Distinguished Medical Engineering Seminar

November 13, 2014 • 4:10 – 5:10 pm • 105 Annenberg
followed by 30-minute social and refreshments

Integrating Hemodynamic Stress and Oxidative Stress to Assess Unstable Plaque

In the U.S., the prevalence of overt coronary artery disease is about 7 million with up to 2 million procedures performed annually. Despite the advent of computed tomographic (CT) angiography, high resolution MRI, intravascular ultrasound (IVUS), near-infrared fluorescence (NIRF),21 and time-resolved laser-induced fluorescence spectroscopy, early identification of mechanically and metabolically unstable plaques remains an unmet clinical need to detect and prevent acute coronary syndromes and stroke. Fluid shear stress, in addition to its mechanical effects on vascular endothelial cells, imparts both metabolic and mechanical effects on vascular endothelial function. A complex flow profile develops at the arterial bifurcations. Oscillatory shear stress (OSS: bidirectional and axially misaligned flow) is considered to be atherogenic, promoting oxidative stress and inflammatory responses, whereas pulsatile shear stress (PSS: unidirectional and axially aligned flow) is deemed atheroprotective, down-regulating pro-inflammatory states. Encouraging results from our interdisciplinary team demonstrated that integration of intravascular shear stress (ISS) and endoluminal electrochemical impedance spectroscopy (EIS) distinguishes pre-atherogenic lesions associated with oxidative stress in fat-fed New Zealand White (NZW) rabbits. In this context, we hypothesize that oxLDL-rich lesions harbor distinct electrochemical properties in the vessel wall that can be measured by frequency-dependent electrochemical impedance to identify metabolically active atherosclerotic lesions. We will integrate a triad of intravascular sensing modalities, shear stress (ISS), ultrasound (IVUS), and electrochemical impedance (EIS), for early detection of metabolically unstable lesions. This integrated sensing system would allow initial detection by disturbed shear, then visualization by IVUS, and then electrochemical characterization by EIS. Overall, by integrating electrochemical signals of active lipid-laden lesions with animal models of atherosclerosis, we will establish early detection of metabolically and mechanically unstable lesions for individualized intervention.

Tzung Hsiai, MD
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Tzung Hsiai received his undergraduate education from Columbia University and his medical education from the University of Chicago. He completed his internship, residency and cardiovascular fellowship at UCLA School of Medicine, followed by an NIH-funded post-graduate training in Biomedical Engineering in 2001. He is a Professor of Medicine and Bioengineering in the Division of Cardiology, UCLA School of Medicine. His research focuses on mechanobiology of cardiovascular diseases. His group has demonstrated that spatial ($\partial\tau/\partial x$) and temporal ($\partial\tau/\partial t$) variations in shear stress modulate post-translational oxidative modifications of low density lipoprotein protein (LDL) and mechano-signal transduction of mitochondrial redox states. These findings led to a first joint textbook for the field of mechanotransduction entitled "Hemodynamics & Mechanobiology of Endothelium." Tzung Hsiai has been actively promoting Team Science, as evidenced by his multi-disciplinary NIH supports with Caltech, USC and UCSD. He has chaired the Biomedical Engineering Society joint meeting with the American Physiological Society (FASEB) to promote transdisciplinary collaboration. He is a member of NIH Bioengineering, Technology, and Surgical Sciences Study Section, the American Society for Clinical Investigation, Fellow of American Heart Association, and the recipient of an American Heart Association John J. Simpson Outstanding Research Achievement Award.