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The Potential of Polarization Imaging of the Eye to Provide a Window on the Brain in Alzheimer's Disease and Malaria

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Imaging the retina may provide a “window on the brain”, potentially enabling diagnosis of neural conditions. Two of these are malaria and Alzheimer's disease (AD). AD is a neuro-degenerative disease, characterized by the formation of insoluble fibrils (plaques) composed of amyloid beta proteins. There is currently no definitive diagnosis available prior to death. Neurotoxic effects of amyloid beta have been demonstrated in the retinas of animal models and human retinal function is affected by AD. Previously, our group was among the first to find amyloid beta in the retinas of those diagnosed with AD and we have demonstrated that polarization imaging could improve the visibility of malaria in retinal vessels. Here we will describe the development of non-invasive imaging methods that might be used for *in vivo* diagnosis of both conditions. Imaging in the human retina in both malaria and Alzheimer's disease (AD) could lead to a better understanding of the diseases and earlier and more accessible diagnoses.

Whole mounts were prepared of post-mortem retinas of subjects with AD and malaria and of age matched subjects without disease. In the AD study, retinas were stained with thioflavin S and examined using a fluorescence microscope. Previously, in some retinas, positive for AD, fluorescently labeled structures near the retinal surface were studied using Atomic Force Microscopy.

The polarization properties of the *ex vivo* retinas were imaged under crossed polarizers along with the surrounding retina. In addition, spatially defined Mueller matrices were found by imaging in a microscope modified with an adjustable polarization generator and an analyzer.

We have confirmed the presence of amyloid beta in the *ex vivo* neural retina of those with AD and not in age matched normal donors without the disease with sensitivity and specificity each at 75%. The polarization properties of amyloid beta deposits differed significantly from those of bare glass from the surrounding retinal tissue and from control retinas. Ours are the first measurements of the polarization properties of unstained amyloid beta. We believe that the *in vivo* imaging methods that we are developing could become a more accessible, less invasive and less expensive technique than others under development for the diagnosis of malaria affecting the brain and Alzheimer's disease.

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