Integrated photoacoustic microscopy, optical coherence tomography and fluorescence microscopy imaging of rabbit ocular neovascularization *in vivo*

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Background, Motivation, and Objective:

Ocular neovascularization is a major cause of vision loss and blindness, and is a main marker of numerous retinal diseases. Early diagnosis can be highly beneficial to the treatment of angiogenesis related ocular diseases. Many imaging modalities have been adapted to the diagnosis and characterization of ocular neovascularization. Although these modalities can provide valuable information, each is suffering by certain limitations. A multi-modality platform that can combine the advantages of current imaging technologies with the access to additional functional and molecular information is in high demand in the field of ophthalmology.

Statement of Contribution/Methods:

A multimodality imaging system with integrated optical coherence tomography (OCT), photoacoustic microscopy (PAM), and fluorescence microscopy (FM) has been developed to evaluate the angiogenesis in clinically relevant larger animal eyes. High resolution in vivo imaging was performed in live rabbit eyes with different disease models, including vascular endothelial growth factor (VEGF)-induced retinal neovascularization, laser induced retinal vein occlusion and high intraocular pressure.

Results/Discussion:

PAM images can selectively show the vasculature grown over the retina. Different retinal layers can be indicated by OCT B-mode image. The leakage property of ocular neovascularization can be shown by FM with fluorescein sodium. Quantitative analysis of ocular neovascularization has been achieved by PAM. The experimental results demonstrate that the multi-modality imaging system can noninvasively visualize neovascularization in both albino and pigmented rabbits for characterization of retinal pathology. Besides imaging based on the endogenous contrast, this system can be further powered by molecular contrast agents. Biomarker-conjugated nanoparticles, including both organic hydrogel based and gold nanostructure based, have been involved in our PAM and OCT imaging of eye diseases, and facilitated imaging of neoangiogenesis at the molecular level. This work presents the first description of a multi-modality PAM, OCT, and FM system for visualization of angiogenesis in large animal eye, and could be an important step toward the clinical translation of the technology.

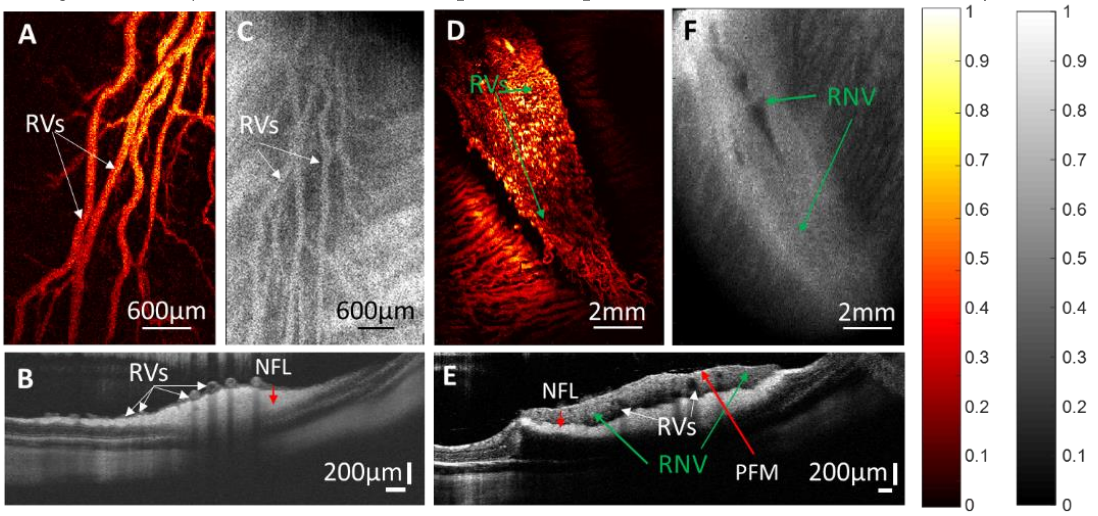

Figure 1. Multi-modality images with rabbit normal retinal vessels and retinal neovascularization. (A-C) PAM, OCT and FM images with normal rabbit retinal vessels. (D-F) PAM, OCT and FM images with normal rabbit retinal neovascularization. RVs: retinal vessels; NFL: nerve fiber layer; RNV: retinal neovascularization; PFM: preretinal fibrovascular membrane.