VISIBLE LIGHT OPTICAL COHERENCE MICROSCOPY OF THE BRAIN WITH ISOTROPIC FEMTOLITER RESOLUTION *IN VIVO*

Shau Poh Chong,[1,†] Conrad William Merkle,[1,†] Aaron Michael Kho,[1] Jun Zhu,[1] Alfredo Dubra,[2] and Vivek Jay Srinivasan[1,*]
[1]Biomedical Engineering Department, University of California Davis, 95616, USA.
[2]Byers Eye Institute, Stanford University, Palo Alto, California 94303, USA.
†Equal contributions * vjsriniv@ucdavis.edu

KEY WORDS: Optical coherence tomography, medical and biological imaging, visible laser, *in vivo* mouse brain imaging, scattering tissues.

1. ABSTRACTS

Most flying-spot Optical Coherence Tomography (OCT) and Optical Coherence Microscopy (OCM) systems use a symmetric confocal geometry, where the detection path retraces the illumination path starting from and ending with the spatial mode of a single mode optical fiber. Here, we describe a visible light OCM instrument [1] that breaks this symmetry to improve transverse resolution without sacrificing collection efficiency. This was achieved by overfilling a water immersion objective on the illumination path, while maintaining a conventional Gaussian mode detection path ($1/e^2$ intensity diameter ~ 0.82 Airy disks), enabling ~1.1 μm full-width at half-maximum (FWHM) transverse resolution. At the same time, a ~ 0.9 μm FWHM axial resolution in tissue, achieved by a broadband visible light source, enabled femtoliter volume resolution. We characterized this instrument according to paraxial coherent microscopy theory, and finally, used it to image the meningeal layers, intravascular red blood cell-free layer, and myelinated axons in the mouse neocortex *in vivo* through the thinned skull (Figure 1).

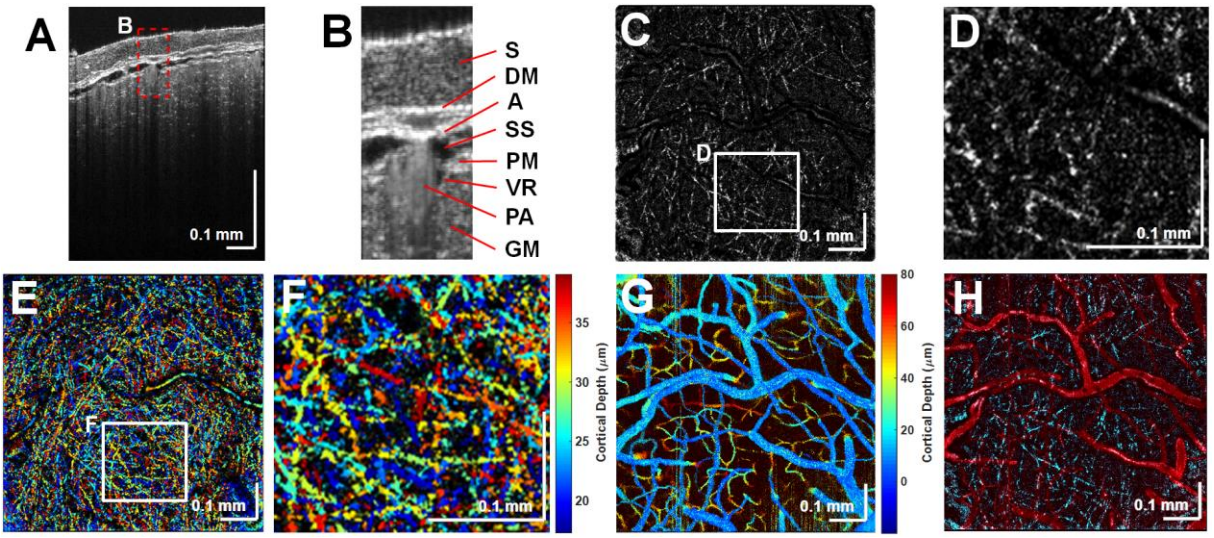

Figure 1 Structural cross-sectional imaging of the mouse neocortex (A) with labeled meningeal layers (B). S: skull, DM: dura mater, A: arachnoid, SS: subarachnoid space, GM: gray matter, PM: pia mater, PA: pial artery, and VR: Virchow-Robin space (dark region next to PA). Myelin is shown in 6 μm thick *en face* maximum intensity projections (C-D). (E) Depth encoded color display of myelinated axons and (F) zoomed in version of white box in (E). (G) Depth-encoded color display of angiogram. (H) Overlay of the *en face* projections of angiogram (red) and the myelinated axons (cyan).

[1] C. W. Merkle, S. P. Chong, A. M. Kho, J. Zhu, A. Dubra, and V. J. Srinivasan, "Visible light optical coherence microscopy of the brain with isotropic femtoliter resolution *in vivo*," Optics Letters 43, 198-201 (2018).