THz Spectroscopic Response of Brain Tissue Exhibiting Alzheimer's Disease

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Alzheimer's disease (AD) is the primary cause of dementia, and its root cause remains uncertain with no effective cure. Pathological inspection typically characterizes AD as amyloid beta ($A\beta_{42}$) plaques buildup, tau protein hyperphosphorylation, and neurofibrillary tangles (NFT) in the gray matter of the brain. As a result, AD has primarily been considered a disease of gray matter, however, recent publications on white matter abnormalities such as axonal loss and demyelination have been also suggested as important characteristics of AD.

Based on the abovementioned neuropathological indicators, particularly the misaggregated state seen with β-amyloid buildup, we embarked on THz-Time Domain Spectroscopy (TDS) reflection spectroscopic studies comparing AD and normal brain tissue specimens. THz waves are safe (non-ionizing), and they can provide highly resolved spectral information corresponding to characteristic responses of biochemical molecules. In addition, the high sensitivity of THz waves to tissue hydration enables contrast between healthy and diseased/damaged areas within the tissue such as with skin burns and malignant tumors. Even for dehydrated tissue specimens, such as with biopsies typically prepared for retrospective pathologic study, morphological variations due to local and metastatic malignancies are also measurable via THz spectroscopy. Previous work, including research conducted in our laboratory, has used time domain spectroscopy (TDS) or continuous wave (CW) THz spectroscopy to examine major human tissue groups and associated diseases ranging from cancer to skin burns.

In this study, we investigate the THz response of human brain tissues with AD using broadband time domain THz spectroscopy, studying both formalin-fixed and paraffin-embedded samples from the hippocampus and cerebral cortex. We demonstrate that the THz response of neuropathological changes in gray and white brain matters for samples with AD exhibits detectable differences compared to healthy control tissues. These results offer the possibility, for the first time, of detecting AD using THz imaging, *ex vivo* as in this study and potentially *in vivo* as THz imaging technologies continue to improve. Considering further case studies, we are formulating a hypothesis to diagnose AD based on THz reflection spectroscopy. At the conference, we will present spectroscopic differences between grey matter exhibiting Alzheimer's disease and normal control samples.