1. Acta Ophthalmol. 2022 Sep;100(6):654-664. doi: 10.1111/aos.15063. Epub 2021 Nov 8.

Dynamic volume-rendered optical coherence tomography pupillometry.

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PURPOSE: To assess intrapupillary space (IPS) changes in healthy subjects with regard to decreased iris motility in patients with pseudoexfoliation glaucoma (PEXG) or non-arteritic anterior ischaemic optic neuropathy (NAION) in a feasibility study in a clinical environment.
METHODS: Scotopic and photopic IPS measurements using three-dimensionally rendered swept-source optical coherence tomography (SS-OCT) data were obtained and compared for all subjects. Intrapupillary space (IPS) parameters were evaluated such as absolute volumetric differences, relative light response for volumetric ratios and pupillary ejection fraction (PEF) for functional contraction measurements.
RESULTS: From a total of 122 IPS from 66 subjects, 106 IPS were eligible for comparison providing values for 72 normal, 30 PEXG and 4 NAION eyes. In healthy,

PEXG and NAION subjects, scotopic overall mean IPS was 8.90, 3.45 and 4.16 mm3 , and photopic overall mean IPS was 0.87, 0.74 and 1.13 mm3 , respectively. Three-dimensional contractility showed a mean absolute difference of 8.03 mm3 for normals (defined as 100% contractility), 2.72 mm3 for PEXG (33.88% of normal) and 3.03 mm3 for NAION (38.50% of normal) with a relative light response ratio between scotopic and photopic volumes of 10.26 (100%), 4.69 (45.70%) and 3.67 (35.78%), respectively. Pupillary ejection fraction (PEF) showed a contractile pupillary emptying of 88.11% for normals, 76.92% for PEXG and 70.91% for NAION patients.
CONCLUSION: This 3D pupillometry OCT assessment allows for quantitative measurements of pupil function, contractility and response to light. More specifically, PEF is presented as a potential (neuro)-pupillary outcome measure that could be useful in the monitoring of ophthalmic disorders that affect pupillary function.

DOI: 10.1111/aos.15063
PMID: 34750988 [Indexed for MEDLINE]

2. J Biophotonics. 2022 Dec;15(12):e202200169. doi: 10.1002/jbio.202200169. Epub 2022 Sep 11.

Volume-rendered optical coherence tomography angiography during ocular interventions: Advocating for noninvasive intraoperative retinal perfusion monitoring.

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We aimed to test for feasibility of volume-rendered optical coherence tomography angiography (OCTA) as a novel method for assessing/quantifying retinal vasculature during ocular procedures and to explore the potential for intraoperative use. Thirty patients undergoing periocular anaesthesia were enrolled, since published evidence suggests a reduction in ocular blood flow. Retinal perfusion was monitored based on planar OCTA image-derived data provided by a standard quantification algorithm and postprocessed/volume-rendered OCTA data using a custom software script. Overall, imaging procedures were successful, yet imaging artifacts occurred frequently. In interventional eyes, perfusion parameters decreased during anaesthesia. Planar image-derived and volume rendering-derived parameters were correlated. No correlation was found between perfusion parameters and a motion artifact score developed for this study, yet all perfusion parameters correlated with signal strength as displayed by the device. Concluding, volume-rendered OCTA allows for noninvasive three-dimensional retinal vasculature assessment/quantification in challenging surgical settings and appears generally feasible for intraoperative use.

DOI: 10.1002/jbio.202200169
PMID: 36089335 [Indexed for MEDLINE]

3. Invest Ophthalmol Vis Sci. 2024 Jun 3;65(6):9. doi: 10.1167/iovs.65.6.9.

Time-Resolved Dynamic Optical Coherence Tomography for Retinal Blood Flow Analysis.

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PURPOSE: Optical coherence tomography (OCT) representations in clinical practice are static and do not allow for a dynamic visualization and quantification of blood flow. This study aims to present a method to analyze retinal blood flow dynamics using time-resolved structural OCT.
METHODS: We developed novel imaging protocols to acquire video-rate time-resolved OCT B-scans (1024 × 496 pixels, 10 degrees field of view) at four different sensor integration times (integration time of 44.8 µs at a nominal A-scan rate of 20 kHz, 22.4 µs at 40 kHz, 11.2 µs at 85 kHz, and 7.24 µs at 125 kHz). The vessel centers were manually annotated for each B-scan and surrounding subvolumes were extracted. We used a velocity model based on signal-to-noise ratio (SNR) drops due to fringe washout to calculate blood flow velocity profiles in vessels within five optic disc diameters of the optic disc rim.
RESULTS: Time-resolved dynamic structural OCT revealed pulsatile SNR changes in the analyzed vessels and allowed the calculation of potential blood flow velocities at all integration times. Fringe washout was stronger in acquisitions with longer integration times; however, the ratio of the average SNR to the peak

SNR inside the vessel was similar across all integration times.
CONCLUSIONS: We demonstrated the feasibility of estimating blood flow profiles based on fringe washout analysis, showing pulsatile dynamics in vessels close to the optic nerve head using structural OCT. Time-resolved dynamic OCT has the potential to uncover valuable blood flow information in clinical settings.

DOI: 10.1167/iovs.65.6.9
PMCID: PMC11160951
PMID: 38837167 [Indexed for MEDLINE]

Conflict of interest statement: Disclosure: P. Valmaggia, Swiss National Science Foundation (Grant 323530_199395) (F), the Janggen-Pöhn Stiftung (F), AlumniMedizin Basel (F), Heidelberg Engineering GmbH (I); P.C. Cattin, None; R. Sandkühler, None; N. Inglin, None; T.P. Otto, Heidelberg Engineering GmbH (E); S. Aumann, Heidelberg Engineering GmbH (E); M.M. Teussink, Heidelberg Engineering GmbH (E); R.F. Spaide, Topcon Medical Systems (C), Roche (C), Bayer (C), Heidelberg Engineering (C), Genentech (C); H.P.N. Scholl, Swiss National Science Foundation (Project funding: “Developing novel outcomes for clinical trials in Stargardt disease using structure/function relationship and deep learning” #310030_201165, and National Center of Competence in Research Molecular Systems Engineering: “NCCR MSE: Molecular Systems Engineering (phase II)” #51NF40-182895) (F), the Wellcome Trust (PINNACLE study) (F), and the Foundation Fighting Blindness Clinical Research Institute (ProgStar study) (F), Scientific Advisory Board of Boehringer Ingelheim Pharma GmbH & Co. (S), Droia NV (S), Eluminex Biosciences (S), Janssen Research & Development, LLC (Johnson & Johnson) (S), Novartis Pharma AG (CORE) (S), Okuvision GmbH (S), ReVision Therapeutics Inc. (S), Saliogen Therapeutics Inc. (S), Alnylam Pharmaceuticals Inc. (C), Gerson Lehrman Group Inc. (C), Guidepoint Global, LLC (C), and Intergalactic Therapeutics Inc. (C), Data Monitoring and Safety Board/Committee of Belite Bio (DRAGON trial, NCT05244304, LBS-008-CT02, NCT05266014), (CT2019-CTN-04690-1) (S), F. Hoffmann-La Roche Ltd. (VELODROME trial, NCT04657289; DIAGRID trial, NCT05126966; HUTONG trial) (S), member of the Steering Committee of Novo Nordisk (FOCUS trial; NCT03811561) (S); P.M. Maloca,

F. Hoffmann-La Roche Ltd. (C), MIMO AG (O), VisionAI (O). Funding organizations had no influence on the design, performance or evaluation of the current study

4. Sci Rep. 2022 Aug 2;12(1):13276. doi: 10.1038/s41598-022-17699-7.

Cynomolgus monkey's choroid reference database derived from hybrid deep learning optical coherence tomography segmentation.

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Cynomolgus monkeys exhibit human-like features, such as a fovea, so they are often used in non-clinical research. Nevertheless, little is known about the natural variation of the choroidal thickness in relation to origin and sex. A combination of deep learning and a deterministic computer vision algorithm was applied for automatic segmentation of foveolar optical coherence tomography images in cynomolgus monkeys. The main evaluation parameters were choroidal thickness and surface area directed from the deepest point on OCT images within the fovea, marked as the nulla with regard to sex and origin. Reference choroid landmarks were set underneath the nulla and at 500 µm intervals laterally up to a distance of 2000 µm nasally and temporally, complemented by a sub-analysis of the central bouquet of cones. 203 animals contributed 374 eyes for a reference choroid database. The overall average central choroidal thickness was 193 µm with a coefficient of variation of 7.8%, and the overall mean surface area of the central bouquet temporally was 19,335 µm2 and nasally was 19,283 µm2. The choroidal thickness of the fovea appears relatively homogeneous between the sexes and the studied origins. However, considerable natural variation has been observed, which needs to be appreciated.

DOI: 10.1038/s41598-022-17699-7
PMCID: PMC9346135
PMID: 35918392 [Indexed for MEDLINE]

Conflict of interest statement: Authors CF, ND and CS are salaried employees of Roche. PMM is a consultant of Roche. The other authors declare no conflict.

5. Transl Vis Sci Technol. 2022 Nov 1;11(11):6. doi: 10.1167/tvst.11.11.6.

Iris Color Matters-A Contractility Analysis With Dynamic Volume-Rendered Optical

Coherence Tomography Pupillometry.

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PURPOSE: To analyze natural variability in pupillary contractility with dynamic volume-rendered optical coherence tomography (OCT) pupillometry regarding iris color, age, and sex in healthy Caucasian participants.
METHODS: The intrapupillary spaces (IPSs) derived from anterior segment swept-source OCT of 71 healthy eyes were retrospectively analyzed. Baseline scotopic and photopic volumes and the functional parameters of pupillary ejection fraction (PEF), three-dimensional (3D) contractility, and relative light response (RLR) were measured on the swept-source OCT volumes. The effect on these parameters of iris color (brown, green, and blue), age, and sex was assessed.
RESULTS: More pigmented irises were more contractile than less pigmented irises. Iris color significantly affected scotopic baseline IPSs (brown, 10.39 ± 4.86 mm3; green, 9.68 ± 3.31 mm3; blue, 6.75 ± 4.27 mm3; P = 0.018), PEF (brown, 90.8% ± 2.7%; green, 89.1% ± 2.5%; blue, 85.0% ± 9.3%; P = 0.010), 3D contractility (brown, 9.52 ± 4.59 mm3; green, 8.66 ± 3.07 mm3; blue, 6.44 ± 4.87 mm3; P = 0.016), and RLR (brown, 11.90 ± 4.03; green, 9.75 ± 2.73; blue, 8.52 ± 3.88; P = 0.026). Absolute scotopic volume (P = 0.022) and 3D contractility (P = 0.024) decreased with age. Sex showed no correlations.
CONCLUSIONS: The natural variability of pupillary contractility can be analyzed with dynamic OCT pupillometry. Iris color and age can impact pupillary response with this method.
TRANSLATIONAL RELEVANCE: Iris contractility parameters can be measured using a

commercially available OCT system, allowing for quantification of the aqueous humor volume inside the pupil.

DOI: 10.1167/tvst.11.11.6
PMCID: PMC9652714
PMID: 36342706 [Indexed for MEDLINE]

Conflict of interest statement: Disclosure: P. Valmaggia, Swiss National Science Foundation (Grant 323530_199395) (F), AlumniMedizin Basel (F); N. Inglin, None; P. Kaiser, Supercomputing Systems AG, Zurich, Switzerland (E); H.P.N. Scholl, Swiss National Science Foundation (Project funding: “Developing novel outcomes for clinical trials in Stargardt disease using structure/function relationship and deep learning” #310030_201165, and National Center of Competence in Research Molecular Systems Engineering: “NCCR MSE: Molecular Systems Engineering (phase II)” #51NF40-182895) (F), the Wellcome Trust (PINNACLE study) (F), and the Foundation Fighting Blindness Clinical Research Institute (ProgStar study) (F), Astellas Pharma Global Development, Inc./Astellas Institute for Regenerative Medicine (S), Boehringer Ingelheim Pharma GmbH & Co (S), Gyroscope Therapeutics Ltd. (S), Janssen Research & Development, LLC (Johnson & Johnson) (S), Novartis Pharma AG (CORE) (S), Okuvision GmbH (S), and Third Rock Ventures, LLC (S), Gerson Lehrman Group (C), Guidepoint Global, LLC (C), and Tenpoint Therapeutics Limited (C), Data Monitoring and Safety Board/Committee of Belite Bio (CT2019-CTN-04690-1), ReNeuron Group Plc/Ora Inc. (NCT02464436), F. Hoffmann-La Roche Ltd (VELODROME trial, NCT04657289; DIAGRID trial, NCT05126966) and member of the Steering Committee of Novo Nordisk (FOCUS trial; NCT03811561) (N); P.M. Maloca, Roche (C), MIMO AG (O), VisionAI (O)

6. Sci Rep. 2023 Apr 9;13(1):5797. doi: 10.1038/s41598-023-32739-6.

Cynomolgus monkey's retina volume reference database based on hybrid deep learning optical coherence tomography segmentation.

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Cynomolgus monkeys (Macaca fascicularis) are commonly used in pre-clinical ocular studies. However, studies that report the morphological features of the macaque retina are based only on minimal sample sizes; therefore, little is known about the normal distribution and background variation. This study was conducted using optical coherence tomography (OCT) imaging to investigate the variations in retinal volumes of healthy cynomolgus monkeys and the effects of sex, origin, and eye side on the retinal volumes to establish a comprehensive reference database. A machine-learning algorithm was employed to segment the retina within the OCT data (i.e., generated pixel-wise labels). Furthermore, a classical computer vision algorithm has identified the deepest point in a foveolar depression. The retinal volumes were determined and analyzed based on this reference point and segmented retinal compartments. Notably, the overall foveolar mean volume in zone 1, which is the region of the sharpest vision, was 0.205 mm3 (range 0.154-0.268 mm3), with a relatively low coefficient of

variation of 7.9%. Generally, retinal volumes exhibit a relatively low degree of variation. However, significant differences in the retinal volumes due to the monkey's origin were identified. Additionally, sex had a significant impact on the paracentral retinal volume. Therefore, the origin and sex of cynomolgus monkeys should be considered when evaluating the macaque retinal volumes based on this dataset.

DOI: 10.1038/s41598-023-32739-6
PMCID: PMC10083168
PMID: 37032376 [Indexed for MEDLINE]

Conflict of interest statement: Research support was granted from Roche (Basel, Switzerland), especially with regard to data collection and the decision to publish. Roche had no role and did not interfere in the conceptualization or conduct of this study. Authors N.D., C.F., S.W., and MV are salaried employees of Roche, Switzerland. P.K. is a P.M.M. is a salaried employee of Supercomputing Systems, Zurich, Switzerland. The funder had no role in design, conduct or submission of the study. The other authors of this paper declare no competing interests. Outside of the present study, the authors declare the following competing interests: P.M.M. is a consultant at Zeiss Forum and holds intellectual property for machine learning at MIMO AG and VisionAI, Switzerland. H.P.N.S. is supported by the Swiss National Science Foundation (Project funding: “Developing novel outcomes for clinical trials in Stargardt disease using structure/function relationship and deep learning” #310030_201165 and National Center of Competence in Research Molecular Systems Engineering: “NCCR MSE: Molecular Systems Engineering (phase II)” #51NF40-182895), the Wellcome Trust (PINNACLE study), and the Foundation Fighting Blindness Clinical Research Institute (ProgStar study). H.P.N.S. is member of the scientific advisory boards of Astellas Pharma Global Development, Inc./Astellas Institute for Regenerative Medicine, Boehringer Ingelheim Pharma GmbH & Co; Gyroscope Therapeutics Ltd.; Janssen Research & Development, LLC (Johnson & Johnson); Novartis Pharma AG

(CORE); Okuvision GmbH; and Third Rock Ventures, LLC. H.P.N.S. is a consultant for Gerson Lehrman Group; Guidepoint Global, LLC; and Tenpoint Therapeutics Limited. H.P.N.S. is member of the Data Monitoring and Safety Board/Committee of Belite Bio (CT2019-CTN-04690-1), ReNeuron Group Plc/Ora Inc. (NCT02464436), and F. Hoffmann-La Roche Ltd (VELODROME trial, NCT04657289; DIAGRID trial, NCT05126966) and member of the Steering Committee of Novo Nordisk (FOCUS trial; NCT03811561). All arrangements have been reviewed and approved by the University of Basel (Universitätsspital Basel, USB) and the Board of Directors of the Institute of Molecular and Clinical Ophthalmology Basel (IOB) in accordance with their conflict of interest policies. Compensation is being negotiated and administered as grants by USB, which receives them in its proper accounts. H.P.N.S. is co-director of the IOB, which is a non-profit foundation and receives funding from the University of Basel, the University Hospital Basel, Novartis, and the government of Basel-Stadt. P.V. received funding from the Swiss National Science Foundation (Grant 323530_199395) and the Janggen-Pöhn Foundation.

7. Retina. 2021 Sep 1;41(9):1948-1957. doi: 10.1097/IAE.0000000000003110.

NEGATIVE VESSEL REMODELING IN STARGARDT DISEASE QUANTIFIED WITH VOLUME-RENDERED OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY.

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PURPOSE: To quantify retinal vasculature changes in Stargardt disease1 (STGD1) with volume-rendered optical coherence tomography angiography.
METHODS: Optical coherence tomography angiography volumes from healthy subjects and two subgroups of patients with STGD1 with the presence/absence of definitely decreased autofluorescence areas were compared. Optical coherence tomography angiography vessel surface area and vessel volume were measured in central zones (Z) of 1-, 2-, and 3-mm diameter.
RESULTS: Twenty nine eyes of 15 patients with STGD1 (20/9 eyes with/without definitely decreased autofluorescence) and 30 eyes of 15 controls contributed data. An enlarged foveal avascular zone was found in patients with STGD1 without and even more with definitely decreased autofluorescence associated with a vessel rarefication in central and also paracentral zones with unnoticeable autofluorescence. Vessel surface area and vessel volume were reduced in both STGD1 subgroups for all zones ($P < 0.0001$). Stargardt disease 1 eyes when compared to without definitely decreased autofluorescence showed reduced vessel surface area and vessel volume in Z2+3 (both $P < 0.05$).
CONCLUSION: Volume rendering of optical coherence tomography angiography in STGD1 shows a reduced retinal flow in the central macula. This is most likely secondary to loss of neurosensory tissue with disease progression and therefore not likely be favorably influenced by gene transfer and retinal pigment epithelial transplantation. Retinal blood flow assessed by 3D volume-rendered optical coherence tomography angiography could serve as surrogate marker for vascular changes of the central retina.

DOI: 10.1097/IAE.0000000000003110
PMID: 33438899 [Indexed for MEDLINE]

Conflict of interest statement: H. P. N. Scholl is a member of the Scientific

Advisory Board of: Astellas Institute for Regenerative Medicine; GenSight Biologics; Ionis Pharmaceuticals, Inc.; Gyroscope Therapeutics Ltd.; Janssen Research & Development, LLC (Johnson & Johnson); and Pharma Research & Early Development (pRED) of F. Hoffmann-La Roche Ltd; Novartis Pharma AG (CORE). H. P. N. Scholl is paid consultant of: Boehringer Ingelheim Pharma GmbH & Co; Gerson Lehrman Group; and Guidepoint. H. P. N. Scholl is a member of the Data Monitoring and Safety Board/Committee of Belite Bio and ReNeuron Group Plc/Ora Inc. and a member of the Steering Committee of Novo Nordisk (FOCUS trial). H. P. N. Scholl is co-director of the Institute of Molecular and Clinical Ophthalmology Basel (IOB) that is constituted as a non-profit foundation and receives funding from the University of Basel, the University Hospital Basel, Novartis, and the government of Basel-Stadt. These arrangements have been reviewed and approved by the University of Basel (Universitätsspital Basel, USB) in accordance with its conflict of interest policies. H. P. N. Scholl is principal investigator of grants at the USB sponsored by the following entities: IVERIC bio (Ophthotech Corporation); Kinarus AG; and Novartis Pharma AG. Grants at USB are negotiated and administered by the institution (USB), which receives them on its proper accounts. Individual investigators who participate in the sponsored project(s) are not directly compensated by the sponsor but may receive support from the institution for their project(s). R. F. Spaide has received personal compensation from Topcon Medical Systems, Roche, Genentech, Bayer, Regeneron, Heidelberg Engineering, Adverum Biotechnologies, and DORC. P. M. Maloca is Group Leader Ophthalmic Imaging, Institute of Molecular and Clinical Ophthalmology (IOB), Basel, Switzerland, and is co-director, OCTlab, University Basel, Mittlere Strasse 91, CH-4056 Basel, Switzerland & Belegarzt Hirslanden St. Anna im Bahnhof, Luzern. Furthermore, he is a Honorary Research Fellow, Moorfields Eye Hospital, 162 City Rd, London EC1V 2PD, London, United Kingdom. P. M. Maloca is a consultant of Zeiss and Roche. The remaining authors have no conflicting interests to disclose.

8. Sci Rep. 2021 Oct 19;11(1):20647. doi: 10.1038/s41598-021-99704-z.

Uncovering of intraspecies macular heterogeneity in cynomolgus monkeys using hybrid machine learning optical coherence tomography image segmentation.

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The fovea is a depression in the center of the macula and is the site of the highest visual acuity. Optical coherence tomography (OCT) has contributed considerably in elucidating the pathologic changes in the fovea and is now being considered as an accompanying imaging method in drug development, such as antivascular endothelial growth factor and its safety profiling. Because animal numbers are limited in preclinical studies and automatized image evaluation tools have not yet been routinely employed, essential reference data describing the morphologic variations in macular thickness in laboratory cynomolgus monkeys are sparse to nonexistent. A hybrid machine learning algorithm was applied for automated OCT image processing and measurements of central retina thickness and surface area values. Morphological variations and the effects of sex and

geographical origin were determined. Based on our findings, the fovea parameters are specific to the geographic origin. Despite morphological similarities among cynomolgus monkeys, considerable variations in the foveolar contour, even within the same species but from different geographic origins, were found. The results of the reference database show that not only the entire retinal thickness, but also the macular subfields, should be considered when designing preclinical studies and in the interpretation of foveal data.

DOI: 10.1038/s41598-021-99704-z
PMCID: PMC8526684
PMID: 34667265 [Indexed for MEDLINE]

Conflict of interest statement: Research support was granted from Roche, Basel, Switzerland, especially with data collection and the decision to publish. Roche had no role and did not interfere in conceptualization or conduct of this study. N.D., C.S., and H.B. are salaried employees of Roche, Switzerland. P.M.M. and P.W.H. are consultants for Roche, Switzerland. The other authors of this paper declare no competing interests. Outside of the present study, the authors declare the following competing interests: P.M.M. is a consultant at Zeiss Forum and holds intellectual properties for machine learning and speckle-denoising. C.E. and A.T. received a financial grant from the National Institute for Health Research (NIHR) Biomedical Research Centre, based at Moorfields Eye Hospital, and also from the NHS Foundation Trust and the UCL Institute of Ophthalmology. The views expressed in this article are those of the authors and not necessarily those of the National Eye Institute, NHS, the NIHR, or the Department of Health. A.T. is a consultant for Heidelberg Engineering and Optovue and has received research grant funding from Novartis and Bayer. C.E. is a consultant for Heidelberg Engineering and has received research grant funding from Novartis.

9. Acta Ophthalmol. 2022 Mar;100(2):e588-e597. doi: 10.1111/aos.14900. Epub 2021

May 14.

Feasibility and tolerability of ophthalmic virtual reality as a medical communication tool in children and young people.

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PURPOSE: Virtual reality (VR) can be useful in explaining diseases and complications that affect children in order to improve medical communications with this vulnerable patient group. So far, children and young people's responses to high-end medical VR environments have never been assessed.
METHODS: An unprecedented number of 320 children and young people were given the opportunity to interact with a VR application displaying original ophthalmic volume data via a commercially available tethered head-mounted display (HMD). Participants completed three surveys: demographics and experience with VR, usability and perceived utility of this technology and the Simulator Sickness Questionnaire. The second survey also probed participants for suggestions on

improvements and whether this system could be useful for increasing engagement in science.
RESULTS: A total of 206 sets of surveys were received. 165 children and young people (84 female) aged 12-18 years (mean, 15 years) completed surveys that could be used for analysis. 69 participants (47.59%) were VR-naïve, and 76 (52.41%) reported that they had previous VR experience. Results show that VR facilitated understanding of ophthalmological complications and was reasonably tolerated. Lastly, exposure to VR raised children and young people's awareness and interest in science.
CONCLUSIONS: The VR platform used was successfully utilized and was well accepted in children to display and interact with volume-rendered 3D ophthalmological data. Virtual reality (VR) is suitable as a novel image display platform in ophthalmology to engage children and young people.

DOI: 10.1111/aos.14900
PMCID: PMC9290670
PMID: 33988309 [Indexed for MEDLINE]