High-Resolution Optical Coherence Tomography in Pathology of the Vitreomacular Interface

Enrico Bernardi[1,2], Lorenzo Ferro Desideri[1,2,3], Karin Paschon[1], Ines Schumacher[1], Nicola Sagurski[1], Yousif Subhi[4,5,6], Janice Roth[1,7], Martin Zinkernagel[1,2], Rodrigo Anguita[1,7]

1. Department of Ophthalmology, Inselspital, Bern University Hospital, University of Bern, Freiburgstrasse 15, CH-3010, Bern, Switzerland; 2 Department of Ophthalmology, Belfast Health and Social Care Trust274 Grosvenor Rd, Belfast BT12 6BA, UK
3. Faculty of Medicine, University of Bern, Murtenstrasse 11, Bern, CH-3008, Switzerland 4. Department of Ophthalmology, Rigshospitalet, Glostrup, Denmark; 5. Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark;
2. 6. Department of Clinical Research, University of Southern Denmark, Odense, Denmark; 7. Moorfields Eye Hospital NHS Foundation Trust, London, UK

Purpose

To evaluate the diagnostic performance of high-resolution optical coherence tomography (HR-OCT) compared with spectral-domain OCT (SD-OCT) in detecting microstructural biomarkers in vitreomacular interface (VMI) diseases.

Methods

- **Design:** Prospective cross-sectional study
- **Imaging:**
  - SD-OCT (Spectralis HRA-OCT)
  - HR-OCT (Heidelberg SPECTRALIS® High-Res OCT-DMR001, 3 µm axial resolution)
- **Analysis:**
  - Biomarkers: EZ, ELM, and IZ integrity; intraretinal cysts; epiretinal glial tissue; hyporeflective dots (ONL and GCL); “cotton ball” sign
  - 3 masked graders; inter-grader agreement via Cohen’s Kappa

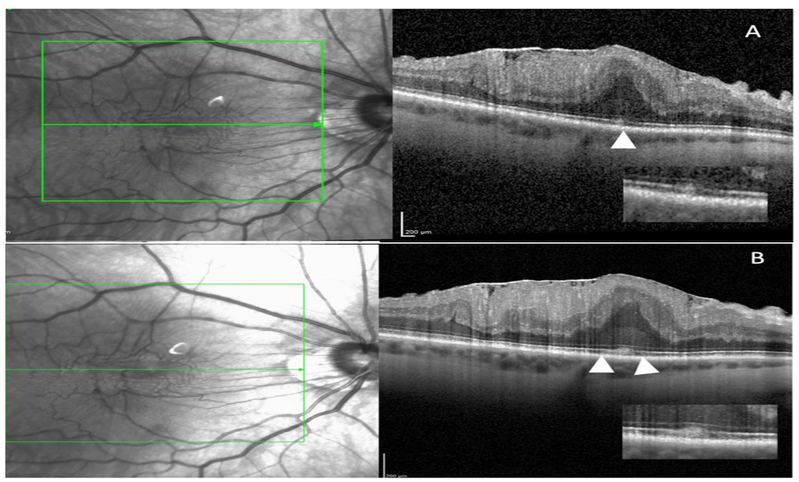

Figure 1 ‘Cotton ball sign’ in a patient with epiretinal membrane. A standard OCT scan reveals the presence of a small hyperreflective vitelliform material in the foveola between the ellipsoid zone and external limiting membrane without clear impairment of interdigitation zone (IZ) (white arrowhead) B) In HR-OCT beside the hyperreflective material it is possible to identify focal disruption of the IZ in the area around the lesion, probably due to mechanical forces compressing and impairing this thin retinal structure (white arrow heads). Moreover, in ONL an hyperreflective halo around the cotton ball is more clearly distinguishable in comparison with the standard acquisition.

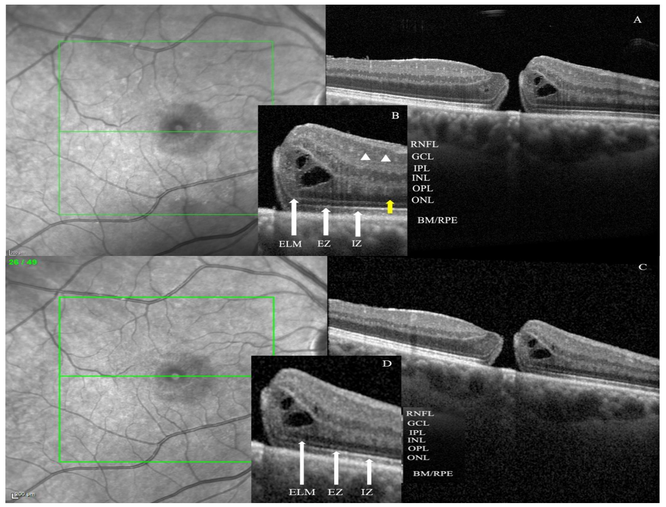

Figure 2. HR-OCT in a patient with full-stage macular hole A) The full-retina defect can be appreciated in the OCT scan with intraretinal cysts and no visible disruption in the outer retinal layer on the edge of the hole. B) In the magnified image all the retinal layers can be identified and the ganglion cell nuclei in the GCL layer s roundish hypo reflective spots (white arrow heads) and similarly subcellular detail is provided in the outer nuclear layer with the possible identification of the rod cell nuclei (yellow arrow). In the standard OCT scan subcellular details cannot be distinguished even in the magnified image (C, D)

OCT Biomarker	HR-OCT n (%)	SD-OCT n (%)	P-Value	CK (95% CI)
Disrupted EZ	5 (27.8)	4 (22.2)	0.148	0.78 [0.72, 0.84]
Disrupted ELM	7 (38.9)	6 (33.3)	0.1204	0.82 [0.76, 0.88]
Disrupted IZ	15 (83.3)	12 (66.7)	0.248	0.85 [0.79, 0.90]
Intraretinal cysts	16 (88.9)	16 (88.9)	1.0	0.89 [0.83, 0.94]
Epiretinal Glial Tissue	7 (38.9)	7 (38.9)	1.0	0.86 [0.80, 0.91]
Hyporeflective dots in ONL	16 (88.9)	0 (0)	<0.001	0.87 [0.81, 0.92]
Hyporeflective areas ganglion cell nuclei	17 (94.4)	3 (16.7)	<0.001	0.83 [0.77, 0.89]
‘Cotton ball sign’ with focal IZ interruption	6 (33.3)	1 (5.6)	0.042	0.84 [0.78, 0.89]
ELM continuity edge of MH	1 (5.6)	3 (16.7)	0.6026	0.80 [0.74, 0.86]
Posterior hyaloid visualization	6 (33.3)	4 (22.2)	0.4567	0.81 [0.75, 0.87]
Gross disruption of inner retinal layers	3 (16.7)	2 (11.1)	0.2323	0.78 [0.72, 0.84]

Results

- **Participants:** 18 eyes (11 male; mean age 66.0 ± 8.9 years)
  - ERM 50%, LH 27.8%, MH 16.7%, VMT 5.6%
- **HR-OCT vs SD-OCT:**
  - Hyporeflective dots (ONL) 88.9% vs 0% (P<0.0001)
  - Hyporeflective dots (GCL) 94.4% vs 16.7% (P<0.001)
  - “Cotton ball” sign 33.3% vs 5.6% (P=0.042)
  - EZ 27.8% vs 22.2%; ELM 38.9% vs 33.3% (P>0.1)
  - Intraretinal cysts 88.9% and glial tissue 38.9% (P=1.0)
- **Reliability:** Inter-grader κ = 0.78–0.89
- **Key Insights:**
  - HR-OCT provides near-histologic visualization of ONL and GCL
  - Detects early IZ, “cotton ball” alterations linked to tractional stress
  - Enhances sensitivity for subtle microstructural biomarkers in VMI

Conclusion

- HR-OCT outperforms SD-OCT in subcellular visualization, supporting earlier diagnosis and improved structural assessment of vitreomacular interface disease.

Figure 3 High-resolution OCT in epiretinal membrane characterization. Standard OCT (B) images show the presence of an ERM (white arrowhead) with limited delineation of its structural components. The corresponding HR-OCT scan more clearly define the epiretinal tissue, with enhanced contrast and layering. In particular, the HR-OCT highlights differences in hyperreflectivity suggestive of glial proliferation and potentially macrophagic cellular components (white arrowhead), which are less distinguishable in the standard acquisition.

Contact: enrico.bernardi@insel.ch

Conflicts of interest: None