



brain+cognitive sciences

2008 Fall Colloquium Series

Speaker Elisa E. Konofagou, Dept. of Biomedical Engineering,
Columbia University, New York, NY

Time 4pm, Departmental Tea immediately following.

Date Friday, 3 October 2008

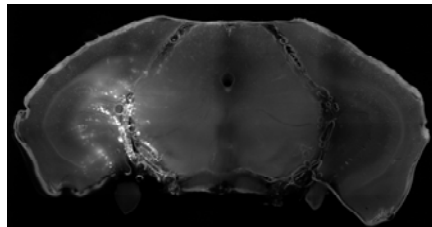
Place BCS Auditorium, 46-3002

Title Brain Molecular Imaging and Molecular Delivery
Through the Blood-Brain Barrier In Vivo.

Host Emery Brown

Abstract:

Current treatments of neurological and neurodegenerative diseases are limited due to the lack of a truly non-invasive, transient, and regionally selective brain drug delivery method. The brain is particularly difficult to deliver drugs to because of the blood-brain barrier (BBB). The impermeability of the BBB is due to the tight junctions connecting adjacent endothelial cells and highly regulatory transport systems of the endothelial cell membranes. The main function of the BBB is ion and volume regulation to ensure conditions necessary for proper synaptic and axonal signaling. However, the same permeability properties that keep the brain healthy are the reason for the difficulty in its pharmacological treatment. The BBB prevents most neurologically active drugs from entering the brain and, as a result, has been isolated as the rate-limiting factor in brain drug delivery. Until a solution to the trans-BBB delivery problem is found, treatments of neurological diseases will remain impeded. In this presentation, the role of focused ultrasound in the non-invasive and localized treatment of neurodegenerative disease is explored. Over the past few years, we have been developing methods that combine Focused Ultrasound (FUS) and microbubbles in order to noninvasively, locally and transiently open the BBB so as to treat neurodegenerative diseases. We will first focus on the feasibility of Magnetic Resonance (MR) and fluorescence imaging enabled by the FUS-induced BBB opening. In addition, the type of molecular delivery that can be induced through the opened BBB will be characterized and its potential role in the treatment of central nervous system (CNS) diseases, such as Alzheimer's and Parkinson's, will be discussed. More specifically, we will determine important properties of the BBB opening such as its size and permeability as well as the range of molecular sizes of compounds that can cross it. The role of the microbubble type, size and concentration on the BBB diffusion properties, its reversibility and the pressure threshold for the opening in vivo will also be described. Finally, results will be shown in both non-transgenic (normal) and transgenic (Alzheimer's) mice in order to determine the variability of the properties of the opened BBB in the presence and absence of disease.



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