Regional & International Glaucoma Societies

American Glaucoma Society

Asia-Pacific Glaucoma Society

Australia and New Zealand Glaucoma Society

Canadian Glaucoma Society

Childhood Glaucoma Research Network

Chinese Glaucoma Society

Commonwealth Independent States Glaucoma Society

European Glaucoma Society

Glaucoma Society of India

International Society for Glaucoma Surgery

Japan Glaucoma Society

Latin American Glaucoma Society

Middle East African Glaucoma Society

Optometric Glaucoma Society

Pan American Glaucoma Society

International Glaucoma Review

VOLUME 22-4
2022

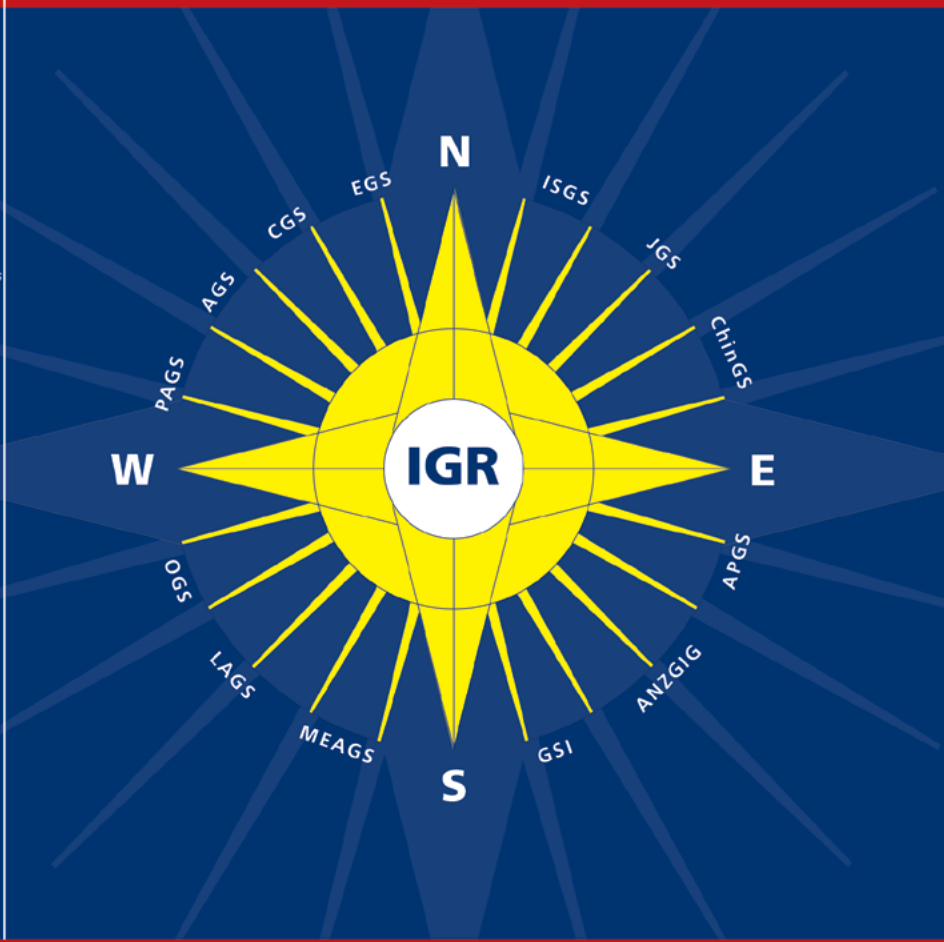
The journal of the World Glaucoma Association

Abstracts and Review of Glaucoma Literature

www.e-IGR.com

SINCE 1984

ISSN 1566-1040



OCULUS Glaucoma Experts

Pentacam® HR
Hey colleagues, I got the angles, depth, volume and pachy

Corvis® ST
Ok, I will check the patient's bIOP and for NTG

Smartfield
Perfect, I complete the data with a fast visual field

Solutions for Detecting Glaucoma

OCULUS has a number of methods and options to offer when it comes to glaucoma screening, follow-up and patient management: Tonometry, perimetry, tomography, pachymetry and, new to the range, the Biomechanical Glaucoma Factor for early detection of normal tension glaucoma as well as biomechanically corrected intraocular pressure.

All this is available from OCULUS.

Click here to learn more

OCULUS®

ISSN 1566-1040

INTERNATIONAL GLAUCOMA REVIEW

A Quarterly Journal
Volume 22 no. 4

Information on the member Glaucoma Societies of the WGA can be found in the WGA Global Directory of Glaucoma Societies at www.wga.one/wga/directory-of-glaucoma-societies

Registration
Access to IGR Online is complimentary for all members of glaucoma societies affiliated to the WGA. As of 2018, access to IGR is arranged through WGA#One; see next page for details. Should you have any questions, please contact us at info@e-igr.com

Find us on Facebook: www.facebook.com/worldglaucoma
Find us on Twitter: www.twitter.com/WorldGlaucoma
Find us on LinkedIn: www.linkedin.com/company/world-glaucoma-association
Find us on Instagram: www.instagram.com/worldglaucoma

ISSN 1566-1040

Contact Information
All correspondence on copies, supplements, content, advertising, etc. should be directed to:
WGA Executive Office
c/o Schipluidenlaan 4
1062 HE Amsterdam
The Netherlands
Tel: +31 20 570 9600
E-mail: info@worldglaucoma.org

Published by Kugler Publications, P.O. Box 20538, 1001 NM Amsterdam, The Netherlands, on behalf of the World Glaucoma Association.
Cover design: Cees van Rutten, The Hague, The Netherlands
Typesetting: 3bergen, www.3bergen.com

WGA#One

WGA#One is the name of the World Glaucoma Association's customer relationship management system. With WGA#One we are moving forward towards one platform, and hence one user profile, for all our services.

WGA#One is facilitating our communications about and access to our services, offers and initiatives. Therefore it's very important to keep your **WGA#One** profile updated. See below for details on how to activate your account for the first time.

Communicating effectively is key, and thus we extended our basic user profile with the option to activate different information preferences:

☑	**1 - Monthly newsletter**	A concise monthly digest of all WGA activities, such as congresses, publications, courses, projects, governance, scientific content, awareness activities etc. Find the archive here to get a taste: wga.one/wga/newsletter
☑	**2 - Glaucoma awareness initiatives**	Information on awareness activities, such as World Glaucoma Week
☑	**3 - Educational & scientific content**	For example: Consensus statements/ publications, International Glaucoma review, Journal of Glaucoma, recorded WGC session/enduring materials, etc.

In just a few clicks you'll be ensured to stay in touch and receive the latest news according to your own preferences. We never share your information with third parties.

Your privacy is very important to us, so please see our privacy policy at wga.one/terms-and-conditions

How to activate your WGA#One profile

1. **Please visit www.wga.one/wga/check-wga-account to check if you have a WGA#One account.**
2. **Enter your email address (use the address where you are currently receiving our communications).**
3. **You will receive an email with an activation link (if not received, check your spam folder first before contacting info@worldglaucoma.org).**
4. **Click on the link, create a new password, and update your WGA#One profile.**

If none of your email addresses is found in the system you can either contact us at info@worldglaucoma.org, or subscribe to our newsletter at: wga.one/wga/newsletter.

Santen

What do you expect from glaucoma surgery?

PRESERFLO™ MICROSHUNT

Indication:

The PRESERFLO™ MicroShunt glaucoma drainage system is intended for the reduction of intraocular pressure in the eyes of patients with primary open-angle glaucoma where IOP remains uncontrollable while on maximum tolerated medical therapy and/or where glaucoma progression warrants surgery.

Please read the PRESERFLO™ MicroShunt Instructions for Use carefully before using the device.
PRESERFLO™ has previously been referred to as Innfocus MicroShunt®

For inquiry on this product, please consult your local Santen representative directly for more information as product registrations may differ across regions and countries.

This product is not yet approved for use in the United States.

PP-PMS-ALL-0002: Date of Preparation: Oct 2020

Table of Contents

All abstracts are available online in the classified IGR searchable glaucoma database
www.e-IGR.com
The affiliations of the contributors to this issue can be found on www.e-IGR.com.

www.e-IGR.com

e-IGR.com

IGR Searchable Glaucoma Database

- Huge time saver to stay on top of the most significant glaucoma developments!
- The IGR abstract database holds **over 21,000 abstracts** related to Glaucoma, **all classified**, and some 10% commented on by leading experts.
- **Only glaucoma abstracts**: no false positives to wade through.
- Expert comments from the Editor's Selection are also **fully searchable** and linked to the abstracts.

Accessible, free of charge, to all members of WGA affiliated Glaucoma Societies

Features

- Searches in the abstracts may be limited to those abstracts that are commented on by experts.
- Limit your search or view abstracts by classification.
- Limit your search to (a range) of year(s) of publication
- Find related abstracts with one click of your mouse.
- Browse abstracts by classification, journal or author.
- Use operators to refine your queries and get better search results.

International Glaucoma Review is published as an online journal only.

If you are not yet receiving **IGR online**, we urge you go to the WGA website and supply us with your email address, so you will not miss any of the IGR content.

www.e-IGR.com

2022 APGC 6TH ASIA-PACIFIC GLAUCOMA CONGRESS

4 - 7 AUGUST 2022
KUALA LUMPUR, MALAYSIA

JOIN US FOR APGC 2022

IN CONJUNCTION WITH
THE 12TH MSO-ASM AND
THE 36TH MSJOC

KUALA LUMPUR CONVENTION CENTRE

4-7 AUGUST 2022

WWW.APGCONGRESS.ORG/REGISTRATION

APGS
Asia-Pacific Glaucoma Society

#APGC2022

MALAYSIAN GLAUCOMA SOCIETY

MALAYSIAN SOCIETY OF OPHTHALMOLOGY

Singapore Society of Ophthalmology

From the WGA

Dear IGR readers,

We are happy to let you know that the WGA continues to expand our educational resources online and to develop numerous opportunities for remote learning by our members. Our collaborative work as a society helps our members to deliver the very best care to our glaucoma patients.

On April 14, we held the second edition of the WGA Surgical Grand Rounds which addressed the topic of, 'The Management of Hypotony following Glaucoma Surgery'. The session was viewed by 1,124 participants across 117 countries. The recorded session is available to everyone with a WGA#One account. The third edition on Malignant Glaucoma and Nanophthalmos with Glaucoma took place on July 7, and will be available on-demand for all as of August 5. Find out more at the WGA website: wga.one/wga/surgical-grand-rounds.

At the recent annual ARVO meeting in Denver (May 1-4), the WGA hosted the 38th Information and Planning Exchange (IPE) meeting in person, with many participants also calling in from around the world. Major stakeholders in glaucoma care and research, including our top industry members, met to collaborate and network with the concerted goal to defeat glaucoma. Additionally, thanks to all of you who attended the ARVO meeting and stopped by the WGA booth. If you did not have the chance to get your copy of the WGA Patient Guide at our booth, you may download it here.

The WGC-2023 Program Planning Committee, chaired by Drs. Kaweh Mansouri and Arthur Sit, came together during the 15th Congress of the European Glaucoma Society (June 4-8) in Athens, Greece. They committee is creating a wonderful scientific and clinical program that will bring together the preeminent researchers, clinicians, and surgeons from around the globe as our faculty to educate and engage with our attending participants. Please mark your calendars for the next World Glaucoma Congress to take place June 28-July 1, 2023, in Rome. Abstract submission and registration will open in August 2022.

In collaboration with the World Society of Pediatric Ophthalmology and Strabismus (WSPOS) we presented the 8th WGA Global Webinar on Saturday, May 21, focusing on the topic of 'Childhood Glaucoma'. If you wish to view this excellent session, we encourage you to watch the recording on our website: wga.one/wga/wga-global-webinars.

The new talks in the Fundamental Questions in Glaucoma Video Lectures series have been released on July 18. Everyone with a WGA#One account will be able to access these talks and other educational resources through the WGA website. If you are a member of one of our affiliate glaucoma societies and do not have a free WGA#One account yet, please be sure to create one today.

Best wishes,

Neeru Gupta	**Shan Lin**	**Kaweh Mansori**
MD PhD MBA FRCSC DABO	MD	MD MPH
President	Executive Vice-President	Associate EVP

GET TO KNOW US!

Lisandro Sakata

Almost 16 years ago, I was invited to participate at the WGA Consensus on Angle Closure Glaucoma. As a young glaucoma fellow at University of Alabama at Birmingham with Prof. Chris Girkin (and previously at the University of Sao Paulo with Prof. Remo Susanna and colleagues), this first opportunity to collaborate with the greatest glaucoma experts in this field to create such important educational material was an amazing experience. A couple of years later, just after finishing my last glaucoma fellowship at the Singapore Eye Research Institute with Prof. Tin Aung, I joined the Associate Advisory Board, together with a group of great young clinician scientists eager to work for the WGA.

And for the past decade, I had the privilege to collaborate in many WGA projects, serving the Education and Nomination Committee; WGC Program Planning Committee in 2015 (Hong Kong), 2017 (Helsinki), and 2023 (Rome); at the Board of Governors; and as co-chair of Patient Committee and Communication and Technology Committee. It is indeed stimulating to note how WGA is continuously evolving: producing high-quality educational material, improving its resources accessibility and communication methods, as well as tackling challenging /inspiring missions such as to better glaucoma care in areas of need, and working to provide reliable, unbiased, easy to understand information for glaucoma patients. Of course, all these represent a continuation of amazing work from previous members and running so many activities is only possible due to the teamwork of outstanding colleagues, industry members, and specially the WGA executive office (Mariska, and now Irene, Marije and so many others – Simon Bakker as well) – all of them truly committed to contribute for a better life for our patients worldwide.

Currently, I am Professor of Ophthalmology and Head of Glaucoma Service at the Universidade Federal do Parana, Brazil; also serving other Regional Glaucoma/ Ophthalmological societies; happily married and father of two young sons – Lucas (12) and Leo (9). And I am quite confident (and proud) to balance my time with an association like WGA – for all it stands for, and the great people involved.

touch OPHTHALMOLOGY®

Join the
touchOPHTHALMOLOGY
online community for FREE access to

Practical articles

Expert interviews

News and insights

NEW
touchREVIEWS in Ophthalmology available now!

VISIT
touchOPHTHALMOLOGY.com

FOLLOW

Your Special Attention For

Standalone XEN45 Gel Stent implantation in the treatment of open-angle glaucoma: A systematic review and meta-analysis
Lim SY, Betzler BK, Yip LWL, Dorairaj S, Ang BCH
Survey of Ophthalmology 2022; 67(4): 1048-1061
abstract no. 98636

Alcohol, intraocular pressure, and open-angle glaucoma: A systematic review and meta-analysis
Stuart KV, Madjedi K, Luben RN, Chua SYL, Warwick AN, Chia M, Pasquale LR, Wiggs JL, Kang JH, Hysi PG, Tran JH, Foster PJ, Khawaja AP
Ophthalmology 2022; 129(6): 637-652
abstract no. 98707

The role of trabeculectomy in the era of minimally invasive glaucoma surgery
Kalarn S, Le T, Rhee DJ
Current Opinions in Ophthalmology 2022; 33: 112-118
abstract no. 98777

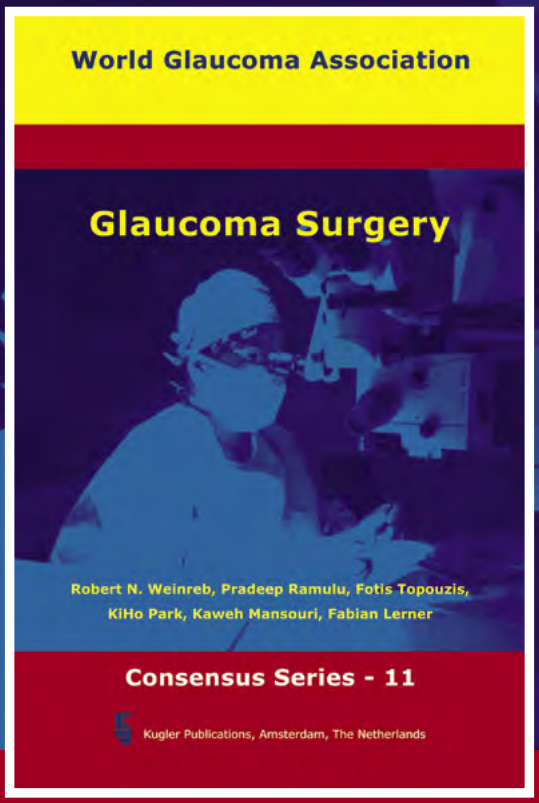
Artificial intelligence for glaucoma: Creating and implementing ai for disease detection and progression
Al-Aswad LA, Ramachandran R, Schuman JS, Medeiros F, Eydelman MB
Ophthalmology. Glaucoma 2022
abstract no. 98965

Intraocular pressure measurement: A review
Da Silva F, Lira M
Survey of Ophthalmology 2022
abstract no. 99032

The physiological and pathophysiological roles of the autophagy lysosomal system in the conventional aqueous humor outflow pathway: More than cellular clean-up
Shim MS, Liton PB
Progress in Retinal and Eye Research 2022; 101064
abstract no. 99343

WGA Consensus Series 11

Glaucoma Surgery



Order online and use discount code WGA1 to get a 10% discount at www.kuglerpublications.com

Editor's Selection

With the multitude and variety of publications it seems almost impossible for the ophthalmologist to intelligently read all the relevant subspecialty literature. Even the dedicated glaucomatologist may have difficulty to absorb 1200+ yearly publications concerning his/her favorite subject. An approach to this confusing situation may be a critical selection and review of the world literature.

Robert N. Weinreb, Chief Editor

Basic Science

Are Pericytes the Missing Link Between IOP and Functional Damage?

Comment by David Calkins, Nashville, TN, USA

98772 Pericyte dysfunction and loss of interpericyte tunneling nanotubes promote neurovascular deficits in glaucoma; Alarcon-Martinez L, Shiga Y, Villafranca-Baughman D, Belforte N, Quintero H, Dotigny F, Cueva Vargas JL, Di Polo A; Proceedings of the National Academy of Sciences of the United States of America 2022; 119(7): e2110329119

Physiological signaling within and between regions of the central nervous system (CNS) involves complex interplay between neurons and vascular elements via intermediary glial cells that bridge the two. Diseases that cause neurodegeneration dysfunction or failure in this interplay or 'neurovascular coupling' creates an imbalance between the metabolic needs struggling neuronal tissue with available bio-energetic resources. Similarly, dysfunctional neurovascular coupling is implicated in degeneration of retinal ganglion cells (RGCs) and their axons in glaucoma, involving reduced capillary blood flow spanning optic nerve to retina. Vascular pericytes are specialized cells that distribute intermittently along the walls of capillaries and contribute to formation of blood vessels and maintenance of the blood-brain barrier which regulates the privileged immunity of the CNS. At the level of microcirculation in the retina, pericytes help regulate neurovascular coupling through tunneling nanotubes that help connect local networks of

pericytes. The important paper by Adriana Di Polo and her colleagues (Alarcon-Martinez *et al.*, 2022) investigates with unprecedented resolution the mechanisms through which vascular pericytes influence retinal capillaries. Using an innovative combination of transgenics and two-photon laser scanning microscopy (TPLSM) to visualize capillary pericytes *in vivo*, the team demonstrated that experimental glaucoma constricts capillaries through calcium-dependent mechanisms that restricts ganglion cell blood supply.

The team demonstrated that experimental glaucoma constricts capillaries through calcium-dependent mechanisms that restricts ganglion cell blood supply

That restoring calcium homeostasis in retinal pericytes restores both vascular and neuronal function while protecting ganglion cells **highlights the potential utility of modulating pericyte physiology as a therapeutic intervention** more generally in CNS degenerative disease.

Clinical Examination Methods

Macular Damage Progression Can Be Missed by Standard Perimetry

Comment by Angelo Tanna, Chicago, IL, USA

99322 The 24-2 visual field Guided Progression Analysis can miss progression of glaucomatous damage of the macula seen with OCT; Hood DC, la Bruna S, Tsamis E, Leshno A, Melchior B, Grossman J, Liebmann JM, de Moraes CG; Ophthalmology. Glaucoma 2022; 0:

Professor Hood and colleagues evaluated the sensitivity and specificity of 24-2 guided progression analysis (GPA) in 29 healthy controls and 70 glaucoma suspects or patients with early glaucoma (baseline MD > –6 dB) with at least four serial VF and OCT studies over a period of at least one year. The reference standard was expert assessment of OCT imaging data and Humphrey visual fields (VF).[1] Subjects prospectively underwent a mean of 9.2 tests over 31 months in the context of the Macular Damage in Early Glaucoma and Progression Study. Among the glaucoma and glaucoma suspect subjects, almost half had normal baseline 24-2 and 10-2 VFs.

The study's reference standard for progression required agreement among three glaucoma specialists on three findings: (1) worsening of the circumpapillary RNFL profile; (2) corresponding change of the RNFL and GCL on probability maps; and (3) worsening of corresponding locations on the 10-2 or 24-2 VFs. The graders used the investigators' custom-made OCT progression report (which only relies on the first and final OCT studies) and commercially available VF reports.

Ten eyes were defined as having progressed by the reference standard criteria and 15 eyes had likely (n = 9) or possible progression (n = 6) on GPA. Two of the healthy control eyes had likely progression on GPA (false positives). The severity of the VF abnormality in these cases is striking, particularly for VFs performed in a research setting, and goes unexplained.

Six of the ten eyes defined as having progressed by the reference standard were not detected as having progressed by GPA (false negatives). All six of these had progression in the central 8° of the VF. There are only 12 locations in the central 10° of the VF represented in the 24-2 test, and macular glaucomatous damage may only affect one or two locations in the 24-2 VF. Since progression by GPA requires the presence of at least three locations of significant deterioration, early progression of focal central VF damage can go undetected by the software algorithm. Glaucoma experts reading this already know a clinician should not accept the GPA progression classification result without a critical review. It has been reported that the central 12 locations in the 24-2 field can be used to characterize central visual field damage.[2] Indeed, in another study, more than 90% of cases of disagreement between GPA and expert graders (who were aware of the GPA result but had no other information) were due to experts calling progression when GPA did not.[3]

Early glaucoma sometimes results in central visual field damage that can be missed by the 24-2 GPA algorithm

Nine eyes that did not meet the reference standard criteria for progression had likely (n = 4) or possible progression (n = 5) with GPA (possible false positives). Most of these eyes had normal and unchanged cpRNFL profiles, suggesting these were indeed false positive progression calls by GPA. This is not a surprise for the five eyes with the GPA classification of possible progression, since it is established that false positive progression calls are common in the absence of three confirmatory tests. The criteria for likely progression with GPA are essentially the same as those for defining VF progression in the Early Manifest Glaucoma Trial (EMGT). Since the subjects in the control group in EMGT were untreated, the progression detection algorithm was designed to be very sensitive for the detection of progression in eyes with glaucomatous VF defects at baseline.

The investigators did not report rates of change in either the visual field or structural parameters. Although some information can be gleaned from viewing the GPA reports in the figures, the duration of observation and the number of visual fields and OCT tests that were performed in the cases in which GPA resulted in false negative or false positive progression calls is not formally reported. Optic disc photographs were not evaluated as part of the study nor were OCT parameters of optic disc morphology. Nevertheless, this study nicely highlights the fact that early glaucoma sometimes results in central visual field damage that can be missed by the 24-2 GPA algorithm.

References

1. Hood DC, La Bruna S, Tsamis E,et al. The 24-2 Visual Field Guided Progression Analysis Can Miss the Progression of Glaucomatous Damage of the Macula Seen Using OCT. Ophthalmol Glaucoma. 2022 Mar 28:S2589-4196(22)00054-0. doi: 10.1016/j.ogla.2022.03.007. Epub ahead of print. PMID: 35358755.
2. Chakravarti T, Moghimi S, Weinreb RN. Prediction of Central Visual Field Severity in Glaucoma. J Glaucoma. 2022;31(6):430-437. doi: 10.1097/IJG.0000000000002031. Epub 2022 Apr 7. PMID: 35649258.
3. Tanna AP, Budenz DL, Bandi J, et al. Glaucoma Progression Analysis software compared with expert consensus opinion in the detection of visual field progression in glaucoma. Ophthalmology. 2012;119(3):468-473. doi: 10.1016/j.ophtha.2011.08.041. Epub 2011 Dec 2. PMID: 22137043; PMCID: PMC3294135.

Clinical Examination Methods

Analysing the Texture of Individual Nerve Fiber Bundles

Comment by Brad Fortune, Portland, OR, USA

98460 Diagnostic assessment of glaucoma and non-glaucomatous optic neuropathies via optical texture analysis of the retinal nerve fibre layer; Leung CKS, Lam AKN, Weinreb RN, Garway-Heath DF, Yu M, Guo PY, Chiu VSM, Wan KHN, Wong M, Wu KZ, Cheung CYL, Lin C, Chan CKM, Chan NCY, Kam KW, Lai GWK; Nature biomedical engineering 2022; 6(5): 593-604

Leung and colleagues have introduced a method for post-processing OCT scans that enhances visualization of axon bundles within the retinal nerve fiber layer when viewed as *en-face* projection images. **Their study also shows that the technique provides improved diagnostic accuracy for detecting glaucoma, as compared to an array of current standard clinical measures.** Leung and colleagues have called their new technique: 'Retinal Nerve Fiber Layer Optical Texture Analysis (ROTA)' and their paper describes in detail each of its five post-processing steps, which serve to: (1) reduce variation of RNFL reflectance intensity from B-scan to B-scan within and between eyes by normalizing to the intensity of a reference layer, the RPE; (2) enhance the contrast between axon bundles and the glial-vascular tissue components surrounding the axon bundles within the RNFL by applying an exponential transformation of the normalized pixel intensities; (3) prepare an *en-face* projection image by summing the normalized, amplified values of RNFL pixels in depth along each A-line; (4) account for RNFL thickness differences across quadrants and eyes by normalizing the *en-face* image values to a constant, alpha); and (5) further enhance

RNFL bundle visibility in the final displayed *en-face* image by applying another exponential transformation (essentially a gamma function), which helps utilize the full range of available gray scale values for display in an optimal manner.

In their paper, Leung *et al.* show that these post-processing steps produce compelling images of RNFL bundles across the entire posterior pole in healthy eyes and most important, also produce high contrast images of RNFL bundle defects in glaucomatous eyes more reliably than other current standard techniques such as 'red-free' fundus photographs, RNFL thickness maps derived from OCT scans and *en-face* projection images of RNFL that are not subject to all of the post-processing steps of ROTA. **Thus, ROTA helps overcome many of the limitations known to constrain the utility of these other common methods.**

Assessment of ROTA images improves diagnostic accuracy over current standards for glaucoma

The study by Leung *et al.* also clearly demonstrates that assessment of ROTA images improves diagnostic accuracy over current standards for glaucoma, albeit by a modest degree, nevertheless likely to have clinical importance going forward. The methodological details underlying this latter aspect of the study were articulated less clearly than other aspects within the paper, but seem to be based in part by applying a criterion size (minimal two-dimensional area of at least 0.29 mm^2) to define an 'RNFL defect' in a ROTA image, as well as some subjective determinations about whether or not a putative defect follows accepted trajectories of RNFL bundles; in any case, there was excellent inter-observer agreement for the latter, which may be further refined in the future to become objective and automated. Similarly, the 'depth' of what defines a ROTA defect was not described in quantitative terms, rather only as being 'hypo-reflective', so, this will also require further scrutiny and verification using other datasets.

Naturally, the ROTA technique also provides insight into RNFL bundle loss (and swelling) due to other forms of optic neuropathy besides glaucoma, as shown clearly in this study by Leung and colleagues. Overall, the paper is excellent (including the supplemental material, which provides additional text to describe methodological details, 25 additional figures and 25 additional tables to further support the conclusions); readers interested in the topic are strongly encouraged to peruse the entire report. It should be mentioned that the history of this particular field (starting with the pioneering work of Robert Knighton and colleagues) was not covered well or credited, nor were the many other previous studies about using RNFL reflectance for assessment of glaucoma. Several earlier reports documented similar if not exactly the same approach as some of the post-processing steps used in ROTA. This omission does not undermine the actual results of the study, which were presented very well in this paper. Finally, there are fundamental challenges remaining to overcome for this field, including for ROTA, such as how use of normalization steps based on RPE reflectance (and/or other depths of an OCT scan), which while beneficial in the short run, may introduce problems due to effects of decreased attenuation through degenerative RNFL bundles (*i.e.*, the OCT beam incident on the RPE under an RNFL defect is less attenuated). And, given that nearly all current OCT image segmentation algorithms depend to a great extent on the reflectance differences to define layer boundaries, it may

become a circular problem for analysis of RNFL reflectance. In context of these challenges, a novel approach contributed recently to this field by Cannon, Bouma and Uribe-Patarroyo also should be recognized.[1]

Reference

1. Cannon TM, Bouma BE, Uribe-Patarroyo N. Layer-based, depth-resolved computation of attenuation coefficients and backscattering fractions in tissue using optical coherence tomography. Biomed Opt Express. 2021;12(8):5037-5056. doi: 10.1364/BOE.427833. PMID: 34513241.

Clinical Examination Methods

Higher Temperatures and Disc Hemorrhage

Comment by Tanuj Dada and Saurabh Verma, New Delhi, India

98896 Analysis of variation in incidence of optic disc hemorrhage according to seasonal and temperature changes; Jang M, Kim YK, Jeoung JW, Park KH; American Journal of Ophthalmology 2022; 239: 84-89

Jang *et al.* evaluated the seasonal variation in optic disc hemorrhage (DH) by review of fundus photographs over two years to answer the research question – **what is the impact of temperature on the incidence of DH in glaucoma patients?**

Fundus images of 13,514 eyes were reviewed, and 454 eyes (3.36%) were confirmed to have DH. The DH incidence ratio was 1.53 (95% CI 1.23-1.91, $P < .01$) for the Temperature (T) < 10 °C group relative to the T ≥ 20 °C group. **The IOP of the patients with DH in winter was significantly higher than that measured in summer** and an increase in temperature by 1 °C, was associated with a reduction in the DH risk ratio to 0.979 (95% confidence interval [CI] 0.969-0.989, $P < .01$). *The study concluded that DH is affected by temperature, and as such, shows seasonal variability.*

This variation is in line with several studies that have shown seasonal variability in IOP which tends to be higher in colder months.[1,2] **Elevated IOP in winter months leading to stretching of the lamina cribrosa and mechanical vascular disruption may be a possible cause for this variation.**

Additionally, more than 64% of eyes with DH were diagnosed cases of normal-tension glaucoma (NTG) an entity where vascular dysregulation is a major contributing factor to disease pathogenesis.[3] Patients of primary vascular dysregulation are known to respond unfavorably to cold temperatures leading to an increase vasospasm. Females constituted

almost two thirds of the total cases of DH and vascular dysregulation is also known to be more common in females.[4] The **higher incidence of DH in winter months can also be attributed to vascular dysregulation due to autonomic dysfunction, which is exacerbated by colder temperatures and impact on blood coagulability and plasma viscosity.** However, this was not evaluated in the present study.

A significant proportion of patients (almost 44%) with DH had diabetes or hypertension which are independent risk factors for DH and a separate analysis evaluating concomitant changes in blood pressure/glycemic control would be a useful addition to study seasonal variation of DH in this subgroup group. Although the study reports variation in DH with temperature, the clinical significance of these results requires further evaluation related to the impact on disease progression and additional imaging modalities such as OCT angiography to establish objective changes in peripapillary circulation.

References

1. Kuze M, Ayaki M, Yuki K, et al. Seasonal variation of intra-ocular pressure in glaucoma with and without dry eye. Sci Rep. 2020;10(1):13949.
2. Mansouri K, Gillmann K, Rao HL, Weinreb RN. Weekly and seasonal changes of intraocular pressure measured with an implanted intraocular telemetry sensor. Br J Ophthalmol. 2021;105(3):387-391.
3. Flammer J, Konieczka K, Flammer AJ. The primary vascular dysregulation syndrome: implications for eye diseases. EPMA Journal. 2013;4(1):14.
4. Grieshaber MC, Mozaffarieh M, Flammer J. What Is the Link Between Vascular Dysregulation and Glaucoma? Survey of Ophthalmology. 2007;52(6):S144-154.

Clinical Examination Methods

Noninvasive Analysis of the Cerebrovascular Autoregulation

Comment by Alon Harris, New York, NY, USA

98779 Prospective Pilot Clinical Study of Noninvasive Cerebrovascular Autoregulation Monitoring in Open-Angle Glaucoma Patients and Healthy Subjects; Hamarat Y, Deimantavicius M, Dambrauskas V, Labunskas V, Putnynaite V, Lucinskas P, Siaudvytyte L, Simiene E, Stoskuviene A, Januleviciene I, Petkus V, Ragauskas A; Translational vision science & technology 2022; 11: 17

Glaucoma has long been associated with alterations in ocular and systemic hemodynamic factors, including faulty autoregulation of the retinal circulation during known vasoactive stimulus.[1-3] Similarities in cerebrovascular and ocular tissues and blood vessel autoregulation pathways suggest the potential for shared mechanisms of disease through impairment of local tissue autoregulation. Diseases such as Alzheimer's and glaucoma both involve changes to microvascular tissues and subsequent neurodegeneration, and these shared pathways may be even more significant in patients of African descent.[4] In the current article, **Hamarat and colleagues present novel findings highlighting compromised cerebral autoregulation in patients with normal tension (NTG) based on a novel non-invasive ultrasonic technique utilizing intracranial blood volume slow-wave measurements**. The authors specifically found the volumetric reactivity index (VRx) and the duration and doses of longest cerebral autoregulation impairment (LCAI) were significantly lower ($P < 0.05$) in healthy subjects than in patients with NTG and high tension (HTG) glaucoma during a Valsalva maneuver (forceful breathing test). **No statically significant differences were identified between healthy and HTG, or NTG and HTG subjects**. Previously in my laboratories, we have used transcranial Doppler to identify an absence of vasoreactivity in the middle cerebral artery (MCA) during hyperoxia in glaucoma patients.[5] These data compliment this finding, with a significant strength of the current approach being the inclusion of cerebrovascular autoregulation assessment over the entire cranium.

The non-invasive ultrasonic approach is highly translatable to a clinical setting

The non-invasive ultrasonic approach is highly translatable to a clinical setting, and may provide diagnostic enhancements for other brain diseases involving the microvasculature including traumatic brain injury (TBI) and patients with cardiac procedures. One limitation is the small patient sample and study power (ten NTG, eight HTG, and ten healthy) while

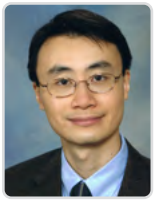
the cross-sectional study design and lack of comparison to a Gold standard for cerebrovascular autoregulation suggest need for confirmation in larger prospective controlled trials. Future studies should also account for potential influence of race, age, gender, and diurnal fluctuation of autoregulation. In summary, the novel findings presented by Hamarat *et al.* are highly impactful in demonstrating the ability to non-invasively identify cerebrovascular autoregulatory deficits in patients with NTG in a clinical setting. These data highlight the potential shared relationship of cerebrovascular and retinal vascular tissues, especially patients with NTG, and suggest a potential utility in the diagnosis of other vascular brain impairments.

References

1. Harris A, Guidoboni G, Siesky B, et al. Ocular blood flow as a clinical observation: Value, limitations and data analysis. J Prog Retin Eye Res. 2020:100841. PMID: 31987983
2. Harris A, Martin BJ, Shoemaker JA. Regulation of retinal blood flow during blood gas perturbation. J Glaucoma. 1994;3 Suppl 1:S82-90.PMID: 19920593.
3. Hosking SL, Harris A, Chung HS, et al. Ocular haemodynamic responses to induced hypercapnia and hyperoxia in glaucoma. Br J Ophthalmol. 2004;88(3):406-411.
4. Hutchins K, Harris A, Thomas J, et al. Alzheimer's disease and primary open-angle glaucoma associated with vascular health in patients of African descent. Acta Ophthalmol. 2018;96(8):e1031.
5. Harris A, Zarfati D, Zalish M, et al. Reduced cerebrovascular blood flow velocities and vasoreactivity in open-angle glaucoma. Am J Ophthalmol. 2003;135(2):144-147.PMID: 12566016.

Telemedicine

Implanted Sensors Can Telemonitor IOP Over 10 Years



Comment by Tyler Kaplan and Arthur Sit, Rochester, MN, USA

99170 Telemetric non-contact intraocular pressure monitoring with an implanted sensor in patients with glaucoma: long-term safety report and monitoring data; Schmidt I, Plange N, Walter P, Koutsonas A; British Journal of Ophthalmology 2022; 0:

The reduction of intraocular pressure (IOP) is currently the only known effective treatment available to reduce glaucomatous progression, but measurement of IOP is usually only performed during office hours every few months. However, as much as 80% of IOP peaks occur outside of scheduled appointments and frequently occur at night,[1] and may be related to disease progression.[2,3] Thus, there is a clear need for telemetric IOP monitoring to assess IOP throughout the day.

The purpose of the study from Schmidt *et al.* was to report the safety, tolerability, and functionality of a telemetric IOP sensor for up to ten years from patients enrolled in the ARGOS study.[4] The device was a first-generation ring-shaped implant with eight capacitive pressure sensors that measure IOP indirectly from mechanical deflections of the capacitor membrane, and was placed in the ciliary sulcus. IOP readings were obtained on demand with a handheld reader or on a continuous basis using a modified sleep mask and eye-patch with built in antennas. The device has since been modified and CE marked as the Eyemate system (Implandata Ophthalmic Products GmbH, Hannover, Germany). Six patients received the device placed at time of cataract surgery and long-term follow-up was available in five patients (one died 13 months after surgery due to unrelated causes). The device was well-tolerated without late onset complications. **Initially after the procedure, all patients had pupillary distortion and iris pigment dispersion. Four patients developed anterior chamber inflammation that resolved shortly after surgery. However, there was no ongoing inflammation beyond the early post-operative period, and pupillary distortion was not progressive. As well, there were no instances of dislocation of the pressure sensors. Importantly, the sensors in all surviving patients were still functional after ten years.**

> Importantly, the sensors in all surviving patients were still functional after ten years

This study provides valuable information regarding the long-term efficacy and safety of an implantable IOP sensor. Safety and tolerability appeared to be excellent even with this first generation device. However, this study was limited by its small sample size of six patients, with the vast majority of sensor measurements coming from a single patient. The remaining four surviving patients stopped regular self-tonometry after 25-51 months due to absence of ability or motivation.

The long-term safety data provided from the pioneering ARGOS study demonstrate that implantable pressure sensors are a viable and well-tolerated method for obtaining IOP measurements outside of the office for management of glaucoma

This suggests that long-term continuous IOP measurement may require a system that minimizes patient effort instead of requiring on-demand reading of the device. Also, there is limited data presented concerning the accuracy of pressure measurements from the implant. While the authors indicate that there was good correlation between Goldmann applanation tonometry and the sensor readings, and adjustments after calibration were not needed after the first few years, details were not presented. Nevertheless, the long-term safety data provided from the pioneering ARGOS study demonstrate that implantable pressure sensors are a viable and well-tolerated method for obtaining IOP measurements outside of the office for management of glaucoma.

References

1. Mansouri K, Weinreb RN, Liu JHK. Efficacy of a contact lens sensor for monitoring 24-h intraocular pressure related patterns. PLoS One. 2015;10(5):e0125530. doi:10.1371/journal.pone.0125530
2. Kim JH, Caprioli J. Intraocular Pressure Fluctuation: Is It Important? J Ophthalmic Vis Res. 13(2):170-174. doi:10.4103/jovr.jovr_35_18
3. Sit AJ. Intraocular pressure variations: causes and clinical significance. Can J Ophthalmol. 2014;49(6):484-488. doi:10.1016/j.jcjo.2014.07.008
4. Schmidt I, Plange N, Walter P, Koutsonas A. Telemetric non-contact intraocular pressure monitoring with an implanted sensor in patients with glaucoma: long-term safety report and monitoring data. Br J Ophthalmol. Published online March 21, 2022:bjophthalmol-2021-319786. doi:10.1136/bjophthalmol-2021-319786

Risk Factors

Myopia as a Risk Factor for POAG

Comment by Linda Zangwill, La Jolla, CA, USA

98897 High myopia as risk factor for the 10-year incidence of open-angle glaucoma in the Beijing Eye Study; Wang YX, Yang H, Wei CC, Xu L, Wei WB, Jonas JB; British Journal of Ophthalmology 2022; 0:

There are very few population-based longitudinal studies that can accurately assess the ten-year incidence of glaucoma and its risk factors. Moreover, with the increasing worldwide prevalence of high myopia, it is of particular interest to determine whether high myopia is a risk factor for the development of glaucoma in an unbiased, population-based sample. This important study by Wang *et al.* filled this gap by re-examining 2695 of the 4430 original participants of the Beijing Eye Study (2001-2011). Specifically, they estimated **the ten-year incidence of open-angle glaucoma (OAG) to be 3% in adult Chinese participants in the population-based Beijing Eye Study.** The strongest risk factor for the development of OAG was high myopia, with a 7.3-fold increased incidence compared to emmetropic eyes. Other risk factors included higher age, IOP, vertical cup disc ratio and thinner central corneal thickness. The incidence estimates are similar to the 3.4% glaucoma incidence rate in the Blue Mountain Study, while slightly lower than the nine-year incidence rate of the Barbardos Eye Study (4.4%)[1] and (accounting for shorter follow-up) lower than the Los Angeles Latino Eye Study (four-year incidence 2.3%).[2] The association between high myopia and incident glaucoma is consistent with other cross-sectional reports on risk factors associated with the prevalence of glaucoma.

> The strongest risk factor for the development of OAG was high myopia, with a 7.3-fold increased incidence compared to emmetropic eyes

Strengths of the study include its unique ten-year follow-up of a large population-based sample, large number of variables assessed in univariable analysis, appropriate and clearly reported multivariable modeling to identify risk factors for incident glaucoma, and its ability to assess high myopia and the experts involved in the assessment of the photograph-based endpoint. A weakness of this report is that some details regarding the definition, reproducibility and comparability of the incident OAG endpoint were not included.

The differentiation between highly myopic eyes with and without glaucoma is often challenging, so clear reproducible criteria for defining glaucoma are important. To exclude Beijing Eye Study participants with OAG at the baseline exam from the assessment of OAG incidence, fundus photographs were reviewed by two expert graders to detect glaucomatous optic neuropathy (GON) defined using both absolute criteria, which is similar to the definition recommended by the International Society of Geographical and Epidemiological Ophthalmology, and relative criteria based on retinal nerve fiber layer and neuroretinal rim thinning and retinal caliber, which has not previously been reported. Flicker chronoscopy was used to detect incident glaucomatous optic neuropathy by a panel of three experts. In case of a disagreement, photographs were reassessed up to three times until consensus was reached. **Although visual fields were used to define glaucoma in the original the Beijing Eye Study glaucoma prevalence report,[3] the authors note as a limitation that visual field test results could not be included in the definition of glaucoma for this ten-year incidence study.** Given that glaucoma was defined was photographs alone, additional details on the masked flicker chronoscopy implementation would have been helpful to better interpret these results. For example: (1) was the temporal sequence of the photographs masked (*i.e.*, order of photographs randomized)?; (2) what was the initial agreement among graders for flicker chronoscopy and what proportion of eyes required three reassessments before consensus was reached?; (3) were high myopes over-represented in the eyes requiring consensus?; and (4) how this GON definition may affect comparison with other population-based estimates of the incidence of OAG? In addition, it is unclear why the relative criteria for defining GON was initiated and how many subjects were excluded at baseline due to the relative criteria for GON alone. Given that flicker chronoscopy has been shown to be reproducible and accurate,[4,5] it is likely that documentation of these details would lead to a strengthening of the manuscript conclusions.

The authors acknowledge another limitation to the study, the participation rate of 66.4%, which is lower than other population-based studies (Blue Mountain 75.6%, and Beaver Dam 82.9%), in part due to the construction of a new airport which led to the relocation of a large number of participants; something that researchers cannot anticipate.

In conclusion, this study provides important new information on the ten-year incidence of glaucoma in a Chinese population, and highlights the importance of high myopia as a risk factor for the development of glaucoma. As the prevalence of high myopia increases worldwide, this study has important implications for public health planning of ophthalmic services for glaucoma detection.

References

1. Leske MC, Wu SY, Honkanen R, et al; Barbados Eye Studies G. Nine-year incidence of open-angle glaucoma in the Barbados Eye Studies. Ophthalmology. 2007;114:1058-1064.
2. Varma R, Wang D, Wu C, et al;, Los Angeles Latino Eye Study G. Four-year incidence of open-angle glaucoma and ocular hypertension: the Los Angeles Latino Eye Study. Am J Ophthalmol. 2012;154:315-325 e311.
3. Wang YX, Xu L, Yang H, Jonas JB. Prevalence of glaucoma in North China: the Beijing Eye Study. Am J Ophthalmol. 2010;150:917-924.
4. Heijl A, Bengtsson B. Diagnosis of early glaucoma with flicker comparisons of serial disc photographs. Invest Ophthalmol Vis Sci. 1989;30:2376-2384.

5. Schaefer JL, Meyer AM, Rodgers CD, et al. Comparing glaucomatous disc change using stereo disc viewing and the MatchedFlicker programme in glaucoma experts and trainees. Br J Ophthalmol. 2018;102:358-363.

Clinical Forms of Glaucoma

Does Ocular Rigidity Have a Special Role in Vasospastic Patients?

Comment by Michael Girard, Singapore

99320 Ocular rigidity and neuroretinal damage in vasospastic patients: a pilot study; Sayah DN, Mazzaferri J, Descovich D, Costantino S, Lesk MR; Canadian Journal of Ophthalmology 2022; 0:

Glaucoma has been referred to by many as a biomechanical disorder. After all, the optic nerve head (ONH) is exposed to high levels of biomechanical stress arising from various loads or pressures – exhibiting constant fluctuations – including, but not limited to: the intraocular pressure (IOP), the cerebrospinal fluid pressure (CSFP), the orbital fat pressure, the traction of the optic nerve (strongest in adduction), and stresses induced by diastole-to-systole choroidal expansion. Such stress levels are known to deform the ONH tissues; when they exceed their homeostatic range, they may be responsible (in part) for the development and progression of glaucoma. **These effects could be exacerbated if stress levels directly alter blood flow, or in the presence of existing vascular dysfunction.** Such interactions have not been studied in enough depth, and more clinical/engineering studies should be warranted.

In this study, the authors aimed to measure (1) ocular rigidity (a 'global' quantity approximating the elasticity of the corneo-scleral shell); and (2) neuroretinal damage (assessed through RNFL thickness) in patients with vasospasticity or atherosclerosis. Why vasospastic patients? Firstly, it has been shown that vasospasticity is a risk factor for glaucoma. Secondly, evidence suggests that patients with vasospasticity could exhibit ocular blood flow dysregulation in response to biomechanical stimuli. Overall, the authors hypothesized that lower values of ocular rigidity (*i.e.*, more ocular tissue deformations in response to IOP elevations) should correlate with greater glaucoma damage (as assessed through OCT-based RNFL thickness measurements). From their results, **the authors were able to confirm their hypothesis but the correlation was only significant for the infero-temporal region. No such correlations were observed in the atherosclerotic group.** The authors concluded that more structural damage could potentially occur in eyes that are

less rigid and in the presence of vasospasticity. These results could potentially suggest strong interactions between ocular tissue biomechanics and vascular dysfunction that could yield glaucomatous damage.

Several limitations in this pilot study were well acknowledged by the authors. Firstly, the sample size was small (ten vasospastic and 37 atherosclerotic participants), and the authors would benefit from reproducing their work in a much larger cohort. Second, the presence of vascular disorders was only assessed through patient questionnaires, and more quantitative tools (*e.g.*, blood flow measurements) should naturally be used to confirm vascular dysfunction. In addition, a wider spectrum of subjects should be considered, and also those with no vascular dysfunction, as atherosclerosis may well be stiffening the nerve.

The measurement of ocular rigidity may have its own limitation

It is also worth noting that the measurement of ocular rigidity may have its own limitation. Ocular rigidity is basically defined as how a change in ocular volume (loosely defined) would result in a change in IOP. Ocular rigidity has been suggested to reflect the biomechanical properties of the sclera. **Mathematical modelling tells us that a higher ocular rigidity is linked to a stiffer sclera, but not in the presence of a higher baseline IOP, thus contradicting previous thinking**.[1] In addition, ocular rigidity will not be able to reflect the robustness (or fragility) of a local region (such as the ONH), and other methods need to be developed to assess ONH robustness.[2] Nevertheless, ocular rigidity may still represent a clinically viable parameter, especially if could be assessed non-invasively. In previous publications, the authors found an elegant way to assess ocular rigidity *in vivo* noninvasively using OCT imaging the choroid during the cardiac cycle, and measurements of the ocular pulse amplitude.[3] Their technique was validated against measurements obtained with a more traditional method.[4] It was employed in the proposed study to assess ocular rigidity in vasospastic patients.

Overall, the proposed study has the merit of bridging the gap (from a clinical point-of-view) between two critical physical phenomena that are known to interact in the eye and that may well be driving glaucomatous damage: soft tissue biomechanics and hemodynamics. As stated in the title, this study remains a pilot study, but it could hopefully encourage more engineering and clinical developments to better understand these interactions.

This study remains a pilot study, but it could hopefully encourage more engineering and clinical developments to better understand these interactions

References

1. Jin Y, Wang X, Zhang L, et al. Modeling the Origin of the Ocular Pulse and Its Impact on the Optic Nerve Head. Invest Ophthalmol Vis Sci. 2018;59:3997-4010.
2. Braeu FA, Chuangsuwanich T, Tun TA, et al. AI-based Clinical Assessment of Optic Nerve Head Robustness Superseding Biomechanical Testing.

3. Beaton L, Mazzaferri J, Lalonde F, et al. Non-invasive measurement of choroidal volume change and ocular rigidity through automated segmentation of high-speed OCT imaging. Biomed Opt Express. 2015;6:1694-1706.
4. Sayah DN, Mazzaferri J, Ghesquiere P, et al. Non-invasive in vivo measurement of ocular rigidity: Clinical validation, repeatability and method improvement. Exp Eye Res. 2020;190:107831.

Clinical Forms of Glaucoma

Edema of the Outflow Pathway May Be the Cause Hypertension in Posner-Schlossman Syndrome

Comment by Ursula Schlötzer-Schrehardt, Erlangen, Nürnberg, Germany

98432 Morphology of the trabecular meshwork and Schlemm's canal in Posner-Schlossman Syndrome; Yan X, Li M, Wang J, Zhang H, Zhou X, Chen Z; Investigative Ophthalmology and Visual Science 2022; 63: 1

Posner-Schlossman syndrome (PSS), also known as glaucomatocyclitic crisis, is a rare unilateral disease characterized by recurrent episodes of anterior uveitis and acute rises in IOP, which may lead to chronic secondary glaucoma. Although etiology and pathophysiology of PSS are still unclear, infectious and autoimmune causes have been proposed as potential triggers. Structural alterations of the trabecular meshwork, including trabeculitis and trabecular outflow obstruction by inflammatory cells or pigment, have been suggested as potential causes of IOP elevation.[1]

This cross-sectional observational study presents the first description of morphological changes of trabecular meshwork (TM) and Schlemm's canal (SC) in 45 patients with PSS using *in-vivo* SS-OCT imaging. The patients revealed transient episodes of IOP elevation, mild anterior chamber inflammation and open chamber angles and were divided into two subgroups with ocular hypertension (OHT) and ocular normal tension (ONT); their unaffected fellow eyes served as controls. TM and SC parameters were measured in nasal and temporal quadrants on 2D cross-sectional images. TM thickness, SC area and SC diameter were found to be significantly greater in the affected eyes of all PSS patients and the OHT subgroup only compared to the fellow eyes. TM thickness was either positively or negatively correlated with IOP in the OHT and ONT subgroups, respectively. From these observations, the authors conclude that edematous thickening of TM, by narrowing trabecular outflow spaces, may contribute to IOP elevation in PSS patients.

The strength of this study is that it is the first to analyze the morphological changes of TM and SC using high-resolution *in-vivo* imaging of anterior segment structures in PSS patients. However, there are several weaknesses, which include: (1) the use of 2D cross-sectional images instead of 3D volumetric scans; (2) the lack of intra- and interobserver reproducibility measurements; (3) no correlation of findings with the presence of viral infection and keratic precipitates; and (4) insufficient methodological details on image acquisition, such as light conditions, anatomical landmarks to ensure comparable area scans, etc. Most importantly, anti-inflammatory and IOP-lowering medications, which might have affected the morphology of TM and SC, have not been taken into account, even though several studies have reported that glaucoma treatments can change the TM and SC morphology.[2] Finally, it may be considered that TM thickening could be also caused by inflammatory infiltrations rather than edema. A histopathological analysis of a trabeculectomy specimen provided evidence of numerous mononuclear cells accumulating in the trabecular spaces, which were suggested to increase aqueous outflow resistance.[3] Although the present study confirms involvement of the trabecular meshwork in PSS-associated hypertension, further studies are needed to provide a more accurate understanding of the mechanisms of IOP elevation in PSS patients.

References

1. Okonkwo ON, Tripathy K. Posner Schlossman Syndrome. 2022 Feb 21. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 35015437.
2. Park JH, Chung HW, Yoon EG, et al. Morphological changes in the trabecular meshwork and Schlemm's canal after treatment with topical intraocular pressure-lowering agents. Sci Rep. 2021;13;11(1):18169.
3. Harstad HK, Ringvold A. Glaucomatocyclitic crises (Posner-Schlossman syndrome). A case report. Acta Ophthalmol (Copenh). 1986;64(2):146-151.

Clinical Forms of Glaucoma

Differentiating Between Non-Glaucomatous Optic Neuropathy and Normal-Tension Glaucoma

Comment by David Greenfield and Yasmin Islam, Miami, FL, USA

98744 Yield of investigations in patients with questionable nonglaucomatous optic neuropathy; Donaldson L, Dezard V, Margolin E; Canadian Journal of Ophthalmology 2022; 0:

Various non-glaucomatous optic nerve (NGON) disorders may produce optic disc cupping and visual field disturbances that resemble the clinical profile of glaucomatous optic neuropathy (GON), and it is important that clinicians recognize them. **These disorders include hereditary optic neuropathy, antecedent optic nerve infarction, trauma, syphilis, demyelinating optic neuritis, fusiform enlargement of the intracranial carotid artery and intraorbital and intracranial mass lesions**. Pallor of the neuroretinal rim has been reported to be highly specific in predicting non-glaucomatous cupping, and focal or diffuse obliteration of the neuroretinal rim is highly specific for predicting glaucomatous cupping. Yet, clinically differentiating non-glaucomatous optic nerve disorders from glaucoma remains a subjective and often difficult challenge. Thus, ancillary tests, in particular neuroimaging, have been proposed in the diagnostic evaluation of glaucoma with normal intraocular pressure.

In this retrospective review, Donaldson and colleagues retrospectively examined 82 patients with atypical features of GON referred by a diverse group of clinicians (ophthalmologists, optometrists and primary care physicians) for neuro-ophthalmic consultation to exclude NGON. All patients underwent perimetry and OCT imaging; bloodwork, genetic testing and neuroimaging were selectively performed. GON was defined as increased optic disc cupping, lack of pallor of the remaining neuroretinal rim, and relative preservation of central visual acuity. **Most patients (71) underwent neuroimaging of whom approximately 70% were diagnosed with GON. Among the 14 patients with NGON a diagnosis could not be identified in approximately 50%.** The others were found to have ischemic optic neuropathy, optic neuritis, or optic neuropathy associated with inherited, toximetabolic, or compressive mechanisms. The three patients with compression included two patients with anomalous vasculature and 1 case with optic nerve sheath meningioma. Neural rim pallor was identified in 86% patients with NGON, however nerve fiber bundle visual field defects were common in both GON and NGON eyes and not found to be a helpful differentiating feature.

Nerve fiber bundle visual field defects were common in both GON and NGON eyes and not found to be a helpful differentiating feature

Unfortunately, due to the relatively small number of patients found to have an identifiable cause for NGON the ability to draw significant conclusions from this study is limited. However, there are a few important lessons to be learned from this interesting study. First, **careful inspection of the optic nerve is critical with attention to neural rim integrity, color, and presence of optic disc hemorrhage**. Among the five optic disc photographs illustrated in Figure 1, the two left images with GON had focal loss of the inferior rim (one with a flame hemorrhage), and the three right images with NGON had obvious rim pallor in excess of cupping. Thus, the classification could have been easily established in these eyes based solely on the disc appearance. Second, most patients referred for neuro-ophalmic consultation are eventually found to have GON. **Third, eyes with NGON often do not yield a definitive diagnosis despite blood work, genetic testing and cranial neuroimaging**. Fourth, routine neuroimaging in patients with GON is costly, and rarely identifies a compressive lesion responsible for the associated visual field abnormality. Selective neuroimaging in eyes with atypical features is warranted.

Routine neuroimaging in patients with GON is costly, and rarely identifies a compressive lesion responsible for the associated visual field abnormality

Laser Treatment

SLT as First-Line Treatment: Patient and Treater Perspectives

Comment by Rupert Bourne, Cambridge, UK

98620 Facilitators and Barriers to Using Selective Laser Trabeculoplasty (SLT) as First-Line Treatment for Glaucoma: Physician and Patient Views Gathered during an Exploratory Descriptive Qualitative Study; Chen Y, Lohfeld L, Song D, Pak C, Gong X, Zhou W, Liang Y, Congdon N; Ophthalmic Epidemiology 2022; 0: 1-8

In this article by Chen *et al,* 11 Chinese glaucoma specialists and 12 patients were recruited from two tertiary-level municipal hospitals in the cities of Wenzhou and Guangzhou, to participate in recorded interviews. These interviews explored perception of relative advantages and disadvantages of selective laser trabeculoplasty (SLT) versus other intraocular pressure-reducing treatments, factors affecting glaucoma treatment decision-making and barriers to the use of SLT as a first-line treatment for glaucoma in China.

All of the patients were on topical medication, 5 had had SLT and most had received incisional surgery (n=6). The majority had open angle glaucoma (n=10) and the patients were relatively young (median age, 41 years). Eligibility criteria for inclusion in the study are not given, the authors simply explaining that patients were 'selected' by a glaucoma clinic nurse after reviewing patient records. Interviews were assisted by 'interview guides', the transcripts recorded and a thematic framework analysis approach used. The results are a series of anecdotes (with occasional frequencies of anecdote given) from individual participants around each of several themes centering around physician treatment preferences, patient's views on treatment types, and decision-making during the physician-patient encounter, and feasibility of SLT as a first-line therapy.

The rationale for the study was a reportedly lower uptake of SLT in China than in Europe/USA. Using anecdotal evidence from these limited interviews (questions are in the supplementary material), the authors promote some possible reasons such as willingness to pay, education and patient profile in clinics, yet one has to agree with the authors when they conclude that unfortunately the study design (a very small sample size [e.g. 5 SLT patients] from only 2 hospitals in China) makes it impossible to draw any generalizable conclusions from this study.

Laser Treatment

SLT and Post-Trabeculectomy Circadian IOP

Comment by Tony Realini, Morgantown, WV, USA

98384 Efficacy of Selective Laser Trabeculoplasty on Circadian Intraocular Pressure Following Trabeculectomy in Advanced Primary Open-angle Glaucoma; Pillunat KR, Herber R, Wolfram S, Jasper CS, Waibel S, Pillunat LE; Journal of Glaucoma 2022; 31: 96-101

Pillunat and colleagues have conducted a retrospective analysis of the effect of selective laser trabeculoplasty (SLT) on 24-hour circadian intraocular pressure (IOP) measured both before and approximately 12 months after SLT in eyes with advanced primary open-angle glaucoma following prior trabeculectomy and now on maximal tolerated medical therapy that would otherwise be candidates for repeat surgery. IOP measurements were taken by Goldmann tonometry seated at 1, 4, 7, and 10 PM, at midnight by Perkins tonometry (supine), and at 7 AM again by Goldmann tonometry seated. **Thirty-three eyes not requiring additional therapy during the 12-month interval were analyzed. Overall, mean 24-hr IOP was reduced from 15.2 mmHg before SLT to 13.2 mmHg 12 months after SLT (p = 0.027), and 54% of eyes were deemed treatment success at 12 months having attained individualized target IOP.** In linear regression analysis, higher pretreatment peak IOP but not higher mean 24-hr IOP was predictive of favorable SLT response.

> SLT should be considered an alternative to repeat surgery in these eyes, especially given the exceedingly low risk of SLT versus repeat surgery

This study confirms prior studies demonstrating reduction of diurnal/circadian IOP by SLT, and extends this knowledge to eyes with advanced POAG that have previously undergone trabeculectomy. It is noteworthy that more than half of eyes were able to avoid repeat trabeculectomy for at least a year with SLT, particularly given the low mean starting IOP of ~15 mmHg. Based on these findings, SLT should be considered an alternative to repeat surgery in these eyes, especially given the exceedingly low risk of SLT versus repeat surgery.

Surgical Treatment

Cataract Surgery is Beneficial for Glaucoma

Comment by Angelo Tanna, Chicago, IL, USA

98129 Cataract Surgery Lowers Intraocular Pressure and Medication Use in the Medication Group of the Ocular Hypertension Treatment Study; Mansberger SL, Gardiner SK, Gordon M, Kass M, Ramulu P; American Journal of Ophthalmology 2022; 236: 53-62

The landmark post-hoc analysis of data from the observation arm of the Ocular Hypertension Treatment Study (OHTS) provided strong evidence that cataract surgery lowers IOP in eyes with untreated OHT.[1] That study, published in 2012, found a mean reduction in IOP after cataract surgery of 4.1 mmHg from a baseline of 23.9 mmHg, with a gradual loss of effect over time. The importance of the body of knowledge regarding the effects of cataract surgery on IOP has grown with the advent of various minimally invasive glaucoma surgeries. In evaluating the efficacy of such procedures when combined with cataract surgery in clinical studies and even in our own clinical practices, we must be cognizant of the IOP lowering effect of cataract surgery alone.

The latest report from OHTS on this topic adds important new information about the effects of cataract surgery on IOP by focusing on the OHTS subjects who were randomized to treatment to achieve a 20% reduction in IOP.[2] Among 1612 eyes of 806 OHTS subjects randomized to treatment, this study included a subset of eyes for which at least two study visits occurred prior to and after cataract surgery. As in their prior report on the effect of cataract surgery among eyes in the observation arm of OHTS, the study visit at which subjects reported they had undergone cataract surgery was defined as the 'split date' – the first post-cataract surgery study visit. Because treatment strategies evolved during the course of the clinical trial, particularly as a result of the approval of latanoprost, it was important to compare temporally matched IOP data from the control group that did not undergo cataract surgery. The investigators attempt to do this by defining the matching split date for the control group as the 15th study visit such that the median number of study visits prior to the split date was the same for both groups. The investigators analyzed 149 eyes of 92 subjects that underwent cataract surgery and 1004 eyes of 531 control subjects, all from the treatment arm.

Subjects in the cataract surgery group were significantly older and had slightly worse mean deviation and pattern standard deviation values. Interestingly, the control group had significantly larger vertical and horizontal cup-disc ratios. The only other notable difference between groups prior to the split date was a higher IOP in the cataract surgery arm, 18.9 vs 18.2 mmHg ($p = 0.053$).

Cataract surgery resulted in a mean IOP change ranging from -2.2 to -1.3 mmHg through 48 months after the split date ($p < 0.001$), compared to the group's own baseline. Contemporaneously, there was a significant and persistent (72 months after the split date) reduction in the mean number of medications ranging from -0.5 to -0.3 classes ($p < 0.001$), with 13.8 to 23.5% of eyes that were medication-free. There was also a slight but statistically significant decrease in the IOP in the control group, ranging from -0.1 to -0.7 mmHg ($p < 0.01$); however, there was no change in the number of medications.

An important question is whether undergoing cataract surgery reduced the risk of the subsequent conversion to POAG. First, it is noteworthy that the presence of a developing, visually significant cataract, did not appear to influence the likelihood of conversion to a POAG endpoint *prior* to cataract surgery, *i.e.*, the eyes that underwent cataract surgery were not more likely to have already converted to POAG prior to surgery. After cataract surgery, the hazard ratio for conversion by either visual field or optic disc criteria was 0.7 (95% CI: 0.32-1.55, $p = 0.38$). There was a lower risk of conversion to POAG in the cataract surgery group based on optic disc criteria alone (HR 0.22; 95% CI: 0.05-0.95; $p = 0.042$, but not significant after adjustment for multiple comparisons). Since OHTS required a protocol-driven target IOP, there was no significant difference in IOP between groups by 12 months after the split date, possibly accounting for the lack of a clear protective effect against conversion to POAG. Moreover, since only ten eyes in the cataract surgery group converted to POAG, there may not have been sufficient statistical power to detect a difference in the risk of conversion should one have existed.

We already knew cataract surgery lowers IOP and reduces the need for medications in medically treated POAG and OHT eyes from the many MIGS clinical trials that have been published. Many of those studies provided additional information based on IOP assessment after medication washout. This study, however, provides more reliable evidence about the magnitude of IOP reduction because it is relatively free of the confounding effect of regression to the mean since the decision to intervene with cataract surgery was independent of the IOP prior to surgery.

References

1. Mansberger SL, Gordon MO, Jampel H, et al., Ocular Hypertension Treatment Study Group. Reduction in intraocular pressure after cataract extraction: the Ocular Hypertension Treatment Study. Ophthalmology. 2012;119(9):1826-1831. doi: 10.1016/j.ophtha.2012.02.050. Epub 2012 May 16. PMID: 22608478; PMCID: PMC3426647.
2. Mansberger SL, Gardiner SK, Gordon M, Kass M, Ramulu P; Ocular Hypertension Treatment Study group. Cataract Surgery Lowers Intraocular Pressure and Medication Use in the Medication Group of the Ocular Hypertension Treatment Study. Am J Ophthalmol. 2022 Apr;236:53-62. doi: 10.1016/j.ajo.2021.07.008. Epub 2021 Jul 17. PMID: 34280363; PMCID: PMC8761780.

Prognostic factors

Corneal Hysteresis as a Risk Factor for Progression

Comment by Gábor Holló, Budapest, Hungary

99092 A Prospective Longitudinal Study to Investigate Corneal Hysteresis as a Risk Factor of Central Visual Field Progression in Glaucoma; Kamalipour A, Moghimi S, Eslani M, Nishida T, Mohammadzadeh V, Micheletti E, Girkin CA, Fazio MA, Liebmann JM, Zangwill LM, Weinreb RN; American Journal of Ophthalmology 2022; 240: 159-169

Low corneal hysteresis (CH) has been considered as one of the several known risk factors of glaucoma progression. It has been associated with both structural and visual field progression measures.[1,2] In their prospective cohort study, Kamalipour *et al.* investigated if low CH represents a special risk factor for central visual field progression.[3.] The impetus for the investigation is the special importance of the central visual field for everyday life activities and quality of life. Trend and event

> While central visual field progression was 0.07 dB/year faster per 1 mmHg lower CH ($p < 0.001$), the relationship did not prove to be significant for the total 24-degree visual field

They found a moderately increased rate of progression in the central (10 degree) visual field for lower CH, which was consistent with both types of statistical analyses. While central visual field progression was 0.07 dB/year faster per 1 mmHg lower CH ($p < 0.001$), the relationship did not prove to be significant for the total 24-degree visual field. Further, the central visual field effect was maintained when the early glaucoma eyes (baseline MD ≥ -6.0 dB) were separately investigated. These results are of clinical importance since they call attention to the role of low CH in assessing the risk for central visual field damage in glaucoma eyes. Although the pathophysiological mechanisms behind the this relationship are not yet clear, and most patients were under various topical medications in the study period which can influence CH, clinicians may want to consider intensification of IOP lowering treatment when the central visual field is involved and CH is low.

> Clinicians may want to consider intensification of IOP lowering treatment when the central visual field is involved and CH is low

References

1. Medeiros FA, Meira-Freitas D, Lisboa R, et al. Corneal hysteresis as a risk factor for glaucoma progression: a prospective longitudinal study. Ophthalmology. 2013;120:1533-1540.
2. Susanna CN, Diniz-Filho A, Daga FB, et al. A Prospective Longitudinal Study to Investigate Corneal Hysteresis as a Risk Factor for Predicting Development of Glaucoma. Am J Ophthalmol.2018;187:148-152.
3. Kamalipour A, Moghimi S, Eslani M, et al. A Prospective Longitudinal Study to Investigate Corneal Hysteresis as a Risk Factor of Central Visual Field Progression in Glaucoma. Am J Ophth. 2022; published online first http://dx.doi.org/10.1016/j.ajo.2022.02.025

Prognostic factors

OCT-A Findings and Progression

Comment by Ki Ho Park, Seoul, South Korea

98922 Association of Initial Optical Coherence Tomography Angiography Vessel Density Loss With Faster Visual Field Loss in Glaucoma; Nishida T, Moghimi S, Wu JH, Chang AC, Diniz-Filho A, Kamalipour A, Zangwill LM, Weinreb RN; JAMA ophthalmology 2022; 140: 319-326

In this retrospective cohort study, Nishida and colleagues evaluated the association between the rate of macular vessel density (VD) loss during an initial follow-up and the rate of visual field (VF) loss during an extended follow-up period in 38 eyes suspected of having glaucoma and 86 eyes with primary open-angle glaucoma. The rate of VD loss was derived from macular whole-image (3 × 3 mm^2) vessel density values from 3 optical coherence tomography angiography (OCTA) scans early during the study. The rate of VF loss was calculated from the visual field mean deviation (MD) during the entire follow-up period (mean, 4.0 years) after the first OCTA visit. **The authors found that faster VD loss during the initial follow-up period was associated with faster concurrent and subsequent rates of VF loss during the extended period.**

One may speculate that macular VD loss is a result of macular ganglion cell complex (GCC) thinning. However, **the data on the association of VF MD loss rate with VD loss rate and GCC thinning is interesting, because the association was stronger for the OCTA model than for the OCT model.**

There are some limitations to this study: (1) the 3x3 mm^2 scan area seems to be too small to represent the global index (VF MD) loss; (2) the results (from a relatively small sample size and short follow-up period) need to be confirmed by future longitudinal follow-up studies.

> The current paper raises the promising possibility that fast progressors identified by OCTA are at higher risk of functional loss and may need more intensive observation and treatment

However, the current paper raises the promising possibility that fast progressors identified by OCTA are at higher risk of functional loss and may need more intensive observation and treatment. A future prospective follow-up study could further clarify the utility of OCTA for assessment of VF progression in patients with glaucoma. In addition, even though it was not in the scope of this study, there is a possibility that training of OCTA images by deep learning will further enhance the effectiveness of VD loss as a predictor of future VF loss.

Artificial Intelligence

A Deep Learning Algorithm to Detect Glaucoma

Comment by Xiulan Zhang, Guangzhou, P.R. China

99124 Detecting Glaucoma in the Ocular Hypertension Study Using Deep Learning; Fan R, Bowd C, Christopher M, Brye N, Proudfoot JA, Rezapour J, Belghith A, Goldbaum MH, Chuter B, Girkin CA, Fazio MA, Liebmann JM, Weinreb RN, Gordon MO, Kass MA, Kriegman D, Zangwill LM; JAMA ophthalmology 2022; 140: 383-391

Deep learning (DL) has been widely used in ophthalmic disease diagnosis and achieved comparable performance with senior ophthalmologists in less time. It is expected to accelerate the efficiency of image labeling in clinical trials.

In this retrospective study, Fan and colleagues investigated the diagnostic performance of DL algorithms in classifying the fundus photos from the OHTS cohort into glaucomatous and non-glaucomatous. ResNet-50 was used as the backbone of the DL algorithm. The fundus photos of 1147 OHTS participants were included in the training set, 167 in the validation set, and 322 in the test set. Three external test sets from the USA, Japan, and China were used to evaluate the generalizability of the DL algorithm.

For the OHTS endpoints based on optic disc or visual field changes, The DL model achieved an AUROC of 0.91 (95% CI, 0.88-0.94) and 0.86 (95% CI, 0.76-0.93), respectively. That indicates the DL algorithm is able to detect the glaucomatous eyes with either structural changes or functional changes with relatively high accuracy. However, the diagnostic performance of the DL model developed based on the optic disc endpoint was worse in the external datasets, with AUROCs ranging from 0.74 to 0.79, possibly due to the different ethnicity, gender and disease distribution in these datasets. In general, the above results suggest that the DL algorithms may help standardize and accelerate the data labeling in large clinical trials, decreasing the number of image graders and improving the consistency of the labels.

The limitations of this study should also be noted. Firstly, the performance of the DL algorithms fell in the external datasets. Better generalizability is necessary for clinical deployment, since the DL algorithms may receive imaging data from various sources. Secondly, poor-quality photos are excluded but are frequently seen in clinical practice. A step of quality control either by ophthalmologists or by DL algorithms is helpful for the application of diagnostic algorithms in the real world.

Advanced Course in Glaucoma

This course consists of 4 modules that address advanced aspects of glaucoma diagnosis:

1. Managing complications of post-surgical hypotony

Ricardo Abe and Vital Costa

2. Primary angles closure suspect

Jesa Nadine Protasio, Augusto Azuara-Blanco, Tin Aung

Access Course

3. Management of PACG

Chang Liu, Monisha Nongpiur, Tin Aung

4. Approach to Exfoliation Syndrome and Exfoliation Glaucoma

Vijaya Lingam, Mona Khurana, Ronnie George

All modules were written by world-renowned experts in the field, and reviewed by members of the WGA Education Committee. They are intended for ophthalmologists and other eye-care providers.

All texts, pictures, and videos were adapted to an online platform by a team of e-learning experts. This will allow you to have a pleasant learning experience. At the end of each module, there is a multiple-choice test that will auto-correct once the exam is completed. You will also be able to download a Certificate of Completion.

JOURNAL OF

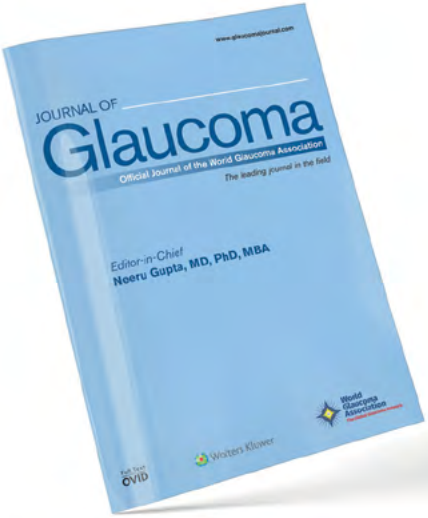
Glaucoma

Official Journal of the World Glaucoma Association

The leading journal in the field

Free access for members of WGA affiliated Glaucoma Societies

As the official journal of the WGA, online access to the Journal of Glaucoma is provided for free to all individual members of our affiliated Glaucoma Societies, including all ophthalmologists from sub-Saharan countries and glaucoma fellows worldwide.



The Journal of Glaucoma (JOG) is the official journal of the World Glaucoma Association (WGA).

The Journal of Glaucoma is the world's premier scientific journal for glaucoma research, devoted to new fundamental understandings, innovations in diagnosis and technology, and advancements in glaucoma medical and surgical care. The Journal of Glaucoma is the only scientific journal dedicated to the field of glaucoma that is both indexed and has an impact factor.

New papers appear online within 72 hours of acceptance. Enjoy **free access** to the Journal of Glaucoma through your WGA#One account and stay abreast of best practices in glaucoma and the latest developments in the field.

Free access for WGA members via www.WGA.one/JOG

World Glaucoma Association
The Global Glaucoma Network

Fundamental questions in Glaucoma

New video lectures will be released on July 18

Make sure to check them out!

www.worldglaucoma.org

A big thank you to all contributors of volume 22

- Youssef Abdelmassih (Paris, France) > view comments on e-igr.com
- Makoto Aihara (Tokyo, Japan) > view comments on e-igr.com
- Dewang Angmo (New Delhi, India) > view comments on e-igr.com
- Makoto Araie (Tokyo, Japan) > view comments on e-igr.com
- Miki Atsuya (Nagoya, Japan) > view comments on e-igr.com
- Rupert Bourne (Cambridge, UK) > view comments on e-igr.com
- Tec Kuan Paul Chew (Singapore) > view comments on e-igr.com
- Tanuj Dada (New Delhi, India) > view comments on e-igr.com
- Gustavo de Moraes (New York, NY, USA) > view comments on e-igr.com
- Crawford Downs (Birmingham, AL, USA) > view comments on e-igr.com
- David Friedman (Baltimore, MD, USA) > view comments on e-igr.com
- Gus Gazzard (London, UK) > view comments on e-igr.com
- Franz Grehn (Wurzburg, Germany) > view comments on e-igr.com
- Neeru Gupta (Toronto, Canada) > view comments on e-igr.com
- Alon Harris (New York, NY, USA) > view comments on e-igr.com
- Minguang He (Guangzhou, P.R. China) > view comments on e-igr.com
- Paul Healey (Sydney, NSW, Australia) > view comments on e-igr.com
- Esther Hoffmann (Mainz, Germany) > view comments on e-igr.com
- Jin Wook Jeoung (Seoul, South Korea) > view comments on e-igr.com
- Chris Johnson (Iowa City, IA , USA) > view comments on e-igr.com
- Thomas Johnson (Baltimore MD, USA) > view comments on e-igr.com
- Ziad Khoueir (Beirut, Lebanon) > view comments on e-igr.com
- Yu-Chieh Ko (Taipei, Taiwan) > view comments on e-igr.com
- Victor Koh (Singapore) > view comments on e-igr.com
- Miriam Kolko (Copenhagen, Denmark) > view comments on e-igr.com
- Ecosse Lamoureux (Singapore) > view comments on e-igr.com
- Fei Li (Guangzhou, China) > view comments on e-igr.com

- Shan Lin (San Francisco, CA, USA) > view comments on e-igr.com
- Catherine Jui-Ling Liu (Taipei, Taiwan) > view comments on e-igr.com
- Ryan Man (Singapore) > view comments on e-igr.com
- Steve Mansberger (Portland, OR USA;) > view comments on e-igr.com
- Kaweh Mansouri (Lausanne, Switzerland) > view comments on e-igr.com
- Heather McGowan (New York, NY, USA) > view comments on e-igr.com
- Sasan Moghimi (La Jolla, CA , USA) > view comments on e-igr.com
- Kouros Nouri-Mahdavi (Los Angeles, CA, USA) > view comments on e-igr.com
- Darryl Overby (London, UK) > view comments on e-igr.com
- Ricardo Paletta Guedes (Juiz de Fora, Brazil) > view comments on e-igr.com
- Ki Ho Park (Seoul, South Korea) > view comments on e-igr.com
- Louis Pasquale (New York, NY, USA) > view comments on e-igr.com
- Pinkal Patel (Fort Worth, TX, USA) > view comments on e-igr.com
- Vincent Michael Patella (Iowa City, IA, USA) > view comments on e-igr.com
- Vittorio Porciatti (Miami, FL, USA) > view comments on e-igr.com
- Luciano Quaranta (Brescia, Italy) > view comments on e-igr.com
- Harry Quigley (Baltimore, MD, USA) > view comments on e-igr.com
- Harsha Rao (Narayana Nethralaya, Bangalore, India) > view comments on e-igr.com
- Arthi Rao (Los Angeles, CA, USA) > view comments on e-igr.com
- Tony Realini (Morgantown, WV, USA) > view comments on e-igr.com
- Cedric Schweitzer (Bordeaux cedex, France) > view comments on e-igr.com
- Brian Song (Los Angeles, CA, USA) > view comments on e-igr.com
- Swapnil Sonkusare (Charlottesville, VA, USA) > view comments on e-igr.com
- Daniel Stamer (Durham, NC, USA) > view comments on e-igr.com
- Min Hee Suh (Busan, South Korea) > view comments on e-igr.com
- Remo Susanna Jr (São Paulo, Brazil) > view comments on e-igr.com
- Angelo Tanna (Chicago, IL, USA) > view comments on e-igr.com
- Andrew Tatham (Edinburgh, UK) > view comments on e-igr.com
- Niklas Telinius (Aarhus, Denmark) > view comments on e-igr.com
- Christopher Teng (New York, NY, USA) > view comments on e-igr.com

- Julien Torbey (Lausanne, Switzerland) > view comments on e-igr.com
- Jessica Tran (New York, NY, USA) > view comments on e-igr.com
- Anja Tuulonen (Tampere, Finland) > view comments on e-igr.com
- Rohit Varma (Los Angeles, CA, USA) > view comments on e-igr.com
- Wei Wang (Guangzhou, P.R. China) > view comments on e-igr.com
- Derek Welsbie (La Jolla, CA, USA) > view comments on e-igr.com
- Tina Wong (Singapore) > view comments on e-igr.com
- Benjamin Xu (Los Angeles, CA, USA) > view comments on e-igr.com
- Kaileen Yeh (Portland, OR USA) > view comments on e-igr.com
- Xiulan Zhang (Guangzhou, P.R. China) > view comments on e-igr.com
- Sarah Zhou (Los Angeles, CA, USA) > view comments on e-igr.com
- Gulab Zode (Fort Worth, TX, USA) > view comments on e-igr.com

WGA Consensus Series 10

Diagnosis of Primary Open Angle Glaucoma

Edited by: R.N. Weinreb, D.F. Garway-Heath, C. Leung, F.A. Medeiros and J. Liebmann

2016

The goal of this consensus is to provide a foundation for diagnosing and managing primary open-angle glaucoma and how it can be best done in clinical practice. Identification of those areas for which we have little evidence and, therefore, the need for additional research always is a high priority. We hope that this consensus report will serve as a benchmark of our understanding. However, this consensus report is intended to be fluid. It is expected that it will be revised and improved with the emergence of new evidence

Download Book at: www.wga.one/wga/consensus-downloads

Through the courtesy of the WGA and Kugler Publications, you may now download the PDF file of Consensus 10 free of charge through your WGA#One account. Consensus 1–9 have previously been made available through IGR and are now also accessible through your WGA#One account.

Robert N. Weinreb
Consensus Initiative Chair
World Glaucoma Association

Consensus 10 participants

SUMMARY CONSENSUS POINTS

Section 1 - Structure

1. Clinical evaluation and documentation of the optic nerve head is essential for the diagnosis and the monitoring of glaucoma.
2. Clinical diagnosis of glaucoma is predicated on the detection of a thinned retinal nerve fiber layer (RNFL) and narrowed neuroretinal rim.
   Comments: These features often are accompanied by deformation of the optic nerve head (ONH) (cupping).
   These features often appear first in the supero- or inferotemporal quadrants.
   Although these features are characteristic of POAG, it is important to exclude non-glaucomatous optic neuropathies.
3. Detecting progressive glaucomatous RNFL thinning and neuroretinal rim narrowing are the best currently available gold standards for glaucoma diagnosis.
   Comment: Disease-related damage should be differentiated from age-related change.
4. The diagnosis of glaucoma does not always require the detection of visual field defects with perimetry.
   Comments: Perimetric defects that correspond to structural findings increase the likelihood of glaucoma.
   Perimetry is indispensable for documentation and monitoring of functional decline in glaucoma.
5. Assessment of the color and the configuration (size and shape) of the neuroret- inal rim is important to differentiate glaucomatous from non-glaucomatous optic neuropathies.
   Comment: A pale rim suggests non-glaucomatous optic neuropathy.
6. Photography is effective to document glaucomatous optic disc appearance and nerve fiber layer damage.
   Comments: Photography is particularly useful for detecting and documenting optic disc hemorrhage and rim color.
   Stereophotography is particularly useful for documenting optic disc topography.
7. Imaging technologies including optical coherence tomography (OCT), confocal scanning laser ophthalmoscopy (CSLO) and scanning laser polarimetry (SLP) provide an objective and quantitative approach to detect and monitor glaucoma.
8. OCT may be the best currently available digital imaging instrument for detecting and tracking optic nerve structural damage in glaucoma.
9. RNFL thickness is the most clinically helpful parameter of the ones currently available with OCT.
   Comments: Macular RGC loss in glaucoma also can be detected by OCT. RNFL thick- ness and macular RGC loss are complementary.
   Pitfalls of OCT such as artifacts and false segmentation should be considered when using OCT.
   GCIPL thickness (macula): The macula has the highest density of RGCs.

10. It is difficult in myopic eyes to differentiate those with and without glaucoma.
Comments: In myopic eyes, documented progressive optic neuropathy can be used to make the differential diagnosis of glaucoma.
Reference databases do not currently include highly myopic eyes and, therefore, are not appropriate for diagnosing RNFL damage in them.

Section 2- Vision function

1. Functional testing is essential for the evaluation, staging and monitoring of glaucoma
Comment: Standard automated perimetry (SAP) is the reference standard for all functional testing.
2. Clinical decisions should be made based on reliable visual field tests. *Comments:* Visual field defects should be reproducible and/or should be consistent with the location of the optic nerve defects.
The most important reliability criterion is the false positive rate.
3. In the presence of glaucomatous optic neuropathy, a Glaucoma Hemifield Test (GHT) 'outside normal limits' in a reliable visual field indicates that glauco- matous visual field loss is present.
Comment: For instruments not calculating a GHT, an abnormal (P < 5%) pattern standard deviation (PSD) or square-root-loss variance (sLV) likely have similar diagnostic value.
4. When glaucomatous optic neuropathy (GON) is suspected, a GHT criterion of 'outside normal limits' or 'borderline' in a reliable visual field increases the probability that an eye has glaucoma.
Comment: The level of probability for glaucoma depends on the presence and magnitude of other risk factors for glaucoma (such as raised intraocular pressure) and the quality of evidence that there is no GON.
5. Before a visual field defect can be confirmed as glaucomatous, retinal and non-glaucomatous optic disc conditions should be excluded by a careful examination of the retina and optic disc.
Comment: If the pattern of visual field loss suggests a neurological origin, or if there is incongruity between the pattern of visual field loss and optic disc and retinal nerve fiber layer appearance, then further investigation is warranted (e.g., color vision testing, neuroimaging).
6. Standard white-on-white automated perimetry (SAP), with a fixed testing matrix covering at least the central 24 degrees, is preferred for the diagnosis of glaucomatous visual field loss.
Comments: Goldmann size III stimuli are conventionally used in most automated perimeters in clinical practice for glaucoma diagnosis.
For more severe cases size V, increases the dynamic range and reduces variability of test results.
Using the 10-2 strategy, in addition to the conventional 24-2 Humphrey grid, can improve the detection of central functional loss

7. Threshold algorithms are preferred over supra-threshold algorithms for glaucoma diagnosis.
   Comment: Supra-threshold algorithms can be helpful in cases of unreliable results from threshold testing algorithms.
8. Neither short-wavelength automated perimetry (SWAP) nor frequency doubling technology (FDT) perimetry have superior diagnostic precision to SAP.
   Comments: Patients should be followed consistently with same visual function test and ideally one with statistical support for recognizing change.
   The more diagnostic tests that are performed, the more likely it is that one will be 'outside normal limits', therefore increasing the number of false positive results.
9. Patients who are at risk for glaucoma and have normal standard automated perimetry (SAP) should have their visual function monitored to detect deteri- oration and hence establish a glaucoma diagnosis.
   Comment: The earliest evidence for glaucoma may be functional or structural. Therefore, both should be measured to ensure that the onset of glaucoma damage is not overlooked.
10. Deterioration may be first detected by the glaucoma hemifield test (GHT) (or summary parameters) or by trend analysis of measurements over time. Which analysis is most sensitive varies between patients and so both should be done.
    Comments: Progressive functional loss identified by SAP may be a generalized reduction in visual field sensitivity alone, or focal loss alone, or a combination of both.
    If trend analysis indicates a change in VFI, MD or mean defect, then one needs to exclude media opacity (e.g., cataract).
11. There only is weak evidence for the use of functional measurements other than SAP to detect the earliest signs of deterioration.
12. There is a limited role for ERG testing in the routine diagnosis and management of glaucoma.
    Comment: PERG and PhNR testing are not substitutes for standard automated perimetry (SAP), nor are they substitutes for optical coherence tomography (OCT) imaging.
13. The classification of glaucomatous functional damage in stages of increasing severity is a useful tool in the management of patients affected with chronic glaucoma.
    Comment: Staging provides a summary metric of disease severity which may guide treatment decisions.
14. While staging systems may be clinically useful, no current staging system shows all the information present in a visual field printout.
    Comment: For instance, staging systems do not identify the location of damage.
15. POAG-related functional impairment affects patients' ability to perform daily activities and also their well-being (vision-related quality of life). Worse vision-related quality of life is associated with greater severity of the disease.
    Comment: Vision-related quality of life may be assessed with question- naires, by performance tasks (e.g., reading), event monitoring (e.g., falls) and measures of behavior (e.g., GPS trackers).

16. Understanding how glaucoma and glaucoma treatment affects patients' quality of life, and how this varies across the severity continuum, can have practical value in the clinic. It can inform treatment choices and communica- tion to patients of the implications of disease worsening.
17. The impact of glaucomatous visual field loss on vision-related function and quality of life depends on the location of the defect in the field of vision and the task involved. *Comment:* risk of falling, eye-hand coordination and mobility may be most affected by loss in the inferior hemifield, whereas reading may be more affected by superior hemifield loss.
18. Aspects of glaucoma other than visual field loss, such as reduced central contrast sensitivity and acuity (in more advanced disease), may affect vision-related function and quality of life.
Comment: Contrast sensitivity is more strongly associated with specific aspects of reading performance than visual field measures.

Section 3 - Structure and function

1. In glaucoma, there is a continuous relationship between standard structural and functional (dB for visual field) measurements, which appears nonlinear with current methods of testing and conventional scaling of metrics. *Comment:* When both are transformed into linear scales, then a linear relation- ship between structure and function can be observed.
2. Current structural and functional measurement methods show considerable variability.
3. Visual field test locations are spatially related to regions on the optic nerve head, peripapillary retina and macular area.
Comment: Understanding these spatial relationships can be useful for the diagnosis of glaucoma.
4. With current technology, detection of structural defects generally precedes detect- able functional defects in glaucoma patients while functional defects can precede structural defects in some patients.
Comment: Structural tests based on the comparison to the normative data tend to show a statistically significant glaucomatous change earlier compared to the functional tests because of a greater variability in functional tests.
5. The likelihood of the diagnosis of glaucoma is increased through corrobora- tion of abnormal structural and functional tests.
Comment: The likelihood of the diagnosis of glaucoma is increased further if there is progressive change or if additional risk factors are present, such as raised intraocular pressure.
6. When available, OCT (or an alternative imaging modality) and disc photographs with acceptable quality at baseline should be performed, against which accurate detection of change can be made.
Comments: Disc photography is a useful adjunct for detecting hemorrhages and pallor, and also for assessing change compared with future clinical exam- inations. Disc hemorrhages can only be seen on clinical examinations and disc photographs.

7. As yet there is no widely-accepted method of combining the results of structural and functional tests.
   Comment: Several proposed methods for combining structural and/or functional measurements offer advantages over traditional parameters and continue to be investigated.

8. Physicians should be aware of false-positive tests and over-diagnosing glaucoma, which are more likely when using a large number of diagnostic tests.
   Comment: Although using multiple parameters may increase overall diagnostic sensitivity, the chance will also increase of falsely labeling a change significant.

Section 4 - Risk factors (ocular)

1. Although POAG may develop at any IOP, there is strong evidence supporting higher mean intraocular pressure during follow-up as a risk factor for development and progression of glaucomatous damage.
   Comments: There is insufficient evidence and further studies are needed to elucidate which IOP parameter(s) (mean, peak and/or fluctuation, area under IOP curve, etc.) is most important in determining risk of glaucoma development or progression.
   There is insufficient evidence implicating IOP fluctuations as an independent risk factor for glaucoma development or progression.

2. Low ocular perfusion pressure (OPP) (the difference between systemic blood pressure and intraocular pressure) is associated with increased prevalence of open-angle glaucoma in cross-sectional studies.
   Comments: The value of OPP monitoring in daily clinical practice is not established. Due to the intrinsic relationship between OPP and IOP, it is difficult to establish an independent contribution of OPP as a risk factor for the development of glaucoma.

3. There is insufficient evidence supporting the role of provocative tests, such as the water-drinking test, as providing independent contribution to assess risk of glaucoma development and progression.
   Comment: Prospective longitudinal studies are necessary to clarify whether the water-drinking provocative test can provide additional information over office-based IOP measurements in establishing risk of glaucoma development or progression.

4. There is strong evidence supporting the role of central corneal thickness (CCT) as an important predictive factor for glaucoma development in ocular hypertensives and glaucoma suspects. Baseline CCT measurements should be obtained in patients suspected of having glaucoma.
   Comments: Algorithms to correct IOP based on CCT measurements are not recommended for routine use in clinical practice.
   There is insufficient evidence to conclude whether or not CCT is a true independent risk factor for glaucoma development or progression, or whether its effect is related to a tonometric artifact.
   There is no evidence that serial CCT measurements have value in clinical evaluation glaucoma.

5. There is strong evidence implicating lower corneal hysteresis as a risk factor for glaucoma development and progression.
   Comments: There is insufficient evidence about the mechanisms by which corneal hysteresis is associated with risk of glaucoma progression.
6. Existing evidence suggests that individuals with myopia have an increased risk of developing open angle glaucoma, with the risk being greater for people with high myopia.
   Comments: Diagnosis of glaucoma among myopic eyes can be challenging. Confirmed evidence of glaucomatous progression from a well-defined baseline is important for a correct diagnosis in many myopic individuals.
7. Disc hemorrhage is associated with increased risk of developing glaucoma and it is a marker for glaucomatous progression.
   Comment: Consideration of treatment escalation or closer follow-up should be given for patients presenting with optic disc hemorrhages.
8. Predictive models (risk calculators) may provide objective assessment of individual risk and their use should be considered in patients suspected of having glaucoma.
   Comment: Current validated risk calculators apply only to OHT patients. Moreover, they do not include all known risk factors.

Section 5 - Risk assessment

1. Primary open-angle glaucoma (POAG) occurs at all ages, and the incidence and prevalence accelerates with age.
2. Populations with the highest incidence and prevalence of POAG have African ancestry.
   Comment: Due to the earlier age of disease onset, the average duration of POAG may be greatest in individuals of African ancestry.
3. Hispanics may have higher incidence and prevalence of POAG than individuals of European ancestry (non-Hispanic whites).
4. Older age is a risk factor for glaucoma onset and progression.
5. Although an increased prevalence of POAG in men has been reported, there is not enough evidence to support an association of POAG risk with male gender.
6. Lower socioeconomic status may be associated with later presentation of POAG.
7. First-degree relatives of POAG patients are at higher risk for glaucoma.
8. Although genetic association studies have revealed multiple associated loci for POAG, there is little value for routine genetic testing to diagnose or predict the development of glaucoma at the current time.
9. There is consistent, but weak, positive association between diastolic blood pressure and IOP and between systolic blood pressure and IOP in popula- tion-based studies.
10. Lower blood pressure (BP) and ocular perfusion pressure are associated with higher glaucoma prevalence and incidence across all racial groups. *Comment:* It is not known whether ocular perfusion pressure (OPP) is an independent risk factor for glaucoma due to the fact that IOP is intrinsically used in the calculation as performed with current methods.

11. The relationships between diastolic blood pressure, systolic blood pressure, systemic hypotension or systemic hypertension, and POAG are inconsistent.
12. The relationship between treatment of systemic hypertension and the development of POAG remains unclear.
    Comment: There are data suggesting that some patients being treated for systemic hypertension may be at greater risk for development of POAG.
13. The role of nocturnal systemic hypotension in the development of glaucoma is not known.
14. The evidence that obstructive sleep apnea is a risk factor for open-angle glaucoma (OAG) is weak and warrants further study.
15. Diabetes mellitus likely increases the risk for glaucoma onset.
16. There is insufficient evidence to determine if thyroid disease is associated with glaucoma.
17. Although there is some evidence that reduction of estrogen production in post-menopausal women increases glaucoma risk, there is insufficient evidence for hormonal replacement.

Section 6 - Screening

1. Glaucoma is the leading cause of irreversible blindness worldwide. *Comment:* In some countries, as many as 90% of glaucoma patients remain undiagnosed.
2. Screening everyone for glaucoma is an ideal proposition, but it is not logis- tically feasible. It would also result in an unacceptably high number of individuals with a false-positive diagnosis of glaucoma.
   Comment: To be effective, screening programs should select participants at substantial risk for glaucoma.
3. The cost-effectiveness of screening for POAG alone has not been demonstrat- ed.
   Comment: Cost-effectiveness for glaucoma may be enhanced when done with other ocular conditions that cause visual impairment, including uncorrected refractive error, cataract, diabetic retinopathy, and age-related macular degen- eration.
4. First-degree relatives of individuals with POAG and those with significant risk factors should be examined.

Glaucoma Industry Members

We acknowledge the unrestricted educational grants of our industry members.

For more information about our Glaucoma Industry Members, please click below on the company names.

PLATINUM

Allergan an AbbVie company

Gold

Santen

Silver

aerie Pharmaceuticals, Inc.

Alcon

GLAUKOS Transforming Glaucoma Therapy

Bronze

BAUSCH + LOMB

iSTAR MEDICAL

NOVARTIS

SENJU

TOMEY

TOPCON YOUR VISION. OUR FOCUS.

ZEISS

News Flashes

- ★ The team demonstrated that experimental glaucoma constricts capillaries through calcium-dependent mechanisms that restricts ganglion cell blood supply
- ★ Early glaucoma sometimes results in central visual field damage that can be missed by the 24-2 GPA algorithm
- ★ Assessment of ROTA images improves diagnostic accuracy over current standards for glaucoma
- ★ The non-invasive ultrasonic approach is highly translatable to a clinical setting
- ★ Importantly, the sensors in all surviving patients were still functional after ten years
- ★ The long-term safety data provided from the pioneering ARGOS study demonstrate that implantable pressure sensors are a viable and well-tolerated method for obtaining IOP measurements outside of the office for management of glaucoma
- ★ The strongest risk factor for the development of OAG was high myopia, with a 7.3-fold increased incidence compared to emmetropic eyes
- ★ The measurement of ocular rigidity may have its own limitation
- ★ This study remains a pilot study, but it could hopefully encourage more engineering and clinical developments to better understand these interactions
- ★ Nerve fiber bundle visual field defects were common in both GON and NGON eyes and not found to be a helpful differentiating feature
- ★ Routine neuroimaging in patients with GON is costly, and rarely identifies a compressive lesion responsible for the associated visual field abnormality
- ★ SLT should be considered an alternative to repeat surgery in these eyes, especially given the exceedingly low risk of SLT versus repeat surgery
- ★ Clinicians may want to consider intensification of IOP lowering treatment when the central visual field is involved and CH is low
- ★ While central visual field progression was 0.07 dB/year faster per 1 mmHg lower CH ($p < 0.001$), the relationship did not prove to be significant for the total 24-degree visual field. Descent and Glaucoma
- ★ The current paper raises the promising possibility that fast progressors identified by OCTA are at higher risk of functional loss and may need more intensive observation and treatment

www.e-IGR.com

Published by the World Glaucoma Association in collaboration with
Kugler Publications, Amsterdam, The Netherlands