VOLUME 25-1
2025

International Glaucoma Review

The journal of the World Glaucoma Association

Abstracts and Review of Glaucoma Literature

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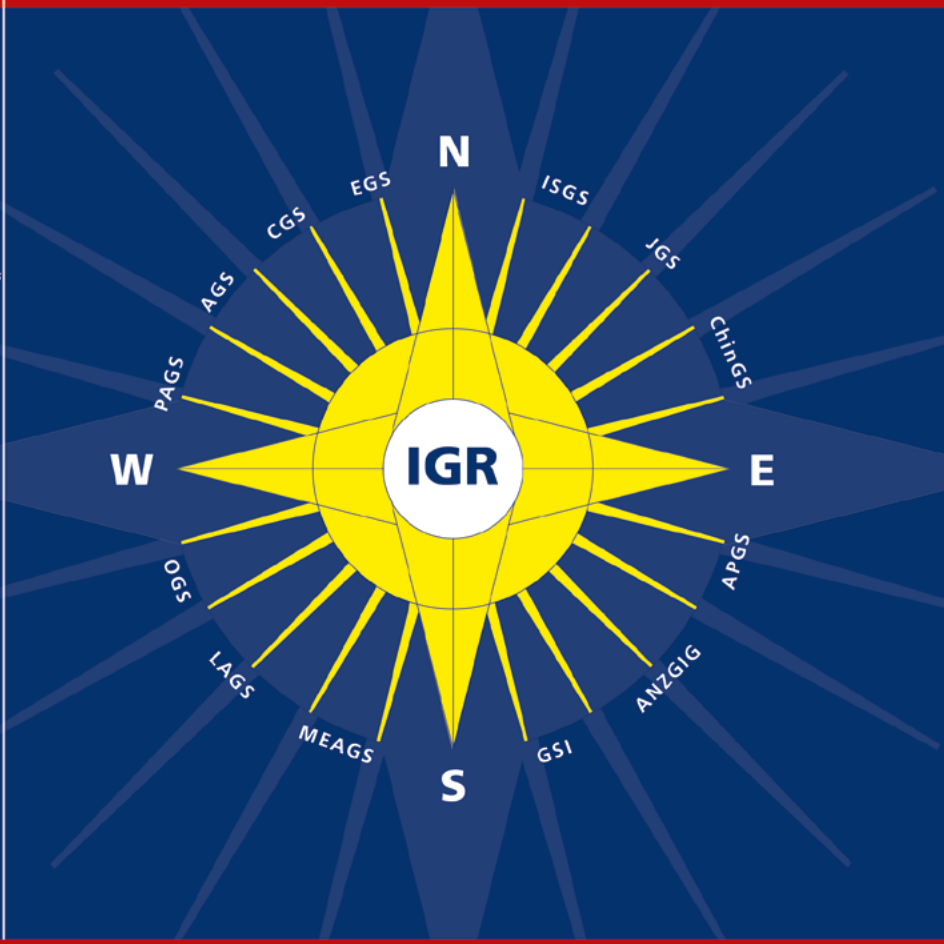

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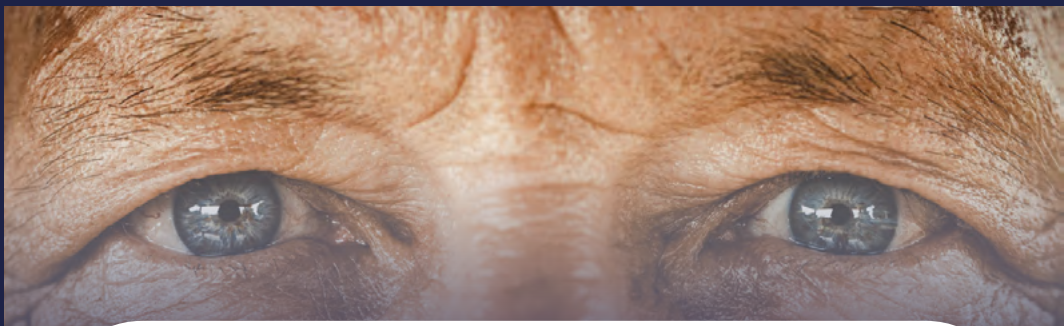

Envisioning a Better Future For Patients With Glaucoma

Glaucoma is one of the leading causes of irreversible blindness worldwide and it is a growing problem, with the number of people affected estimated to reach 111.8 million people by 2040.[1] More than 11 million people are estimated to be bilaterally blind (in both eyes) from glaucoma.[2]

Early diagnosis and treatment initiation is critical to help prevent vision loss from glaucoma, as symptoms may be hard to detect when the condition first develops.[3,4] AbbVie focuses on clinically relevant science to make a meaningful difference for patients and seeks to elevate the standard of care by addressing areas of unmet need.

With over two decades of experience researching eye diseases, Jie Shen, Ph.D., AbbVie's Vice President of Local Delivery Translational Sciences, leads a team of scientists responsible for designing and conducting studies, evaluating drug behavior in the eye, and testing promising drug candidates in early-stage clinical trials. Jie and team utilize state-of-the-art imaging modalities found in world-class clinical research institutions, digital technologies, statistical modeling, and data science to accelerate the translation of science to new medicines.

It is the people around the world living with eye conditions like glaucoma that motivate AbbVie's eye care scientists to push forward with leading-edge translational research, with the aim to deliver medicines with best-in-class outcomes to patients.

In this quest to meet patient needs, AbbVie is leveraging capabilities at its Genetic Research Center and investing in technology to accelerate and

optimize R&D, for example, identifying biomarkers that can help indicate at an early stage whether a drug may be effective. Jie also highlights the importance of AbbVie's biostatistics support, including machine learning, which can help to derive more benefit from available data in the early discovery phase.

Pursuing these goals is enabled by an eye care journey that began as Allergan over 75 years ago, bolstered today by AbbVie's legacy in complex diseases and global scale.

While eye care may seem simple, with some vision issues being solved by people wearing glasses, contact lenses, or using eye drops, the reality is what works for some does not work for others. With a background in academia and many years as a practicing ophthalmologist, Mike Robinson, M.D., AbbVie's Vice President, Clinical Development, Ophthalmology has seen firsthand the great need to elevate the standard of care and continuously improve existing options. This is why AbbVie is focused on addressing unmet needs in glaucoma.

"We continue to look for solutions in our clinical trials. Our goal has been and continues to be identifying ways to meet people where they are in their ability to preserve their vision, and our clinical trials are looking at ways to provide glaucoma patients additional options," says Mike.

AbbVie will continue to push the envelope through R&D and collaborations, to accelerate the development of better treatments for patients.

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Date of preparation: February 2024. ROC-EMEA-240001.

INTERNATIONAL GLAUCOMA REVIEW

Volume 25 no. 1

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

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ISSN 1566-1040

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1062 HE Amsterdam
The Netherlands
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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

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Welcome to the 11th World Glaucoma Congres

A Message from the Executive Vice President

Dear Colleagues and Friends, Aloha!

On behalf of the World Glaucoma Association (WGA), it is my pleasure to extend a warm welcome to all delegates attending the 11th World Glaucoma Congress (WGC) in beautiful Honolulu. As the premier global event in glaucoma education, the WGC represents the core mission of the WGA: to advance knowledge, foster collaboration, and ultimately improve the lives of patients living with glaucoma.

Education is the cornerstone of our work at the WGA, and the WGC is our flagship platform for sharing knowledge. This year's Congress brings together a truly international faculty of thought leaders—clinicians, surgeons, and scientists who represent the very best in global glaucoma expertise. We are honored to host sessions led by distinguished colleagues from over 50 countries, highlighting diverse perspectives, emerging evidence, and new paradigms of care.

We are equally proud to feature our Society Symposia, which exemplify the spirit of international cooperation that defines the WGA. These sessions are a testament to the strength we gain through collaboration—across borders, specialties, and disciplines. Our shared goal is clear: to elevate the standard of glaucoma care around the world.

We also want to acknowledge the invaluable support of our glaucoma industry partners. Their innovations continue to drive progress in diagnostics, therapeutics, and surgical technologies. We thank them for their ongoing collaboration and encourage all delegates to engage with our industry colleagues in the exhibit hall and sponsored events.

One of this year's major highlights is the 12th Consensus Meeting, (directed by Dr Weinreb and Dr Xu and their team of co-chairs) will presents a comprehensive update on angle closure and angle closure glaucoma—an area of pressing global importance. We also encourage you to attend the hands-on workshops, which offer practical training and direct interaction with experts in surgical techniques, imaging, and laser therapies.

Beyond the scientific program, the WGC is also a place to connect, share stories, and build lifelong professional relationships. Whether you're attending a session, meeting a new colleague over coffee, or exchanging ideas during a social event—network, collaborate, and enjoy every moment.

Thank you for joining us. Your participation is what makes the World Glaucoma Congress a truly global forum. Let's learn, share, and work together to move the field forward.

Warm regards,

Kaweh Mansouri, MD, MPH
Executive Vice President
World Glaucoma Association

Welcome to WGC-2025
from Co-Chairs WGC Program Committee

Dear IGR Readers,

The World Glaucoma Congress is truly a unique and global scientific meeting which showcases the latest research and developments in glaucoma diagnostics and care, from basic science to advanced surgical techniques.

While we attend local and national meetings, and perhaps international meetings in nearby countries, how often do we learn from experts around the world? The care of glaucoma, and the scientific approach to answering questions, is not homogenous across the world. We benefit tremendously by listening to doctors and scientists from other systems of care and schools of thought who might challenge our paradigms and push us to rethink our scientific understand and clinical approach to glaucoma.

No meeting brings together the best clinical, surgical, and scientific experts in glaucoma from across the world like the World Glaucoma Congress (WGC). This year's congress will be held from June 25th to 28th in Honolulu, and hopefully most of you will be there (if you're on the fence – it is not too late to register at https://worldglaucomacongress.org/registration/). The Congress covers the full range of topics in glaucoma, from case studies to clinical debates, to practical sessions on medical/laser therapy, functional testing and imaging, to innovative video-heavy surgical sessions. It includes dedicated scientific sessions covering epidemiology with public health strategies, genetic breakthroughs and cutting edge research including artificial intelligence that will change how we diagnose and treat glaucoma in the coming years. Whether you're looking to learn the basics of glaucoma diagnostics and management, understand the latest practice innovations, pick up surgical tips to adopt new techniques or immerse yourself in the science that will change our future care of patients, there is something for each one of you.

This year's Congress will include 286 faculty from 50 countries, and will include 25 symposia, 23 courses, 4 workshops, 35 society symposiums. and over 838 poster presentations. The congress stars of with the Presidential symposia on cutting edge research and included are Plenary Symposia on ways to modify disease risk through lifestyle modifications, novel ways to revitalize conventional outflow, and a summary of the 12th consensus meeting on angle closure and angle closure glaucoma. Other highlights

include a Glaucoma Surgical Grand Rounds, a WGA-ASCRS Symposium on cataract and refractive surgery in glaucoma patients, an engaging debate session , case based interactions and a Symposium on the “Beautiful Basics” of glaucoma care – taught by the world’s best doctors with decades of experience.

We hope that all attendees will have a unique learning experience , utilize this wonderful opportunity to collaborate with the global glaucoma network and move towards our ultimate goal of positively impacting the lives of glaucoma patients worldwide.

We offer our sincere thanks to Drs. Lisandro Sakata, Chelvin Sng, Anthony Khawaja, and Yvonne Ou who worked with their teams to organize sessions on clinical care/science, glaucoma surgery, epidemiology/genetics, and basic sciences, respectively.

We look forward to seeing you in Hawaii.

Sincerely,

Tanuj Dada and **Pradeep Ramulu**
Co-Chairs WGC Program Committee

12th Consensus Meeting:
Angle Closure and Angle Closure Glaucoma

Honolulu, HI, USA, June 26, 2025

Leadership

WGA Consensus Initiative Chair
Robert N. Weinreb (USA)

WGA Consensus 12 Co-Chairs
Benjamin Xu (USA), David Friedman (USA), Paul Foster (UK), Tin Aung (Singapore), Xiulan Zhang (China)

Section Leaders
Ching-Yu Cheng (Singapore), Christopher Leung (Hong Kong), Clement Tham (Hong Kong), Do Tan (Vietnam), Gus Gazzard (UK), Kyung Rim Sung (Korea), Lisandro Sakata (Brazil), Mani Baskaran (India), Mingguang He (Hong Kong), Monisha Nongpiur (Singapore), Ningli Wang (China), Ronnie George (India), Sasan Moghimi (USA), Shan Lin (USA), Tanuj Dada (India), Vijaya Lingham (India)

Introduction

In the 19 years since the last World Glaucoma Association (WGA) consensus meeting on angle closure glaucoma (published in 2006), our understanding of this visually devastating disease has been significantly transformed by a series of landmark studies.

Population-based epidemiological research has shed new light on the global burden of primary angle closure glaucoma (PACG) and its associated ocular morbidity. Insights into disease pathogenesis have deepened, particularly regarding racial anatomical differences and dynamic iris-related mechanisms.

Anterior segment optical coherence tomography (AS-OCT) is emerging as a potential new standard for detecting and risk-stratifying angle closure, superseding gonioscopy, the long-standing clinical standard. The integration of artificial intelligence (AI) with AS-OCT has further enhanced its utility and accessibility for widespread clinical use.

At the same time, evidence-based care for angle closure disease has improved, driven by pivotal trials such as EAGLE and ZAP. These studies support a broader spectrum of treatment strategies, including clear lens extraction (CLE), goniosynechiolysis (GSL), and minimally invasive glaucoma surgeries (MIGS), and a reconsideration of which patients should be treated.

Given the depth and breadth of these advances, it is an ideal time is to synthesize current knowledge for the global glaucoma community and identify critical knowledge gaps to guide research over the next two decades.

As with all the previous WGA consensuses, the Angle Closure and Angle Closure Glaucoma Consensus is based on the published literature and expert experience. Although consensus does not replace and is not a surrogate for scientific investigation, it does provide considerable value, especially when the desired evidence is lacking. The goal of this consensus is to establish what we 'know' and what we need to 'know'. It is expected that this consensus report will serve as a benchmark for our current knowledge and that it will be revised and improved with the emergence of new evidence.

Sections

Section 1: Epidemiology

Section 2: Pathophysiology and Risk Factors

Section 3: Diagnosis and Evaluation

Section 4: Medical and Laser Management

Section 5: Surgical Management

Section 6: Acute Primary Angle Closure

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Suspicious eyes - Elvis's glaucoma battle

Zegers RH, Liu KC, Heutink J, Tennant F, Weinreb RN
Journal of Medical Biography 2024; 0: 9677720241273624
abstract no. 119172

The Benefit of Nocturnal IOP Reduction in Glaucoma, Including Normal Tension Glaucoma

Huang AS, Mai AP, Goldberg JL, Samuelson TW, Morgan WH, Herndon L, Ferguson TJ, Weinreb RN
Clinical Ophthalmology 2024; 18: 3153-3160
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Federated Learning in Glaucoma: A Comprehensive Review and Future Perspectives

Hallaj S, Chuter BG, Lieu AC, Singh P, Kalpathy-Cramer J, Xu BY, Christopher M, Zangwill LM, Weinreb RN, Baxter SL
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The AI revolution in glaucoma: Bridging challenges with opportunities

Li F, Wang D, Yang Z, Zhang Y, Jiang J, Liu X, Kong K, Zhou F, Tham CC, Medeiros F, Han Y, Grzybowski A, Zangwill LM, Lam DSC, Zhang X
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Evaluating the impact of caloric restriction, body mass index and exercise on primary open-angle glaucoma: A review

Lai JY, Mclarnon P, Sheridan C, Vallabh NA
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Glaucoma: now and beyond

Jayaram H, Kolko M, Friedman DS, Gazzard G
Lancet 2023; 402: 1788-1801
abstract no. 121901

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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

Join the discussion online at e-igr.com using your WGA#One account.

Epidemiology

Newest data on Glaucoma prevalence in the US

Comment by Rupert Bourne, Cambridge, UK

119744 Prevalence of Glaucoma Among US Adults in 2022; Ehrlich JR, Burke-Conte Z, Wittenborn JS, Saaddine J, Omura JD, Friedman DS, Flaxman AD, Rein DB; JAMA ophthalmology 2024; 142: 1046-1053

This meta-analysis is an advance on what we know of prevalence of glaucoma in the USA, the authors estimating that in 2022, **4 million people had glaucoma (all forms combined) with approximately 35% (1.5 million) of them with associated poor visual acuity or visual field damage**. Glaucoma was estimated to affect 2.56% (95% Uncertainty Interval, UI, 2.10%-3.16%) among those 40 years or older, rising to 5.20% (UI, 4.12%-6.49%) among those aged 65 years or older.

In 2022 in USA, "4 million people had glaucoma ……". It also is "estimated to affect 2.56% among those 40 years or older, rising to 5.20% among those aged 65 years or older."

As with other meta-analyses, males were found to have higher age-standardised prevalence of glaucoma and vision-affecting glaucoma than females.[1,2] This recent meta-analysis incorporated data from the 2005-2008 National Health and Nutrition Examination Survey (NHANES)- a cross-sectional survey that uses a stratified multistage probability design to obtain representative health data of the civilian, noninstitutionalized US population.[3] The NHANES oversamples elderly participants and certain age and minority groups, making it well suited to estimate glaucoma prevalence in the United States, and prior NHANES studies had relied on only self-reported glaucoma. By analysing optic nerve photographs from 5,746 participants, NHANES 2005-2008 reported a glaucoma prevalence of 2.1% (95% confidence interval [CI], 1.7%–2.6%) in the population aged 40 years and older, of whom **half the cases were undiagnosed**.[4] In this current meta-analysis, the authors also used data from the Los Angeles Latino Eye Study (2000 to 2003);[5] a meta-analysis by the Eye Diseases Prevalence Research Group (EDPRG; that analyzed studies conducted from 1985 to 2000);[6] the Salisbury Eye Evaluation Glaucoma Study (2001-2003),[7] and two medical claims databases. The authors acknowledge the limitations associated with differing glaucoma definitions between studies/sources. They report substantial variation in prevalence across US states and counties and in demographic subgroups, for example non-Hispanic black adults were approximately twice as likely as non-Hispanic white adults to have glaucoma and nearly 3 times as likely to have vision-affecting glaucoma after adjusting for age and sex/gender. In summary, this report demonstrates the importance of population-based data collection that quantifies the met and unmet need for glaucoma care. **We eagerly await the imminent NHANES survey which will employ both optic disc photography and OCT which should provide additional insight into glaucoma trends in the US population**.

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Basic Science

IOP is not the only culprit, genome studies say

Comment by Mahantesh Biradar and Anthony Khawaja, London, UK

119085 GWAS-by-subtraction reveals an IOP-independent component of primary open angle glaucoma; Huang Y, Plotnikov D, Wang H, Shi D, Li C, Zhang X, Zhang X, Tang S, Shang X, Hu Y, Yu H, Zhang H, Guggenheim JA, He M; Nature communications 2024; 15: 8962

High intraocular pressure (IOP) is the most important modifiable risk factor for primary open-angle glaucoma (POAG), and recent genome-wide association studies (GWAS) have identified hundreds of genetic signals linked to IOP and glaucoma [1,2]. The etiology of POAG involves both IOP-dependent and IOP-independent mechanisms[3], but GWASs focused on IOP-independent traits remain limited.

To address this issue, Huang Y and colleagues applied GWAS-by-subtraction—a genomic structural equation modelling approach—to dissect POAG into IOP-dependent and IOP-independent components. This method subtracts genetic effects from an IOP GWAS (n = 97,644) from those in a POAG GWAS (14,853 cases; 106,544 controls), separating IOP-independent genetic contributions to POAG. Seventeen independent genome-wide significant SNPs were identified for the IOP-independent component.

These components display distinct genetic associations with other traits. **The IOP-independent component correlates with glaucoma endophenotypes (cup area, disc area, cup-to-disc ratio), whereas the IOP-dependent component is associated with blood pressure**.

Pathway enrichment analysis identified "Apolipoprotein A-1 binding" as significantly enriched for the IOP-independent component, while "negative regulation of vascular permeability" was most enriched for the IOP-dependent component.

Single-cell and tissue enrichment analyses revealed distinct gene expression patterns: IOP-dependent genes were enriched in the juxtacanalicular region of the trabecular meshwork and retinal fibroblasts, while IOP-independent genes were enriched in photoreceptors and the visual cortex.

A genetic risk score (GRS) derived from the IOP-independent component was associated with 26 distinct retinal microvascular features, unlike the IOP-dependent GRS.

This study highlights the importance of separating POAG genetics into IOP-dependent and IOP-independent components

This study highlights the importance of separating POAG genetics into IOP-dependent and IOP-independent components, offering deeper insights into the distinct biological pathways driving disease risk. Future genetic research using similar approaches may improve our understanding of the causal mechanisms underlying normal-tension glaucoma (NTG) and enable earlier prediction through NTG-specific polygenic risk scores.

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Basic Science

Can Insulin be neuroprotective for RGCs?

Comment by James Morgan, Cardiff, UK

121602 Insulin restores retinal ganglion cell functional connectivity and promotes visual recovery in glaucoma; El Hajji S, Shiga Y, Belforte N, Solorio YC, Tastet O, D'Onofrio P, Dotigny F, Prat A, Arbour N, Fortune B, Di Polo A; Science advances 2024; 10: eadl5722

Our understanding of the processes underpinning retinal ganglion cell degeneration in glaucoma has changed considerably in recent years. Evidence from animal models and human studies indicates that retinal ganglion cell (RGC) death in glaucoma is preceded by dendritic degeneration, likely occurring before axon loss. In a landmark study, Hajji *et al.* explore whether dendrite remodelling can be used as a neural substrate for the reversal of retinal ganglion cell damage in glaucoma. If dendritic structure can be restored, vision could be recovered and RGC death prevented.

They use a mouse model of glaucoma in which the iridocorneal angle was blocked using magnetic microbeads to elevate the intraocular pressure (OHT). **For RGC recovery they applied topical insulin (eye drops) to stimulate mTORC (mammalian target of rapamycin complex), an important factor in maintaining neuronal dendritic integrity**. RGC dendrites were traced using the genetically expressed label, YFP. They demonstrate significant dendritic degeneration following OHT, which could be reversed following the application of topical insulin (treatment was started after the onset of RGC degeneration); this reversal in degeneration was not observed following the reduction in IOP. Critically, they confirm elevated insulin levels in the vitreous and retina following treatment. In a series of intricate experiments knocking down effector molecules they show that SIN1 (a stress induced protein) mediated linked mTORC1 and 2 activities in a positive feedback process to enhance dendritic remodelling. Dendritic recovery was associated with restoration of pre and post synaptic connectivity, laying the foundation for a recovery in visual function as demonstrated in this model by enhanced oculomotor responses.

The results are exciting since they support the concept that vision can be recovered in glaucoma. Insulin treatment is associated with increased RGC survival, but we do not yet know how RGC afferent connections are affected and how this might influence higher level visual responses. Since dendritic pruning could be an adaptive response to damage,

forcing the recovery of dendrites could increase cell stress and increase the risk of axon loss(1). While this does not appear to be the case in this study of short-term OHT in mice, further careful study will be required to confirm that this is the case with long-term glaucoma in man.

The results are exciting since they support the concept that vision can be recovered in glaucoma

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Clinical Examination Methods

Could a "central 24-2 index" replace a 10-2 test?

Comment by Zhi Wu, Melbourne, Australia

122394 Enhancing Detection of Glaucoma Progression: Utility of 24-2 Visual Field Central Points vs. 10-2 Visual Fields; Ashrafkhorasani M, Besharati S, Mohammadzadeh V, Zou J, Figueroa J, Mohammadi M, Nouri-Mahdavi K; Ophthalmology. Glaucoma 2024; 0:

Preserving the central visual field (VF) is crucial to preventing functional disability in glaucoma. This study examined if the mean deviation (MD) derived from the central 12 points (or 10° radius) of 24-2 VFs (termed "MD12") can "*enhance detection of disease progression in the macular region*" compared to MD from the entire 10-2 and 24-2 VF.

The authors reported that **there was *"a low level of agreement"* in the rate of change in MD12 and 10-2 MD (correlation coefficient = 0.49), and in the eyes showing a significant negative slope.** Specifically, of the 33 eyes with a significant negative MD12 or 10-2 MD slope, only one-third was detected by both parameters (whilst one-third each was detected by MD12 and 10-2 MD only). **The authors thus conclude that evaluating MD12 does not *"replace the need for 10-2 VF MD to monitor central damage"*.**

Is this a valid inference of the data? Large measurement variability is an inherent characteristic of subjective VF tests. To appropriately conclude that 10-2 VF tests *cannot* be replaced, one would need to show that the agreement between the 10-2 MD and MD12 is lower than with measurement variability alone. This could be evaluated with test-retest data, or with careful computer simulations using paired clinical data.[1] This study reported instead that *more* eyes had a significant negative slope with MD12 than 10-2 MD (35% vs. 30% respectively), when using permutation analyses to achieve matched specificities.

Substituting 24-2 VFs with 10-2 VFs could delay detection of disease progression more broadly, without providing meaningful gains in detecting central VF progression

Substituting 24-2 VFs with 10-2 VFs could delay detection of disease progression more broadly,[2] without providing meaningful gains in detecting central VF progression. It thus remains prudent to consider the conclusion of the recent American Academy of Ophthalmology report[3]: "Evidence to date does not support routine testing using 10-2 VF for patients with early glaucoma." Careful review of central 24-2 VF sensitivities also remains critical clinically, until device manufacturers incorporate the simple-to-derive MD12 measure in their progression analysis software.[4]

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Clinical Examination Methods

Smartphone-based perimeters: Are we there yet?

Comment by Vincent Michael Patella, Iowa City, IA, USA and Anders Heijl, Malmo, Sweden

121251 Comparing a Head-Mounted Smartphone Visual Field Analyzer to Standard Automated Perimetry in Glaucoma: A Prospective Study; Wang SK, Tran EM, Yan W, Kosaraju R, Sun Y, Chang RT; Journal of Glaucoma 2024; 33: 742-747

The authors compared test results from an FDA-registered head-mounted smartphone perimeter (PalmScan VF2000, Micro Medical Devices, Calabasas, California) to HFA SITA Standard 24-2 results in terms of MD and PSD using t-tests, and Bland-Altman plots. Bland-Altman analyses also were applied to quadrant means of deviations from age normal sensitivity, The authors also assessed PalmScan's test-retest repeatability using Spearman's correlations and intraclass correlation coefficients but made no comparisons to the HFA.

Perhaps more interesting than what the authors assessed is what they did not assess. The authors pointed out that this was only a pilot study, which may explain why they did not recruit normal subjects in order to compare the specificities of the two devices, and also why they did not collect HFA test-retest data so as to compare the inter-test variabilities of the two devices in the same patient cohort. However, they also seem to have ignored possibly interesting analyses of data that they appear to have had at hand.

Example: The authors compared pointwise decibel deviations from age-normal but did not compare how often test points were outside normal limits for Total and Pattern Deviation. If the two devices were found to identify similar patterns of VF damage in the probability plots and similar numbers of test points outside normal limits, we might have said, "Wow, as a follow-on study, let's go see how similar the specificities of the two devices are." And if the results were significantly dissimilar that might have suggested a different next step.

Other Examples: What about comparison of test duration as a function of the severity of VF loss? How about comparing PalmScan's test-retest variability, for instance in the 32 available eyes with mild glaucoma to reports in the literature of HFA variability in similar cohorts? Does PalmScan software have analyses that are functionally similar to the HFA's Glaucoma Hemifield Test and/or Visual Field Index? If so, how did those analyses compare? How do the authors' Bland-Altman plots of Mean Deviation differences presented in Figure 3 compare to similar plots for the HFA in the literature, for instance in Heijl *et al,* 2019?[1]

In our experience, pilot studies are performed during product development as a way of confirming proposed design decisions. Clinical evaluations of FDA cleared commercially released devices should not be treated as pilot studies, but should be scaled to address and document clinically critical performance metrics. Critical metrics include comparisons of diagnostic sensitivities to early, moderate, and advanced disease, specificity of pointwise and summary analyses, pointwise inter-test variability across the dynamic range, and test durations across the full range of VF damage. Devices being evaluated must be equipped with testing strategies, normative data and analysis methods that are intended for actual clinical use; otherwise study findings may not usefully apply to clinical care.

We view publication of instrument evaluations that deal solely with correlations and/or only evaluate MD & PSD and/or worry about comparisons of raw threshold sensitivities as totally insufficient and, therefore misleading

We view publication of instrument evaluations that deal solely with correlations and/or only evaluate MD & PSD and/or worry about comparisons of raw threshold sensitivities as totally insufficient and, therefore misleading. Of course the results are correlated; how could they not be, given that the instruments being compared were designed to measure visual field sensitivity? MD & PSD are poor tools for diagnosing of glaucoma or other disease; point-wise analyses should instead be used. And, of course the raw sensitivities found by the devices being compared do not have to match; that's what normative databases are for.[2]

If we are going to spend time and energy performing and publishing diagnostic studies involving devices that are FDA cleared and commercially available, we must think carefully about which metrics are critical for clinical success. Sensitivity, specificity, test-retest reproducibility, and testing time all have to be on the list.

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Clinical Examination Methods

Smartphone-based perimeters: Are we there yet?

Comment by Chris Johnson, Iowa City, IA , USA

121251 Comparing a Head-Mounted Smartphone Visual Field Analyzer to Standard Automated Perimetry in Glaucoma: A Prospective Study; Wang SK, Tran EM, Yan W, Kosaraju R, Sun Y, Chang RT; Journal of Glaucoma 2024; 33: 742-747

The use of inexpensive, portable devices such as tablets and virtual reality headsets to perform visual field testing is an area that is receiving an increased amount of attention. In this view, Dr. Wang and colleagues performed a comparison of the PalmScan VF100 Visual Field Analyzer to the Humphrey Field Analyzer SITA Standard 24-2 test procedure in 81 eyes of 51 patients with glaucoma. Classification of glaucomatous deficits as mild, moderate and severe were performed according to the Hodapp, Parrish and Anderson criteria. The authors report that **there was reasonably good agreement between the two devices, but some differences were also noted, indicating that results from the two methods cannot be interchangeable**. This is not surprising, given that (1) there was missing information concerning the PalmScan device (test strategy, characteristics of the normative database, refractive correction employed, analysis method, statistical procedures, etc.) and (2) there were difference in the test characteristics of the two devices (background luminance, calibration procedures, dynamic intensity range, eye tracking capability, test strategy, etc.).

The use of portable visual field devices such as virtual reality headsets is still in its infancy and there are presently a wide variety of approaches that are being employed, none of which have been able to achieve the highest degree of compatibility with the methods employed by the Humphrey Field Analyzer

It is therefore not clear what information in the present study is of interest or value to practitioners who read this article. The use of portable visual field devices such as virtual reality headsets is still in its infancy and there are presently a wide variety of approaches that are being employed, none of which have been able to achieve the highest degree

of compatibility with the methods employed by the Humphrey Field Analyzer. Although this may be regarded as a problem, it can also be viewed as an opportunity for clinical investigators to approach this challenging topic to refine current procedures. Future investigations should include a larger sample of patients with glaucomatous losses spanning the entire range of peripheral visual impairment.

Clinical Examination Methods

Structure-function association in the papillomacular RNFL bundle

Comment by Laura A. Meliante and Anthony Khawaja, London, UK

120542 Retinal Nerve Fiber Layer Optical Texture Analysis and 10-2 Visual Field Assessment in Glaucoma; Kamalipour A, Moghimi S, Khosravi P, Tansuebchueasai N, Vasile C, Adelpour M, Gunasegaran G, Nishida T, Zangwill LM, Lam AKN, Leung CKS, Weinreb RN; American Journal of Ophthalmology 2024; 266: 118-134

Retinal Optical Texture Analysis (ROTA) is a novel imaging approach that enhances traditional OCT-based assessment of the retinal nerve fibre layer (RNFL) by capturing optical texture changes along nerve fibre bundle trajectories. Unlike conventional RNFL thickness maps, ROTA combines reflectance and thickness data through nonlinear transformations to produce detailed visual representations of axonal integrity.[1–3] This new algorithm may improve detection of glaucomatous damage in the macular region, where early structural changes are often subtle and easily overlooked.[1]

In this cross-sectional study of 841 eyes from 442 participants, the authors applied ROTA to visualize papillomacular and papillofoveal RNFL bundle defects and assessed their association with 10-2 and 24-2 visual field (VF) sensitivity loss. The cohort included 380 glaucoma eyes (45.2%), 317 glaucoma suspects (37.7%), and 144 controls (17.1%). Papillomacular defects were present in 92.1% of glaucoma eyes, with strong topographic concordance to abnormal 10-2 VF points on pattern deviation probability (PDP) maps (ORs reaching 38.60, 95% CI: 36.17, 41.18 at $P < .01$). In univariable analyses, this association exceeded that observed between ROTA-detected defects and the central 24-2 VF points (OR = 21.25, 95% CI: 19.22–23.49). **In multivariable models including both predictors, ROTA remained more strongly associated with 10-2 abnormalities (OR = 22.21, 95% CI: 20.74–23.79) than central 24-2 test points (OR = 7.47, 95% CI:**

6.93–8.06), highlighting its superior independent predictive value for detecting central glaucomatous damage. Perhaps most striking is how common even papillofoveal defects are in glaucoma (37.9%).

The authors present a biologically informed structure-function model that accounts for ganglion cell displacement and axonal bundle trajectories, supporting ROTA as a promising tool for identifying early macular damage

This study adds to the growing evidence that glaucoma has important effects on central vision, even early in the disease. The authors present a biologically informed structure-function model that accounts for ganglion cell displacement and axonal bundle trajectories, supporting ROTA as a promising tool for identifying early macular damage and guiding targeted 10-2 VF testing in eyes with papillomacular texture abnormalities.[4] Longitudinal studies are needed to assess ROTA's ability to detect pre-perimetric glaucoma and monitor disease progression.

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Clinical Examination Methods

RNFL thickness accuracy may vary with ethnicity

Comment by Jin Wook Jeoung, Seoul, South Korea

121032 Racial Differences in Diagnostic Accuracy of Retinal Nerve Fiber Layer Thickness in Primary Open-Angle Glaucoma; KhalafAllah MT, Zangwill LM, Proudfoot J, Walker E, Girkin CA, Fazio MA, Weinreb RN, Bowd C, Moghimi S, De Moraes CG, Liebmann JM, Racette L; American Journal of Ophthalmology 2023; 0:

Glaucoma is a progressive optic neuropathy characterized by the degeneration of retinal ganglion cells, with evaluation of retinal nerve fiber layer thickness (RNFLT) and optic nerve head (ONH) morphology being central to its diagnosis and monitoring. Spectral-domain optical coherence tomography (SD-OCT) has been widely adopted as the standard imaging modality owing to its capacity for high-resolution structural assessment. Previous studies have reported a higher prevalence and more rapid progression of glaucoma in individuals of African descent compared to those of European descent.[1-3] In this context, KhalafAllah *et al.*[4] investigated whether the diagnostic accuracy of RNFLT varies by race. The study analyzed data from 821 eyes (379 healthy and 442 glaucomatous) drawn from two large, prospective cohorts. RNFLT was assessed using both Spectralis and Cirrus OCT platforms, and diagnostic accuracy was evaluated using area under the receiver operating characteristic (AUROC) curves, with statistical adjustments for key ocular and demographic covariates.

There is reduced diagnostic sensitivity of RNFLT measurements in individuals of African descent

The findings revealed that the diagnostic accuracy of RNFLT was significantly lower in eyes of African descent compared to those of European descent, particularly when using the Spectralis OCT device (AUROC: 0.85 vs. 0.91; P = .04). A similar trend was noted with Cirrus OCT (AUROC: 0.86 vs. 0.90), although this difference did not reach statistical significance (P = .33). These differences remained consistent after adjusting for age, axial length, central corneal thickness, disc area, intraocular pressure, and visual field mean deviation. there is reduced diagnostic sensitivity of RNFLT measurements in individuals of African descent, emphasizing potential limitations of applying uniform diagnostic thresholds across racially diverse populations.

The strengths of this study include its large, racially diverse sample and the use of two widely implemented OCT platforms, which enhances the generalizability and clinical relevance of the findings. The rigorous multivariable adjustment increases the methodological robustness, while the real-world applicability of the OCT devices supports clinical translation. From a clinical perspective, these results highlight the necessity of considering racial and ethnic differences in OCT interpretation. Development of race-specific normative databases and adjustment of diagnostic criteria may improve the accuracy of glaucoma diagnosis across diverse populations.

Several limitations should be considered when interpreting the findings. The cross-sectional design limits the ability to assess longitudinal changes and the temporal dynamics of structure-function relationships. Racial categorization was based on self-identification, which may not fully capture underlying genetic variation. The analysis was limited to global RNFLT measurements, without assessment of sectoral or clock-hour data, which may differ in diagnostic utility between racial groups. Additionally, Cirrus OCT data were not available for all eyes, and current OCT devices lack the capability to image deeper structures such as the lamina cribrosa, which may contribute to racial differences in diagnostic accuracy. Although visual field mean deviation was similar between groups, the unknown timing of disease onset may have confounded structural-functional comparisons.

In conclusion, **this study demonstrates that the diagnostic performance of RNFLT is lower in eyes of African descent compared to those of European descent. These findings, consistent across multiple OCT platforms and robust to adjustment for known confounders, emphasize the importance of integrating race-specific considerations into glaucoma diagnostic protocols**. Future investigations should aim to elucidate the anatomical factors underlying these disparities and assess the utility of alternative or complementary imaging biomarkers. Longitudinal studies, along with the development of comprehensive and inclusive normative databases, will be essential to enhancing diagnostic accuracy and reducing disparities in glaucoma detection and management.

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Clinical Examination Methods

Self-tonometry and self-perimetry may comlement glaucoma monitoring in some patients

Comment by David Friedman, Baltimore, MD, USA

121434 Glaucoma Home Self-Testing Using VR Visual Fields and Rebound Tonometry Versus In-Clinic Perimetry and Goldmann Applanation Tonometry: A Pilot Study; Berneshawi AR, Shue A, Chang RT; Translational vision science & technology 2024; 13: 7

Berneshawi and colleagues evaluated home monitoring of glaucoma using the Icare Home tonometer and virtual reality perimetry (VRP) using the Olleyes device. Fifteen patients (28 eyes) were enrolled; however, only nine patients (16 eyes) completed the study. **Six participants were unable to use the Icare device.** In-office intraocular pressures (IOPs) ranged from 9 to 42 mmHg, and the mean deviation (MD) on Humphrey visual field (HVF) testing averaged -10 dB (range: -2 to -28 dB). Patients were instructed to perform VRP daily and Icare measurements four times per day over three consecutive days. Home IOP measurements correlated with in-office Goldmann IOPs, and the averaged VRP MD showed concordance with HVF MD.

This small study primarily confirms that VRP-derived MD correlates with HVF MD. Sectoral analysis revealed no correlation between VRP and HVF in the superonasal field, and only a weak correlation in the superotemporal field.

Sectoral analysis revealed no correlation between VRP and HVF in the superonasal field, and only a weak correlation in the superotemporal field

A larger sample is needed to determine whether these discrepancies reflect device limitations or variability due to the small and heterogeneous study population.

Importantly, not all patients were able to use the Icare tonometer, which in this study was an older-generation model. Despite training, several patients either failed to generate reliable values or could not operate the device. This limitation has been noted previously. A next-generation home tonometer requiring less user manipulation would be a welcome development for home monitoring.

In sum, the authors show that select patients can measure IOP and perform perimetry at home. However, substantial work remains before this approach can be broadly integrated into clinical practice.

Risk Factors

The potential role of blood pressure in VF progression - I

Comment by Alon Harris, New York, NY, USA

121260 Long-Term Blood Pressure Variability and Visual Field Progression in Glaucoma; Pham VQ, Nishida T, Moghimi S, Girkin CA, Fazio MA, Liebmann JM, Zangwill LM, Weinreb RN; JAMA ophthalmology 2024; 0:

Risk factors for primary open angle glaucoma (POAG) include elevated intraocular pressure (IOP), genetics, myopia, high and low blood pressure (BP) and retinal/optic nerve head (ONH) vascular impairments.[1-2] Diurnal fluctuations and variability in physiological biomarkers have also been associated with POAG. Specifically, non-physiologic nocturnal BP dipping and wider circadian fluctuations in ocular perfusion pressures (OPP-calculated from IOP and BP) have been identified in POAG patients.[3] Higher daytime baseline standard deviation (SD) in mean arterial pressure (MAP) and OPP have also previously been found to be predictors of visual field (VF) progression in patients with normal tension glaucoma.[4]

In the current study Pham *et al.* present novel data on the long-term variability of BP and how it is associated with VF progression in patients with suspected or confirmed glaucoma. **The researchers found higher mean BP and higher SD of BP were associated with faster rates of VF progression**. Specifically, they identified how the variability of BP readings over 8 years was associated with steeper VF MD slopes. Their work indicates faster disease progression associated with both MAP and diastolic arterial pressure (DAP), especially when combined with higher mean BP and IOP. Perhaps more interesting, both low MAP and DAP, when combined with low mean IOP and increased SD, also resulted in steeper MD slopes.

Both low MAP and DAP, when combined with low mean IOP and increased SD, also resulted in steeper MD slopes

Strengths of the current work include the uniformity of dual protocols used in the Diagnostic Innovations in Glaucoma Study and the African Descent and Glaucoma Evaluation Study and the sample size of 1,674 eyes from 985 patients. Limitations include absence of blood flow assessments (*i.e.* optical coherence tomography angiography-OCTA), not accounting for systemic and ocular medication use, and not assessing diurnal fluctuations or structural assessments including the retinal nerve fiber layer.

Pham and coworkers should be congratulated for this important contribution on BP variability and its relationship to functional POAG progression. The combination of machine learning (ML) and mathematical modeling has previously demonstrated how subjects with both low BP and high IOP are more susceptible to POAG progression.[5-6] The Singapore Epidemiology of Eye Diseases study (SEED) of 19,587 eyes found that low systolic BP coupled with high IOP may result in reduced perfusion to the ONH in ocular hypertensive eyes (OR=3.90).[7] **The highly interesting results presented here by Pham and coworkers are therefore in strong agreement with the large and growing body of evidence linking BP, and potentially its variability, to the onset and progression of POAG**. Future work may consider including direct vascular assessments using OCTA or other advanced imagery to reveal the metabolic impact of BP and IOP combinations and their variability on retinal and ONH tissues.

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Risk Factors

The potential role of blood pressure in VF progression - II

Comment by Alon Harris, New York, NY, USA

120591 Relationship between Blood Pressure and Rates of Glaucomatous Visual Field Progression: The Vascular Imaging in Glaucoma Study; Donkor R, Jammal AA, Greenfield DS; Ophthalmology 2025; 132: 30-38

The multifactorial nature of primary open angle glaucoma (POAG) creates unique challenges for advancing diagnostics and precision patient care. Many previous studies have found both high and low blood pressure (BP) to be strongly associated with POAG.[1-4] **Low ocular perfusion pressure (OPP), calculated from BP and intraocular pressure (IOP), has also been identified as a risk factor for POAG prevalence, incidence and progression** in in several population-based studies.[5-7] Studies have suggested the importance of maintaining blood flow and metabolic autoregulation across physiological ranges of BP and IOP. Non-physiological dips or spikes in BP and IOP in combination with faulty autoregulation may result in imbalances that cause low retinal and optic nerve head (ONH) perfusion and ultimately retinal ganglion cell (RGC) death and visual field (VF) loss.

In this new prospective analysis, Donkor and colleagues examine the relationship between 24-hour ambulatory BP monitoring (ABPM) and the rate of change in standard automated perimetry (SAP) in 124 eyes with glaucoma (91) and suspected glaucoma (33)

over 4 years. The researchers found lower mean arterial pressure (MAP) and systolic BP at baseline, as well as low systolic BP during follow-up were significantly associated with faster rates of SAP mean deviation (MD) loss.

Lower mean arterial pressure (MAP) and systolic BP at baseline, as well as low systolic BP during follow-up were significantly associated with faster rates of SAP mean deviation (MD) loss

The results are in line with the Early Manifest Glaucoma Trial[6] and complement the previous work of Jammal *et al.* who found that when adjusted for IOP, lower MAP and diastolic arterial pressure during follow-up were significantly associated with faster rates of retinal nerve fiber layer (RNFL) loss in subjects from the Duke Glaucoma Registry.[2] Strengths of the study by Donkor *et al.* include diurnal 24-hour ABPM and adjusting for potential confounding variables including age, IOP during follow-up, central corneal thickness, and the severity of VF loss. Limitations include absence of structural assessments including OCT assessed-RNFL, inclusion of both glaucoma and glaucoma suspects in a single cohort and no healthy controls, mixed medication use among patients and not directly assessing retinal and ONH blood flow.

The outstanding work by Donkor and associates provides exciting new prospective data linking lower systolic BP and MAP to glaucomatous VF progression. This novel contribution strengthens the paradigm that certain POAG patients may benefit from including BP in their risk assessment, especially those when a patient's IOP is low. Interestingly, another recently highlighted article by Pham *et al.* (JAMA Ophthalmol. 2025;143(1):25-32. doi:10.1001/jamaophthalmol.2024.4868) (see preceding comment- 121260) confirmed glaucoma and suspects over 8 years found both high and low mean BP combined with higher SD of BP and high or low IOP respectfully, were associated with faster VF progression (MD slopes). **Both studies would benefit from using OCTA or other techniques to understand the impact of lower BP, MAP and OPP on retinal and ONH perfusion and metabolism.** Overall, these complimentary results further reinforce the need for using advanced data science tools, including artificial intelligence and mathematical applications, to identify the combinations of BP and IOP that elevate an individual's risk for the onset and progression of glaucoma.[8]

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Risk Factors

Unaffected eyes of unilateral NTG patients: Beware!

Comment by Hitomi Saito, Tokyo, Japan

121632 Rapid Retinal Nerve Fiber Layer Thinning in the Unaffected Contralateral Eyes of Patients with Unilateral Normal-Tension Glaucoma: A Retrospective Observational Study; Song JE, Lee EJ, Kim TW; Ophthalmology. Glaucoma 2024; 7: 431-439

This study by Song JE *et al.* compared the rates of retinal nerve fiber layer (RNFL) thinning over a four-year period among eyes with unilateral normal tension glaucoma (NTG), their contralateral unaffected eyes, and healthy control eyes. The findings revealed that **the untreated contralateral eyes exhibited a faster rate of RNFL thinning compared**

to the healthy controls, while their thinning rate was comparable to that of the medically treated NTG eyes. Additionally, a worse baseline visual field mean deviation (VF-MD) and a thicker baseline RNFL were associated with more rapid RNFL thinning in the contralateral unaffected eyes.

> **"….healthy contralateral eyes in patients with unilateral NTG are at significant risk of structural progression. As such, prophylactic treatment should be considered for these eyes"**

These results highlight that the seemingly healthy contralateral eyes in patients with unilateral NTG are at significant risk of structural progression. As such, prophylactic treatment should be considered for these eyes. Notably, although worse baseline VF-MD in the NTG eye correlated with faster progression in the contralateral eye, the average VF-MD in NTG eyes whose contralateral eye progressed to glaucoma during the study period was -5.58 dB. This suggests that prophylactic treatment should not be dismissed solely based on the NTG eye not appearing to be in an advanced stage.

While the study provides valuable insights into the management of unilateral NTG, certain limitations should be acknowledged. First, only the NTG eyes received medical treatment, while the contralateral eyes did not. This treatment disparity may have obscured differences in natural disease progression between the NTG and contralateral eyes. Nevertheless, the contralateral eyes still showed faster RNFL thinning than the healthy controls, indicating an intrinsic susceptibility of the contralateral eyes to progression.

Second, the observed association between thicker baseline RNFL and faster thinning should be interpreted with caution. The study population largely comprised early-stage NTG eyes (mean MD of -2.92 dB), in which structural changes are typically more detectable than functional ones. RNFL thinning may have been more easily observed in eyes with initially thicker RNFL, and this characteristic alone may not necessarily predict future progression.

Third, given that NTG progression is generally slow, a longer follow-up period and a more comprehensive assessment—including factors such as disc hemorrhage, deep optic nerve head morphology, and systemic conditions—are required to fully understand the true risk factors for progression in the contralateral, clinically unaffected eyes of unilateral NTG patients.

Glaucoma and Systemic Diseases

GLP-1 agonists could be protective against glaucoma incidence in diabetic patients

Comment by Keith Martin, Melbourne, Australia

122655 Comparative Effects of Glucagon-like Peptide 1 Receptor Agonists and Metformin on Glaucoma Risk in Patients with Type 2 Diabetes; Muayad J, Loya A, Hussain ZS, Chauhan MZ, Alsoudi AF, De Francesco T, Ahmed IIK; Ophthalmology 2024; 0:

There has been growing interest in the potential for systemic metabolic treatments to influence the risk of glaucoma onset and progression, especially given the complex interplay between vascular, metabolic, and neurodegenerative factors in the disease. In this context, the retrospective cohort study by Muayad *et al.* is both timely and thought-provoking.

Using the extensive TriNetX global database and careful propensity score matching, the authors compared outcomes in patients with type 2 diabetes mellitus (T2DM) initiated on either GLP-1 receptor agonists or metformin. They report a significantly reduced risk of developing primary open-angle glaucoma (POAG), ocular hypertension, and need for first-line glaucoma therapies in the GLP-1 cohort after 1, 2, and 3-years of follow-up.

The findings are compelling and align with preclinical studies suggesting that GLP-1 receptor agonists exert neuroprotective and anti-inflammatory effects on retinal ganglion cells. Importantly, the authors also propose several plausible mechanisms, including enhanced glycaemic control, reduction in intraocular pressure (IOP), and modulation of nitric oxide signalling. The breadth of the cohort—drawn from over 120 healthcare systems across 17 countries—lends weight to the generalisability of the results, and the consistent protective effect across multiple outcome measures is interesting.

There are, however, several caveats. The study relies entirely on coded health record data, with no access to individual clinical measures such as actual IOP values or visual field loss, limiting the precision with which glaucoma incidence and severity can be assessed. Although the authors attempted to match for ophthalmology access, surveillance bias remains a concern: patients receiving more frequent care are more likely to be diagnosed. Additionally, while the authors used sophisticated matching techniques, the potential for

residual confounding factors - particularly related to unmeasured socioeconomic status, prescribing biases, and access to GLP-1 therapies - remains. It is also worth noting that the apparent protective effect emerged early, which may be difficult to reconcile with the slow, insidious course of POAG in many individuals.

Despite these limitations, the study significantly advances our understanding of the systemic factors that may modulate glaucoma risk. While causality cannot be established in this observational setting, these results offer an intriguing suggestion that GLP-1 receptor agonists may confer ocular benefits beyond glucose control. Further prospective, mechanistic, and interventional studies are now warranted to determine whether these agents might one day play a role in glaucoma prevention or therapy.

Medical Treatment

IOP lowering does not affect VF status in the short term, study finds


Comment by Boel Bengtsson, Lund, Sweden and Anders Heijl, Malmo, Sweden

122140 Does the Visual Field Improve After Initiation of Intraocular Pressure Lowering in the United Kingdom Glaucoma Treatment Study?; Reddingius PF, Kelly SR, Ometto G, Garway-Heath DF, Crabb DP,; American Journal of Ophthalmology 2025; 269: 346-354

The idea that visual field status can improve after IOP reduction has often been raised, and several publications have supported this view, as recently summarized in a review paper.[1] It has even been suggested that the lack of such an improvement may indicate that the IOP reduction might be non-optimal.[2] It is, however, important to realize that visual field status can improve over time in untreated eyes, so-called perimetric learning,[3] and studies claiming improvement in visual field status as a result of IOP reduction, therefore, need to be controlled, for instance by including a group that has not been subjected to IOP lowering therapy during the study period.

The United Kingdom Glaucoma Treatment Study (UKGTS) was controlled in this way, and its authors have analyzed data from that study to address the question of whether visual field status really can improve after introducing pressure-lowering therapy. In the UKGTS, untreated patients with newly detected glaucoma were randomized to treatment

with latanoprost or placebo. The authors compared the baseline visual fields of the two groups to follow-up visual fields obtained an average of 3 months later. **Changes in Mean Deviation were almost the same in the two groups. Further, there was no difference in the proportions of patients with MD improvements of 1 dB or more, and there was no association between MD change and IOP reduction**. Stratifying data by IOP, level of VF loss or age also did not reveal any differences, nor did pointwise analyses.

Medical IOP reduction in early glaucoma did not result in an improvement of visual field status

The authors' conclusions are well supported by data in this carefully designed study, and their results convincingly show that medical IOP reduction in early glaucoma did not result in an improvement of visual field status. This is in accordance with previously published results from the Early Manifest Glaucoma Trial.[4]

As the authors point out, strong evidence requires agreement in results from two independent well-designed studies. We agree with the authors' opinion that there is now strong evidence that VF sensitivity, as measured by SAP, does not improve as a result of medical IOP lowering, and this issue can be put to rest.

The UKGTS and EMGT results do not, however, provide evidence that no improvement can be seen after more dramatic, for instance, surgical reductions of IOP in glaucoma patients with very high intraocular pressures.

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Surgical Treatment

MIGS and MIBS take center-stage vs. traditional surgery

Comment by Michele Figus and Chiara Posarelli, Pisa, Italy

119234 Trends in glaucoma surgery in a tertiary hospital in Spain: 2010-2022; Morales-Fernandez L, Garcia-Bardera J, Pérez-García P, Saenz-Frances F, Garcia-Saenz S, Martinez-de-la-Casa JM, Garcia-Feijoo J; European Journal of Ophthalmology 2024; 0: 11206721241295291

The manuscript offers a comprehensive interpretation of the evolving trends in glaucoma surgery over a 13-year period. One of the key strengths of the paper lies in its large dataset, encompassing nearly 13,000 surgical cases, which allows for meaningful trend analysis within a publicly funded healthcare system. **The authors successfully demonstrate the paradigm shift from traditional surgeries—primarily trabeculectomy and GDD—to MIGS and MIBS, which now represent nearly 75% of glaucoma procedures**. This aligns with global surgical practice changes and is reinforced through international comparisons with datasets from China, Germany and UK.

The discussion is well-grounded in the literature, referencing studies that explain the declining use of traditional procedures due to their higher complication profiles and the rise of MIGS/MIBS as safer, less invasive alternatives. The analysis of combined surgeries and the increasing role of MIGS with cataract surgery is particularly relevant, offering practical insight into clinical decision-making.

However, the study presents some limitations. The retrospective design and lack of patient-level outcome data restrict conclusions regarding the clinical effectiveness and safety of each procedure. Importantly, individual patient data were not analyzed, limiting the ability to assess factors such as disease severity, treatment response, or longitudinal intraocular pressure control**. Furthermore, the categorization of MIGS and MIBS as a single group masks differences between individual procedures**, making it impossible to determine which specific techniques are most frequently used or preferred in clinical practice. While the cost-effectiveness discussion is addressed, it would benefit from more robust economic analysis. Moreover, the findings may not be directly generalizable to private healthcare systems or countries without universal coverage.

Overall, the manuscript underscores a significant transition in glaucoma surgical practice, affirming the growing role of MIGS/MIBS. Further long-term prospective studies are advisable to better understand safety, efficacy and economic impact—crucial for guiding future ophthalmic surgical guidelines and policy decisions.

Surgical Treatment

XEN-45 Gel stent implantation is effective and safe

Comment by Sunee Chansangpetch and Shan Lin, San Francisco, CA, USA

119503 Clinical study on the efficacy and safety of glaucoma drainage implants in the treatment of different types of glaucoma; Wu KK, Liang ZQ, Lyu K, Ma Y, Lu Y, Yin SY, Wu HJ; Chinese Journal of Ophthalmology 2024; 60: 430-439

The Xen Gel Stent is a minimally invasive subconjunctival drainage implant for glaucoma, proven effective in primary open-angle glaucoma (POAG) and increasingly used in other glaucoma types such as primary angle-closure glaucoma (PACG) and secondary glaucoma. As a result, the use of the Xen Gel Stent has recently expanded to include various types of glaucoma, such as pseudophakic angle-closure and secondary glaucoma. Surgical techniques have also evolved from ab interno to more widely adopted ab externo approaches. However, few studies have directly compared Xen outcomes across different glaucoma types and surgical approaches.

In this prospective observational study, Kuankuan *et al.* reported 1-year outcomes of the Xen-45 Gel Stent in 48 Chinese eyes. The cohort included patients with three glaucoma diagnoses: POAG, pseudophakic PACG, and secondary glaucoma. **The study showed a significant reduction in intraocular pressure (IOP), from 20.5 to 13.5 mmHg, and a decrease in the number of medications from 3 to 0.** Success rates were 91.3% (qualified success) and 73.9% (complete success), in line with a prior meta-analysis (74.0%-89.2%).[1] The IOP, number of medications, and visual acuity outcomes were equivalent across the three diagnosis types. These findings are consistent with Sng *et al.*, who reported no difference in IOP reduction between POAG and PACG eyes,[2] and with Schargus *et al.*, who found similar outcomes between POAG and secondary glaucoma.[3] Eyes that underwent the ab interno approach had significantly higher IOP at 1 month postoperatively compared to those treated with ab externo approaches.

A notable finding was the relatively high needling rate of 56.3%. Although no significant risk factors—including glaucoma subtype or surgical technique—were identified, needling appeared more frequent in the ab interno group (71%) than in the transconjunctival (48%) and open conjunctiva (60%) ab externo groups. This high rate may be attributable to the inclusion of eyes with previous glaucoma surgery or to ethnic differences, as all participants in this study were Chinese. Supporting this, Tan *et al.* found that Asian ethnicity was associated with a higher risk of not achieving complete success.[4]

In terms of safety, the most common complication reported was shallow anterior chamber (12.5%), followed by transient hypotony (6.3%) and tube obstruction (6.3%). In contrast, a meta-analysis of Xen implants reported rates of shallow anterior chamber and lumen obstruction to be less than 1%.[1] The higher rates observed in this study may be attributed to anatomical differences in the Chinese eyes.

Limitations included a small sample size, particularly in the pseudophakic PACG group, potentially affecting statistical power. Despite this, the study provides valuable data on the efficacy and safety of the Xen-45 Gel Stent in a Chinese population. As surgical outcomes may differ across ethnic groups, this dataset offers important insights into ethnic-specific outcomes. The results also suggest broader applicability of the device beyond POAG, with a comparison of three surgical techniques revealing a slight trend toward higher needling rates with the ab interno approach.

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Surgical Treatment

Sectorial cyclodialysis with bio-scaffold scleral reinforcement to enhance uveoscleral outflow and reduce IOP


Comment by Patrick Wu and Robert Feldman, Houston, TX, USA

121940 Bio-Interventional Cyclodialysis and Allograft Scleral Reinforcement for Uveoscleral Outflow Enhancement in Open-Angle Glaucoma Patients: One-Year Clinical Outcomes; Ianchulev T, Weinreb RN, Calvo EA, Lewis J, Kamthan G, Sheybani A, Rhee DJ, Ahmed IK; Clinical Ophthalmology 2024; 18: 3605-3614

This article reports on a novel surgical intervention called bio-interventional cyclodialysis with allograft scleral reinforcement for treating open-angle glaucoma. The surgical technique aims to enhance the uveoscleral pathway, a less commonly targeted drainage route in glaucoma surgery. This procedure utilizes a bio-scaffold made of acellular donor scleral allograft tissue, which theoretically prevents closure of a surgical cyclodialysis cleft. After 12 months, results showed a significant reduction in intraocular pressure by 6.3 mmHg, and a decrease in the number of IOP-lowering medications required in a mixed standalone and cataract combined population. However, the information provided has significant limitations. **The results are limited to a follow-up one year**. While this does provide some preliminary insight into the procedure's outcomes, it can only be considered a mid-term assessment. A one-year timeframe limits the ability to assess late complications, disease progression, or regression of benefits especially when the procedure has been combined with cataract surgery. A particular concern arises with the attribution of cystoid macular edema (CME). The authors do not provide a clear basis for distinguishing whether CME is attributable to the cataract surgery or the cleft procedure. Without specific differentiation strategies, such claims remain speculative and potentially misleading. Additionally, the study does not present sufficient data to support comparisons with other techniques. Drawing conclusions or implying comparability or superiority relative to other MIGS or surgical approaches is beyond the scope of this case series. Any such comparisons are speculative until comparative studies are performed. **While the presented data can be considered a useful first step, it is not definitive.** Further research, ideally in the form of randomized controlled studies with standardized techniques, is warranted given the reported efficacy and safety but there is not enough data to support widespread use at his time.

In conclusion while the data are interesting and suggest potential for this intervention the conclusions are limited to those in the abstract: "IOP lowering through uveoscleral outflow enhancement can be achieved by means of a bio-interventional cyclodialysis procedure with allograft scleral reinforcement."

Prognostic factors

Oxygen consumption rates in peripheral mononuclears could be a biomarker for progressive glaucoma

Comment by Jost Jonas, Heidelberg, Germany

120564 Peripheral blood mononuclear cell respiratory function is associated with progressive glaucomatous vision loss; Petriti B, Rabiolo A, Chau KY, Williams PA, Montesano G, Lascaratos G, Garway-Heath DF; Nature Medicine 2024; 30: 2362-2370

While several risk factors have been identified for the development and progression of glaucoma, the therapeutic reduction in intraocular pressure (IOP) has remained the only evidence-proven method to reduce risk of development and progression of glaucoma.[1] In a new study, Petriti, Garway-Heath and colleagues reported that a lower oxygen consumption rate in mononuclear cell of the peripheral blood was strongly associated with faster perimetric glaucoma progression in patients under IOP-lowering therapy.[2] **It explained 13% of the variance in the rate of glaucoma progression**. In another group of untreated patients with glaucoma, IOP explained 16% of the variance in perimetric glaucoma progression. Interestingly, the **oxygen consumption rate was lower in patients with glaucoma than in controls, and it was lower in patients with glaucoma and low baseline IOP than those with high baseline IOP**. In a parallel manner, the nicotinamide adenine dinucleotide levels in peripheral blood mononuclear cells were lower in patients with glaucoma than in controls and it was strongly correlated with the oxygen consumption rate.

If the results of this pilot study are confirmed, the oxygen consumption of peripheral mononuclear blood cells and the nicotinamide adenine dinucleotide level may become new biomarkers for progressive glaucoma

If the results of this pilot study are confirmed, the oxygen consumption of peripheral mononuclear blood cells and the nicotinamide adenine dinucleotide level may become new biomarkers for progressive glaucoma. The results of this study may also be of interest for ongoing studies on the use of nicotinamide for the therapy of patients with normal-pressure glaucoma.[3]

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Prognostic factors

Glaucoma could be more severe and faster progressing in longer eyes

Comment by Kyung Rim Sung, Seoul, Korea

120643 Assessing Glaucoma Severity and Progression in Individuals with Asymmetric Axial Length: An Intrapatient Comparative Study; Huh MG, Jeong Y, Shin YI, Kim YK, Jeoung JW, Park KH; Ophthalmology 2025; 132: 39-51

In this compelling intrapatient comparative study, Huh *et al.* explore the association between intereye axial length asymmetry and glaucoma severity and progression.[1] By studying 95 patients with bilateral glaucoma and axial length differences exceeding 1.0 mm, the authors eliminate intersubject variability—a common confounder in glaucomatous research—and focus instead on structural and functional disparities within

individuals. Their findings are both intuitive and striking: **longer eyes consistently demonstrated lower thinner retinal nerve fiber layer (RNFL) and ganglion cell inner plexiform layer, worse baseline visual field indices, and faster progression rates**. Importantly, these differences persisted even after correcting for ocular magnification, reinforcing that the observed anatomical discrepancies are not mere imaging artifacts, but rather reflective of true pathophysiological divergence.[1, 2).]

Equally important is the study's use of a long-term follow-up cohort (mean ~10 years), which lends robustness to their progression analysis. The authors further enhance interpretability by excluding patients with RNFL floor effects—often an underappreciated pitfall in structural glaucoma monitoring—thereby increasing the sensitivity of detecting true progression.[1,3]

The study also identifies potential mechanistic correlates: intereye differences in intraocular pressure fluctuation and b-zone parapapillary atrophy were significantly associated with differences in progression rates, particularly in RNFL and visual field measures.[1,4] This highlights the multifactorial nature of glaucomatous damage and the added susceptibility of highly myopic eyes to lamina cribrosa deformation (LCD), as corroborated by higher rates of LCDs observed in longer eyes.[5]

These results underscore the need for clinicians to incorporate axial length differences in their interpretation of structural and functional glaucoma metrics

While the retrospective design and relatively narrow axial length asymmetry range (>1 mm, with few >2 mm cases) limit generalizability, the intrapatient model stands as a methodological strength. The study convincingly positions axial length asymmetry—not simply as a biometric footnote—but as a clinically relevant modifier of glaucomatous risk.

Taken together, these results underscore the need for clinicians to incorporate axial length differences in their interpretation of structural and functional glaucoma metrics. They also raise the possibility that asymmetric patients may benefit from closer surveillance and earlier therapeutic intervention in the longer eye.

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Artificial Intelligence

Ophthalmolgy-specific "chatbots" may contribute significantly to better glaucoma detection


Comment by Fei Li and Zefeng Yang, Guangzhou, China

119903 Predicting Glaucoma Before Onset Using a Large Language Model Chatbot
Huang X, Raja H, Madadi Y, Delsoz M, Poursoroush A, Kahook MY, Yousefi S
American Journal of Ophthalmology 2024; 266: 289-299

Predicting glaucoma onset is critical for preventing vision loss, and Artificial Intelligence (AI) offers promising solutions for this challenge. Recent advancements in AI, particularly the development of large language models (LLMs) like ChatGPT, represent significant progress in forecasting glaucoma development even before clinical signs manifest. Evaluating the performance of these AI tools, including LLMs, in accurately predicting glaucoma onset based on data like fundus photographs and clinical information is a crucial area of ongoing research.

In this retrospective case-control study by Huang *et al.*, researchers analyzed 1,504 participants (3,008 eyes) from the Ocular Hypertension Treatment Study (OHTS), using longitudinal visual field (VF) and optic disc photo data to define conversion to glaucoma. Tabular clinical parameters, including demographic, clinical, and ocular measurements, were converted into text prompts for input into ChatGPT. Through iterative prompt engineering, **ChatGPT-4.0 achieved an accuracy of 75% (AUC = 0.67, sensitivity = 56%, specificity = 78%) in predicting glaucoma conversion, outperforming ChatGPT-3.5 (accuracy = 61%, AUC = 0.62). Sensitivity improved to 61% in cases where both VF loss and optic nerve damage were present. However, logistic regression matched the accuracy of ChatGPT-4.0 (75%) while achieving a higher AUC (0.73)**.

Future endeavors should focus on developing ophthalmology-specific LLM-based systems to maximize predictive performance, rather than utilizing generic and commercially available models like ChatGPT

The initial exploration of this study reported a moderate sensitivity (56%) of ChatGPT in predicting glaucoma onset, providing valuable insights for future research. Firstly, it suggested that using only 15 clinical text variables from a single timepoint may not provide sufficient information for accurate prediction. Multimodal integration of image data or the combination of longitudinal tracking of IOP, VF, and optic nerve at multiple timepoints may enhance LLMs' ability to recognize relevant features for glaucoma onset because it better reflects real-world clinical decision-making. Moreover, the pre-defined structured variable input format, similar to that of a logistic regression model, meant that the predictive task did not leverage ChatGPT's core capabilities for processing and integrating complex, less structured, or multimodal data. Finally, these experimental results highlight that future endeavors should focus on developing ophthalmology-specific LLM-based systems to maximize predictive performance, rather than utilizing generic and commercially available models like ChatGPT. Bridging these clinical-technological gaps will be essential to transform LLMs from a proof-of-concept tool into a reliable adjunct for ophthalmologists detecting high-risk patients.

Dialogue

120394 Virtual Reality Visual Perceptual Plastic Training Promotes Retinal Structure and Macular Function Recovery in Glaucoma Patients; Zhao M, Lu Y, Wiederhold M, Wiederhold BK, Chu H, Yan L; Cyberpsychology, behavior and social networking 2023; 26: 861-868

Note: The corresponding author was sent the comments for him or co-authors to respond. At this time, he was unable to respond. Their comments would be welcomed in the future.

Comment by Hary Quigley, Baltimore, MD, USA

I provide here a list of the considerable weaknesses of the study:

1. No control group.
2. Inclusion of both eye's data without accounting interocular correlation.
3. Methods state "paired sample t test" used, but data are group mean comparisons.
4. Bonferroni correction not applied to multiple sector comparisons of OCT data.
5. If Bonferroni applied, OCT regional data are not statistically significant.
6. No comparison of areas of abnormal field to degree of change.
7. No comparison of findings between eyes of each patient.
8. No presentation of degree of overall glaucoma damage in fields at baseline.
9. No presentation of statistical abnormality of OCT damage at baseline.
10. Use of mean sensitivity in dB rather than total or pattern deviation values in fields.
11. Apparent use of only one field and OCT at baseline and one at 3 months.
12. Failure to compare field data change in all points in the field.
13. No definition of what "good" eye and "poor" eye meant in field or OCT.
14. The description of the patterns shown to the patient are mixed with foregone conclusions about what the results might be.

15. Thickening of localized retinal areas is assumed to be beneficial to function, ignoring effects of visual effort on retinal and choroidal thickness known to be associated with emmetropization, which are temporary and not associated with better visual function.
16. Cited references by the same authors or using similar methods have insufficient sample sizes and a lack of controlled observations.
17. The authors fail to cite the IOP as an individual variable in analysis, in fact omitting what if any treatment the patients were undergoing and how adherence with therapy was monitored if at all.
18. Does the intense visual task for as much as one hour per day alter IOP?
19. There is no citation of methods reported to improve visual function, such as (among others) nicotinamide/pyruvate administration as means of improving short-term visual function.[1]

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Comment by Chris Johnson, Iowa City, IA , USA

This publication reports that there were statistically significant increases in thickness in the superior temporal macular ganglion cell layer-inner plexiform layer (mGCIPL) and superior mGCIPL thickness, and an increase in mean macular sensitivity (mMS) in a small group of glaucoma patients (27 patients, 54 eyes), The glaucoma patients underwent daily viewing of stereoscopic images for 15 to 20 minutes while wearing glasses with a red filter over one eye and a blue filter over the other eye. The authors attribute these findings to neural cell plasticity that was produced by the 3 months of visual perceptual plastic training. While the primary goal of glaucoma treatment is to prevent or delay progressive changes, there has also been interest in developing methods to improve the visual performance of eyes with glaucomatous damage. The findings of this investigation suggest that certain training procedures may accomplish this goal, although the lack of

important clinical patient information, inferences of causative factors responsible for this improvement based on descriptive findings, the lack of a control group, and the optimistic interpretation of results draws these conclusions into question, as indicated below.

Many of the measurements did not produce a statistically significant difference in the pre and post training period. Those that did show a statistically significant difference were rather small. Thus, while they may be statistically significant, they may not be clinically meaningful.

Although the authors had participants undergo two prior visual fields before enrolling in the study, it has been reported that improvements in visual field sensitivity can occur for up to six years (Gardiner *et al,* Optometry and Visual Science,2008, 85: 1043-1048). This could certainly account for the pre and post sensitivity differences, and it also indicates why a control group would have been useful to include in the present study.

There is very little information (visual field status, refractive errors, mode of treatment, etc) that is provided for the participants in this study, making it difficult to determine the underlying characteristics of the population tested.

It is not clear why the authors chose to use stereoscopic images on a vr headset as the method for enhancing performance, and why the macula was selected as the visual field location to evaluate. Much more is known about peripheral visual field impairment produced by glaucoma than for the macula, and the use of stereoscopic images also seems quite remote from what the authors were evaluating. Why would stereoscopic images be the most preferred means of improving performance in glaucomatous eyes ?

Although the authors provide a possible mechanism for this improvement in performance and in the thickness of certain portions of the mGCIPL, this is mainly based on a speculative inference rather than a direct evidence-based outcome. Although this may be a possible explanation for this finding, much further work will be needed to establish this as the basis for this effect.

Although the investigators attempt to provide an objective, unbiased effort towards exploring a research problem, there is a strong incentive to report positive results rather than negative or neutral ones. In this view, it is important for other researchers to determine if they are able to replicate these findings because they do not have a direct interest in the outcome becoming successful. It will be informative to see if the results reported by these authors can also be found by other investigators who do not have a direct interest in a successful outcome of this research.

Comment by Giovanni Montesano, London, UK

Extraordinary claims require extraordinary evidence

In their research, Zhao *et al.* report on the effects of a virtual-reality (VR) training protocol on 54 patients with glaucoma. The hypothesis was that, through neuroplasticity, their training protocol could induce structural changes in the retina and, *crucially*, improvements in visual function, tested with white-on-white perimetry (24-2 SITA fast). This is an attractive proposition, because it would offer a non-invasive approach to improving visual function in patients with glaucoma. They show a small borderline statistically significant increase in the thickness of the superior macular ganglion cell and inner plexiform layer (mGCIPL) and a similarly small improvement in the average sensitivity of the central 12 locations of the 24-2 test. They conclude that "VR visual training has some positive effects on retinal ganglion cells and the central visual sensitivity of glaucoma patients."

This might well be true. However, several methodological shortcomings make their evidence far from conclusive. Perimetry, or static visual field (VF) testing, is the most important test to assess functional damage and its progression in glaucoma patients and has been successfully used to demonstrate the effect of therapeutic intervention in landmark clinical trials. However, it is also affected by an important learning effect, by which the measured sensitivity can improve over time simply because of improved performance with experience[1,2]. This makes showing true improvement challenging. The authors mention that patients were required to have produced at least two reliable VF tests prior to recruitment. However, this does not prevent the influence of learning, whose effect has been shown to carry on, on average, for up to 7 tests[1,2]. A similar critique could be made for research claiming to show improvement after pressure lowering interventions[3,4]. As for many other challenging scientific questions, the answer comes from the magic of randomization[4,5]: the authors should have randomised an equal number of patients to either receiving their VR training or a sham treatment, comparing the results in the two groups. This procedure would have equated patients' characteristics and, importantly, the learning effect between the two groups, allowing the authors to isolate the true effect of their protocol on functional improvement. There are also technical shortcomings in their choice of the testing approach, such as the use of a SITA Fast algorithm (instead of Standard) and the use of a 24-2 grid to investigate macular sensitivity (instead of a 10-2). These choices reduce the precision of the measurements and the confidence in the results.

The structural assessments suffer from similar issues. Although structural data are not affected by systematic learning, they are influenced by noise, especially when relying only on a single scan per patient at each time-point. Moreover, similarly to their VF testing, the authors did not adapt their methodology to target the specific scientific question. Their hypothetical explanation for possible changes in mGCIPL increase was related to plastic changes in the retina after training. This could have been better investigated by analysing the GCL and IPL thickness separately, since the latter would be more influenced by hypothetical synaptic changes induced by their VR training protocol. Once again, any refinement of their methodology would not overcome the strong limitation of lacking a control group.

There are additional methodological issues in their approach to the analysis and reporting of their results. Despite being registered as a clinical trial, the registered protocol does not report any pre-specified analysis or outcome. This is concerning, because their statistically significant findings resulted from multiple comparisons, with no attempt to correct for the increased false discovery rate derived from multiple testing. In fact, even their smallest p-value would not stand up to a relatively conservative multiple test correction (in Table 4, $p = 0.024$ is < 0.05, but the threshold should be lowered to at least 0.017). An even stronger point of concern is that the original published protocol *does* mention a plan to recruit a control group. The authors not only do not mention it in the final paper, but explicitly state that a control group was not recruited.

The topographical concordance between the increased superior macular sensitivity and the inferior mGCIPL thickness is, however, promising and might warrant additional investigation into the potential of VF training for glaucoma patients. The evidence presented in this paper is, however, insufficient to support the author's *extraordinary* claims.

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Miscellaneous

Can acupuncture be an effective adjunct therapy for glaucoma? This rigorous RCT may provide answers

Comment by Vivek Gupta and Tanuj Dada, New Delhi, India

119684 Acupuncture as Adjuvant Therapy for Glaucoma: Protocol for a Randomized Controlled Trial; Liao YF, Lee YC, Lin HJ, Shao YC; JMIR research protocols 2024; 13: e57888

There are conflicting reports about the utility of acupuncture for glaucoma with evidence both in favour of benefit [1] and lack of it.[2] Studies have also indicated increase in IOP right after acupuncture sessions.[3] The primary objective of this single-center, parallel-arm, randomized controlled trial (ClinicalTrials.gov NCT05753137) is to evaluate acupuncture in patients with mild-moderate POAG. In addition to standard routine ophthalmic care, intervention group (n=25) receives traditional Chinese medicine–style acupuncture at the six bilateral ophthalmic related acupoints, and control group (n=25) on six bilateral non-ophthalmic acupoints, once a week for 6 weeks. Participant, assessor and statisticians will be masked to group allocation. Primary outcome measures are change in IOP between baseline and 12 weeks, and IOP measured pre-acupressure and 15 minutes post-acupressure session. Secondary outcomes include best corrected visual acuity, visual fields, optical coherence tomography (OCT), OCT angiography, Glaucoma Symptom Scale, Glaucoma Quality of Life-15 questionnaire, heart rate, and blood pressure.

We note a few methodological issues in the present protocol. **The inclusion criterion of age ≥20 years will not be appropriate for POAG alone as Juvenile glaucoma cases may be included**. Excluding those using any drugs that affect IOP, conflicts with inclusion criteria (1 or 2 glaucoma drugs). Criteria for success / failure are not defined. Authors are not assessing change in diurnal fluctuations of IOP which may influence the measure of effect. In sample size calculation, statistical power mentioned as 95% CI, is confusing since CIs are linked to type 1 error probability and not to power (1-type 2 error probability). Based on our estimates using G*Power calculator, for an effect-size *d* of 0.4, 5% type-1 error probability, and 80% power, a sample size of 100+100 is needed for independent samples comparison, indicating the study may be underpowered. Authors

also need to specify use of intention to treat or per-protocol analysis. We are hopeful that the trial will address shortcomings in existing studies noted by Law and colleagues in their systematic review.[2]

Results of this trial, if conducted well, would be a valuable addition. Traditional forms of medicine such as yoga and mindfulness have been shown to be beneficial in POAG and OHT. Allostatic load is also emerging as a risk factor for glaucoma.[4]diastolic BP, homocysteine, triglycerides, total cholesterol, high-density lipoprotein, low-density lipoprotein, body mass index, serum cortisol, glycosylated hemoglobin, albumin, creatinine clearance, and C-reactive protein. High-risk thresholds were determined based on biological cutoffs of each biomarker. One point was assigned for each biomarker reading above cutoff and were summated to obtain AL score; score ≥4 was considered high.\nRESULTS: Mean age of glaucoma patients was 60.82±6.26 and 60.14±6.72 years in controls (P =0.602 **It may be worth exploring biophysiological parameters and assess changes in stress and allostatic load among the trial participants to gain insights on the holistic impact of this intervention.**

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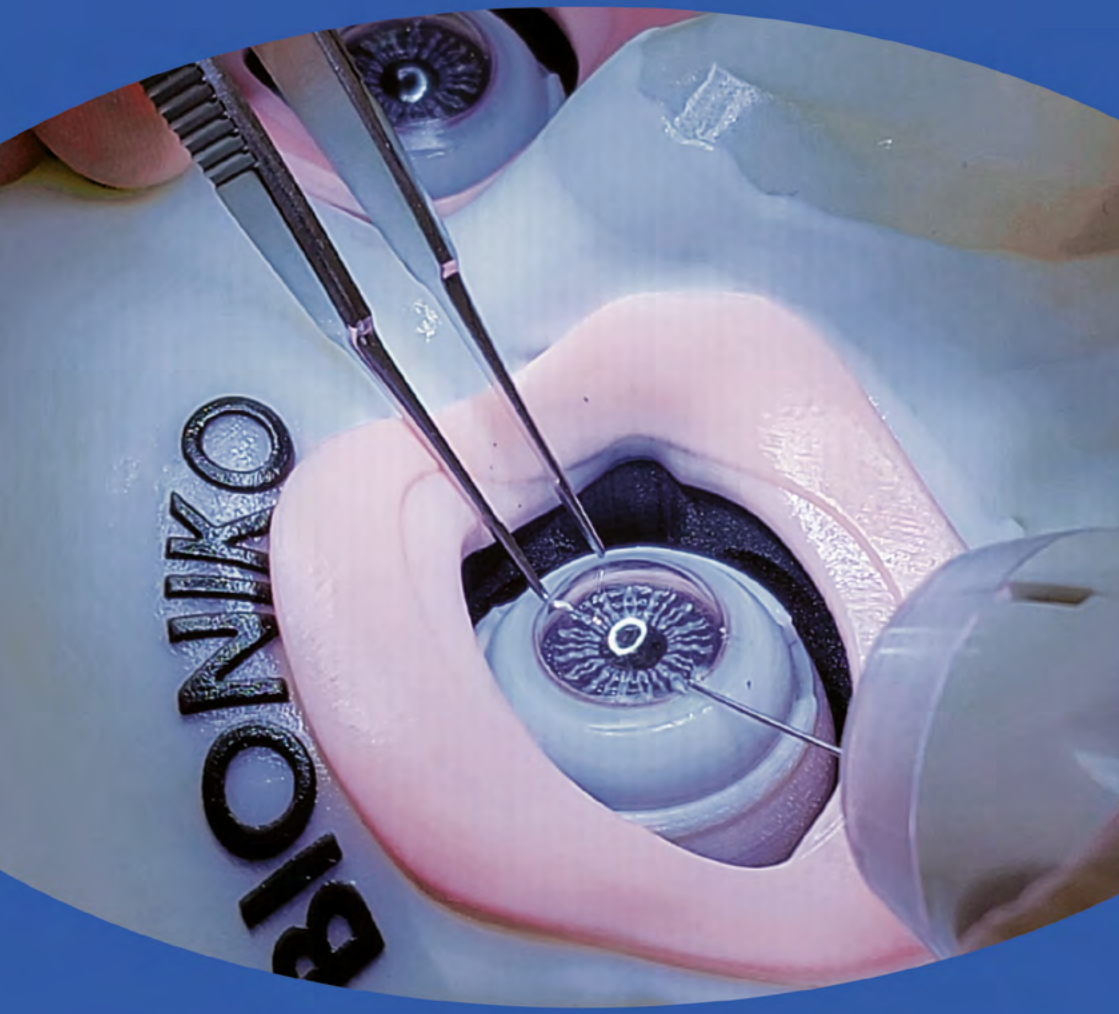

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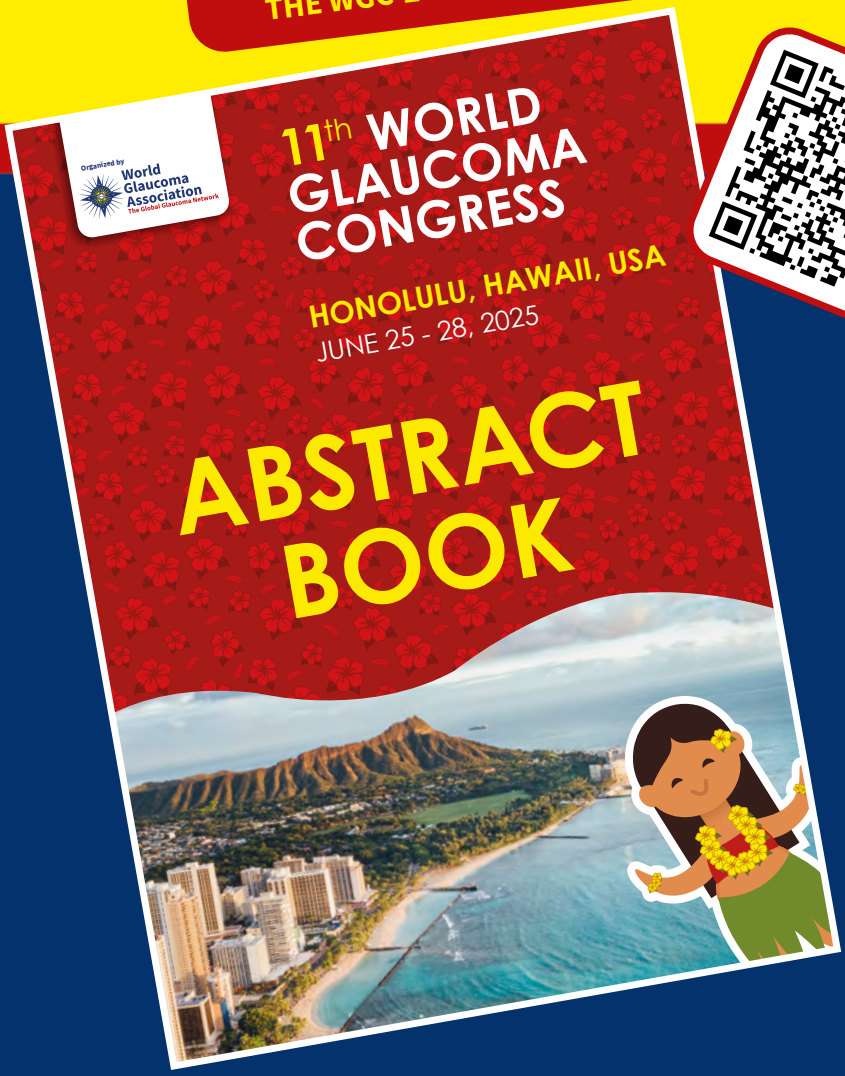

Published by the World Glaucoma Association in collaboration with Kugler Publications, Amsterdam, The Netherlands