MEDICAL UNIVERSITY OF VIENNA

Quantification of intrinsic optical signals in the outer human retina using optical coherence tomography

R.M. Werkmeister[1,2], Alina Messner[1], H. Stegmann[1,2], L. Schmetterer[1,2,3], Doreen Schmidl[4], Rainer Leitgeb[1], V. Aranha dos Santos[1]

1 Center for Medical Physics and Biomedical Engineering, Medical University Vienna, Austria
2 Christian Doppler Laboratory for Ocular Effects of Thiomers, Vienna, Austria
3 Singapore Eye Research Institute, Singapore
4 Department of Clinical Pharmacology, Medical University Vienna, Austria

Objective

Optoretinography comprises technologies that, based on optical methods such as OCT, measure stimulus-evoked changes in the optical properties of the retina. The changes evoked by visible light are called **intrinsic optical signals (IOS)** and can serve as an indicator of the state of the photoreceptor function, making them a promising biomarker for early detection of retinal diseases.
We employed a commercial OCT system and an OCT signal model for evaluation of optical path length (OPL) changes in the temporal outer retina of healthy subjects during light adaptation.

Methods

OCT

- Zeiss Meditec Cirrus HD-OCT
- Central wavelength: 840 nm
- Resolution: 5 µm axial, 15 µm
- Acquisition speed: 27 000 A-scan/s

White light stimulation

- Light therapy device

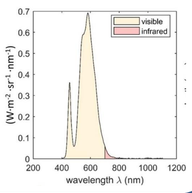

Image acquisition

- 5 healthy subjects
- Temporal retina
- Retinal eccentricity of 14 degrees
- 3.0 x 2.4 mm², 320 x 300 x 1024 voxels
- 15 baseline, 15 light stimulation

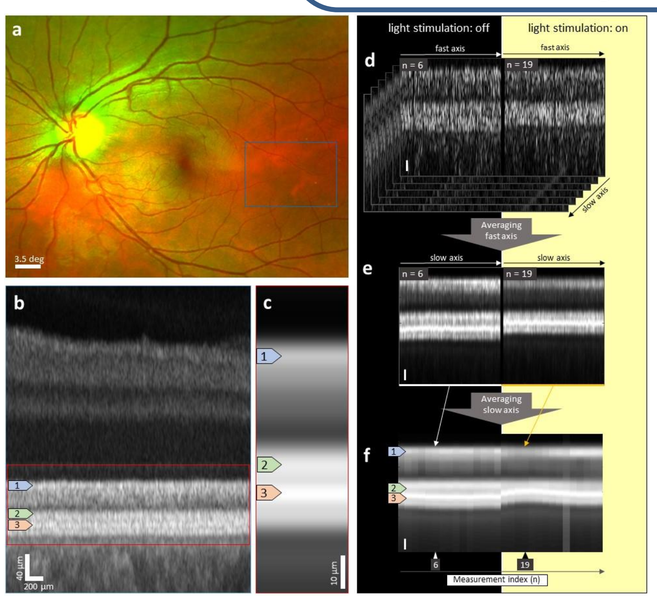

Fig. 1 Measurement scheme for assessment of IOS in the peripheral retina. (a) Exemplary ROI in a fundus image. (b) B-scan in the centre of ROI with marked measurement area in the outer retina. The A-scans were registered to the IS/OS junction and the B-scan was flattened. (c) A-scan average - Average of all registered A-scans. (d-f) Measurements with varying degree of averaging before (left) and after (right) light stimulation. Scale bars correspond to 10 µm. n is the measurement number and therefore provides a non-linear axis of time. (d) Flattened, native B-scans in which each column is one A-scan. (e) Each tomogram was averaged along the fast axis and represents one volume. Each column in an image represents one B-scan. (f) After averaging all A-scans of one volume (= A-scan average at one time point), the graph shows the OPL change between IS/OS junction and RPE over time [1].

OCT signal model

A **signal model** for the A-scan averages, based on the sum of seven Gaussian curves and linear slope correction for compensation of the sensitivity decay of the OCT signal, was developed.

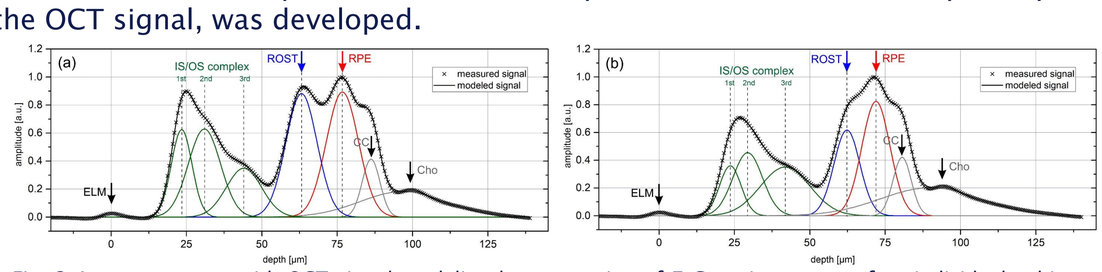

Fig. 2 A-scan averages with OCT signal modeling by summation of 7 Gaussian curves of an individual subject before and after light stimulation. Crosses represent the measured data points, the black line is the summation of the individual model curves. (a) Measurement during **ambient room light** before light stimulation. (b) Measurement during **white light stimulation**. ELM, external limiting membrane; IS/OS, inner segment/outer segment complex; ROST, rod outer segment tips; RPE, retinal pigment epithelium; CC, choriocapillaris; Cho, choroid [2].

Fig. 3 Positions of retinal boundaries in the OCT amplitude signal and the OCT signal model and corresponding distances to the ELM as internal reference [2].

Results

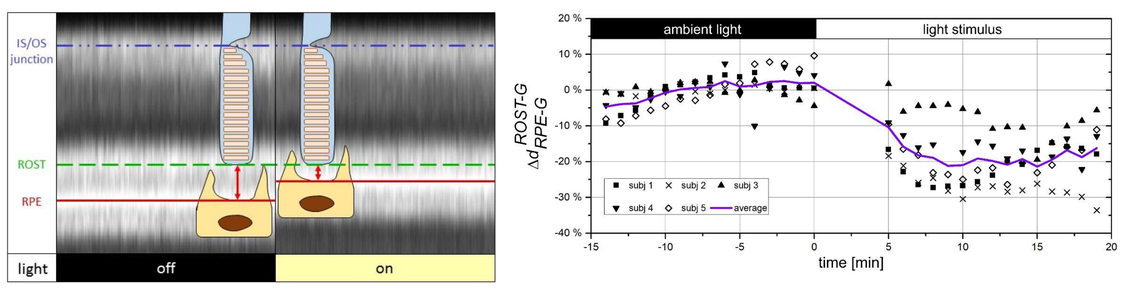

Fig. 4 OPL change between ROST and RPE. (a) B-scans of the outer retina before and after light stimulation and schematic interpretation of the cells' involvement in the OPL decrease between IS/OS junction and RPE after light stimulation. (b) Relative distance change between the peaks attributed to ROST and RPE [1,2].

The OPL between the ELM and the RPE decreased by 5.2 ±0.9% versus baseline, while OPL between ELM and ROST showed an initial decrease by 2.1 ±1.6% versus baseline and, thereafter, increased by 2.8 ±2.1% versus baseline. OPL changes of the other outer retinal layers during light stimulation are depicted in Fig. 5.

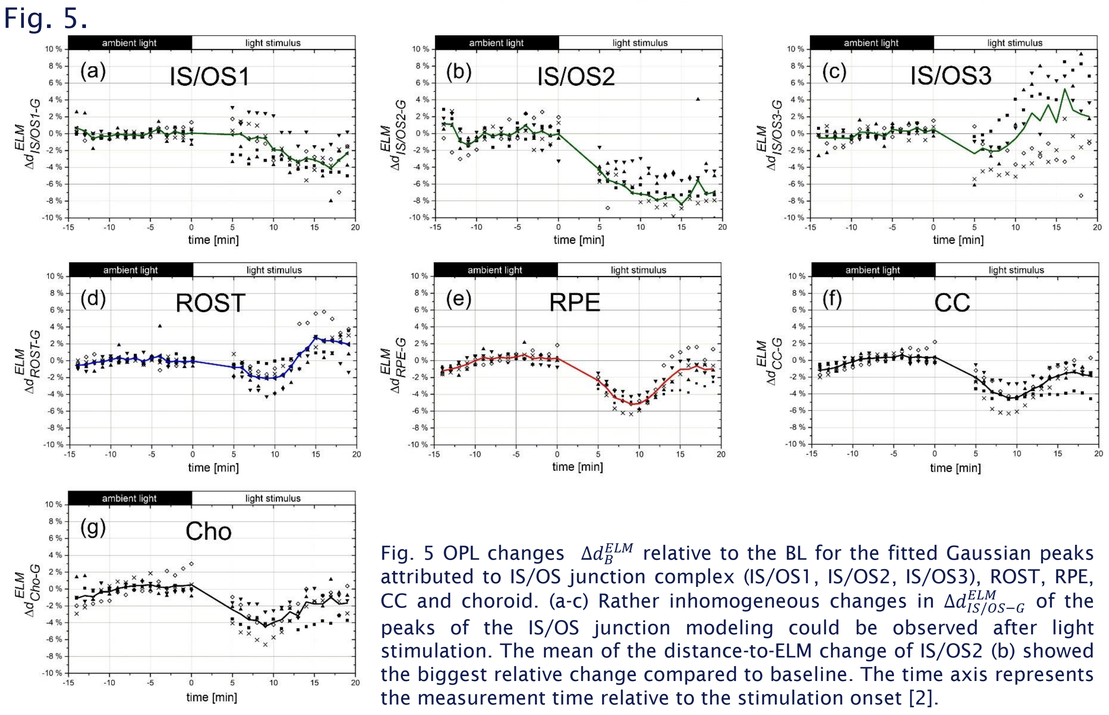

Fig. 5 OPL changes Δd_B^{ELM} relative to the BL for the fitted Gaussian peaks attributed to IS/OS junction complex (IS/OS1, IS/OS2, IS/OS3), ROST, RPE, CC and choroid. (a-c) Rather inhomogeneous changes in $\Delta d_{IS/OS-G}^{ELM}$ of the peaks of the IS/OS junction modeling could be observed after light stimulation. The mean of the distance-to-ELM change of IS/OS2 (b) showed the biggest relative change compared to baseline. The time axis represents the measurement time relative to the stimulation onset [2].

Origin of the IS/OS3 peak

Measurements at five locations at retinal eccentricities of 0, 3.5, 7, 10.5, and 14 degrees (Fig. 6) revealed position-related alteration of the signal of the IS/OS junction complex.

Fig. 6 Measurement positions at retinal eccentricities of 0, 3.5, 7, 10.5, and 14 degrees.

IS/OS3-G that showed an increase in $\Delta d_{IS/OS3-G}^{ELM}$ with decreasing eccentricity (Fig. 7). A possible explanation could be that IS/OS3 is not part of IS/IS junction complex, but represents the **cone outer segment tips** (COST), a hypothesis that is supported by the fact that cone OS length is greatest in the fovea and decreases with increasing retinal eccentricities.

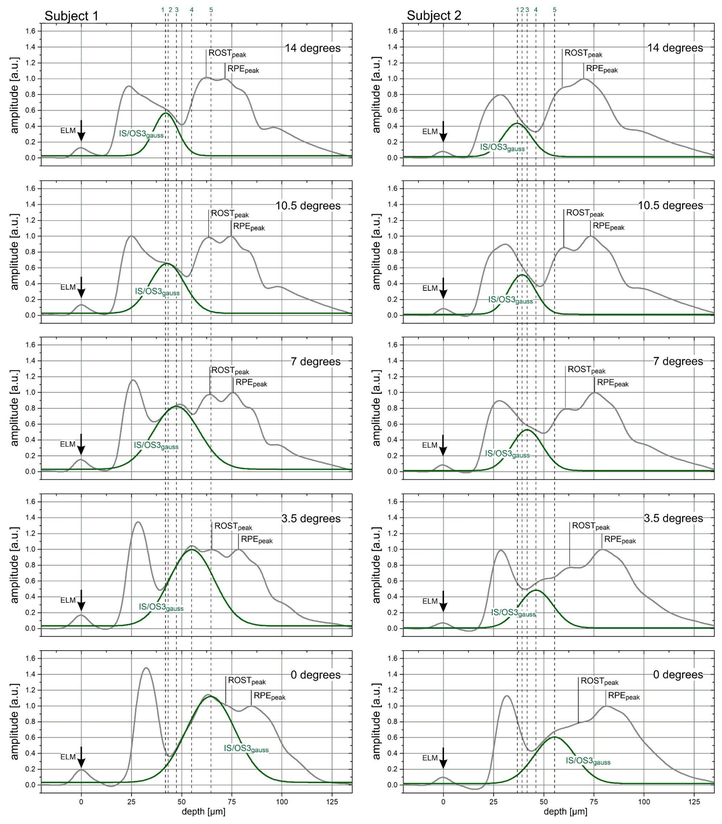

Fig. 7 Position of the IS/OS3 peak at different retinal eccentricities. The profile in the upper panel (14 deg.) correspond to the measurement location employed for the assessment of IOS during white-light stimulation of the retina while in the lowest panel (0 deg.), the volumetric OCT scan was centered at the macular region [2].

Conclusion

Change in the subretinal space occurring in the context of light adaptation could be measured using a standard OCT platform and a dedicated signal model. The measured IOS could ultimately serve as biomarkers for the investigation of the health of the outer retina.

References

[1] Messner A, Werkmeister RM, Seidel G, Stegmann H, Schmetterer L, Aranha Dos Santos V "Light-induced changes of the subretinal space of the temporal retina observed via optical coherence tomography" Scientific Reports, Volume 9, Issue 1: 13632 (September 2019)
[2] Messner A, Aranha dos Santos V, Stegmann H, Puchner S, Schmidl D, Leitgeb R, Schmetterer L, and Werkmeister RM "Quantification of intrinsic optical signals in the outer human retina using optical coherence tomography" Ann N Y Acad Sci, Volume 1510, Issue 1: 145-157 (December 2021)