with a collection of linear impactors, ballistic pendulums, and hydraulic loading machines. In addition to these are high-speed biaxial tissue testers. One such device is designed to test cruciate samples using strain rates up to 1000 s^{-1}. This custom device is used to examine tissue response to rapid biaxial stretch, and to estimate strain energy density functions. High-speed, high resolution video cameras and lasers are used to measure strain and tissue thickness, respectively. Load is measured using miniature load cells attached to the clamps used to grasp the tissue. The tissue characteristics obtained from using this device have direct application to finite element models of the human body. One organization funding research examining high-speed tissue properties is the Global Human Body Models Consortium.

Karen Richardson

Wake Forest Institute for Regenerative Medicine

From working to solve the challenges of engineering a human limb to using regenerative medicine technologies to improve meniscus replacement surgery, School of Biomedical Engineering and Sciences (SBES) students assigned to the Wake Forest Institute for Regenerative Medicine (WFIRM) in Winston-Salem, N.C., are involved in projects with the potential to make dramatic improvement in patients' lives. The common goal is to harness the body's natural healing powers to promote healing from within or to develop replacement organs and tissues in the laboratory.

Masters' and doctoral students in the Cell and Tissue Engineering Track work under the guidance of institute faculty members and have increasing responsibility as they progress in the program.

Anthony Atala

"The SBES students in this program make significant contributions to the work of the institute," said **Anthony Atala, M.D.**, institute director. "With their backgrounds in engineering and biotechnology, they are productive members of our team and are helping us make strides to bring new therapies to patients. We are delighted to be an SBES partner."

Engineers bring a unique perspective that complements that of the physicians and basic science researchers at WFIRM. Some of the current projects that show this collaboration are described below, and include such engineering disciplines as biomechanics, fluid flow, and material science.

Engineering Segments of a Human Limb

Almost 2 million people in the United States have amputated limbs. Being able to one day replace those limbs may sound like science fiction, but scientists in the field of regenerative are actively at work to make it a reality. At WFIRM, researchers are working to develop replacement limbs in the laboratory by first engineering the component parts: skin, bone, muscle, tendons, and blood vessels.

Mitchell R. Ladd, B.S., a fifth-year MD/PhD student, is part of a project to solve one of many technical challenges – engineering tissue that will function like the muscle-tendon junction, the area where tendon and muscle join together and make pulling movements possible, such as flexing the arm and bending the leg. Ladd's advisor is **James Yoo, M.D., Ph.D.**, associate professor of regenerative medicine and WFIRM's assistant director.

In the project, Ladd and colleagues are using two biodegradable polymers to create a scaffold, or three-dimensional shape, to support muscle cells as they develop and form this junction.

"The challenge of the project is that there is a 'mismatch' in the mechanical properties of tendon and muscle," said Ladd. "Muscle tissue must be compliant and contractile in order to generate force for movement. The tendon, on the other hand, is designed to transfer the force generated by the muscle to a bone and create movement and therefore must be strong and stiff."

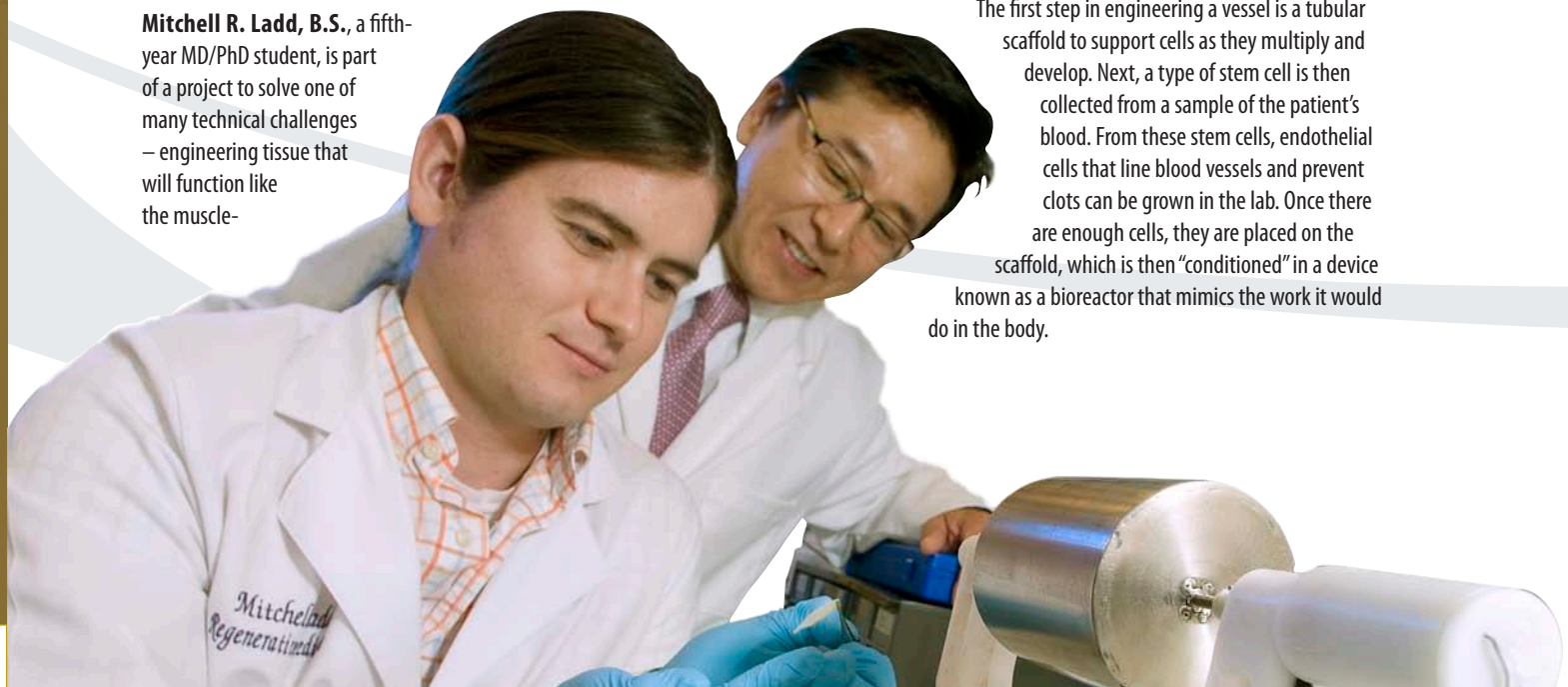
The scaffold used to engineer this tissue must have three distinct regions in order to mimic the native junction – areas destined to become muscle tissue, tendon tissue and the area where they overlap. In a project to engineer the scaffold, Ladd and colleagues begin by spraying liquid biomaterials onto a spinning mandrel – using different materials for the muscle and tendon regions and allowing them to overlap and create the junction. They are using tensile testing, including uniaxial, cyclic and stress-relaxation, to test mechanical properties of each region.

The scaffold is then seeded with muscle cells to promote tissue formation. The work continues, but so far, the results look promising.

Vessels for Bypass Surgery or Dialysis Access

Being able to engineer a blood vessel in the laboratory from a patient's own cells would solve several challenges in medicine. These custom-made vessels could be used for heart bypass surgery, for example, instead of harvesting a vessel from the patient's legs. And, they could also benefit dialysis patients: creating an access for the dialysis equipment that would replace synthetic options that are prone to infection.

The first step in engineering a vessel is a tubular scaffold to support cells as they multiply and develop. Next, a type of stem cell is then collected from a sample of the patient's blood. From these stem cells, endothelial cells that line blood vessels and prevent clots can be grown in the lab. Once there are enough cells, they are placed on the scaffold, which is then "conditioned" in a device known as a bioreactor that mimics the work it would do in the body.




George Christ

Masood Machingal, M.S., a fifth-year student whose advisor is **George Christ, Ph.D.**, professor of regenerative medicine, has been part of a project showing that the bioreactor system is an important step in accelerating the formation of smooth muscle tissue on the vessel. The team is currently working to identify the best scaffold to engineer vessels. In a recent project, they evaluated two options: veins and arteries that have been "decellularized" to remove cells from the donor and leave only the support structure.

The research showed that with arterial scaffolds, there is limited migration of smooth muscle cells into the medial, or middle, layer of the vessel – even with the use of the bioreactor. With venous scaffolds, on the other hand, there was cell migration and growth in the medial layer.

"Our long-term goal is to develop a vessel in the lab that mimics the architecture and physiological characteristics of native arteries," said Machingal. "These preliminary data seem encouraging, but there is more work to be done to characterize the function of these engineered vessels and to determine the ideal length and pulsatile flow rate and pressure for pre-conditioning."

Improving Meniscus Surgery

In the United States, a torn meniscus is the most common reason for knee surgery. These two C-shaped pieces of cartilage distribute body weight across the knee joint and are responsible for stability and cushioning. While damage to the tissue can sometimes be repaired; in other cases all or large parts of the meniscus must be removed and replaced by cadaver tissue. These implants do not appear to function as well or last as long, possibly because the patient's own cells do not grow into the central portion of the tissue. As a result, there are no cells there to maintain the tissue's structure and strength.


Mark Van Dyke

Julie Steen, B.S., a fourth-year student, works with advisers **Cristin M. Ferguson, M.D.**, an assistant professor of orthopaedic surgery and regenerative medicine, and **Mark Van Dyke, Ph.D.**, an assistant professor of regenerative medicine, and a team of researchers with the goal of developing an improved meniscus scaffold that could be used as an alternative to current methods when the meniscus must be replaced.

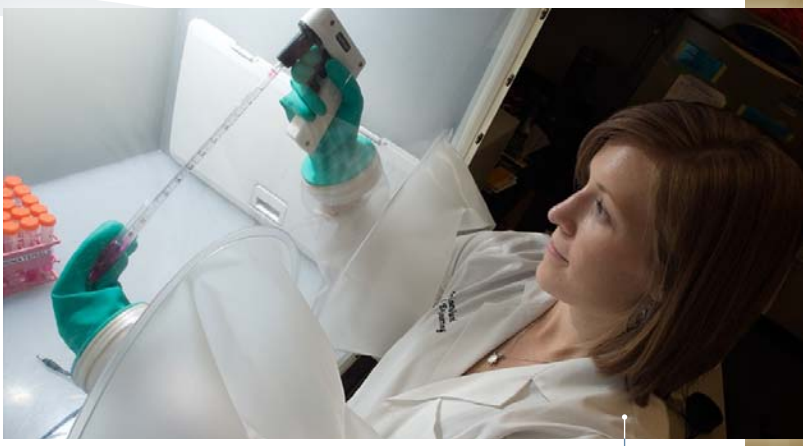
The project's goal is to incorporate a patient's own cells into the donated tissue to improve its function. To accomplish this, the team first processed donor menisci from an animal model to remove the cells – leaving behind the support structure. The processing also had an additional function – to increase the porosity of the tissue. An important part of the work was to determine the ideal level of porosity – enough to encourage the growth of cells in the tissue, but not too much to weaken the tissue. The next step was to attempt to "grow" cells on the scaffold, which was performed in culture using bone marrow derived stem cells.

"The decellularization process didn't change the integrity of the meniscus and did result in increased porosity," said Steen. "Results from our animal study are promising. It appears our new approach to transplants decreases osteoarthritis occurrence and the tissue is able to maintain its integrity in vivo. These results are promising and suggest that this technique may provide an alternative to allograft transplantation."

Further research is needed, including refining seeding techniques to achieve uniform cell density and adding culture conditions that support meniscus tissue differentiation.

Oxygen Producing Gel

When tissues in the body are deprived of oxygen, the irreversible process of tissue death begins. For example, if immediate medical attention isn't available when a traumatic wound damages blood vessels in the leg, the tissue may begin to decompose and amputation is often required. But what if there was a way to temporarily provide oxygen to muscle tissue and keep it alive until surgery could restore the blood supply?



Catherine L. Ward, B.S., a third-year student, her adviser **Benjamin Harrison, Ph.D.**, assistant professor of regenerative medicine, and a team of researchers are working to develop an injectable gel that could do just that. Ward recently won an award at the SBES 8th Annual Graduate Student Research Symposium for her work on the project, which is part of an $85-million federally funded program to apply regenerative medicine therapies to battlefield injuries.

"Our goal is to develop a treatment that medics could carry with them," said Ward. "It would offer a way to buy time and provide a temporary burst of oxygen until a patient could get medical treatment."

The technology may also have other applications, such as organ transplantation. The idea would be to provide oxygen to donated organs as a way to increase the amount of time they can safely remain outside the body before transplantation.

The gel is made from a peroxide-based chemical that generates oxygen. The team's challenge is to optimize the gel to produce specific amounts of oxygen. In preliminary studies, the team has assessed the gel's biocompatibility and its ability to keep tissue in a viable state outside the body. Early testing has been promising and the group continues to refine the technology, including working to prolong the length of oxygen production for extended release.

For additional information, please see *www.wfirm.org*.

Faculty

Anthony Atala, MD
Professor, *Clinical Translation of Regenerative Medicine*
SBES Core/WFIRM

Stefan Duma, PhD
Professor & Head
Auto Safety, Sports, Military, Biomechanics
SBES Primary

Ben Harrison, PhD
Assistant Professor
Tissue Engineering
SBES Core/WFIRM

Bahareh Behkam, PhD
Assistant Professor, *Biophysics, Microbial Motility and Adhesion, Medical Devices*
SBES Core/ME

Joseph W. Freeman, PhD
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Musculoskeletal Tissue – Regeneration
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Katherine Holzbaur, PhD
Assistant Professor,
Musculoskeletal Biomechanics & Control, Human Movement
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Joel Berry, PhD
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H. Clay Gabler, PhD
Associate Professor, Center for Injury Biomechanics
EDR, Crash, Alcohol Studies
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Robert Kraft, PhD
Assistant Professor,
Quantitative MR Imaging
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J. Daniel Bourland, PhD
Assistant Professor,
3D Radiation
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Yaorong Ge, PhD
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YongWoo Lee, PhD
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Biomaterials, Tissue Eng. Mechanotransduction
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Thurmon Lockhart, PhD
Associate Professor,
Locomotion Research, Balance, Biomechanics
SBES Core/ISE

George Christ, PhD
Professor, *Muscle Physiology, Bioreactors*
SBES Core

J. Wallace Grant, PhD
Professor, *Mathematical Modeling of Inner Ear, Vestibular Mechanics*
SBES Core/ESM

Michael Madigan, PhD
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Rafael Davalos, PhD
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Craig Hamilton, PhD
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Cardiovasular MRI, Biosignal Processing
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Michael Munley, PhD
Associate Professor,
Radiation Effects, Molecular Imaging, Radiation Therapy
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Assistant Professor,
Constitutive Modeling, Cardiovascular Mechanics
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Warren Hardy, PhD
Associate Professor, Center for Injury Biomechanics
Neurotrauma, Thorax, Spine
SBES Core/ME

Maury A. Nussbaum, PhD
Professor, *Occupational Biomechanics & Ergonomics, Balance, Aging*
SBES Core/ISE

Our Biomedical Engineering program is a joint venture between Virginia Tech and Wake Forest University. Since the program spans two universities and grants degrees with both seals, the program is called the School for Biomedical Engineering and Sciences (SBES) and involves 107 faculty:

39 Tenure Track Biomedical Engineering Faculty: 16 Primary + 23 Core (Joint Appointments)

68 Affiliate Biomedical Engineering Faculty at Virginia Tech and Wake Forest University

During the 2008 – 2009 academic year, the 39 biomedical engineering faculty at Virginia Tech and Wake Forest University published nearly 400 articles with 184 of those as full length peer reviewed journal papers.

184 Journal Papers

206 Conference papers

SBES Faculty ■ Virginia Tech ■ Wake Forest

Padma Rajagopalan, PhD
Assistant Professor, *3D Tissue Mimics, Polymeric Scaffolds, Biopolymers*
SBES Core/CHE

Jake Socha, PhD
Assistant Professor, *Internal Flow Sys. in Animals Gliding Flight in Vertebrates*
SBES Core/ESM

Mark Van Dyke, PhD
Associate Professor, *Biomaterials, WFIRM*
SBES Core/WFIRM

Christopher Rylander, PhD
Assistant Professor, *Optical Devices for Imaging & Therapeutics, Biotransport*
SBES Primary

Shay Soker, PhD
Associate Professor, *Stem Cell Vascular, Biology*
SBES Core/WFIRM

Ge Wang, PhD
Samuel Reynolds Pritchard Professor, *X-Ray Computed & Tomography, Inverse Problems*
SBES Primary

M. Nichole Rylander, PhD
Assistant Professor, *Nanotechnology, Bioheat Transfer, Cancer Therapies*
SBES Primary

Jessica Sparks, PhD
Assistant Professor, *Liver Biomechanics, Impact Injury, Surgical Simulation*
SBES Primary

Pavlos P. Vlachos, PhD
Associate Professor, *Fluid Biomechanics, Cardio and Vascular Flow Analysis*
SBES Core/ME

Pete Santago, PhD
Professor & Associate Head, *Image & Signal Analysis, Mach. Learning & Pattern Recognition*
SBES Primary

Anne E. Staples, PhD
Assistant Professor, *Biological Fluid Dynamics, Biomechanics*
SBES Core/ESM

Christopher Wyatt, PhD
Associate Professor, *Biomedical Image Analysis*
SBES Core/ECE

Justin Saul, PhD
Assistant Professor, *Biomaterial Scaffolds, Controlled Release Systems*
SBES Primary

Joel Stitzel, PhD
Associate Professor, Center for Injury Biomechanics
Modeling, Imaging, CIREN
SBES Primary

James Yoo, MD, PhD
Associate Professor
Tissue Engineering
SBES Core/WFIRM

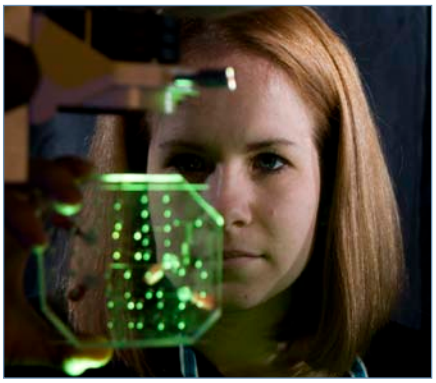
Pavlos Vlachos

Fluid Mechanics in Cardiovascular Flow

Left Ventricular Diastolic Dysfunction (LVDD)
Left ventricular diastolic dysfunction (LVDD) and diastolic heart failure are conditions that affect the filling dynamics of the heart and remain difficult to diagnose using current clinical methods. According to the 2008 AHA Statistical Update, one in every three adults in the United States suffers from hypertension which is a significant precursor to LVDD. The most commonly used technologies for the noninvasive analysis of diastolic function include echocardiography and magnetic resonance imaging (MRI).

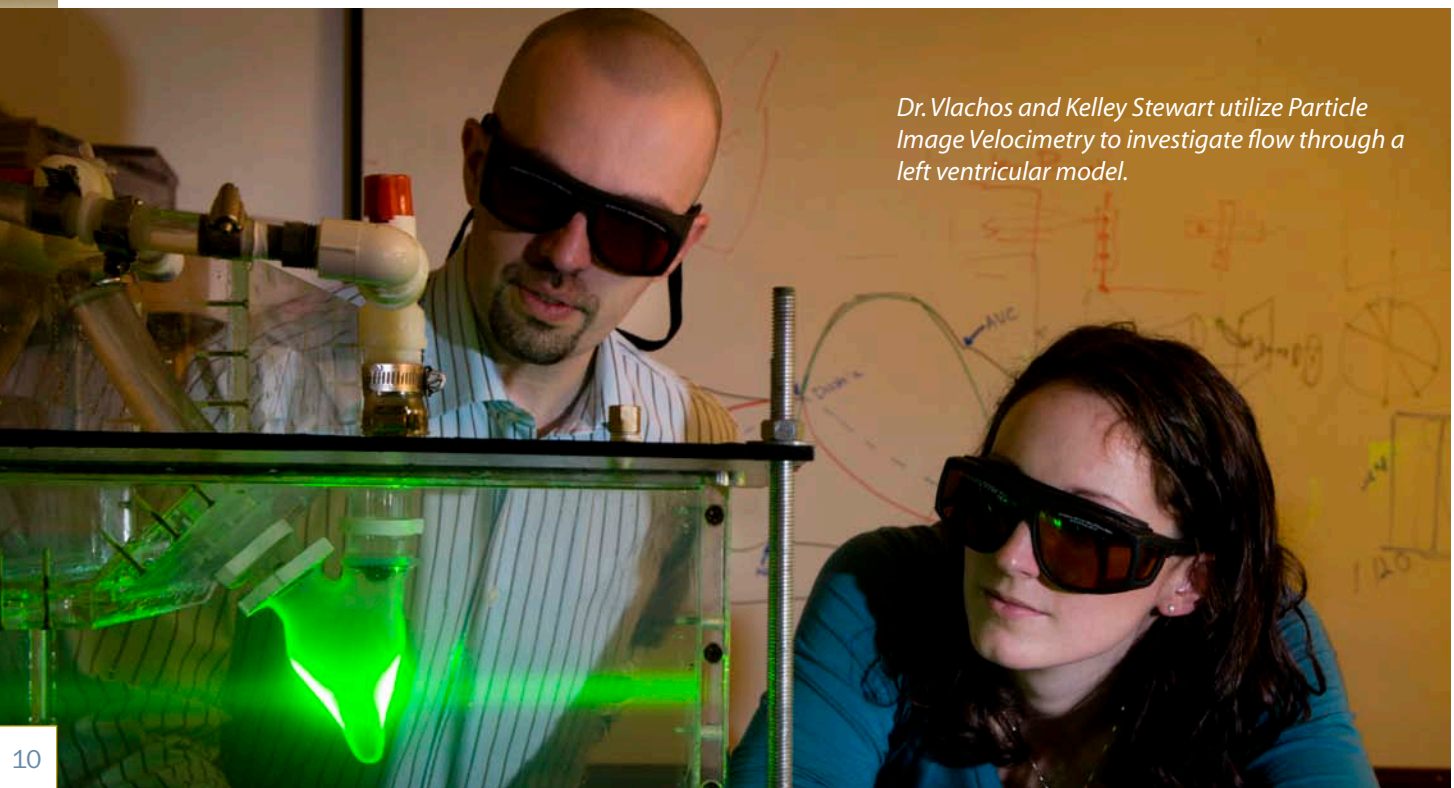
A team of researchers in the AEThER laboratory (Mechanical Engineering Ph.D. student Kelley Stewart and Dr. John Charonko) headed by Prof. Pavlos Vlachos in conjunction with cardiologists Dr. William Little and Dr. Rahul Kumar at Wake Forest Baptist Medical Center are researching the hydrodynamics of the progression of LVDD.

Magnetic Drug Targeting (MDT)
Magnetic drug targeting (MDT) is an active drug delivery technique which utilizes an external magnetic field to drive magnetically altered drug particles to a diseased location within the body. Much of the current research involving MDT systems focuses on delivery in diffusion dominated capillaries. Unfortunately, this delivery approach has suffered in larger arteries where the magnetic force on the particles must compete with large hydrodynamic forces acting to sweep the particles away from the diseased location. In response to this limitation, SBES Ph.D. Jaime Schmieg and Dr. Pavlos Vlachos of the AEThER Laboratory at Virginia Tech have begun efforts to investigate the parameters which govern MDT, in hopes of discovering new approaches to increase efficacy in coronary flow conditions. In doing so, the group has centered their investigation on drug particle characterization to measure the responsiveness of individual particles to external magnetic fields, as well as the design of magnetic field configurations capable of favoring localized drug capture. It is a unique and strategic combination of these two factors which provides optimal delivery within a particular flow environment.



This project utilizes Micro Particle Image Velocimetry (μPIV) to visualize the movement of magnetic particles in response to an external magnetic field, thus providing a means of particle characterization. μPIV is a well-known imaging technique which utilizes a high speed camera, a microscope and a laser to capture the location of laser-illuminated particles over time. In doing so, the responsiveness of particles to steady or transient magnetic field and flow conditions may be determined to allow for complete particle characterization.

For more information, visit *www.me.vt.edu/AEThER/index.html.*



Dr. Vlachos and Kelley Stewart utilize Particle Image Velocimetry to investigate flow through a left ventricular model.

Childress Institute for Pediatric Trauma and SBES

Joel Stitzel

ANNUAL CHILDHOOD DEATHS FOR CHILDREN 18 AND UNDER:

674 from Heart Disease

1,117 from Birth Defects

1,930 from Cancer

12,399 from Trauma

CHILDRESS INSTITUTE *for* Pediatric Trauma
Wake Forest University Baptist Medical Center

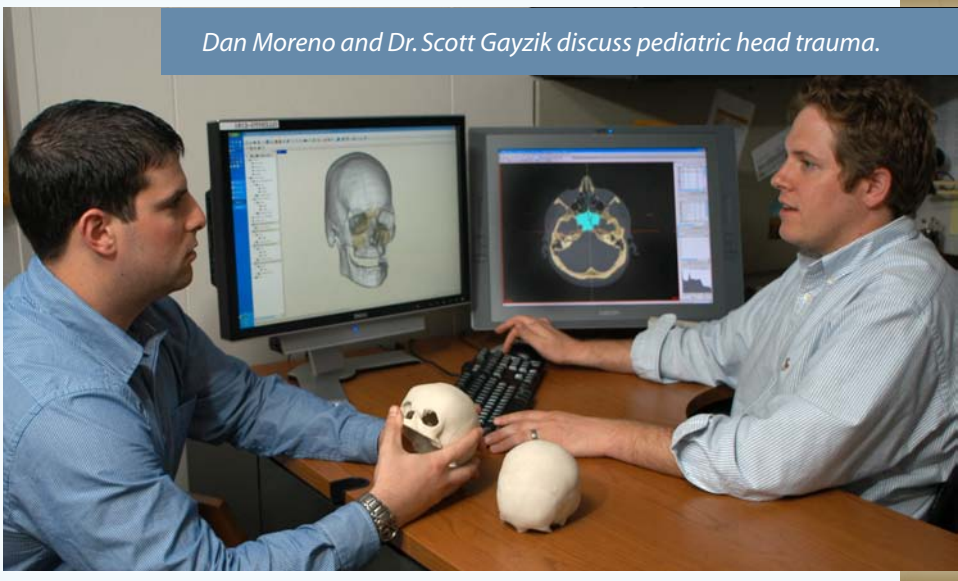
The Childress Institute for Pediatric Trauma is dedicated to preventing and treating life-threatening injuries to children. Its goal is to save lives and to help kids affected by these injuries recover to lead a more normal life. Each year, serious injuries claim the lives of more than 12,000 children – more than all other causes combined. The work of the Institute addresses this situation through advocacy, education, prevention, research and rehabilitation. In founding the Institute in 2008, Richard and Judy Childress pledged money, time and energy to its cause, and they continue to work tirelessly for its mission.

The Institute works through a network of partners that includes the School of Biomedical Engineering and Sciences, jointly established by Wake Forest University and Virginia Tech; the Pediatric Medical Device Institute; and the Center for Injury Biomechanics. To this network, the Childress Institute provides opportunities to evaluate and clinically test new devices that show promise for helping seriously injured children. As part of the Childress mission, the Institute is helping to speed the development of pediatric medical devices into tangible tools that benefit kids.

One ongoing research initiative in SBES and the Center for Injury Biomechanics, through a collaboration established with the CIPT, is to better understand the anatomical and physiological differences between adults and children affected by trauma. Kerry Danelson, a graduate student in the CIB and her team have quantified the shape differences between the pediatric and adult skull. This study demonstrated that a pediatric skull has a more rounded shape and an adult skull has a more elongated shape. These differences can then be integrated into existing injury prediction tools, such as computer models of the brain. These models contains the primary anatomic structures of the brain and can be used to predict possible injuries.

Using the research conducted, these models can be scaled to the correct size and shape of a newborn. When these changes are implemented and a simulation is conducted, the results show a difference in the location of high strain elements in the brain. Areas of high strain in the computer model can be indicative of areas of potential injury. Further research into this area will refine the computer model to more accurately represent the material properties of the pediatric brain and skull. This scaled model can be used in many safety applications, by providing injury prediction for safety system design for child seats, restraints, and air bags.

Collaborations with SBES through the Center for Injury Biomechanics and other researchers in SBES will help to ensure the success of the CIPT as it forms more partnerships and accomplishes its mission. More info at www.childresspediatrictrauma.org.



Dan Moreno and Dr. Scott Gayzik discuss pediatric head trauma.

Jeffrey Douglas

VMRCVM Contributing, Prospering Through SBES

The Virginia-Maryland Regional College of Veterinary Medicine (VMRCVM) a founding partner with Virginia Tech's College of Engineering and Wake Forest Medical School on the establishment of Virginia Tech Wake Forest School of Biomedical Engineering and Sciences (SBES), has played a significant role in many of the school's accomplishments in biomechanics, cell and tissue engineering, biomedical imaging and medical physics, and instructional areas. But a value-added dividend to its association with SBES has been the opportunity to build a galaxy of new relationships with other health science researchers at WFU and at Virginia Tech. Many of these have sparked additional research initiatives and collaborations, many which intersect and in some cases transcend the actual structure of the school.

One of the most recent and the most exciting collaborations has been developed with the world-class Wake Forest Institute for Regenerative Medicine. Dr. Anthony Atala invited VMRCVM Dean Gerhardt Schurig and Senior Associate Dean Roger Avery to visit the center, which has led to an important new collaborative opportunity.

WFIRM is making considerable progress in the treatment of urogenital disorders. By engineering new muscle tissue for a damaged or age-degenerated urethral sphincter, for example, the technology could help eliminate vexing human incontinence problems. Urinary incontinence is a major problem with some companion animals as well, so the technology has important applications in veterinary medicine. Dogs and cats presenting for clinical care in the VTH represent a spontaneous animal model for the human disorder, and animal modeling work will need to be conducted before such an innovative technology is eventually approved for human clinical applications. What's more, the VMRCVM could become a portal for WFIRM's eventual migration into the world of veterinary medicine.

The VMRCVM views this opportunity so appealing that they have assigned research scientist **Dr. Will Eyestone,** an associate professor in the Department of Large Animal Clinical Sciences who has extensive experience in cloning and familiarity with regenerative medicine, to work full-time at the WFIRM research installation in Winston-Salem. "One of my goals is to keep up with what they're doing and look at ways to apply it in veterinary medicine," said Eyestone.

The Veterinary Teaching Hospital's clinical caseload provides a continuous stream of animals suffering from spontaneous disease and injuries that can be evaluated for comparative purposes, for example, and veterinarians are well versed with devising and operating protocols in animal modeling that can support the pioneering experimental work being accomplished by SBES researchers.

Dr. John Robertson, a professor in the Department of Biomedical Sciences and Pathobiology (DPSP) and an affiliated faculty member in SBES, has been collaborating with **Dr. John Rossmeisl,** an associate professor in the Department of Small Animal Clinical Sciences (DSACS), **Dr. Kumaran Subbiah,** an assistant professor in DPSP, and Dr. Rafael Davalos, an assistant professor in SBES to develop novel methods for treating brain tumors in dogs and people. These methods involve rapid pulsed electrical fields and introduction of tumor-killing viruses. This research group also widely collaborates with a large number of colleagues at the Brain Tumor Center for Excellence at Wake Forest University **(Drs. Robbins, Bourland, Shaw, Debinski, Ellis, and Tatter)** to refine methods to detect and treat brain tumors, which are very similar in dogs and people.

"SBES has been the portal through which a number of programs have evolved," said **Dr. Lud Eng,** assistant dean for strategic innovations in the VMRCVM and a member of the SBES Governing Board. "Collaboration and an interdisciplinary approach to scientific problem solving is absolutely

Research Associate professor Dr. Will Eyestone has been assigned responsibilities for developing the collaboration between the VMRCVM and WFIRM.

the most efficient approach there is. When I look at all that has been accomplished so far, and the things that are being set in place for the future, I think we can certainly view SBES as a 'best practices' model for inter-institutional collaboration."

Dr. William Huckle, an associate professor in the DBSP, has been collaborating with SBES since its inception. Huckle's area of interest—mechanisms of communication among cells in the cardiovascular system—has applications ranging from cancer to ophthalmological disorders and is well suited for collaboration with a number of different scientists working with SBES.

Dr. Huckle's laboratory is interested in gaining a greater understanding of how chemical signals control the development, repair and growth of blood vessels. These processes are crucial biologically in the formation of the vasculature de novo during embryonic development and in the response of adult vasculature to tissue ischemia or traumatic injury. Moreover, dysregulation of new blood vessel formation ("angiogenesis") underlies a variety of serious pathologic states, notably the growth of solid tumors, diabetic retinopathy and macular degeneration — all serious medical conditions with significant unmet therapeutic needs. Age-related macular degeneration, for example, is the primary cause of blindness and vision loss in Americans 65 and over. Mild forms of this condition affect some 30% of individuals 75 years or older, with 6-8% progressing to an advanced form that can include substantial loss of vision and reduced quality of life. Dr. Huckle's work has been supported by diverse organizations (the American Heart Association, the American Cancer Society, the NIH, and AstraZeneca), reflecting the central role that angiogenesis is believed to play in a variety of diseases.

Research in the Huckle lab currently is focused on elucidating the biochemical mechanisms by which vascular endothelial cells, the cells that form the inner lining of blood vessels, maintain their responsiveness to signaling molecules that promote their growth. Vascular endothelial growth factor (VEGF), an important angiogenic agent, produced in low oxygen or hypoxic tissue and frequently overexpressed in tumors, interacts with receptor proteins on the surface of endothelial cells, activating pathways leading to cell proliferation, migration, and assembly into vascular structures capable of carrying blood. Owing to their central role in both adaptive and pathologic angiogenesis, VEGF and its receptor proteins have become attractive targets for the therapeutic manipulation blood vessel growth.

Matt Rittler (SBES Ph.D. '08), a graduate student in Dr. Huckle's lab, devised a mathematical model that sought to predict how receptors could alter the duration and magnitude of cellular responses to VEGF in the presence of VEGF-related growth factors with differential binding affinities. Dr. Rittler then tested his model in a VEGF-responsive cell culture system that enabled measurement of receptor binding, receptor activation, and the engagement of key downstream signaling components. Dr. Rittler's model successfully predicted cellular behavior within certain boundaries, and, where correspondence between modeled and actual behavior was lower, pointed to assumptions or estimated parameters that should be reassessed. Work of this nature is viewed as essential to optimally design therapeutic strategies revolving around VEGF-receptor interactions that either promote or inhibit angiogenesis.
Please see: www.vetmed.vt.edu/org/dbsp/faculty/huckle.asp.

This complete article can be viewed at *www.sbes.vt.edu/news/feature_articles.html*. For additional information, please see *www.vetmed.vt.edu*.

Coupling Modeling and Experimentation to Investigate Collagen (Type I) Biomechanics *By Albert Kwansa, graduate student (Joseph Freeman, advisor)*

Fiber-forming collagens such as collagen type I are the main load-bearing component of connective tissues such as tendon, ligament, bone, and skin. These collagens provide tensile strength and mechanical support to the extracellular matrix, and they can provide mechanical and chemical cues for cells. We are interested in how factors present in the extracellular matrix (i.e., hydration, presence or absence of crosslinking, and changes in amino acid sequence) influence the mechanical properties of fiber-forming collagens at the molecular level.

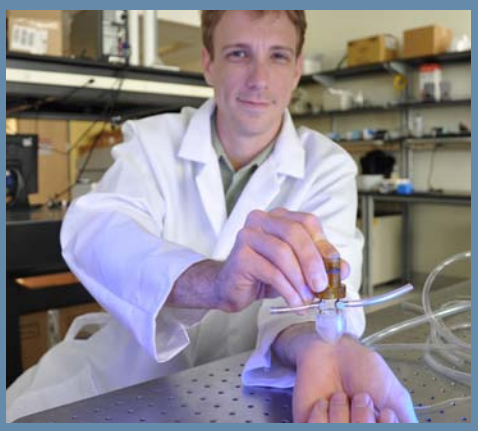
The images above represent a molecular model of type I collagen that we are using to investigate how tissue hydration and collagen crosslinking affects elastic energy storage in collagen type I, thus potentially gaining more insight into how tissues store elastic energy at the molecular level. Specifically, we are using molecular modeling programs on a computer to assemble the above structures and then to apply unidirectional virtual strain to the models. These simulations are being used to compute the amount of elastic energy stored in these models and to observe how the elastic energy storage is distributed throughout the length of the models. This molecular modeling is being validated by experimental work involving the reconstitution of aligned collagen fibers and their mechanical characterization in vitro.

The dimensions of the molecular model shown above are approximately 67 nanometers in length and 5 nanometers in diameter, whereas the diameter of the reconstituted collagen fiber shown below is on the order of 50 micrometers. Thus, these reconstituted collagen fibers (below) are 10,000 times larger in diameter than the molecular model (shown above).

Tissue Optical Clearing Devices for Deeper Light-based Imaging and Therapy *By Chris Rylander*

Optical techniques for in vivo imaging and therapy hold great promise for improving healthcare due to their relatively low-cost and safety. Unfortunately, because of the shallow penetration depth of light in tissue such as skin (on the order of millimeters), optical techniques have not seen widespread clinical implementation. To overcome the light penetration barrier, and permit deeper light delivery, Assistant Professor, Chris Rylander is developing Tissue Optical Clearing Devices, TOCDs. These non-invasive devices consist of an array of pins which induce spatially localized skin compression using vacuum pressure. TOCDs exert a mechanical transduction force on skin, causing stretching and compression of tissue between and underneath the pins, respectively.

This technology-driven research is inspired by our hypothesis that compression induced by the TOCDs will cause localized water transport, decrease blood perfusion, and reduce physical distance to target tissues. The modification of tissue water and blood concentration will cause a change in the optical scattering and absorption properties. Upon delivery of optical radiation we predict less-divergent, deeper transport of light within the tissue and a correspondingly sharper focused beam profile. Preliminary results suggest the TOCDs permit an approximately two-fold increase in penetration depth of light into skin. The ability of TOCDs to deliver a collimated or focused light beam deeper into tissue should allow increased sensitivity for optical detection and diagnosis of disease such as cancer as well as increased specificity of photothermal heating of target tissue leading to better treatment outcome.



In collaboration with Virginia Tech Professors John Robertson (Vet Med) and Ge Wang (SBES) as well as Wake Forest University Professors Suzy Torti and Steve Akman (Cancer Biology), Dr. Rylander is investigating application of tissue optical clearing technology to enhance photothermal treatment of cancer. In addition, collaboration is underway to explore a wide range of optical imaging and sensing techniques utilizing TOCDs such as optical coherence tomography, optical molecular tomography, diffuse optical tomography, fluorescence confocal microscopy, and spectroscopy to improve the early detection of cancer.

Dr. Rylander has presented his research on optical clearing at invited talks at the 2009 SPIE Photonics West Conference, and the 2009 D.C. Metropolitan Biophotonics Symposium. His student, Yajing Liu, received a travel grant by the American Society of Lasers in Medicine and Surgery to present her research at their 2009 annual meeting. Dr. Rylander's recent work was published on the cover of the December 2008 issue of Lasers in Surgery and Medicine. For more information see: C.G. Rylander, T.E. Milner, J.S. Nelson, "Mechanical tissue optical clearing devices: Enhancement of light penetration of ex-vivo porcine skin and adipose tissue," Lasers Surg. Med. 40(10): 688-694, 2008.

Dr. Clay Gabler Named SAE Fellow

SBES is pleased to announce that Dr. H. Clay Gabler has been elected Fellow of the Society of Automotive Engineering in April 2009. Dr. Gabler was recognized by SAE for his pioneering contributions to automotive safety in crash compatibility, side-impact protection, and the use of event data recorders for crashworthiness research. His research has led to fundamental advances in the understanding of injury risk in vehicle collisions. His technical paper on light-truck aggressivity was instrumental in establishing the scientific foundation on compatibility, which has led to industry-wide voluntary agreements that will be phased in this year. The SAE Fellow Grade of Membership was established as a prestigious and honorary grade bestowed on individuals whose extraordinary leadership, engineering, or scientific achievements have brought about meaningful advances in the various fields of mobility engineering. Election to Fellow is an exceptional professional distinction.

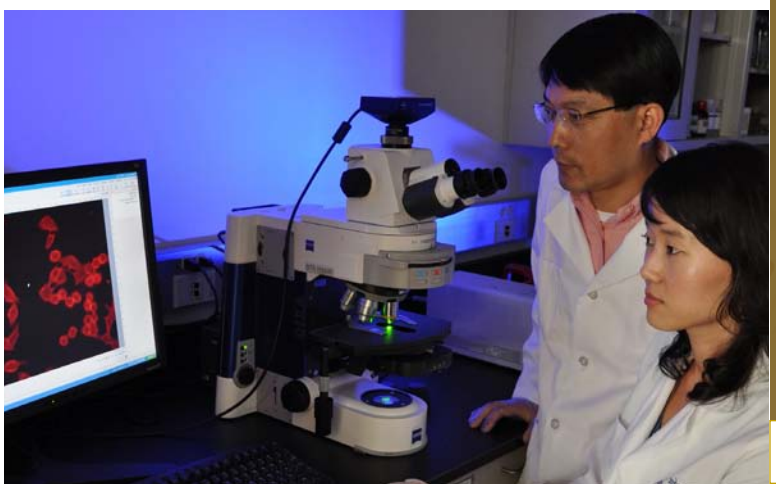
In addition, Dr. Gabler led the research effort on vehicle upper interior/head impact protection in side impact, which was enacted by the National Highway Traffic Safety Administration into a federal law that is estimated will prevent more than a thousand serious brain injuries each year in the U.S. He also conducted the first studies on the use of event data recorder data to develop new crash injury risk relationships, evaluate traditional crash reconstruction techniques, and evaluate the performance of occupant restraints. Dr. Gabler has published one book and more than 100 technical papers. Among his achievements are the Ralph H. Isbrandt Automotive Safety Engineering Award, the SAE Lloyd L. Withrow Distinguished Speaker Award, the Ralph R. Teetor Educational Award, and the NHTSA Superior Achievement Award. Dr. Gabler earned his PhD in mechanical and aerospace engineering from Princeton University.

Dr. Clay Gabler is an Associate Professor of Mechanical and Biomedical Engineering at Virginia Tech. Currently, Dr. Gabler serves as the Associate Head of the Virginia Tech-Wake Forest School of Biomedical Engineering and Sciences and is a faculty member of the Center of Injury Biomechanics. His research focus has expanded to include alcohol sensors in vehicles as a measure to reduce drunk driving deaths.

NanoMedicine: Small Revolution for a Big Splash

By YongWoo Lee

The use of conventional pharmaceutical drugs has been significantly limited by inadequate delivery of therapeutic doses of drugs to the target tissues as well as by occurrence of massive side effects on healthy tissues. One of the most attractive biomedical applications of nanotechnology ("NanoMedicine") is the creation of drug delivery system by conjugating target molecules and therapeutic drugs onto a functionalized nanoparticle. A variety of nanoparticles including polymer, liposomes, dendrimers, quantum dots, and noble metals have been investigated to develop multi-functional and targeted drug delivery systems. This technique has provided great possibilities in developing novel systems that can deliver drugs selectively to targeted tissues or cells and minimize systemic side effects. The potential for using nanoparticles bioconjugated with specific ligands and biologically active compounds to target cell surface molecules, however, has not yet been fully explored. The long-term goal of Dr. Lee's research is to create an innovative and multi-disciplinary research program by developing novel, effective intervention strategies to improve the quality of health through biomedical applications of nanotechnology. Dr. Lee's laboratory, http://www.vascular.sbes.vt.edu, currently focuses on the development of bioconjugated nanoparticles and validation of their effectiveness for targeted drug delivery. The specific objectives are: (1) to design, synthesize, and characterize bioconjugated nanoparticles for targeted drug delivery; and (2) to determine the effectiveness of the bioconjugated nanoparticles in the treatment of human chronic diseases such as atherosclerosis and cancer using cell culture and experimental animal model systems. Studies in this area are anticipated to advance the understanding of how nanotechnology can contribute to improvements in human health as well as to providing new opportunities for diagnostic and therapeutic explorations. Dr. Lee's research will generate and disseminate knowledge to improve human health by interdisciplinary collaborations in biomedical sciences, molecular imaging, polymer chemistry, and nanotechnology. It will also have the potential to translate basic laboratory discoveries into clinically effective treatments that eventually make great contributions to the development of new therapeutic approaches. Dr. Lee's research has been funded by American Heart Association, National Institutes of Health, National Science Foundation, etc.



Virginia Tech
Wake Forest University

School of **Biomedical Engineering and Sciences**

OUR HISTORY WITH BMES

1990 BMES

Virginia Tech hosted the first annual fall BMES conference in Blacksburg Virginia nearly two decades ago. Until that time, BMES had combined with other conferences each year. In light of this new growth opportunity, the 1990 conference theme was "Biomedical Engineering: Opening New Doors." Dr. Donald Mikulecky and Dr. Alexander Clarke, both from Virginia Commonwealth University, were the two Editors of the annual proceedings that year.

2009 BMES

We are bringing over **50 biomedical engineering faculty** and graduate students from Virginia Tech and Wake Forest University for the BMES conference in Pittsburg. These faculty and graduate students will present over **50 papers and posters** highlighting their recent research accomplishments. Please look for these papers and stop by our booth (2324 – 2326) for a chance to learn more about our program and possibly win some great prizes!

Pamela M. Stiff editor

Stefan Duma contributing editor

Alex Parrish graphic artist

Photos by Stefan Duma, Ellen Henson, John McCormick, Alex Parrish, Pamela M. Stiff, and Department of Creative Communications, Wake Forest University Baptist Medical Center.

Wake Forest University School of Medicine

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