**APOSTEL 2.0 Recommendations for Reporting Quantitative Optical Coherence Tomography Studies**

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**Abstract**

**Objective**

To update the consensus recommendations for reporting of quantitative optical coherence tomography (OCT) study results, thus revising the previously published Advised Protocol for OCT Study Terminology and Elements (APOSTEL) recommendations.

**Methods**

To identify studies reporting quantitative OCT results, we performed a PubMed search for the terms “quantitative” and “optical coherence tomography” from 2015 to 2017. Corresponding

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Glossary

APOSTEL = Advised Protocol for OCT Study Terminology and Elements; GRADE = Grading of Recommendations Assessment, Development and Evaluation; OCT = optical coherence tomography; OCT-A = optical coherence tomography angiography.

authors of the identified publications were invited to provide feedback on the initial APOSTEL recommendations via online surveys following the principle of a modified Delphi method. The results were evaluated and discussed by a panel of experts and changes to the initial recommendations were proposed. A final survey was recirculated among the corresponding authors to obtain a majority vote on the proposed changes.

Results

A total of 116 authors participated in the surveys, resulting in 15 suggestions, of which 12 were finally accepted and incorporated into an updated 9-point checklist. We harmonized the nomenclature of the outer retinal layers, added the exact area of measurement to the description of volume scans, and suggested reporting device-specific features. We advised to address potential bias in manual segmentation or manual correction of segmentation errors. References to specific reporting guidelines and room light conditions were removed. The participants’ consensus with the recommendations increased from 80% for the previous APOSTEL version to greater than 90%.

Conclusions

The modified Delphi method resulted in an expert-led guideline (evidence Class III; Grading of Recommendations, Assessment, Development and Evaluations [GRADE] criteria) concerning study protocol, acquisition device, acquisition settings, scanning protocol, funduscopic imaging, postacquisition data selection, postacquisition analysis, nomenclature and abbreviations, and statistical approach. It will be essential to update these recommendations to new research and practices regularly.

Increases in the numbers of quantitative optical coherence tomography (OCT) studies have raised the need for consistent and coherent standardized reporting recommendations. In 2016, the Advised Protocol for OCT Study Terminology and Elements (APOSTEL) recommendations were published to provide a 9-point checklist of relevant aspects for reporting quantitative retinal OCT studies. The original APOSTEL recommendations were conceived as expert opinion (level D evidence according to the Grading of Recommendations Assessment, Development and Evaluation [GRADE] working group criteria; grade-workinggroup.org) from discussions among the authors, the IMSVISUAL consortium (imsvisual.org), and consideration of the literature. Without a formal consensus-building approach, and without involving a broader audience, further validation was warranted. We aimed to revise and achieve consensus on these recommendations by using a modified Delphi method, including a larger group of OCT scientists and clinicians, in a formal procedure to review the consensus and develop level C evidence-based guidelines (GRADE criteria). The long-term goal was to improve the reproducibility and interoperability of OCT studies for retinal and neuro-ophthalmology diseases.

Methods

In order to identify experts in the field while minimizing the risk of selection bias, we chose to contact corresponding authors of studies reporting quantitative retinal OCT results published within 24 months prior to our initial survey by email. A total of 892 authors of 1,189 publications were identified by a PubMed search (performed 3 July 2017) using the search terms “quantitative” and “optical coherence tomography” for 2015 to 2017. The Delphi method is a systematic, multistage survey to obtain consensus on a specified question. The process involves multiple rounds of questionnaires presented to participants. The responses are analyzed by a panel of experts and fed back to participants and assessed for consensus. Most of the members of the panel of experts were also corresponding authors of quantitative retinal OCT studies and were therefore also invited to participate in the survey. Following the consensus-building procedure of a modified Delphi method (figure 1), we conducted the following steps:

1. We contacted all corresponding authors of the identified publications and asked them to evaluate and give feedback on the initial APOSTEL recommendations. The participants were asked about their agreement on each item of the recommendations, rating from 1 (full disagreement) to 4 (full approval). Participants were given the opportunity to provide comments. In a blinded fashion, we collected feedback and suggestions using a free online survey via Google Forms (initial questionnaire; raw data of survey results can be obtained from the corresponding author upon qualified request).

2. We then formed a panel of 54 international experts who gathered at congress meetings and during 4 rounds of telephone conferences. The aggregated results of the initial questionnaire were reviewed online through a second questionnaire by the panel, who also revised the original APOSTEL recommendations and proposed a list of changes.
3. This list was then reviewed in a second Delphi round by
the original group of corresponding authors through a
third online questionnaire (Google Forms). In this last
Delphi round, the participants were given the opportu-
nity to approve or reject the
final list of suggestions of the
panel of experts by majority vote.

Results

Initial Questionnaire: Survey About the Initial
APOSTEL Recommendations Among
Corresponding Authors
Seventy-three (8%) of the 892 contacted corresponding au-
thors of quantitative OCT studies completed the first online
questionnaire and provided feedback, the majority of these
being ophthalmologists (71%), followed by neurologists
(10%) and neuro-ophthalmologists (10%). Eighty percent of
participants agreed with the recommendations as they were
published and 95% planned to adhere to the recommenda-
tions in future publications. At the same time, 64% stated
having reported their previous research with less detail than
suggested.

Second Questionnaire: Consensus Building
With the Panel of Experts
Based on the feedback obtained during the first survey, the
panel of 54 experts drafted a list of 15 suggested changes to
the original APOSTEL recommendations. Twelve (80%) of
these suggestions (see below) were accepted through the
second questionnaire, while proposals already covered in the
original recommendations or to include OCT angiography
(OCT-A) were rejected. With this feedback, we generated a
revised version of the APOSTEL recommendations with an
updated 9-point checklist.

Third Questionnaire: Second Delphi Round
With Corresponding Authors
A total of 116 (13%) of the 892 corresponding authors responded
to the third survey. Among them, 53% were ophthalmologists,
35% neurologists, and 12% non-MD researchers. The overall
acceptance of the proposed changes was over 95%, with the only
exception of the recommendation to report the pixel to millimeter
ratio and the image format if the images are exported from the
device for analysis, which was accepted by 84% of the authors.

Summary of Revisions
After the modified Delphi process for consensus building, we
decided to maintain the initial recommendations of stating the
acquisition protocol and imaging modalities and addressing
concomitant eye pathologies with the exact scanning protocol.
The changes made to the original APOSTEL recommendations
checklist are highlighted in the table and summarized below:

1. As already addressed in correspondence to the initial
recommendations,5 we harmonized the nomenclature of
the outer retinal layers to match the 2014 consensus
article by Staurenghi et al.6 (figure 2).

2. We removed references to specific reporting guidelines to
avoid favoring any guidelines or omitting relevant
recommendations.

3. When utilized, we suggest reporting device-specific
features (e.g., enhanced depth imaging, swept-source
OCT, adaptive optics).

4. We added the exact area of measurement (e.g., analysis
grids) to the description of volume scans.

5. We added a commentary regarding the importance of
addressing potential bias in manual segmentation or
manual correction of segmentation errors (masking). In
several comments, concerns were raised regarding the
length of the methodology section of articles that fully adhered to the APOSTEL recommendations. In case of limited word count availability, we now advise submitting the exact OCT methodology as supplementary material, if permitted.

6. Another issue raised by several comments was concerning the relevance of some of the details to be reported regarding the acquisition setting, namely the room lighting conditions and whether pupils were dilated. The panel of experts agreed that reporting the ambient lighting condition is likely to be of low clinical importance, although shaded room lighting is suggested. However, off-axis beam placement could affect the results of OCT imaging studies, and the risk for this phenomenon increases with pupil dilation and is greater for the outer retinal layers (outer plexiform layer/outer nuclear layer) compared to the inner retinal layers (peripapillary retinal nerve fiber layer to inner nuclear layer).\(^7\) Oberwahrenbrock and colleagues\(^8\) showed that the greatest error is for the outer retinal layers. Therefore, pupil dilation is relevant because it can directly affect quantitative OCT measures. We thus omitted room light conditions but retained pupil dilation.

**Discussion**

The formal consensus-building approach of a modified Delphi method was used to revise the APOSTEL recommendations for the reporting of quantitative OCT studies.

We observed a high consensus of the participants already with the initial APOSTEL recommendations in the first survey. The majority of the participants acknowledged the need for guidance.

Whereas the original APOSTEL recommendations were conceived by a panel dominated by neurologists, a more heterogeneous mix of specialties, with broader expertise, contributed to this new version, the majority being ophthalmologists. Ninety-seven percent of all participants agreed that that the APOSTEL 2.0 guidelines should apply to all studies reporting on quantitative retinal OCT research and not be restrained to certain disorders or disciplines. Furthermore, choosing to identify the experts to be addressed by the survey as the corresponding authors of relevant research articles based on a PubMed search assured a broad consensus-building approach, eliminating the selection bias typically immanent to expert consortia. However, there was a low response rate\(^9\): 8% of the contacted corresponding authors responded to the first round of the survey and 13% to the second round. Possible explanations for this limitation may include the fact that corresponding authors are senior supervisors or principal investigators and are not necessarily as involved in the technical details and specifications addressed by the APOSTEL recommendations. Likewise, there are time constraints to consider. This can be viewed as a limitation of the study but we have to assume that those who participated in the survey were knowledgeable about the matter and contact details for the first authors or technicians involved in these studies were not available.

The modified Delphi method tends to eliminate extreme (but possibly relevant) positions and steers a middle-course consensus. However, all survey participants were given the opportunity to provide feedback in free text and all comments were critically discussed among the panel of experts. The achieved consensus is based on the opinion of the participants and the panel of experts and therefore it should be regularly counterchecked and revised along with evolving scientific evidence.
These recommendations do not cover all aspects and techniques possibly amenable to OCT research and are based on expert opinion and a single consensus finding investigation rather than on a systematic review of a large body of literature. Therefore, they are not intended as an indispensable premise for all experimental OCT research. The APOSTEL recommendations are intended for clinical OCT studies using established techniques and help to provide the necessary comparability between studies.

Some additions suggested during the revision process were not included in the final version as consensus was not reached. One of these suggestions was to incorporate a section on OCT-A. However, the inclusion of details pertaining to OCT-A.

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**Table** Nine-Point Advised Protocol for OCT Study Terminology and Elements (APOSTEL) Checklist (Adapted From Cruz-Herranz et al.1)

| Item | Category | Recommendation |
|------|----------|----------------|
| 1    | Study protocol | (1) Describe how many OCT operating sites and graders were included  
|      |           | (2) Report the timing of OCT compared to other measurements (same day, delayed)  
|      |           | (3) Describe the inclusion and exclusion criteria  
|      |           | (4) In case of limited word count, consider submitting the exact methodology as supplementary materiala |
| 2    | Acquisition device | For all OCT devices used, report data on:  
|      |           | (1) Manufacturer  
|      |           | (2) Model  
|      |           | (3) Version  
|      |           | (4) Software version  
|      |           | (2) Device type (time/spectral domain, swept-source, adaptive optics)b |
| 3    | Acquisition settings | Clearly describe the settings in which OCT scans were obtained:  
|      |           | (1) Pupils dilated before examination (y/n)  
|      |           | (2) Number of operators and devicesb |
| 4    | Scanning protocol | Clearly describe the scanning protocol, including:  
|      |           | (1) Type of scan (circular, volume, star, line, other)  
|      |           | (2) Location (area of interest, macula, optic nerve head, papillomacular bundle, other)  
|      |           | (3) Scan parameters (with or without eye tracking)  
|      |           | Volume scan: size of scan, area and location of measurement (degrees or millimeters), number of B-scans, alignment of B-scans, number of A-scans per B-scan  
|      |           | Radial scan: size of scan area (degrees or millimeters), 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    | Funduscopic imaging | (1) Report other imaging modalities used in addition to OCT (funduscopy, confocal scanning laser ophthalmoscope, retinal angiography, autofluorescence imaging, etc.)  
|      |           | (2) Describe acquisition protocol, including:  
|      |           | Excitation wavelength  
|      |           | Filter sets  
|      |           | Number of frames averaged (if applicable)  
|      |           | Report device specific features when utilized (e.g., enhanced depth imaging, swept-source OCT, adaptive optics)a |
| 6    | Postacquisition data selection | Describe image selection process, including:  
|      |           | (1) Quality control criteria  
|      |           | (2) Postacquisition discard (number and criteria)  
|      |           | (3) Eye selection strategy (if applicable) |
| 7    | Postacquisition analysis | Describe all postacquisition steps:  
|      |           | (1) Software used for processing scans and segmentation (may be different from acquisition software)  
|      |           | (2) Which individual retinal layers were segmented/included  
|      |           | (3) Method of segmentation (automated, semi-automated, or manual)  
|      |           | (4) How potential bias was addressed in the case of manual segmentation or manual correction of automated segmentation errors (masking)b  
|      |           | (5) Grid used for data extraction (size, shape, selected sections)  
|      |           | (6) Pixel to millimeter ratio if images are exported (caliper need)b |
| 8    | Nomenclature and abbreviations | Define:  
|      |           | (1) Anatomical structures analyzed  
|      |           | (2) Units of provided measurements (e.g., volume or thickness)  
|      |           | (3) Report the number of eyes presenting additional retinal pathology; describe qualitative retinal changes and report exact methodology of quantificationa |
| 9    | Statistical approach | Describe:  
|      |           | (1) Statistical models used for the analyses of OCT data  
|      |           | (2) Whether data were analyzed by eye or by patient |

Abbreviation: OCT = optical coherence tomography.

The modified APOSTEL checklist contains 9 important items when reporting quantitative OCT studies.

a Changes made to the original APOSTEL recommendations checklist.
b Room light conditions were removed.
A in the APOSTEL 2.0 recommendations would be premature. The field of OCT-A, both clinically and academically, is in a phase of rapid evolution and essentially in its infancy. Its use is not well established in routine clinical care in either the fields of ophthalmology or neurology. Interpretation of OCT-A scans across devices is challenging and standardized quantitative OCT-A metrics are lacking or vary across OCT platforms. Moreover, there is a lack of consensus regarding quality control criteria for image acquisition and the implementation of such standards as they pertain to OCT-A. These limitations are likely to change in the future. For these reasons, the evidence and corresponding investigative and clinical recommendations for OCT and OCT-A should remain on separate tracks.

A future revision of the APOSTEL criteria likely will also need to consider the role of artificial intelligence–based data from image analyses.

We present revised APOSTEL recommendations based on this investigation using a modified Delphi process that involves a broad group of experts. Therefore, the resulting APOSTEL 2.0 can be considered an expert-led guideline (evidence class C, GRADE criteria) covering all relevant aspects of quantitative retinal OCT research. It will be necessary to update these recommendations to new research and practices regularly.

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Friedemann Paul has served on the scientific advisory boards of Novartis and MedImmune; received speaker honoraria and travel funding from Bayer, Novartis, Biogen, Teva, Sanoﬁ-Aventis/Genzyme, Merck Serono, Alexion, Chugai, MedImmune, and Shire; serves as academic editor of PLoS ONE and associate editor of Neurology®: Neuroimmunology & Neuroinflammation; consulted for Sanoﬁ-Genzyme, Biogen, MedImmune, Shire, and Alexion; and received research support from Bayer, Novartis, Biogen, Teva, Sanoﬁ-Aventis/Genzyme, Alexion, Merck Serono, German Research Council, Werth Stiftung of the City of Cologne, German Ministry of Education and Research, Arthur Arnstein Stiftung Berlin, EU FP7 Framework Program, Guthy Jackson Charitable Foundation, and NMSS. Axel Petzold is supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology and is part of the steering committee of the ANGI network, which is sponsored by Zeiss; steering committee of the OCTiMS study, which is sponsored by Novartis; and reports speaker fees from Heidelberg-Engineering. Gorm Pihl-Jensen, Jana Lizrova Preiningerova, and Gema Rebollo‐de la report no conflicts of interest. Marius Ringelstein received speaker honoraria from Novartis, Bayer, Roche, Alexion, and Ipsen and travel reimbursement from Bayer Schering, Biogen Idec, Merz, Genzyme, Teva, Grifols, Roche, and Merck, none related to this study. Shiv Saidha has received consulting fees from Medical Logic for the development of CME programs in neurology and has served on scientific advisory boards for Biogen, Genzyme, Genentech Corporation, EMD Serono, and Celgene; is the PI of investigator-initiated studies funded by Genentech Corporation and Biogen Idec; received support from the Race to Erase MS foundation; was the site investigator of a trial sponsored by MedDay Pharmaceuticals; and has received equity compensation for consulting from JuneBrain LLC, a retinal imaging device developer. Sven Schippling reports no conflicts of interest. Joel S. Schuman reports the following: Aerie Pharmaceuticals, Inc., Ocular Therapeutics, Inc., Opticent: consultant/advisor, equity owner; Bright Focus...
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| Laura J. Balcer, MD   | Departments of Neurology, Population Health, and Ophthalmology, NYU Grossman School of Medicine, New York, NY | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
| Lisanne J. Balk, PhD  | Muller Institute, Centre for Research on Sports in Society, Utrecht, the Netherlands | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
| Augusto Azuara Blanco, MD | Centre for Public Health, Queen's University Belfast, Northern Ireland, UK | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
| Peter A. Calabresi, MD | Division of Neuroimmunology, Johns Hopkins University, Baltimore, MD | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
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| Delia Cabrera DeBuc, PhD | Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, FL | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
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### Appendix (continued)

| Name                        | Location                                                                 | Contribution                                                                 |
|-----------------------------|---------------------------------------------------------------------------|------------------------------------------------------------------------------|
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| Jennifer S. Graves, MD, PHD, MAS | Department of Neurosciences, University of California, San Diego       | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
| Ari J. Green, MD            | Department of Neurology, University of California San Francisco, CA      | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
| Hans-Peter Hartung, MD, FRCP | Department of Neurology, Medical Faculty, Heinrich-Heine University Düsseldorf, Medical Centre, University of Sydney, Australia; Department of Neurology, Medical University of Vienna, Austria | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
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| Frank G. Holz, MD           | Department of Ophthalmology, University of Bonn, Germany                  | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |

### Appendix (continued)

| Name                        | Location                                                                 | Contribution                                                                 |
|-----------------------------|---------------------------------------------------------------------------|------------------------------------------------------------------------------|
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| Scott Kolbe, MD             | Department of Medicine and Radiology, University of Melbourne, Australia  | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
| Julia Krämer, MD            | Department of Neurology with Institute of Translational Neurology, University of Münster, Germany | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
| Wolf A. Lardrèze, MD        | Eye Center, Medical Center, Faculty of Medicine, University of Freiburg, Germany | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
| Letizia Leocani, MD, PhD    | Experimental Neurophysiology Unit, Institute of Experimental Neurology (INSPE), IRCCS San Raffaele, University Vita-Salute San Raffaele, Milan, Italy | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
| Oliver Maier, MD            | Department of Neurology, Medical Faculty, Heinrich-Heine University Düsseldorf, Germany | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |

Continued
### Appendix (continued)

| Name                         | Location                                                                 | Contribution                                                                 |
|------------------------------|--------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Elena H. Martinez-Lapiscina, MD, PhD | Instituto de Investigaciones Biomedicas August Pi i Sunyer (IDIBAPS) and Hospital Clinic, University of Barcelona, Spain | Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions |
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Appendix (continued)

| Name              | Location                                                                 | Contribution                                                                                                                                                                                                 |
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