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## The APOSTEL 2.0 Recommendations for Reporting Quantitative Optical Coherence Tomography Studies

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## **Abstract**

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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 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: One hundred sixteen 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; we 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, GRADE criteria) concerning study protocol, acquisition device, acquisition settings, scanning protocol, fundoscopic imaging, post-acquisition data selection, post-acquisition analysis, nomenclature and abbreviations, and statistical

approach. It will still be essential to update these recommendations to new research and practices regularly.

ACCEPTED

## Introduction

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<sup>1</sup>. 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, [www.gradeworkinggroup.org](http://www.gradeworkinggroup.org)) from discussions among the authors, the IMSVISUAL consortium ([www.imsvisual.org](http://www.imsvisual.org)), and consideration of the literature<sup>2</sup>. 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)<sup>3</sup>. The long-term goal was to improve the reproducibility and inter-operability 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. Eight hundred ninety-two authors (892) of 1189 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, multi-stage 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<sup>4</sup>. 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 four 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 opportunity 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 authors 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 recommendations 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.*

One hundred sixteen (13%) of the 892 corresponding authors responded to the third survey. Among them, 53% were ophthalmologists, 35% neurologists, and 12% were non-MD researchers. The overall acceptance of the proposed changes was above 95%, with the only exception of the recommendation to report the pixel to mm 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, imaging modalities and addressing concomitant eye pathologies with the exact scanning protocol. The following changes made to the original APOSTEL recommendations checklist are printed in bold in Table 1 and summarized below:

- 1) As already addressed in correspondence to the initial recommendations<sup>5</sup>, we harmonized the nomenclature of the outer retinal layers to match the consensus paper by Staurenghi et al 2014 (Figure 2)<sup>6</sup>.
- 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 also 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 that the relevance of some of the details to be reported regarding the acquisition setting, namely the room lighting conditions and if 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 (OPL/ONL) compared to the inner retinal layers (pRNFL to INL)<sup>7</sup>. Oberwahrenbrock and colleagues showed that the greatest error is for the outer retinal layers<sup>8</sup>. Therefore, pupil dilation is relevant since it can directly affect quantitative OCT measures. We, thus, omitted room light conditions but retained pupil dilation.

ACCEPTED

## 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 vast majority of the participants acknowledged the need for guidance.

While 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, we believe that 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<sup>9</sup>: eight percent 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.

It has to be acknowledged that 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. We believe the inclusion of details pertaining to OCT-A to the APOSTEL 2.0 recommendations would be presently 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 either lacking and/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 it pertains to OCT-A. We acknowledge that these limitations are likely to change in the future. For these reasons, we believe

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 very likely will also need to consider the role of Artificial Intelligence based data from image analyses<sup>10</sup>.

In summary, 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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**Table 1**

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 <b>(d) In case of limited word count consider submitting the exact methodology as supplementary material</b>
2 Acquisition device	For all OCT devices used, report data on:  (a) Manufacturer (b) Model (c) Version (d) Software Version <b>(e) Device type (time/spectral domain, swept source, adaptive optics)</b>
3 Acquisition Settings	Clearly describe the settings in which OCT scans were obtained:  (a) Pupils dilated before exam(y/n) (b) 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, papillomacular bundle, other?) (c) Scan parameters (with or without eye tracking) <ul style="list-style-type: none"> <li>- 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</li> <li>- Radial scan: size of scan area (degrees or mm), number of B-scans, alignment of B-scans, number of A-scans per B-scan</li> <li>- Ring scan: diameter, A-scans/B-scan, manual or automatic placement of ring or method of centering, depth resolution.</li> <li>- Line scan: angle, location, number of A-scans, depth resolution.</li> </ul>
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: <ol style="list-style-type: none"> <li>1. Excitation wavelength</li> <li>2. Filter sets</li> <li>3. Number of frames averaged (if applicable)</li> <li><b>4. Report device specific features when utilized (e.g. enhanced depth imaging, swept source OCT, adaptive optics)</b></li> </ol>
6 Post-acquisition data	Describe image selection process including:  (a) Quality control criteria

selection	(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) <b>How potential bias was addressed in the case of manual segmentation or manual correction of automated segmentation errors (masking)</b> (e) Grid used for data-extraction (size, shape, selected sections) (f) <b>Pixel to mm ratio if images are exported (caliper need)</b>
8 Nomenclature and abbreviations	Define:  (a) Anatomical structures analyzed (b) Units of provided measurements (e.g. volume or thickness) (c) <b>Report the number of eyes presenting additional retinal pathology. Describe qualitative retinal changes and report exact methodology of quantification</b>
9 Statistical approach	Describe:  (a) Statistical models used for the analyses of OCT data (b) Whether data was analyzed by eye or by patient

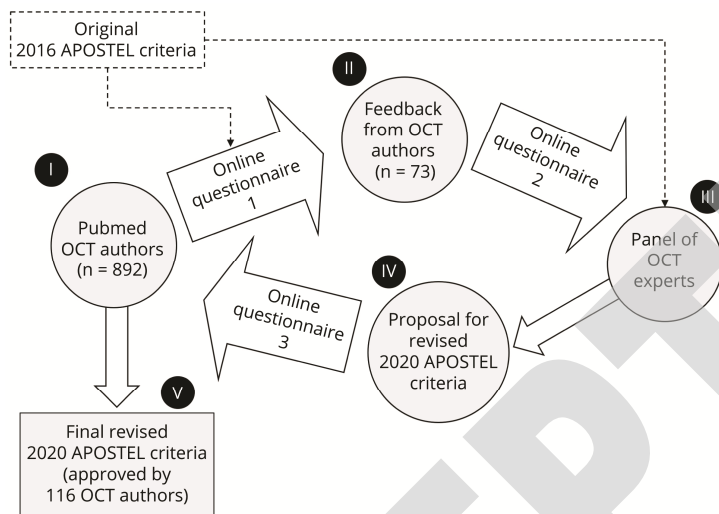
\*Room light conditions were removed.

**Table 1: 9-point APOSTEL checklist (adapted from (Cruz-Herranz et al., 2016))**

Above is the modified APOSTEL checklist containing nine important items when reporting quantitative OCT studies. The changes are in bold.

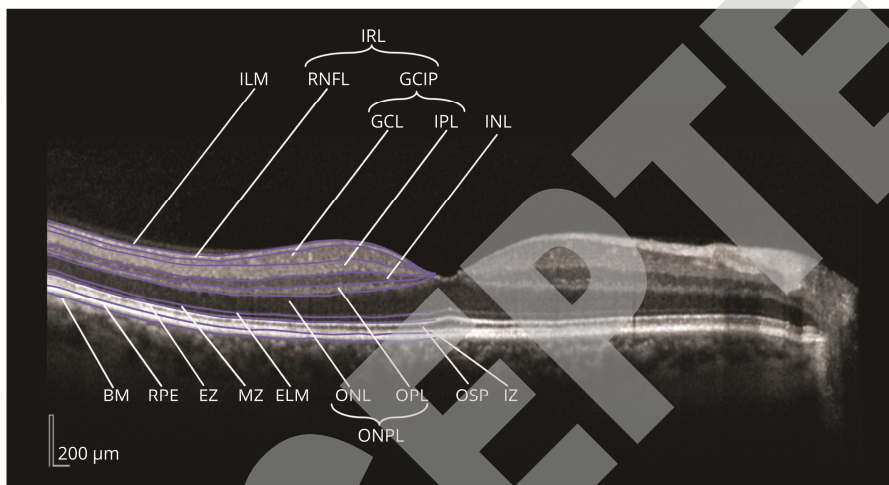
**Figure 1: The modified DELPHI method**

The modified DELPHI method is described as a consensus-building process. We contacted 892 authors of quantitative OCT studies identified by pubmed (I) using an online survey, in which a feedback on the original APOSTEL 2016 criteria was requested. The feedback of the 72 responding OCT authors was analyzed by a panel of experts (II), and changes of the APOSTEL recommendations were proposed (III). A revised version (IV) was proposed to the OCT authors (n=116), who approved the revisions by majority vote, which lead to the final revised 2020 APOSTEL criteria (V).



**Figure 2: The consensus nomenclature for retinal structures**

The different layers (and their boundaries) are illustrated in a central horizontal spectral domain OCT scan through the middle of the fovea. 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 the 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). Copyright by IMSVISUAL and licensed under CC BY 4.0 for this publication (<http://imsvisual.org/resources/media>).





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## The APOSTEL 2.0 Recommendations for Reporting Quantitative Optical Coherence Tomography Studies

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