**Project Title:** Sonoreperfusion Therapy for Microvascular Occlusion

**Participating Labs/Departments:** Microcirculation Laboratory, Center for Ultrasound Molecular Imaging and Therapeutics, University of Pittsburgh

**Primary Investigator:** John Pacella, MS, MD, Associate professor of Medicine

**Additional Investigators:** John Pacella, MS, MD, Francois Yu, PhD, Xucai Chen, PhD

**Research Description:** There are a number or research studies in the microcirculation laboratory, mostly geared toward optimization of microvascular perfusion. The student will have the opportunity to observe studies pertaining to the following projects (this is not all inclusive):

1. **Microcirculation:**
   a. Studying microembolization and no reflow, which occurs during coronary stenting. This process involves the iatrogenic release of atherosclerotic debris from the vessel wall downstream into the microcirculation. Many of the parameters mentioned above will be assessed, and in addition, we will investigate endothelial function, flow reserve, and functional capillary density.
   b. Studying the microvascular mechanisms of microbubble facilitated sonothrombolysis. This involves the application of ultrasound to acoustically active bubbles, which resonate in the vicinity of blood clot to cause mechanical disruption and clot lysis. The bubbles can be targeted to clot and loaded with drugs to facilitate clot lysis. I am using a one of a kind high-speed (25 million frames per second) microscopic camera to study microbubble-clot surface interactions. These studies involved both in vitro and in vivo models.

2. **Drug Delivery using liposomes.** Drugs encapsulated into liposomes can be released using microbubble cavitation targeted by ultrasound energy. We have encapsulated chemotherapeutic drugs into liposomes (doxorubicin) and are looking at loading other compounds such as nitric oxide donors or tissue plasminogen activator to improve sonoreperfusion therapy.

3. **Microscopy study of sonoporation using voltage sensitive and calcium sensitive dyes.** We are exploring using voltage and calcium sensitive dyes to track sonoporated cells. The advantage of using this approach over usual fluorescent markers (propidium iodide and Calcein AM) is that it can provide real time readout of poration and viability (Live sonoporated cell would exhibit a transient change in fluorescence; Permanently compromised cells (dead cells) would show a permanent fluorescence change) and has the potential to be used in vivo. We need to perform in vitro validation studies comparing these new dyes with gold standard fluorescent markers. These include microscopy studies with cells plated in Opticells for static conditions and designing a microscopy setup with flow ([www.Ibidi.com](http://www.Ibidi.com) for microchannels). This could potentially lead to in vivo experiments (possibly intravital microscopy or hindlimb prep).

4. **Interventional cardiology:** Studying angioplasty balloon pressure-volume relation before, during, and after vessel wall contact.

This is a link to the website of the Center for Ultrasound Molecular Imaging and Therapeutics, where this work is being performed. [http://www.imagingtherapeutics.pitt.edu/](http://www.imagingtherapeutics.pitt.edu/)

**Laboratory/Clinical Exposure:** During the course of the semester, the student will have the opportunity to observe a number of research studies. Additionally, the student will gain clinical
exposure by shadowing in the catheterization laboratory to observe right heart catheterization, left heart catheterization, percutaneous coronary intervention, insertion of left ventricular assist device, percutaneous aortic valve replacement. This will give the student a chance to see the equipment and devices used, and how they relate to human anatomy. The student will have the chance to participate during rounds in the coronary care unit, to gain some exposure to clinical decision-making and to learn how our technologies relate to people.
**Project Title:** Saving lives while not destroying kidneys.

**Participating Labs/Departments:** Rosenbloom Laboratory, Institute for Complex Engineered Systems (ICES), Biomedical Engineering

**Location:** Second Floor, Mellon Institute

**Primary Investigator:** Alan Rosenbloom

**Research Description:** In the U.S. and other industrialized nations, seriously ill patients are admitted to Intensive Care Units (ICU) for close monitoring and around-the-clock care. In the U.S., there are about 5 million ICU admissions each year. Technological advances now allow many patients that would have perished to survive. However, many ICU survivors develop kidney damage (acute kidney injury, AKI) in the process of their illness or its therapy. AKI has reached epidemic proportions, causing diminished kidney function or outright kidney failure in large numbers of patients. Kidney dysfunction can markedly increase medical costs and severely diminish quality of life.

My group is developing an “end to end” robotic system that will collect both patient data and samples for measuring kidney biomarkers related to AKI. This system will allow, for the first time, a detailed matching of molecular and clinical events, with the goals of: (1) Improving the way we care for patients by defining optimal clinical strategies and, (2) Strengthening clinical trials by early recognition of side effects that are harmful to the kidneys. A major goal of our work is to develop a device that can be obtained and operated at a low cost and with minimal staffing requirements. This will allow dissemination of the technology to hospitals of all sizes, not just to select academic medical centers. This is important because, in the U.S., about 75% of patients receive their care in community hospitals.

**Significance:** This project will introduce students to three promising directions in next generation medical practice: (1) Use of biomarkers, (2) Personalized medicine and, (3) Use of “big data” in medicine, i.e. the gathering of high quality data on thousands of patients to optimize their care.

**Engineering Component:** The SURP student who selects this project will build an automated sample dispenser that is crucial to translate patient samples into a laboratory-ready form. This intelligent dispenser will be based on 3D printer technology, for precise X-Y-Z positioning and sample delivery. The student will build the hardware and write the software to create a compact, user friendly device. This work will promote an understanding of the engineering challenges of 3D printing technology, and create practical experience in creating a robotic positioner.

**Clinical Component:**

**Didactics:** Review articles will be used to explore 3 areas in the medical literature: (1) The importance of AKI, (2) the promise of biomarkers, focusing on those detecting kidney injury, and (3) the rapidly expanding role of “big data” in medicine.

**Patient Exposure:** The student will make physician-guided visits to a local Intensive Care Unit to identify patients at risk of AKI and those actually evolving AKI. Patients will then be tracked remotely (without any identifying data), using current clinical indicators (blood urea nitrogen
aka. BUN, creatinine, and urine output). The student will rate the degree of AKI using standard AKI rating scales and follow its course. Schedule permitting, the student will also join Dr. Rosenbloom on ICU rounds (usually available in July and August, 2016).
Project Title: Analyzing CMRI and V-Scan Data

Participating Labs/Departments: Cardiology

Location: AGH Cardiac MRI Lab

Primary Investigator: Robert W.W. Biederman, MD

Research Description: The V-Scan is a portable hand-held ultrasound scanner that can be carried in the physician’s lab-coat pocket. We have an ongoing project to compare V-scan measures in patients with similar measures obtained from Cardiovascular MRI. This project is to compare the V-Scan measures with the CMRI measures using various statistical techniques.

Major/Course/Skill Prerequisites: N/A