

Neurology Publish Ahead of Print
DOI: 10.1212/WNL.0000000000012125

The APOSTEL 2.0 Recommendations for Reporting Quantitative Optical Coherence Tomography Studies

This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (CC BY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Neurology[®] Published Ahead of Print articles have been peer reviewed and accepted for publication. This manuscript will be published in its final form after copyediting, page composition, and review of proofs. Errors that could affect the content may be corrected during these processes.

Aykut Aytulun^{1,43*}, Andrés Cruz-Herranz^{2,43*}, Orhan Aktas^{1,43}, Laura J. Balcer^{3,43}, Lianne Balk^{4,43}, Piero Barboni⁵, Augusto Azuara Blanco⁶, Peter A. Calabresi^{7,43}, Fiona Costello^{8,43}, Bernardo Sanchez-Dalmau⁹, Delia Cabrera DeBuc¹⁰, Nicolas Feltgen¹¹, Robert P. Finger¹², Jette Lautrup Frederiksen^{13,43}, Elliot Frohman^{14,43}, Teresa Frohman^{14,43}, David Garway-Heath¹⁵, Iñigo Gabilondo^{16,43}, Jennifer S. Graves^{17,43}, Ari J. Green^{2,43}, Hans-Peter Hartung^{1,18,19,43}, Joachim Havla^{20,43}, Frank G. Holz¹², Jaime Imitola^{21,43}, Rachel Kenney^{3,43}, Alexander Klistorner^{22,43}, Benjamin Knier^{23,43}, Thomas Korn^{23,43}, Scott Kolbe²⁴, Julia Krämer^{25,43}, Wolf A. Lagrèze²⁶, Letizia Leocani^{27,43}, Oliver Maier¹, Elena H. Martínez-Lapiscina^{9,43}, Sven Meuth^{1,43}, Olivier Outteryck^{28,43}, Friedemann Paul^{29,43}, Axel Petzold^{30,43}, Gorm Pihl-Jensen^{13,43}, Jana Lizrova Preiningerova^{31,43}, Gema Rebolleda³², Marius Ringelstein^{1,33,43}, Shiv Saidha^{7,43}, Sven Schippling^{34,43}, Joel S. Schuman^{35,36}, Robert C. Sergott^{37,43}, Ahmed Toosy³⁸, Pablo Villoslada^{9,43}, Sebastian Wolf³⁹, E. Ann Yeh^{40,43}, Patrick Yu-Wai-Man⁴¹, Hanna G. Zimmermann^{29,43}, Alexander U. Brandt^{29,42,43†} and Philipp Albrecht^{1,43‡}

1) Department of Neurology, Medical Faculty, Heinrich-Heine University Düsseldorf, Germany

2) Department of Neurology, University of California San Francisco, San Francisco, USA.

3) Departments of Neurology, Population Health and Ophthalmology, NYU Grossman School of Medicine, New York, USA

4) Mulier Institute, Centre for Research on Sports in Society, Utrecht, Netherlands

5) Scientific Institute San Raffaele, Milan, Italy

6) Centre for Public Health, Queen's University Belfast, Belfast, Northern Ireland, UK

7) Division of Neuroimmunology, Johns Hopkins University, Baltimore, USA

- ⁸⁾ Departments of Clinical Neurosciences and Surgery (F.E.C.), University of Calgary, Alberta, Canada
- ⁹⁾ Institut d'Investigacions Biomediques August Pi iSunyer (IDIBAPS) and Hospital Clinic, University of Barcelona, Barcelona, Spain
- ¹⁰⁾ Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, USA
- ¹¹⁾ Department of Ophthalmology, University Medical Center, Goettingen, Germany
- ¹²⁾ Department of Ophthalmology, University of Bonn, Bonn, Germany
- ¹³⁾ Department of Neurology, Rigshospitalet Glostrup and University of Copenhagen, Denmark
- ¹⁴⁾ Distinguished Senior Fellow, Laboratory of Neuroimmunology, Professor Laurence Steinman, Stanford University School of Medicine, CA, USA
- ¹⁵⁾ Institute of Ophthalmology, University College London; Moorfields Eye Hospital NHS Foundation Trust, UK
- ¹⁶⁾ Biocruces Bizkaia Health Research Institute, Barakaldo, Spain
- ¹⁷⁾ Department of Neurosciences, University of California, San Diego
- ¹⁸⁾ Brain and Mind Centre, University of Sydney
- ¹⁹⁾ Department of Neurology, Medical University of Vienna, Austria
- ²⁰⁾ Institute of Clinical Neuroimmunology, LMU Hospital, Ludwig-Maximilians Universität München, Munich, Germany
- ²¹⁾ UConn Health Comprehensive MS Center, Division of Multiple Sclerosis and Neuroimmunology, Department of Neurology, University of Connecticut School of Medicine, Farmington, CT 06030, USA
- ²²⁾ Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia

- ²³⁾ Department of Neurology, Klinikum rechts der Isar, School of Medicine, Technical University of Munich, Germany
- ²⁴⁾ Department of Medicine and Radiology, University of Melbourne, Australia
- ²⁵⁾ Department of Neurology with Institute of Translational Neurology, University of Münster, Münster, Germany.
- ²⁶⁾ Eye Center, Medical Center, Faculty of Medicine, University of Freiburg, Freiburg, Germany.
- ²⁷⁾ Experimental Neurophysiology Unit, Institute of Experimental Neurology (INSPE), IRCCS San Raffaele, University Vita-Salute San Raffaele, Milan, Italy
- ²⁸⁾ Univ. Lille, Inserm, CHU Lille, U1172 - LiINCog (JPARC) - Lille Neurosciences & Cognition, F-59000 Lille, France
- ²⁹⁾ Experimental and Clinical Research Center, Max Delbrück Center for Molecular Medicine and Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Germany
- ³⁰⁾ Moorfields Eye Hospital, City Road, The National Hospital for Neurology and Neurosurgery, Queen Square, UCL Institute of Neurology, London, UK and Neuro-ophthalmology Expert Center, Amsterdam UMC, The Netherlands
- ³¹⁾ Department of Neurology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic
- ³²⁾ Department of Ophthalmology, Ramon y Cajal Hospital, Medicine University of Alcalá, Madrid, Spain
- ³³⁾ Department of Neurology, Center for Neurology and Neuropsychiatry, LVR-Klinikum, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany
- ³⁴⁾ Department of Neurology, University Hospital Zurich, Switzerland

³⁵⁾ Departments of Ophthalmology, Neuroscience and Physiology, NYU Langone Health, NYU Grossman School of Medicine, New York, NY, USA

³⁶⁾ Departments of Biomedical Engineering, Electrical and Computer Engineering, NYU Tandon School of Engineering, Brooklyn, NY, USA

³⁷⁾ Thomas Jefferson University Medical College, Philadelphia, USA

³⁸⁾ Queen Square MS Centre, Department of Neuroinflammation, UCL Institute of Neurology, University College London, London, UK

³⁹⁾ Department of Ophthalmology and Department of Clinical Research, Bern University Hospital, University of Bern, Switzerland

⁴⁰⁾ Division of Neurology, Department of Pediatrics, Hospital for Sick Children, Division of Neurosciences and Mental Health SickKids Research Institute, University of Toronto, Canada

⁴¹⁾ Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK, and Moorfields Eye Hospital, London, UK

⁴²⁾ University of California, Irvine, CA, USA

⁴³⁾ IMSVISUAL, International Multiple Sclerosis Visual System Consortium

*Equally contributing first authors

‡Equally contributing senior authors

Correspondence should be addressed to Philipp Albrecht, phil.albrecht@gmail.com

Word count:

-Title: 95<96 characters

-Abstract: 265<250 words

References:10 < 10

Figures: 2

Tables: 1

-Main manuscript: 1757 <1250 words

Neurology search terms:

- [186] All Neuro-ophthalmology

- [191] Retina

- [118] All Imaging

Study funding:

None.

Disclosure:

All authors declare no financial disclosures that are relevant to the manuscript.

Financial disclosures outside of the work submitted:

Aykut Aytulun reports no conflicts of interest.

Andrés Cruz-Herranz reports grants from the National Multiple Sclerosis Society (FG 20102-A-1) and the UCSF Program for Breakthrough Biomedical Research (PBBR).

Orhan Aktas reports grants from the German Research Foundation (DFG, GRK 2578) and the German Ministry of Education and Research (BMBF, FKZ01G11602B), grants and personal fees from Bayer HealthCare, Biogen,

Genzyme, Novartis, and Teva, and personal fees from Alexion, Almirall, MedImmune, Merck Serono, and Roche.

Laura Balcer received research funding from Biogen; Editor-in-Chief, Journal of Neuro-Ophthalmology

Lisanne Balk reports no conflicts of interest.

Piero Barboni reports no conflicts of interest.

Augusto Azuara Blanco reports no conflicts of interest.

Peter A. Calabresi reports no conflicts of interest.

Fiona Costello reports no conflicts of interest.

Bernardo Sanchez Dalmau received consulting services and/or speaking activities from Chiesi, Esteve, Thea.

Delia Cabrera DeBu reports grants from the NIH (P30-EY014801 to the University of Miami), Research to Prevent Blindness Inc. (unrestricted grant to the University of Miami), the NIA, and the Alzheimer's Association.

Nicolas Feltgen Consultant to Bayer, Novartis, Roche, Allergan, Alimera, Heidelberg Engineering.

Robert Finger Consultant to Bayer Novartis, Roche, Allergan, Alimera, Santhera, Ellex, Novelion, Inositec, Opthea, ProQR, Research Funding by Novartis, Heidelberg Engineering, Zeiss, CentreVue.

Jette Lautrup Frederiksen has received no funding to support the presented work.

She has served on scientific advisory boards for and received funding for travel related to these activities as well as honoraria from Biogen Idec, Merck Serono,

Sanofi-Aventis, Teva, Novartis and Almirall. She has received speaker honoraria from Biogen Idec, Teva and Novartis. She has served as advisor on preclinical development for Takeda. Jette Frederiksen participate in advisory board meetings with Alexion and Chiesi.

Elliot Frohman received speaker fees from Novartis, Biogen, Genzyme, Alexion.

Teresa Frohman received advisory board fees from Alexion.

David Garway Heath reports no conflicts of interest.

Íñigo Gabilondo reports grants from "Ikerbasque: The Basque Foundation for Science" and Carlos III Health Institute (Ministry of Science and Innovation of Spain) and personal fees and nonfinancial support from Zambon Group and Alter Medica.

Jennifer S. Graves reports no conflicts of interest.

Ari J. Green reports no conflicts of interest.

Hans-Peter Hartung reports no conflicts of interest.

Joachim Havla reports grants for OCT research from the Friedrich-Baur-Stiftung and Merck, personal fees and non-financial support from Celgene, Merck, Alexion, Novartis, Roche, Santhera, Biogen, Heidelberg Engineering, Sanofi Genzyme and non-financial support of the Guthy-Jackson Charitable Foundation, all outside the submitted work. JH is (partially) funded by the German Federal Ministry of Education and Research (Grant Numbers 01ZZ1603[A-D] and 01ZZ1804[A-H] (DIFUTURE)).

Frank G. Holz reports: Research Grant Support: Acucela, Allergan, Apellis, Bayer, Bioeq/Formycon, CenterVue, Ellex, Roche/Genentech, Geuder, Kanghong, NightStarx, Novartis, Optos, Zeiss; Consultant: Acucela, Allergan, Apellis, Bayer, Boehringer-Ingelheim, Roche/Genentech, Geuder, Grayburg Vision, LinBioscience, Kanghong, Novartis, Pixium Vision, Oxurion, Stealth BioTherapeutics, Zeiss.

Jaime Imitola reports no conflicts of interest.

Rachel Kenney reports no conflicts of interest.

Alexander Klistorner reports no conflicts of interest.

Benjamin Knier reports a research grant from the Else Kröner-Fresenius-Stiftung and a research grant (Oppenheim grant) and travel support from Novartis outside the submitted work.

Thomas Korn reports no conflicts of interest.

Scott Kolbe receives project support from Biogen and has received honoraria from Biogen, Merck and Novartis for work unrelated to this manuscript.

Julia Krämer received honoraria for lecturing from Biogen, Novartis, Genzyme, Merck, Mylan, Roche, and Teva, and financial research support from Sanofi Genzyme and Novartis.

Wolf A Lagrèze reports no conflicts of interest.

Letizia Leocani consulting services and / or speaking activities from Novartis, Merck, Biogen, Roche, Almirall.

Oliver Maier reports no conflicts of interest.

Sven Meuth received honoraria for lecturing and travel expenses for attending meetings from Almirall, Amicus Therapeutics Germany, Bayer Health Care, Biogen, Celgene, Diamed, Genzyme, MedDay Pharmaceuticals, Merck Serono, Novartis, Novo Nordisk, ONO Pharma, Roche, Sanofi-Aventis, Chugai Pharma, QuintilesIMS, and Teva. His research is funded by the German Ministry for Education and Research (BMBF), Deutsche Forschungsgemeinschaft (DFG), Else Kröner

Fresenius Foundation, German Academic Exchange Service, Hertie Foundation, Interdisciplinary Center for Clinical Studies (IZKF) Muenster, German Foundation Neurology, and by Almirall, Amicus Therapeutics Germany, Biogen, Diamed, Fresenius Medical Care, Genzyme, Merck Serono, Novartis, ONO Pharma, Roche, and Teva.

Elena H. Martínez-Lapiscina is, since 16th April 2019, an employee of European Medicines Agency (Human Medicines). This article is related to her activity at the Hospital Clinic of Barcelona / IDIBAPS affiliation and consequently, as external activity, it does not represent the views of the Agency, its Committees or working parties. Before joining the EMA, she was granted funds from IDIBAPS and the Clinic of the University of Barcelona Foundation for research and educational purposes, and from the Instituto de Salud Carlos III (Spain) & Fondo Europeo de Desarrollo Regional (JR16/00006; MV17/00021; PI17/01228; RD16/0015/0003, a grant for MS Innovation GMSI, 2016), the Fundació Privada Cellex, the Marató TV3 Charitable Foundation (20142030), Sanofi-Genzyme and Novartis. Before joining the EMA, she received travel support for international and national meetings from Roche and Sanofi-Genzyme, and she also received honoraria for consultancies from Novartis, Roche and Sanofi. She is a member of the International Multiple Sclerosis Visual System (IMSVISUAL) Consortium.

Olivier Outteryck reports grant for research from Novartis and Bayer; grant for research and personal fees from Biogen-Idec, funding for travel from Biogen, Genzyme-Sanofi, Merck-Serono, Novartis and Teva Pharmaceutical Industries, outside the submitted work.

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. AP 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 reports no conflict of interest.

Jana Lizrova Preiningerova reports no conflicts of interest.

Gema Rebolleda reports no conflict 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 Logix for the development of CME programs in neurology and has served on scientific advisory boards for Biogen, Genzyme, Genentech Corporation, EMD Serono & Celgene. He is the PI of investigator-initiated studies funded by Genentech Corporation and Biogen Idec, received support from the Race to Erase MS foundation, and was the site investigator of a trial sponsored by MedDay Pharmaceuticals. He has received equity

compensation for consulting from JuneBrain LLC, a retinal imaging device developer.

Sven Schippling reports no conflicts of interest.

Joel S Schuman Disclosures: Aerie Pharmaceuticals, Inc.: Consultant/Advisor, Equity Owner; Bright Focus Foundation: Grant Support; Boehringer Ingelheim: Consultant/Advisor; Carl Zeiss Meditec: Patents/Royalty/Consultant/Advisor; Massachusetts Eye and Ear Infirmary and Massachusetts Institute of Technology: Intellectual Property; National Eye Institute: Grant Support; New York University: Intellectual Property; Ocugenix: Equity Owner, Patents/Royalty; Ocular Therapeutix, Inc.: Consultant/Advisor, Equity Owner; Opticent: Consultant/Advisor, Equity Owner; Perfuse, Inc.: Consultant/Advisor; Regeneron, Inc.: Consultant/Advisor; SLACK Incorporated: Consultant/Advisor; Tufts University: Intellectual property; University of Pittsburgh: Intellectual property; Financial Support: Funding from the National Institutes of Health (Bethesda, MD, USA) R01-EY013178. An unrestricted grant from Research to Prevent Blindness (New York, NY) to the Department of Ophthalmology, NYU Langone Health, NYU Grossman School of Medicine, New York, NY (PI: JSS).

Robert C Sergott reports no conflicts of interest.

Ahmed Toosy has received speaker honoraria from Biomedica, Sereno Symposia International Foundation, Bayer and meeting expenses from Biogen Idec and Novartis He was the UK PI for two clinical trials sponsored by MEDDAY pharmaceutical company (MD1003 in optic neuropathy [MS-ON] and progressive MS [MS-SPI2]).

Pablo Villoslada has stocks and have received consultancy fees from Accure Therapeutics SL, Health Engineering SL, QMENTA Inc, Attune Neurosciences Inc, Spiral therapeutics Inc, CLight Inc and NeuroPrex Inc.

Sebastian Wolf has served as a consultant for Allergan, Bayer, Chengdu Kanghong Biotech, Heidelberg Engineering, Novartis, Zeiss, and Roche; he has received grant support from Heidelberg Engineering and Zeiss.

E. Ann Yeh reports grants from CMSC, NMSS, MS Society of Canada/MS Scientific Research Foundation, Biogen, CIHR, OIRM, SCN, SickKids Foundation, CBMH, meeting support from the Guthy Jackson Foundation, Honoraria from MS At the Limits, Excemed, Alexion, Biogen. All outside of the submitted work.

Patrick Yu Wai Man reports no conflicts of interest.

Hanna G. Zimmermann received research grants from Novartis and speaking fees from Bayer Healthcare.

Alexander U. Brandt reports no conflicts of interest.

Philipp Albrecht reports grants, personal fees and nonfinancial support from Allergan, Biogen, Celgene, Ipsen, Merz Pharmaceuticals, Merck, Novartis, and Roche; personal fees and nonfinancial support from Bayer Healthcare and TEVA; and nonfinancial support from Sanofi-Aventis/Genzyme outside the submitted work.

Abstract

Word count: 265<250

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 studies¹. 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) from discussions among the authors, the IMSVISUAL consortium (www.imsvisual.org), and consideration of the literature². 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)³. 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 consensus⁴. 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 recommendations⁵, we harmonized the nomenclature of the outer retinal layers to match the consensus paper by Staurengi et al 2014 (Figure 2)⁶.
- 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)⁷. Oberwahrenbrock and colleagues showed that the greatest error is for the outer retinal layers⁸. 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 rate⁹: 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 analyses¹⁰.

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.

Acknowledgements:

We want to thank all the contributors for taking part in our surveys: Solmaz Abdolrahimzadeh (University of Rome Sapienza, Italy); Fahmy Aboulenein-Djamshidian (Department of Neurology, Sozialmedizinisches Zentrum Ost, Donauspital, Vienna, Austria); Kaveh Abri Aghdam (Eye Research Center, The Five Senses Institute, Rassoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran); Asaf Achiron (Wolfson Medical Center Tel Aviv University, Israel); Lillian Aly (Dept. of Neurology, TU Munich, Germany); Sofia Androudi (Department of Ophthalmology, University of Thessaly, Larissa, Greece); J. Fernando Arevalo (Wilmer Eye Institute at Johns Hopkins University, Baltimore, Maryland, USA); Jennifer Arnold (Marsden Eye Specialists, Parramatta, Australia); Nicole Balducci (Policlinico Sant'Orsola-Malpighi Bologna, Italy); Francesco Bandello (San Raffaele Scientific Institute, Milan, Italy); Rajani Battu (Centre for Eye Genetics and Research, Bangalore, India); Raed Behbehani (Al-Bahar Ophthalmology Center, Kuwait); Ivan Bodis-Wollner (SUNY Downstate Medical Center, New York, USA); Enrico Borrelli (San Raffaele Scientific Institute, Milan, Italy); Livia Brandao (University of Basel, Switzerland); Josefine Britze (Department of Neurology, Rigshospitalet Glostrup, Copenhagen, Denmark); Troels Brynskov (Dept. Ophthalmology, Glostrup Hospital, Copenhagen, Denmark); Pilar Calvo (IIS-Aragon, Miguel Servet University Hospital, Zaragoza, Spain); Adriana Carrá (MS Center Hospital Británico, Buenos Aires, Argentina); Alfonso Casado (Hospital Universitario Marqués de Valdecilla, Santander, Spain); Irimi Chatziralli (2nd Department of Ophthalmology, University of Athens, Athens, Greece); Fred K. Chen (Centre for Ophthalmology and Visual Science, The University of Western Australia); Gemmy Cheung (Singapore National Eye Center, Malaysia); Salomon Cohen (Centre d'Imagerie et de Laser Paris, France); Sara Collorone (NMR Research Unit, Department of Neuroinflammation, Institute of Neurology, Faculty of Brain Sciences, University College London,

London, United Kingdom); Christian Cordano (University of California, San Francisco, USA); Christine A. Curcio (University of Alabama at Birmingham, USA); Floriana De Angelis (Queen Square MS Centre, UCL, London, UK); Roberto Dell'Omo (University of Molise, Campobasso, Italy); Mauricio Della Paolera (Hospital de Olhos City, São Paulo, Brazil); Nabil El Ayoubi (American University of Beirut and Medical Center / Department of Neurology / Multiple Sclerosis Center, Lebanon); Brian Fernández (Heidelberg Engineering, Franklin, Massachusetts, USA); Antonio Ferreras (Miguel Servet University Hospital, University of Zaragoza, Spain); Ignacio Flores-Moreno (Puerta de Hierro University Hospital, Madrid, Spain); K. Bailey Freund (Vitreous Retina Macula Consultants of New York, USA); Simona Frontoni (Dept. of Systems Medicine, University of Rome "Tor Vergata", Italy); Steven Galetta (New York University Lagone Medical Center, USA); Ignacio García Basterra (Hospital Costa del Sol, Marbella, Spain); Stuart Gardiner (Devers Eye Institute, Portland, Oregon, USA); Barbara Giambene (Al Emadi Hospital, Doha, Qatar); Steffen Hamann (Department of Ophthalmology, Rigshospitalet, University of Copenhagen, Denmark); Poya Hård af Segerstad (Lund University, Scania, Sweden); Pascal Hasler (Eye Department, University Hospital Basel, Switzerland); Xiangui He (Shanghai Eye Disease Prevention and Treatment Center, Shanghai Eye Hospital, China); Carsten Heinz (Eye Center at St. Franziskus Hospital Muenster, Germany); Yoshio Hirano (Nagoya City University Graduate School of Medical Sciences, Japan); Jyh Yung Hor (Department of Neurology, Penang General Hospital, Penang, Malaysia); Ragnhild Wivestad Jansson (University of Bergen, Norway); Jost B. Jonas (Department of Ophthalmology, Medical Faculty Mannheim, Heidelberg University, Germany); Motohiro Kamei (Aichi Medical University, Nagakute, Japan); Niro Kasahara (Santa Casa de São Paulo School of Medical Sciences, Brazil); Amir Kashani (University of Southern California, Los Angeles, USA); Rajiv Khandekar (King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia);

Albert Khouri (Rutgers New Jersey Medical School, USA); Sidsel Ehlers Klug (Department of Ophthalmology at Aarhus University Hospital, Denmark); Chiara La Morgia (IRCCS Institute of Neurological Sciences of Bologna; University of Bologna, Italy); Timothy Y Y Lai (The Chinese University of Hong Kong, Hong Kong); Marco Lana-Peixoto (Federal University of Minas Gerais Medical School, Belo Horizonte, Brazil); Paolo Lanzetta (University of Udine, Department of Medicine, Italy); Michael Larsen (Rigshospitalet and University of Copenhagen, Denmark); Eun Ji Lee (Seoul National University Bundang Hospital, South Korea); Shu Yen Lee (Singapore National Eye Centre, Singapore); Theodore Leng (Byers Eye Institute at Stanford, Stanford University School of Medicine, Palo Alto, California); Nicolas Leveziel (Dpt. of Ophthalmology, CHU Poitiers, France); Kenneth Li (United Christian Hospital, Hong Kong); Marco Lombardo (Vision Engineering, Rome, Italy); Iuliano Lorenzo (Vita-Salute University, Ospedale San Raffaele Scientific Institute, Milan, Italy); Brandon Lujan (OHSU Casey Eye Institute, Portland, Oregon, USA); Amir-Hadi Maghzi (Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA); Maureen Maguire (University of Pennsylvania, USA); Idit Maharshak (Wolfson Medical Center Holon Israel); Christian Mardin (Department of Ophthalmology, University Erlangen, Germany); Joao Pedro Marques (Department of Ophthalmology, Centro Hospitalar e Universitário de Coimbra (CHUC), Coimbra, Portugal); Battaglia Parodi Maurizio (Vita-Salute San Raffaele University, Milan, Italy); Martin McKibbin (Leeds Teaching Hospitals NHS Trust, West Yorkshire, UK); Carlos Moreira-Neto (Hospital de Ohos do Paraná, Brazil); Adriana Morgan (Santa Casa de São Paulo School of Medical Sciences, Brazil); Inger Christine Munch (Zealand University Hospital, Roskilde, Denmark); Marion Munk (Department of Ophthalmology, University Hospital Bern, Switzerland); Maria Nilsson (Karolinska Institutet, Solna, Sweden); Susana Noval (La Paz Children Hospital, Madrid, Spain); Frederike Cosima Oertel ((1) Dept. Neurology, UCSF, USA (2) NCRC & ECRC

Charité-Universitätsmedizin Berlin, Germany); Akio Oishi (Kyoto University, Japan); Abdullah Ozkaya (Beyoglu Eye Training and Research Hospital, Istanbul, Turkey); Lekha Pandit (Nitte University, Mangalore, India); Athina Papadopoulou (University Hospital Basel, Switzerland); Isabel Pinilla (Hospital Clinico Universitario Zaragoza, Spain); Giuseppe Querques (San Raffaele Scientific Institute, Milan, Italy); Richard Rosen (New York Eye and Ear Infirmary of Mount Sinai, USA); Richard Roxburgh (Auckland City Hospital, New Zealand); Ana Rita Santos (AIBILI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, Portugal); Kaur Savleen (Department of Ophthalmology, Post Graduate Institute of Medical Education and Research, Chandigarh, India); Reinier O. Schlingemann (Academic Medical Center, University of Amsterdam, The Netherlands); Steffen Schmitz-Valckenberg (Department of Ophthalmology, University of Bonn, Germany); Carlos Schönfeldt-Lecuona (Department of Psychiatry and Psychotherapy III, University Clinic Ulm, Germany); Ori Segal (Sackler School of Medicine, Tel Aviv University, Israel); Oudy Semoun (Centre Hospitalier Intercommunal Creteil, France); Aleksandra Shelankova (Research Institute of Eye Diseases, Moscow, Russia); Elizabeth Silbermann (Oregon Health & Science University, Portland, Oregon, USA); Travis Smith (Oregon Health & Science University, Portland, Oregon, USA); Gabor Mark Somfai (Department of Ophthalmology, Semmelweis University, Budapest, Hungary); Elias Sotirchos (Johns Hopkins University, Baltimore, Maryland, USA); Richard Spaide (Vitreous, Retina, Macula Consultants of New York, USA); Rosa Tang (Eye Wellness Center, Houston, Texas); Angelo Tanna (Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA); Lisa Toto (Ophthalmology Clinic, University "G. d'Annunzio" of Chieti-Pescara, Italy); Umut Duygu Uzunel (Izmir Bozyaka Training and Research Hospital, Turkey); Anneke Van der Walt (Alfred Health, Monash University, Melbourne, Australia); Clemens Vass (Medical University Vienna, Austria); Gianni Virgili (University of Florence, Italy);

Stela Vujosevic (University Hospital Maggiore della Carita', Novara, Italy); Nadia Waheed (Tufts University Medical School, Boston, Massachusetts, USA); Maria Waizel (University Hospital Basel, Switzerland); Lihteh Wu (Asociados de Macula Vitreo y Retina de Costa Rica); Yih Chian Yew (Bukit Mertajam Hospital, Malaysia); Glenn Yiu (UC Davis); Hyeong Gon Yu (Seoul National University Hospital, South Korea); Shen Yuan (Tenth Hospital of Tongji University, Shanghai, China); Lucia Ziccardi (IRCCS Fondazione Bietti, Rome, Italy); Martin Zinkernagel (Department of Ophthalmology, University Hospital Bern, Switzerland).

ACCEPTED

Appendix 1. Authors

Name	Location	Contribution
Aykut Aytulun	Department of Neurology, Medical Faculty, Heinrich- Heine University Düsseldorf, Germany	Study concept and design, acquisition of data, analysis and interpretation, drafting and critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Andrés Cruz-Herranz	Department of Neurology, University of California San Francisco, San Francisco, USA	Study concept and design, acquisition of data, analysis and interpretation, drafting and critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Orhan Aktas	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.
Laura J. Balcer	Departments of Neurology, Population Health and Ophthalmology, NYU Grossman School of Medicine, New York, USA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Lisanne J. Balk	Mulier Institute, Centre for Research on Sports in Society, Utrecht, Netherlands	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Piero Barboni	Scientific Institute San Raffaele, Milan, Italy	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Augusto Azuara Blanco	Centre for Public Health, Queen's University Belfast, 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	Division of Neuroimmunology, Johns Hopkins University, Baltimore, USA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Fiona Costello	Departments of Clinical Neurosciences and Surgery (F.E.C.), University of Calgary, Alberta, Canada	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Bernardo Sanchez-Dalmau	Institut d'Investigacions Biomediques August Pi iSunyer (IDIBAPS) and Hospital Clinic, University of Barcelona, Barcelona, Spain	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Delia Cabrera DeBuc	Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, USA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Nicolas Feltgen	Department of Ophthalmology, University	Analysis and interpretation, critical

	Medical Center, Goettingen, Germany	revision of the manuscript for important intellectual content, took part in the panel discussions.
Robert P. Finger	Department of Ophthalmology, University of Bonn, Bonn, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Jette Lautrup Frederiksen	Department of Neurology, Rigshospitalet Glostrup and University of Copenhagen, Denmark	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Elliot Frohman	Distinguished Senior Fellow, Laboratory of Neuroimmunology, Professor Laurence Steinman, Stanford University School of Medicine, CA, USA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Teresa Frohman	Distinguished Senior	Analysis and

	Fellow, Laboratory of Neuroimmunology, Professor Laurence Steinman, Stanford University School of Medicine, CA, USA	interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
David Garway-Heath	Institute of Ophthalmology, University College London; Moorfields Eye Hospital NHS Foundation Trust, UK	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Iñigo Gabilondo	Biocruces Bizkaia Health Research Institute, Barakaldo, Spain	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Jennifer S. Graves	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	Department of Neurology, University of California San Francisco, San Francisco, USA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Hans-Peter Hartung	Department of Neurology, Medical Faculty, Heinrich- Heine University Düsseldorf, Germany Brain and Mind Centre, University of Sydney 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.
Joachim Havla	Institute of Clinical Neuroimmunology, LMU Hospital, Ludwig- Maximilians Universität München, Munich, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Frank G. Holz	Department of Ophthalmology, University of Bonn, Bonn, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual

		content, took part in the panel discussions.
Jaime Imitola	UConn Health Comprehensive MS Center, Division of Multiple Sclerosis and Neuroimmunology, Department of Neurology, University of Connecticut School of Medicine, Farmington, CT 06030, USA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Rachel Kenney	Departments of Neurology, Population Health and Ophthalmology, NYU Grossman School of Medicine, New York, USA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Alexander Klistorner	Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Benjamin Knier	Department of Neurology, Klinikum rechts der Isar,	Analysis and interpretation, critical

	School of Medicine, Technical University of Munich, Germany	revision of the manuscript for important intellectual content, took part in the panel discussions.
Thomas Korn	Department of Neurology, Klinikum rechts der Isar, School of Medicine, Technical University of Munich, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Scott Kolbe	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	Department of Neurology with Institute of Translational Neurology, University of Münster, Münster, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Wolf A. Lagrèze	Eye Center, Medical Center, Faculty of Medicine, University of	Analysis and interpretation, critical revision of the manuscript

	Freiburg, Freiburg, Germany	for important intellectual content, took part in the panel discussions.
Letizia Leocani	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	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.
Elena H. Martínez- Lapiscina	Institut d'Investigacions Biomediques August Pi iSunyer (IDIBAPS) and Hospital Clinic, University of Barcelona, Barcelona, Spain	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Sven Meuth	Department of Neurology, Medical Faculty, Heinrich-	Analysis and interpretation, critical

	Heine University Düsseldorf, Germany	revision of the manuscript for important intellectual content, took part in the panel discussions.
Olivier Outteryck	Univ. Lille, Inserm, CHU Lille, U1172 - LiNCog (JPARC) - Lille Neurosciences & Cognition, F-59000 Lille, France	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Friedemann Paul	Experimental and Clinical Research Center, Max Delbrück Center for Molecular Medicine and Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Axel Petzold	Moorfields Eye Hospital, City Road, The National Hospital for Neurology and Neurosurgery, Queen Square, UCL Institute of	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the

	Neurology, London, UK and Neuro-ophthalmology Expert Center, Amsterdam UMC, The Netherlands	panel discussions.
Gorm Pihl-Jensen	Department of Neurology, Rigshospitalet Glostrup and University of Copenhagen, Denmark	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Jana Lizrova Preiningerova	Department of Neurology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Gema Rebolleda	Department of Ophthalmology, Ramon y Cajal Hospital, Medicine University of Alcalá, Madrid, Spain	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Marius Ringelstein	Department of Neurology, Center for Neurology and Neuropsychiatry, LVR-	Analysis and interpretation, critical revision of the manuscript

	Klinikum, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany	for important intellectual content, took part in the panel discussions.
Shiv Saidha	Division of Neuroimmunology, Johns Hopkins University, Baltimore, USA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Sven Schippling	Department of Neurology, University Hospital Zurich, Switzerland	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Joel S. Schuman	Departments of Neurology, Population Health and Ophthalmology, NYU Grossman School of Medicine, New York, USA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Robert C. Sergott	Thomas Jefferson University Medical College, Philadelphia, USA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the

		panel discussions.
Ahmed Toosy	Queen Square MS Centre, Department of Neuroinflammation, UCL Institute of Neurology, University College London, London, UK	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Pablo Villoslada	Institut d'Investigacions Biomediques August Pi iSunyer (IDIBAPS) and Hospital Clinic, University of Barcelona, Barcelona, Spain	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Sebastian Wolf	Department of Ophthalmology and Department of Clinical Research, Bern University Hospital, University of Bern, Switzerland	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
E. Ann Yeh	Division of Neurology, Department of Pediatrics, Hospital for Sick Children, Division of Neurosciences and Mental Health SickKids Research Institute, University of	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.

	Toronto, Canada	
Patrick Yu-Wai-Man	Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK, and Moorfields Eye Hospital, London, UK	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Hanna G. Zimmermann	Experimental and Clinical Research Center, Max Delbrück Center for Molecular Medicine and Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions.
Alexander U. Brandt	Experimental and Clinical Research Center, Max Delbrück Center for Molecular Medicine and Charité– Universitätsmedizin Berlin, corporate member of Freie Universität Berlin,	Analysis and interpretation, Study concept and design, acquisition of data, drafting and critical revision of the manuscript for important intellectual content, study

	Humboldt-Universität zu Berlin, and Berlin Institute of Health, Germany University of California, Irvine, CA, USA	supervision, took part in the panel discussions.
Philipp Albrecht	Department of Neurology, Medical Faculty, Heinrich-Heine University Düsseldorf, Germany	Analysis and interpretation, Study concept and design, acquisition of data, drafting and critical revision of the manuscript for important intellectual content, study supervision, took part in the panel discussions.

References

1. Cruz-Herranz A, Balk LJ, Oberwahrenbrock T, et al. The APOSTEL recommendations for reporting quantitative optical coherence tomography studies. *Neurology* 2016;86:2303-2309.
2. Balcer LJ, Balk LJ, Brandt AU, et al. The International Multiple Sclerosis Visual System Consortium: Advancing Visual System Research in Multiple Sclerosis. *Journal of Neuro-Ophthalmology* 2018;38.
3. Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the *Journal of Clinical Epidemiology*. *Journal of clinical epidemiology* 2011;64:380-382.
4. de Villiers MR, de Villiers PJ, Kent AP. The Delphi technique in health sciences education research. *Medical teacher* 2005;27:639-643.
5. Cameron JR, Albrecht P, Cruz-Herranz A, Petzold A, Lagreze WA, Brandt AU. The APOSTEL recommendations for reporting quantitative optical coherence tomography studies. *Neurology* 2016;87:1960.
6. Staurengi G, Sadda S, Chakravarthy U, Spaide RF. Proposed lexicon for anatomic landmarks in normal posterior segment spectral-domain optical coherence tomography: the IN•OCT consensus. *Ophthalmology* 2014;121:1572-1578.
7. Balk LJ, de Vries-Knoppert WA, Petzold A. A simple sign for recognizing off-axis OCT measurement beam placement in the context of multicentre studies. *PLoS One* 2012;7:e48222.
8. Oberwahrenbrock T, Weinhold M, Mikolajczak J, et al. Reliability of Intra-Retinal Layer Thickness Estimates. *PLoS one* 2015;10:e0137316.
9. Cunningham CT, Quan H, Hemmelgarn B, et al. Exploring physician specialist response rates to web-based surveys. *BMC Med Res Methodol* 2015;15:32-32.
10. Petzold A, Albrecht P, Balcer L, et al. Artificial Intelligence extension of the OSCAR-IB criteria. *Annals of Clinical and Translational Neurology* [in print].

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 (d) In case of limited word count consider submitting the exact methodology as supplementary material
2 Acquisition device	For all OCT devices used, report data on: (a) Manufacturer (b) Model (c) Version (d) Software Version (e) Device type (time/spectral domain, swept source, adaptive optics)
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"> - 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 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: <ol style="list-style-type: none"> 1. Excitation wavelength 2. Filter sets 3. Number of frames averaged (if applicable) 4. Report device specific features when utilized (e.g. enhanced depth imaging, swept source OCT, adaptive optics)
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) How potential bias was addressed in the case of manual segmentation or manual correction of automated segmentation errors (masking) (e) Grid used for data-extraction (size, shape, selected sections) (f) Pixel to mm ratio if images are exported (caliper need)
8 Nomenclature and abbreviations	Define: (a) Anatomical structures analyzed (b) Units of provided measurements (e.g. volume or thickness) (c) Report the number of eyes presenting additional retinal pathology. Describe qualitative retinal changes and report exact methodology of quantification
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).

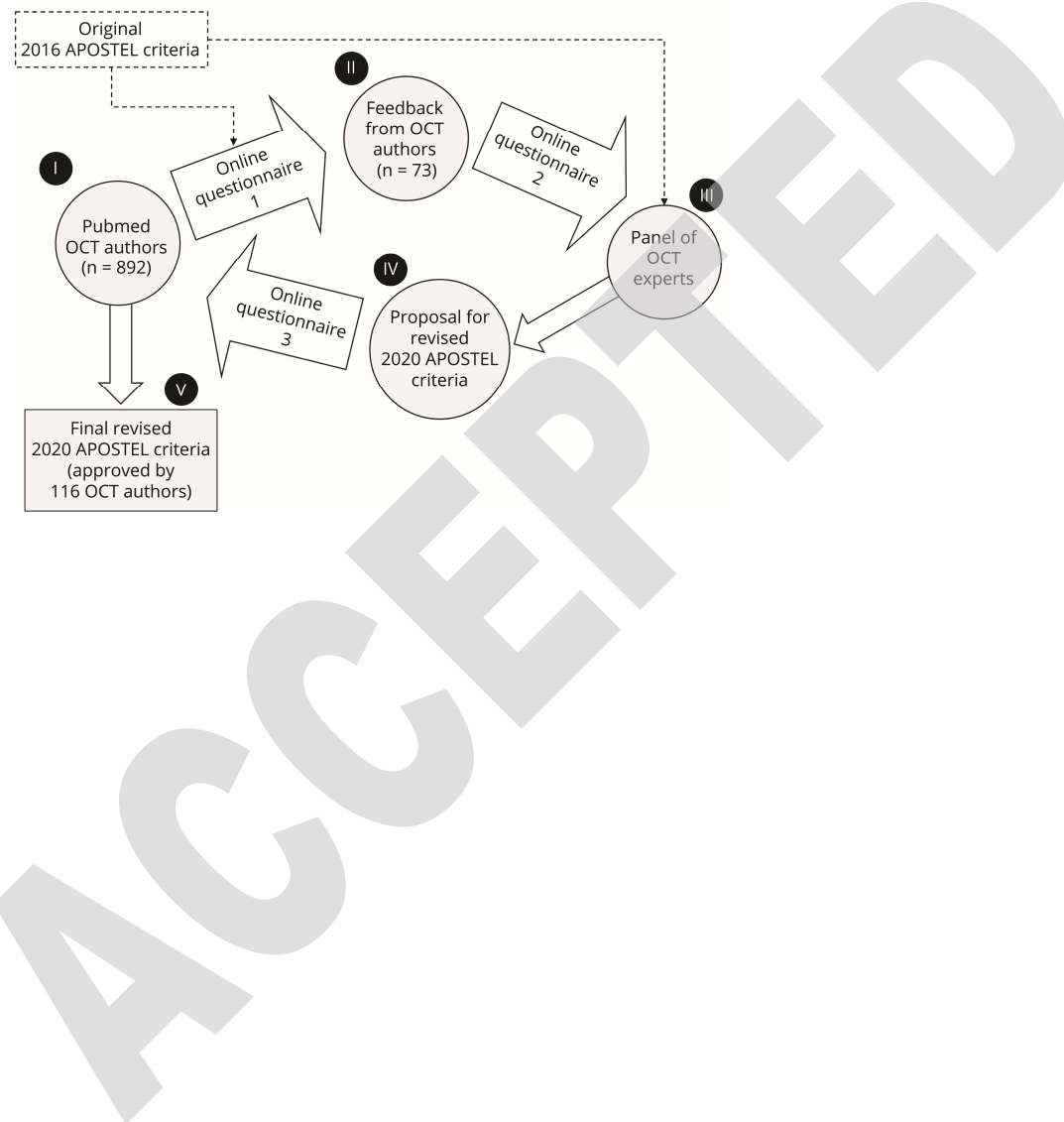
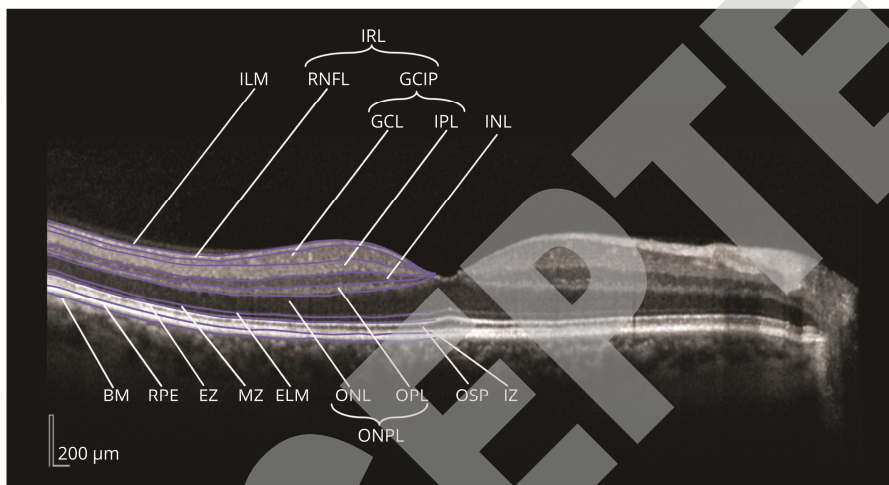


Figure 2: The consensus nomenclature for retinal structures

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>).



Neurology®

The APOSTEL 2.0 Recommendations for Reporting Quantitative Optical Coherence Tomography Studies

Aykut Aytulun, Andrés Cruz-Herranz, Orhan Aktas, et al.

Neurology published online April 28, 2021

DOI 10.1212/WNL.0000000000012125

This information is current as of April 28, 2021

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/early/2021/04/28/WNL.0000000000012125.full
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): All Imaging http://n.neurology.org/cgi/collection/all_imaging All Neuro-ophthalmology http://n.neurology.org/cgi/collection/all_neuroophthalmology Retina http://n.neurology.org/cgi/collection/retina
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright Copyright © 2021 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Academy of Neurology.. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

