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Recent advances in Spatio-Temporal Optical Coherence Tomography (STOC-T) for *in vivo* cellular-level imaging of the human retina

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1. Introduction

The human retina consists of specialized cells such as ganglion cells, amacrine cells, and photoreceptors, whose degeneration leads to vision disorders and neurodegenerative diseases. Early detection and monitoring of structural changes in the retina are crucial for diagnosis and treatment. A well-established method for non-invasive *in vivo* retinal imaging at the cellular level is Optical Coherence Tomography (OCT) with adaptive optics; however, this method is costly, time-consuming, and requires complex calibration. The Fourier Domain Optical Coherence Tomography (FD-OCT) method for signal acquisition enables rapid, non-invasive and volumetric imaging of retinal structure in the living human eye, which are one of the most important challenges of modern ocular disease diagnosis. The conventionally FD-OCT devices which are based on scanning method have a trade-off between transverse resolution and depth of field. Therefore, in recent years the method which allows simultaneous imaging of retina structure with large depth of field in the full field of view (Full Field FD-OCT, FF-FD-OCT) has been developed. The FF-FD-OCT method provides: (a) access to stable spatial phase information, (b) consistent and high power density over the axial direction, and (c) possibilities to design the illuminating beam shape. What is more due to the lack of the confocal parameter in FF-FD-OCT, there is no need to balance between the lateral resolution against the imaging range. FF-FD-OCT utilizes a rapidly tunable laser sources and data acquisition with an ultrafast camera at 10 GHz voxel rate. However, due to the use of a spatially coherent illumination, the acquired signal is vulnerable to strong amplitude modulation caused by multiple interference of multiply scattered light arising from different structures of the measured object [1]. This modulation is a part of the speckle pattern, which contains both object information and coherent cross-talk noise. Unfortunately, the cross-talk noise limits the imaging depth range of FF-FD-OCT and makes imaging of the deeper layers of the retina unavailable in high image quality. In recent years, a new imaging technique named Spatio-Temporal Optical Tomography (STOC-T) [2], [3] has been proposed to address this limitation. This method uses light source with controlled spatial and temporal coherence and enabled the acquisition of high-contrast and high-resolution projection images of the retina. STOC-T reducing spatial coherence in the system by connecting a swept-source laser to the imaging system with appropriately selected multimode optical fiber. The result is selective interference, depending on the spatial coherence at a given point, which allows suppression of noise in the full illumination field. The developed STOC-T system modification provides: increased transverse resolution of approximately 3 μm and an enhanced signal-to-noise ratio of ~12dB through the use of a deformable mirror (vibration frequency ~1.5 MHz) at the input to the measurement system [4].

2. Methods and results

This work presents the latest structural data from the *in-vivo* imaging of the human retina, collected using the updated STOC-T system (with respect to the previously one reported in [4]). The key advancement involves replacing the previously used active mode control module, which consisted of a deformable membrane and a 300-meter multimode fiber, with a passive solution utilizing a 600-meter multimode fiber. This change not only simplifies the optical setup by eliminating the need for dynamic control but also ensures the spatio-temporal phase randomization, which is essential for speckle noise suppression. This solution provides the same improvement in SNR when using the magnitude averaging technique ~11dB. During the data acquisition several 3-D volumes containing 512 images with 512x512 pixels each at a rate of 60000 fps were collected sequentially. Figure 1 shows B-scan and *en face* images reconstructed from measurement of healthy 20-years volunteer. The study protocol was approved by the ethics committee appointed in accordance with the regulations (approval no. KB 87/ 2021). The following cross-sectional views are shown in Fig. 1: inner plexiform layer (IPL), inner nuclear layer (INL), combined IPL and INL, the layers corresponding to the location of the ends of the photoreceptor outer segments for the S cones, M and L cones. We demonstrate a modified STOC-T experimental system, with an increased lateral resolution of ~3 μm, and optimized illumination to enable *in vivo* cellular-level imaging of the human retina.

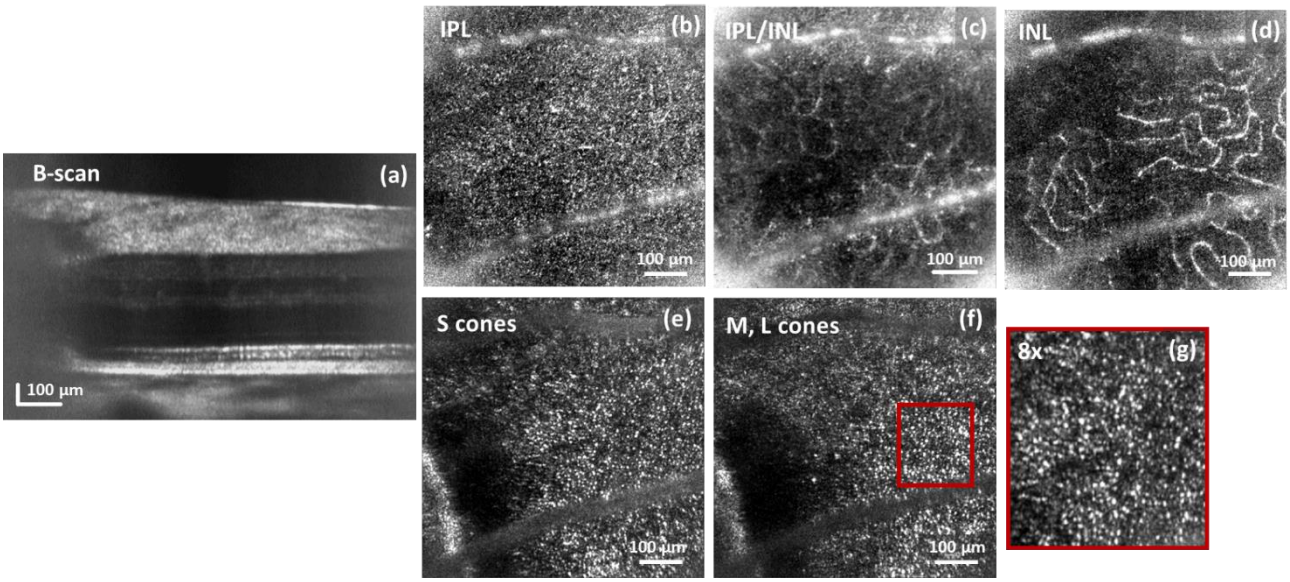

Fig. 1. STOC-T imaging of retinal microstructure: (a) cross-sectional image of the internal microstructure (B-scan), (b) inner plexiform layer (IPL), (c) combined IPL and inner nuclear layer (INL), (d) inner nuclear layer (INL), the layers corresponding to the location of the ends of the photoreceptor outer segments for the (e) S cones, (f-g) M and L cones.

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4. References

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