Five decades of PET neurochemical imaging:

What the images contributed to the understanding of neuropsychopharmacology and CNS drug development

Come and join us for this interesting talk.

- **Time:** Thursday 2 July at 14:00
- **Place:** Forum Lunch Room, A701-104
- **Speaker:** Dean F Wong MD PhD FACNP FSNMMI
- **Title:** Five decades of PET neurochemical imaging: What the images contributed to the understanding of neuropsychopharmacology and CNS drug development

  Organized by: Albert Gjedde and Translational Neuropsychiatry Unit
- **Registration:** Everyone is welcome and no registration is required

ABSTRACT

Over the past four decades, positron emission tomography (PET) neurochemical imaging has transformed our ability to quantify human brain neurotransmitter systems in vivo and to rationally develop central nervous system (CNS) therapeutics. As Professor in the Kahlert Institute for Addiction Medicine and the Department of Neurosurgery at the University of Maryland Baltimore, I now work within a unique preclinical and translational ecosystem that integrates molecular imaging, addiction neuroscience, and interventional neuromodulation. In this talk, I will review key advances from early dopamine D2 receptor imaging and the first demonstrations of age-related changes and elevations of D2 receptors in schizophrenia, through to contemporary applications that span psychosis, addiction, movement disorders, and dementia.

I will highlight how quantitative receptor imaging and occupancy studies at Johns Hopkins and Washington University enabled mechanism-based dose selection and target engagement for multiple FDA-approved antipsychotics (including partial D2 agonists and novel D2 antagonists), as well as for emerging treatments such as the investigational agent LB-102 and psilocybin acting at 5-HT2A receptors. I will then discuss lessons learned from the development and comparative evaluation of novel PET radiopharmaceuticals for memory and neurodegeneration, including first-in-human studies of F-18 florbetapir for amyloid imaging and second-generation tau tracers such as F-18 RO948, and how these approaches inform current translational studies in addiction and neuroinflammation.

Building on this foundation, I will describe ongoing collaborations in Neurosurgery that leverage focused ultrasound as a noninvasive tool to modulate circuits that have been characterized with PET, bridging my prior Brain Initiative work on voltage-sensitive probes and photoacoustic readouts with current preclinical and clinical translation at the Kahlert Institute. Within this framework, we aim to link receptor-level pharmacology, neuroimmune imaging (e.g., S1P1 and related targets), and circuit-level interventions to develop and test novel therapeutic strategies for substance use disorders and related neuropsychiatric conditions. Finally, I will outline future directions that exploit the unique imaging and neuromodulation environment at the University of Maryland Baltimore, which includes three focused ultrasound systems for clinical and preclinical studies (with a human FUS system adjacent to the Siemens PET–MRI facility) and a 7 T MRI with a PET insert for preclinical imaging, perhaps as a basis for potential PET–MRI and focused ultrasound collaborations with the Martinos Center.

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