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High resolution, non-invasive multimode optical imaging: A proposed diagnostic and assessment tool in Alzheimer's Disease

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Statement of the Problem: Alzheimer's Disease (AD) is a major unmet health challenge characterized by (a) fast increasing incidence and costs; (b) very late diagnosis.

Methodology: Our group has recently [1] introduced optical imaging in the retina as a non-invasive method for mapping the occurrence, size and location of beta amyloid plaques, the primary pathology in AD. We have shown that using the fluorescence of curcumin, which attaches specifically to these plaques, we could quantitate the features of these plaques, including in vivo, and even document their reduction by immune treatments. These preclinical studies were also extended to the clinical domain, by using archival human eyes from patients with known levels of AD, as assessed both by brain histopathology and cognitive impairment (prior to death). We present a method for extending such studies to living patients, still using the retina as the window to the brain and plaques as indicators, but without the use of an extrinsic biomarker such as curcumin (as in [1]). This raises the level of experimental difficulty, thus requiring new technologies that we invented and/or perfected.

Findings: We designed a multimode optical imaging instrument, essentially a new type of confocal scanning laser ophthalmoscope, with some (needed) performance advantages over current commercial offerings. Our system consists of the following elements, all proprietary, and patent-protected: (a) A highly versatile light source: pulsed, 400-1400 nm, with ~1 nm resolution; (b) A new galvanometric method of scanning, with synthesized pivot point, not requiring a custom coupling lens; (c) Spectral analysis of imaging data, including hyperspectral image segmentation and elimination of background; (d) A more sensitive method of detecting light, via parametric

Conclusion & Significance: This new instrument achieves significant improvements in all of the following: spatial resolution, imaging depth, imaging angle in the retina (and thus spatial coverage), sensitivity and specificity. It will be used to image, fast and non-invasively, amyloid plaques in the retina, and any other retinal features of interest. We envisage that this instrument and the approach it enables should be used in AD drug/treatment trials, as it allows the repeatable, non-invasive and quantitative imaging of amyloid plaques (via both their autofluorescence and scattering), and of their relationships with important structures in the eye, such as blood vessels.

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