

CARNEGIE MELLON UNIVERSITY

BME 2020 SUMMER SEMINAR SERIES



FUS-mediated localized disruption of drug-plasma protein-binding as a new mode of neuromodulation



PRESENTED BY

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SCHEDULE

**Thursday, September 3,
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(10:00 AM-11:00AM)

Transcranial focused ultrasound (tFUS)-based strategies for non-invasive and localized neuromodulation are rapidly expanding. The experiences in this field through animal models and human studies will be briefly discussed. As a new mode of brain functional modulation, we introduce the evidence that low-intensity ultrasound modified the plasma protein binding (PPB) whereby PPB plays an important role in drug pharmacokinetics, particularly for central nervous system drugs. We demonstrate the non-invasive and localized unbinding of PPB from phenytoin, an anti-epileptic drugs with high affinity to albumin, using FUS delivered in a pulsed manner. No microbubble-based ultrasound contrast agent was used. Equilibrium dialysis was performed on the sonicated saline sample containing therapeutic concentration of phenytoin and bovine serum albumin, which yielded elevation in the level of unbound phenytoin compared to an unsonicated control. Sonication of a brain hemisphere in rats that received intraperitoneal phenytoin showed elevated regional phenytoin uptake compared to the unsonicated hemisphere. Temperature change was not seen without evidence of disruption of the blood brain barrier (BBB). FUS, as a novel technique for spatially-selective unbinding of PPB, may alter a wide range of drug-plasma protein interactions and enhancing drug delivery.

