The APOSTEL Recommendations

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Aykut Aytulun, Andrés Cruz-Herranz, Lisanne Balk, Alexander U. Brandt, and Philipp Albrecht

As the number of quantitative OCT studies rapidly increases, there is an obvious need for standardization on how these studies should be performed and reported. Important steps for standardization were the development of quality control criteria and of a consensus on the nomenclature of retinal structures accessible to OCT imaging. The OSCAR-IB Consensus Criteria for Retinal OCT Quality Assessment [1] were developed to validate the accuracy and quality of peripapillary ring scans assessing the retinal nerve fiber layer (RNFL) in multiple sclerosis (MS). The majority of these criteria not only apply to imaging of the peripapillary RNFL in

A. Aytulun · P. Albrecht (✉)
Department of Neurology, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, Germany
e-mail: ahmetaykut.aytulun@med.uni-duesseldorf.de; philipp.albrecht@med.uni-duesseldorf.de

A. Cruz-Herranz
Department of Neurology, University of California, San Francisco, CA, USA
e-mail: Andres.CruzHerranz@ucsf.edu

L. Balk
Departments of Neurology and Ophthalmology, VU University Medical Centre, Amsterdam, The Netherlands
e-mail: l.balk@vumc.nl

A. U. Brandt
NeuroCure Clinical Research Center, Berlin, Germany

Charité-Universitätsmedizin Berlin, Berlin, Germany

Freie Universität Berlin, Berlin, Germany

Humboldt-Universität zu Berlin, Berlin, Germany

Berlin Institute of Health, Berlin, Germany

Department of Neurology, University of California, Irvine, CA, USA
e-mail: alexander.brandt@charite.de

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MS but can also be used to rate e.g. macular scans or be applied in other conditions associated with quantitative changes of retinal layers (e.g. neurodegenerative disorders). The International Nomenclature for Optical Coherence Tomography (INOCT) Panel has proposed a consensus nomenclature for the classification of retinal and choroidal layers and bands visible on spectral-domain optical coherence tomography (SD-OCT) images of a normal eye [2].

However, despite these recommendations, imprecise reporting of quantitative OCT studies has sometimes led to uncertainty about methodological aspects, such as scan protocols, analysis software, the use of quality control criteria and inclusion or exclusion of patients and/or eyes. This impacts the interpretability and generalizability of these reports. Therefore, a panel of experts from the International MS Visual (IMSVISUAL) consortium convened at two international meetings in 2015 to develop the Advised Protocol for OCT Study Terminology and Elements recommendations ("APOSTEL recommendations"). These recommendations include a checklist of nine items of particular relevance when reporting quantitative OCT studies.

In the following, a short overview of the nine items is provided:

3.1 Describe the Study Protocol

The study design should be reported in line with the applicable guidelines STROBE, CONSORT or CARE [3]. Additionally, for OCT studies, authors should define if inclusion and exclusion criteria were applied at the eye or patient level and if/how confounding ocular pathologies, e.g. as listed in the OSCAR-IB criteria [1], were ruled out. Reporting the history of and time span from events of particular relevance for the OCT outcomes at study, i.e. optic neuritis (ON) in neuroinflammatory diseases or first symptoms in Leber's hereditary optic neuropathy, is of major importance.

3.2 State the Acquisition Device Type, Name and Version

As OCT technology is continuously evolving, it is important to provide not only the specifications of the devices used (manufacturer, model, interferometric technique) but also the exact version of the software used for the acquisition.

3.3 Define the Acquisition Setting

The exact conditions, under which and how OCT measurements were performed, should be reported, including the use of methods to facilitate imaging such as the use of device-specific control for movement artifacts or pupil dilation.

3.4 Define the OCT Scanning Protocol

It is essential to report the target structures imaged and the exact acquisition parameters of the full measurement protocol, including a detailed description of all scan types employed in a study.

3.5 Define Fundoscopic Imaging

In case additional fundus imaging modalities such as confocal scanning laser ophthalmoscopy (cSLO), retinal angiography and auto-fluorescence imaging are reported, these should be described. Likewise, the acquisition protocol, including the excitation wavelength, filter sets and the number of frames averaged (if applicable), should be indicated.

3.6 Describe Post-acquisition Data Selection

A crucial point of all studies is the quality of the scans, which can have a major impact on the results and their interpretation. If strategies to select or exclude scans from analyses were applied, these should be described in detail. In order to ensure a high quality of scans and interpretability of the results, the use of quality control criteria is recommended. For example, an extensive set of quality control criteria has been published in the form of the OSCAR-IB criteria [1, 4].

3.7 Describe Post-acquisition Data Analysis

Authors should precisely report how the post-processing analysis (e.g. intraretinal layer segmentation) was performed (e.g. fully automated, semi-automated with manual correction of obvious errors or fully manual) [5].

To obtain thickness or volume data from volume scans, differently sized and/or shaped grids can be employed, such as the ring-shaped grid defined for the Early Treatment of Diabetic Retinopathy Study (ETDRS) [6]. Area shape and size of these analysis grids should be reported in addition to the size and location of the source scan (see scanning protocol) [7].

3.8 Use Common Nomenclature and Abbreviations

All structures analyzed should be precisely defined and described ideally using the recommended nomenclature proposed by the IN-OCT consortium (Fig. 3.1) [2]. If additional (composite) structures are reported, these should clearly be defined .

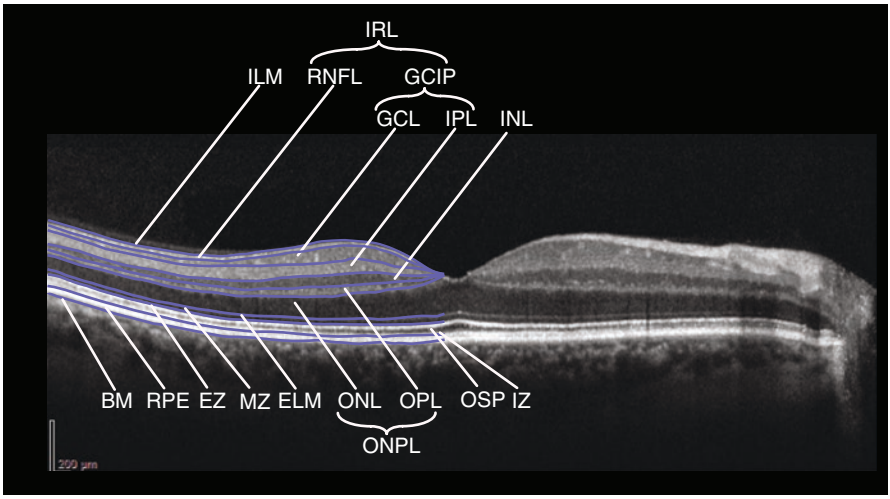

Fig. 3.1 The consensus nomenclature for retinal structures. The different layers (and their borders) are illustrated in a central vertical scan through the middle of the foveola. Abbreviations of retinal structures and layers: ILM (Inner limiting membrane), RNFL (Retinal nerve fiber layer), GCL (Ganglion cell layer), IPL (Inner plexiform layer), INL (Inner nuclear layer), OPL (Outer plexiform layer), ONL (Outer nuclear layer), ELM (External limiting membrane), MZ (Myoid Zone), EZ (Ellipsoid Zone) (Inner and Outer segment Junction), OSP (Outer segment of photoreceptors), IZ (Interdigitation zone), RPE (Retinal pigment epithelium), BM (Bruch's Membrane). Compound layers are Ganglion cell and inner plexiform layer (GCIP) composite of macular GCL and IPL, Inner retinal layers (IRL) composite of macular RNFL, GCL and IPL, and Outer nuclear and plexiform layer (ONPL) composite of ONL and OPL (Image courtesy of Philipp Albrecht and Aykut Aytulun)

3.9 Define the Statistical Approach with Exact Model Description

Reporting of statistical analyses should adhere to the applicable reporting guidelines [3]. As data for both eyes of each subject are usually available in OCT studies, it is important to describe how the inter-eye within-patient dependencies are accounted for. Strategies to deal with this include either randomly selecting one eye, calculating the mean of both eyes or applying statistical methods accounting for these dependencies, such as general mixed effects models or generalized estimating equation models (GEE). Specific questions may require different strategies [8] and advanced statistical models should be reported in sufficient detail.

3.10 Outlook/Future Development

Shortly after their publication, a letter to the editor by James Cameron has commented on the retinal layer nomenclature proposed by the APOSTEL recommendations. He pointed out that additional structures can be described below the external limiting membrane (ELM), which have been detailed in the International

Nomenclature for Optical Coherence Tomography (IN-OCT) consensus paper. Between the inner segment/outer segment junction (ISOS) and the ELM, a myoid zone can be defined; between the ISOS and the outer photoreceptor tips (OPT), an ellipsoid zone; and between the OPT and the retinal pigment epithelium (RPE), an interdigitation zone. These structures are already included in Fig. 3.1. The APOSTEL recommendations are currently being revised using the formalized consensus finding approach of a Delphi process involving a large public of neurologists and ophthalmologists. The nomenclature proposed by the revised recommendations will be harmonized with the IN-OCT consensus (Table 3.1).

Table 3.1 9-Point APOSTEL checklist (adapted from [9])

Item		Recommendation	
1	Study protocol	(a) Describe how many OCT operating sites and graders were included	❑
		(b) Report the timing of OCT compared to other measurements (same day, delayed)	❑
		(c) Describe the inclusion and exclusion criteria	❑
2	Acquisition device	For all OCT devices used, report data on:	
		(a) Manufacturer	❑
		(b) Model	❑
		(c) Version	❑
		(d) Software version	❑
3	Acquisition settings	Clearly describe the settings in which OCT scans were obtained:	
		(a) Room light conditions	❑
		(b) Pupils dilated before exam (y/n)	❑
		(c) Number of operators and devices	❑
4	Scanning protocol	Clearly describe the scanning protocol, including:	
		(a) Type of scan (circular, volume, star, line, other)	❑
		(b) Location (area of interest, macula, optic nerve head, papillo-macular bundle, other?)	❑
		(c) Scan parameters (with or without eye tracking) – *Volume scan: size of scan area (degrees or mm), number of B-scans, alignment of B-scans, number of A-scans per B-scan,* – *Radial scan: size of scan area (degrees or mm), number of B-scans, alignment of B-scans, number of A-scans per B-scan* – *Ring scan: diameter, A-scans/B-scan, manual or automatic placement of ring or method of centering, depth resolution* – *Line scan: angle, location, number of A-scans, depth resolution*	❑
5	Fundoscopic imaging	(a) Report other imaging modalities used in addition to OCT (fundoscopy, CSLO, retinal angiography, autofluorescence imaging, etc.)	❑
		(b) Describe acquisition protocol, including: 1. Excitation wavelength 2. Filter sets 3. Number of frames averaged (if applicable)	❑

(continued)

Table 3.1 (continued)

Item		Recommendation	
6	Post-acquisition data selection	Describe image selection process including:	
		(a) Quality control criteria (i.e. OSCAR-IB [1] or other criteria)	❑
		(b) Post-acquisition discard (number and criteria)	❑
		(c) Eye selection strategy (if applicable)	❑
7	Post-acquisition analysis	Describe all post-acquisition steps:	
		(a) Software used for processing scans and segmentation (may be different from acquisition software)	❑
		(b) Which individual retinal layers were segmented/included	❑
		(c) Method of segmentation (automated, semi-automated or manually)	❑
		(d) How potential bias was addressed in the case of manual segmentation (masking)	❑
		(e) Grid used for data-extraction (size, shape, selected sections)	❑
8	Nomenclature and abbreviations	Define:	
		(a) Anatomical structures analyzed	❑
		(b) Units of provided measurements (e.g. volume or thickness)	❑
9	Statistical approach	Describe:	
		(a) Statistical models used for the analyses of OCT data	❑
		(b) Whether data was analyzed by eye or by patient	❑

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