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Review

Early diagnostics and interventional glaucoma

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***Abstract*:** The glaucoma treatment paradigm is starting to change from a more reactive approach that relies on topical medications to a more proactive approach that leverages procedural interventions. This evolution toward interventional glaucoma has been enabled by a growing array of lower-risk minimally invasive procedures such as laser trabeculoplasty, minimally invasive glaucoma surgery, and procedural pharmaceuticals. A common feature of these glaucoma interventions—as with all glaucoma interventions—is the need for early, prompt, and accurate diagnosis. The present review summarizes new and upcoming developments in glaucoma diagnostics. These include technologies and techniques for home-based intraocular pressure measurement, novel visual field platforms, photography- and optical coherence tomography-based visualization, and artificial intelligence applications. They also include emerging technologies such as mitochondrial flavoprotein fluorescence imaging, detection of apoptosing retinal cells, collector channel visualization, and genetic testing. These diagnostic modalities have the potential to circumvent the limitations of traditional diagnostic methods. By increasing the frequency and feasibility of obtaining valuable glaucoma data with more rapid detection of disease and progression, these diagnostics may enable an interventional approach to glaucoma treatment for the betterment of patient care.

Plain language summary

Diagnostics in glaucoma

The treatment of glaucoma, the leading cause of irreversible blindness worldwide, relies on timely and accurate diagnosis and monitoring. Diagnosis may involve pressure-based, visual, molecular, genetic, and artificial intelligence modalities. This article reviews the new and upcoming diagnostic technologies in these areas. These technologies have the potential to overcome some of the challenges of traditional diagnostics, thereby enabling more rapid and accurate detection of disease and progression and a more effective interventional approach to glaucoma treatment.

Keywords: diagnosis, glaucoma, intervention/interventional, MIGS, technology

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Introduction

Change is underway within the glaucoma community. Over the course of approximately two decades, the eye care community has witnessed the rise of minimally invasive interventions to treat glaucoma, in conjunction with a more proactive stance toward care. The pre-existing treatment paradigm may be considered reactive, with a heavy reliance on topical medications while reserving procedural interventions to later stages of glaucoma. This approach was understandable when invasive higher-risk surgeries were the only

option, compounded by an era of incredible pharmacotherapeutic innovation. However, newer interventions, such as selective laser trabeculoplasty (SLT), minimally invasive glaucoma surgery (MIGS), and procedural pharmaceuticals, have afforded the option of intervening earlier in the disease trajectory rather than relying on topical medications and waiting for visual decline to warrant an intervention.[1,2] This paradigm shift has been coined by many as *interventional glaucoma*,[1–3] and it might positively impact patients, providers, healthcare systems, caregivers, and potentially the disease trajectory itself.

The traditional reliance on topical medications has numerous caveats that limit its sustainability as a long-term strategy for glaucoma management. Topical glaucoma medications are associated with local and systemic side effects, high rates of nonadherence, costs, increased risk of future surgical failure, intraocular pressure (IOP) fluctuations, and diminished quality of life.[2] In addition, ocular surface disease is particularly problematic and prevalent, affecting 30%–70% of glaucoma patients on topical medical therapy.[4–9] Chronic exposure to the common preservative benzalkonium chloride is cytotoxic to ocular surface cells including conjunctival, goblet, and corneal epithelial cells (Baudouin, Goldstein). Ocular surface disease in turn is associated with higher rates of nonadherence, which increases risk of glaucoma progression over time.[10–12] This can create a negative pattern in which ocular surface disease leads to nonadherence, which causes increased IOP, which leads to more medications, more side effects, further nonadherence, and resultant visual field loss.

Rather than relying on reactive use of topical medications, the interventional glaucoma paradigm proactively leverages three main types of procedural interventions: SLT, MIGS, and procedural pharmaceuticals. SLT has overtaken topical medications in many settings for the initial treatment of glaucoma, as supported by the robust findings of the Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial.[13,14] MIGS procedures such as trabecular micro-bypass or angle-based procedures can be efficacious lower-risk alternatives to more invasive filtering surgery, and they may be particularly appropriate in patients whose disease does not yet warrant the risks of such filtering surgery. Procedural pharmaceuticals for glaucoma include the bimatoprost intracameral implant or the travoprost intracameral implant, which achieve reductions in IOP and topical medications for varying lengths of follow-up.

As with any medical issue, one must be aware of a problem before intervention can be considered. Even the most effective and safe procedure is rendered useless if providers and patients do not fully understand the disease they are treating and the trajectory it is taking. Thus early, prompt, and accurate diagnosis is critical. Optimal diagnostics enable us to not only sustainably screen for patients who are at high risk of developing glaucoma, but ideally also to proactively determine which patients are at greatest risk of developing sight or quality of life threatening compromise. Furthermore, optimal diagnostics will help us determine the best method of providing sight-saving therapeutics, a challenge that is particularly daunting given the breadth and depth of interventional options available today. The truth is, there are still too many individuals with glaucoma advancing to visually impaired status,[15] many of whom never even know they have a preventable disease. Glaucoma is known to be more challenging to control as disease severity increases, and the cost of care also increases with disease stage.[16] Indeed, governments and payers are interested in screening, as timely detection has positive implications in terms of disease progression and cost avoidance in the general population[17] and in targeted high-risk populations.[18]

The importance of glaucoma screening was underscored in a recent article which explores the potential role of targeted glaucoma screening within the primary care setting.[19] Since primary care offices are the only point of contact with healthcare for the majority of the population, equipping them with diagnostic capability is a logical and much-needed intervention.[19] Such diagnostic capability could be as simple as a question-based risk assessment that is asked of patients during their visit,[20] or it could incorporate specialized equipment such as ophthalmic photography. In the Philadelphia Telemedicine Glaucoma Detection and Follow-Up Study, for example, a mobile screening program was conducted at primary care offices and Federally Qualified Health Centers.[21] Telemedicine evaluations included optic disc and anterior segment photography, in addition to IOP measurements and medical and ocular history. The program successfully detected a high rate of previously undiagnosed ocular hypertension, concerning optic nerves, and

Table 1. Novel diagnostic modalities.

Portable IOP measurement	Home-based rebound tonometer
	Contact lens-based IOP sensor
	Intraocular telemetric IOP sensor
Visual field examination	Virtual reality perimeter
	Tablet-based perimeter
Photography and visualization innovations	Portable and hand-held optic nerve photography
	Portable and hand-held fundus photography
	Home-based OCT machine
	UBM
	AS-OCT
New diagnostics on the horizon	Mitochondrial FPF imaging
	DARC technology
	OCT-based imaging of collector channels
	Genetic testing
Artificial intelligence	MLM

AS-OCT, anterior segment OCT; DARC, detection of apoptosing retinal cells; FPF, flavoprotein fluorescence; IOP, intraocular pressure; MLM, machine learning methods; OCT, optical coherence tomography; UBM, ultrasound biomicroscopy.

retinal pathology. It is conceivable that programs such as this could be used to screen for other anterior segment and retinal diseases in addition to glaucoma.[22] Indeed, there has been considerable work in telemedicine-based screening for diabetic retinopathy at primary care offices, which potentially could serve as a model for glaucoma screening and could be particularly useful for detecting patients who are at high risk of missing regular screening visits.[23–26]

Early diagnostic modalities have been present elsewhere in the medical system for years, including many devices that are designed for home use, such as home blood pressure monitors, COVID tests, pregnancy tests, glucose monitors, pulse oximeters, and cardiac Holter monitors. Furthermore, some medical monitoring devices can be implanted within the human body and actually can be programmed to provide targeted intervention in certain circumstances (e.g., insulin pump, cardiac defibrillator). Despite such advances in other areas of medicine, many of the diagnostic modalities for glaucoma have remained relatively unchanged for decades. In the present article, we will outline some of the latest advancements in glaucoma diagnostics (Table 1), along with how they may be able to enable an interventional glaucoma treatment approach for the betterment of patient care and the prevention of blindness.

Home-based IOP measurement

Measurement of IOP is a cornerstone of glaucoma diagnosis and management, with treatment decisions often dependent upon IOP values. Indeed, the single most powerful modifiable risk factor in glaucoma is IOP. The current standard of care for measuring IOP is Goldmann applanation tonometry (GAT), which is typically completed at periodic clinic visits. However, IOP is known to vary from day to day and at various times of day, meaning that periodic office tonometry may not detect a meaningful portion of the IOP fluctuations a patient experiences. A cross-sectional study of self-tonometry with the iCare HOME tonometer, for example, revealed significantly greater IOP fluctuation in home tonometry

than clinic tonometry ($p < 0.001$).[27] Maximum daily IOP occurred outside of clinic hours on 50% of days, a finding which has been documented before.[28] Thus, even if a clinic visit had been scheduled, it still may not have detected a spike. IOP fluctuations, in turn, are associated with increased risk of glaucomatous visual field loss,[29,30] and in fact may be an independent risk factor beyond the absolute IOP itself.

Given that in-office IOP measurement is an incomplete representation of a patient's IOP-mediated glaucoma risk, out-of-office testing could be highly valuable. The ability to correctly detect errant IOP variability or spikes and to implement subsequent treatment can mean the difference between preserving or losing visual function.[31,32] This may be especially important for patients who progress despite low or normal clinic IOP.[33]

Most home-based IOP tests are either based on rebound tonometry or are wearable ocular or intraocular implants. Portable rebound tonometers (such as the aforementioned iCare Home Tonometer) consist of a magnetized probe being launched against the eye that detects impact and motion when the probe collides with the eye and decelerates upon bouncing back. Rebound tonometers have been used in a variety of home-based serial-IOP studies, and have shown high reproducibility and concordance with GAT.[34–37] They are particularly helpful in children, elderly patients, and patients with cognitive or physical disabilities who cannot tolerate GAT; they are portable; and they require minimal cooperation and no topical anesthesia.[38]

Although rebound tonometry provides single-point IOP data, emerging contact lens-based IOP sensors can provide continuous IOP measurement. For example, the Sensimed Triggerfish (currently the only FDA-approved device in this space) is a soft contact lens with a microsensor that measures corneal curvature changes, which can be used to calculate relative IOP changes. Research on the device has reported relatively high patient safety and tolerability.[39] Key limitations include its cost, inaccuracies due to changes in environmental factors such as air temperature, inability to be used in patients intolerant to contact lenses, and the fact that another device is still necessary to establish baseline IOP (since the Triggerfish measures only *relative* IOP changes).[38].

Meanwhile, intraocular IOP sensors are also being developed that perform around-the-clock IOP measurement. The first prospective clinical study (ARGOS) of an intraocular telemetric IOP sensor was for the EyeMate device, in a single-center clinical trial in Germany.[40] This study was followed by the ARGOS-02 trial for the second-generation EYEMATE-IO device.[41] Both studies showed comparability between EyeMate readings and in-office GAT readings, with favorable tolerability in the short and long term.[40–42]

Advancement in visual field examinations

Although IOP magnitude and variability help in determining the likelihood of future progression, visual field examinations are critical to staging glaucoma, as well as detecting disease progression and rate of progression. A minimum of 5–6 visual fields are estimated to be necessary to achieve optimal sensitivity and specificity,[43] and 6 visual fields are required to detect rapid progression during the first 2 years after a patient's diagnosis.[44] Current glaucoma guidelines include performing at least one visual field test per year,[45] and many individuals may require even more frequent testing.[46] However, this is far from realized, with over 75% of glaucoma patients receiving less than one visual field test per year in a U.S. nationwide cohort of over 380,000 individuals with glaucoma.[45]

There are significant barriers to obtaining the optimal number of visual fields. Due to patient comfort, stress, or even wakefulness, visual fields can be highly unreliable; they are also cumbersome and ultimately an undesirable part of the glaucoma patient's existence. Furthermore, conventional visual field testing is exceedingly resource intensive, requiring trained technicians, expensive machinery, and an optimized setting to achieve the best possible representation of the patient's disease state.

There are several new technologies that facilitate easier visual field tests in both clinic- and home-based settings. Most of these new perimetry modalities are either virtual reality headsets or tablet-based perimeters. By making perimetry more easily incorporable into clinic flow, more ergonomically comfortable for patients, and more feasible in the home environment, these new perimeters potentially could allow for earlier, more reliable, and more frequent visual field testing.[46–48]

Two prominent virtual reality perimeters which have been tested against the Humphrey Field Analyzer (HFA) are the RadiusXR VR perimeter (RadiusXR, Pleasanton, CA)[49] and the Olleyes VisALL-K pediatric perimeter (Olleyes, Summit, NJ).[50] The RadiusXR VR platform consists of a lightweight purpose-built VR headset that presents stimulus on the same standardized 10 cd/m^2 background luminance as the HFA; this is a key component of achieving parity with HFA, and is a key distinguisher of RadiusXR from other virtual reality headsets. Indeed, the Novel Virtual Reality Field Assessment (NOVA) Trial was the first study to show parity of a VR-based perimetry algorithm (the RadiusXR Adaptive Test Algorithm (RATA)) against the Swedish Interactive Thresholding Algorithm (SITA) of the HFA. Results showed statistical non-inferiority of estimated sensitivities at individual test locations, as well as non-inferiority of glaucoma staging.[49] A second novel VR perimetry platform is the Olleyes VisuALL-K platform, which is a videogame-based static threshold perimeter using a virtual reality headset. The platform was shown to have similar mean sensitivities of diminution from maximum light intensity, and similar mean interparticipant variability, as the HFA; it also had higher patient satisfaction than the HFA.[50]

Using a wearable VR headset allows patients to complete visual field testing in any location in the clinic, and with limited need for clinical assistance, thereby freeing up valuable clinic space and staff time.[49,50] VR perimeters also may be more ergonomically comfortable for patients for whom arthritis, kyphosis, scoliosis, body habitus, and/or being in a wheelchair make visual fields an uncomfortable experience. Additionally, most VR headsets host a library of educational videos for patients to view while in the clinic waiting room, thereby making use of the extra waiting time patients experience.

Alongside virtual reality perimeters, tablet-based perimeters offer another option for at-home and in-office VF testing. A proof-of-concept study by Jones et al. of the Eyecatcher tablet-based perimeter showed that 98% of patients were able to perform monthly home monitoring, with good concordance between at-home and in-office visual fields ($r = 0.94$, $p < 0.001$).[48] The study found that adding home perimetry to two standard in-office perimetry tests completed 6 months apart reduced between-test variability in 97% of eyes. The authors asserted that "the status quo of hospital-only VF monitoring is costly and insufficient," and that home monitoring may deliver earlier and more reliable detection of disease progression.[48] However, one important caveat is that the ability to standardize background illumination can be challenging, which is critical since different background luminance can cause stimulation of a different set of retinal photoreceptors than those stimulated in the photopic range. Among portable and home-based perimeters, only Radius XR has demonstrated such parity with HFA, as previously discussed.

Photography and visualization innovations

Portable and hand-held optic nerve and fundus photography can be another adjunct to in-clinic glaucoma assessment. Visualization of the posterior segment can be a cost-effective screening method for glaucoma as well as other eye diseases; it is already utilized by a number of teleophthalmology programs, such as for diabetic retinopathy screening.[26] Several portable and hand-held technologies now exist that can provide high-quality images in various settings, making them useful for widespread and/or community-based screening.[51–53] Most of these devices are nonmydriatic, which broadens the potential reach of these technologies, adding to their value in screening applications. Although such technologies are indeed promising, one must remember that their images are likely subject to the same limitations as in-office photography: notably, that photographic interpretation is highly subjective, which can lead to low reproducibility and low interrater repeatability.[54–56]

In contrast, the utilization of optical coherence tomography (OCT) in the diagnosis and management of glaucoma has quickly become invaluable. Due to its high reproducibility and accuracy, OCT can provide direct objective quantification of glaucomatous damage as part of glaucoma screening.[57,58] Given the fact that mild glaucoma often does not manifest in visual field changes, OCT may be particularly useful in identifying disease trajectory earlier than functional tests like visual fields. Typically OCT is performed at a dedicated machine in an ophthalmology clinic. However, the widespread use of OCT is often constrained by its cost and the need for skilled operators. As with VF perimetry, in-office testing is often not convenient or possible. Additionally, different OCT machines often use different proprietary algorithms, preventing direct comparison

between results obtained on different instruments. One way to make OCT more feasible is a home-based OCT device, which could enable daily or weekly fundus scans in the home setting. Home testing with one continual device also could reduce or eliminate the variability of different OCT machines. A prospective longitudinal study by Liu et al. showed that daily self-imaging was feasible in patients with neovascular age-related macular degeneration (nAMD), with on average 5.7 scans completed per week using the Notal Vision Home OCT (NVHO) system.[59] Importantly, home imaging demonstrated good agreement with human grading for retinal fluid identification, and excellent agreement with in-clinic OCT scans.[59] Although optic nerve OCT for glaucoma may not need to be repeated as frequently as for nAMD, it is conceivable that in the future such technology could be incorporated for patients who otherwise may not be able to attend clinic visits as frequently as needed, or in those with advanced glaucomatous damage who need more vigilant monitoring.

Visualization of the anterior segment is also clearly important in characterizing glaucoma. Despite being recommended as part of any glaucoma evaluation, slit-lamp gonioscopy examination has been shown to be performed in only half of U.S. Medicare beneficiaries during the 4–5 years preceding glaucoma surgery, including in only 58% of patients with narrow angles or angle-closure glaucoma.[60] Gonioscopy also may be unattainable in telemedicine settings or large-scale screening programs. Two potential technologies have been proposed to circumvent this barrier and supply anterior segment imaging without gonioscopy: ultrasound biomicroscopy (UBM) and anterior segment OCT (AS-OCT). UBM has the potential to distinguish between various types of primary angle-closure glaucoma and primary open-angle glaucoma; it is known as the best tool to assess the structures posterior to the iris, even in eyes with opaque corneas.[61] UBM also can be performed in dark conditions, which may allow angle closure to be detected more readily than in light conditions.[62] Indeed, a study by Kong et al. showed that iridotrabecular meshwork contact was detected more frequently by UBM than by regular static gonioscopy in primary angle-closure glaucoma suspects in China[62]; however, this did not always correlate with actual clinical risk of developing angle-closure damage. Thus, this modality could be a valuable supplement to, but not replacement of, ophthalmologists' static gonioscopy.[63]

AS-OCT also has been proposed as a rapid non-contact method to assess the anterior segment in glaucoma. A study by Nolan, for example, found that noncontact AS-OCT was highly sensitive in detecting angle closure when compared with gonioscopy.[64] AS-OCT was able to detect angle closure in a substantial portion of cases that had been undetected via gonioscopy. Similar to UBM, AS-OCT found more eyes to have closed angles than did static gonioscopy, but a patient's entire clinical picture was still needed to contextualize the findings. In eyes at highest risk of angle closure, identification of the scleral spur (which is critical in determining the location of the trabecular meshwork) is particularly fraught—as such, clinical gonioscopy remains the gold standard in angle assessment, augmented by imaging modalities as mentioned above. Thus, both UBM and AS-OCT are useful components—not whole replacements—of a comprehensive glaucoma evaluation. They also may be informative for telemedicine settings or screening programs where an initial UBM or AS-OCT could identify at-risk patients who could then be referred for ophthalmologist evaluation.

New diagnostics on the horizon

In addition to more widely used diagnostic tools, a number of newer diagnostic modalities have been developed and are garnering interest within the ophthalmic community. One example is mitochondrial flavoprotein fluorescence (FPF) imaging, which has been used to noninvasively detect mitochondrial dysfunction in both retinal diseases and glaucoma. Under oxidative stress, mitochondrial flavoproteins emit green autofluorescence which can be captured using a specially designed camera that detects peak FPF wavelengths (Ocumet Beacon Fundus Camera; OcuSciences, Inc., MI).[65] Studies have demonstrated higher FPF measurements at the optic disc rim in glaucoma patients compared to controls,[66] increased macular FPF in eyes with ocular hypertension compared to controls,[67] and significant improvement in FPF scores at the optic disc rim after application of negative pressure using the Balance Goggles System (BGS; Equinox Ophthalmic Inc., Sioux Falls, SD).[68]

A second area of interest is detection of apoptosing retinal cell technology, which is designed to detect retinal ganglion cell apoptosis in vivo. The technology relies on the properties of Annexin V, which is a phospholipid-binding protein with a high

affinity for phosphatidylserine on the outer leaflet of cell membranes, making it a sensitive probe for identifying apoptosing cells.[69] The Annexin V is labeled with a fluorescent marker and the resultant fluorescent white spots, representing apoptotic cells, are detected with a specially designed confocal scanning laser ophthalmoscope.[70]

Another novel diagnostic tool is OCT-based imaging of collector channels. Swept-source and spectral-domain OCT have been used to visualize and identify collector channels' entrance, the inner wall of the trabecular meshwork, and the aqueous plexus.[71] This technology also can be used to assess collector channel patency, including evaluation of episcleral venous outflow, episcleral venous fluid wave, and tracer studies with fluorescein and indocyanine green.[72] Such visualization of the distal outflow system can help determine the anatomic location of resistance in glaucoma, as well as potentially enable optimal placement of devices such as stents in angle-based MIGS surgery.

A fourth new diagnostic modality is genetic testing, which has largely been used in early-onset forms of glaucoma (e.g., primary congenital glaucoma, juvenile open-angle glaucoma), where a disease phenotype can be predicted by a single gene mutation. Such testing can motivate closer follow-up and earlier treatment for carriers of the mutation, as well as proactive screening of family members.[73] For adult forms of glaucoma, the disease has a polygenic and complex inheritance pattern, so single-gene mutations are not sufficient to produce a disease phenotype. In these cases, polygenic risk scores have been developed to estimate the cumulative effect of multiple single nucleotide polymorphisms in different genes on risk.[74–76] For both childhood and adult-onset forms of glaucoma, gene-based testing can use the Genetic Eye Disease Panel for Optic Nerve Disease and Early Manifest Glaucoma (GEDi-O) from the Ocular Genomics Institute at Massachusetts Eye and Ear Infirmary. This panel tests for mutations in 22 genes (such as FOXC1, CYP1B1, MYOC) which are known to be associated with various forms of glaucoma and thus can be a useful adjunct to clinical examination.[77]

Artificial intelligence: progress and challenges

Given the large amount of data produced by newer and easier diagnostic modalities, it becomes even more critical to be able to readily interpret it. For screening programs to be effective, real-time assessment of clinical parameters such as optic disc photographs and OCT is needed, so that treatment decisions and appropriate referrals can be made. To this end, the potential use of artificial intelligence (AI) bears mention. Preliminary studies have shown that, by incorporating both qualitative and quantitative endpoints (and their respective strengths and weaknesses), AI algorithms may be able to attain a high level of sensitivity and specificity.[78] This may be particularly useful in glaucoma diagnosis which requires reconciling inherently distinct measures such as optic nerve photography (subjective) and optic disc OCT values (objective).

Among AI-based screening algorithms, machine learning methods (MLMs) may be particularly well-suited to handling imbalanced datasets, such as those seen with relatively uncommon diseases like glaucoma. Given the appropriate reference standards, the clinical accuracy of AI-based screening algorithms may match or in some cases surpass that of expert clinical graders. This was observed in a study of MLMs to detect glaucomatous fundus images based on optic nerve head topographic features.[79] High accuracy was also seen in a study by Oh et al. of an MLM program that incorporated visual field tests, retinal nerve fiber layer values, fundus images, and general examination results.[80] However, these favorable findings must be balanced against studies that show lower sensitivity and/or specificity using AI programs, such as a population-based study by Maupin et al. using certain optic disc characteristics alone.[81] Many AI algorithms are well-suited for selected datasets, but show poorer results when used more widely. The "black box" effect is also a concern: there is a lack of transparency and interpretability of AI algorithms, where no specific algorithm or information can be pinpointed to have led to a given conclusion.[82] Indeed, AI programs—although promising—are still in their infancy. Further refinement is needed before their widespread adoption may be able to facilitate earlier diagnosis and monitoring of glaucoma.

Conclusion

Given the importance of detecting glaucoma earlier in the disease process, and the potential new modalities for doing so, it is noteworthy and sobering that traditional glaucoma diagnostic techniques have remained relatively unchanged

for decades. As highlighted in this article, traditional glaucoma diagnostics have well-known limitations. For example, single-point GAT IOP measurements at periodic clinic visits do not capture patients' diurnal and nocturnal IOP fluctuations. HFA visual field examinations are cumbersome, ergonomically challenging, and require valuable practice space and staffing. Slit-lamp gonioscopy is effective in characterizing anterior segment pathology, but is performed far less frequently than is recommended. Optic nerve OCT and mydriatic office-based optic nerve examinations are not well-suited for widespread glaucoma screening.

The diagnostic technologies covered in this paper can circumvent or lessen many of these limitations of traditional diagnostics. However, they also may have downsides of their own that should be taken into consideration. For example, changes to clinic workflow may be necessary when new testing is added. Certain equipment may not be portable enough or time-efficient enough to easily implement into clinical care. Or there may be lack of standardization or limited reproducibility across different technology platforms. In addition, newer diagnostic tools can have substantial costs, posing a barrier to widespread incorporation into clinics.

The issue of cost may be particularly challenging in developing countries where healthcare resources are limited. In these settings, diagnostic tools that are both cost-efficient and scalable are critical. Regarding cost, some newer diagnostic modalities may be less expensive than traditional machines, such as with virtual reality perimeters versus HFA, or with portable rebound tonometers versus tabletop tonometers. Regarding scalability, fundus photography, optic nerve photography, and portable rebound tonometers can be used in cost-effective screening programs and telemedicine settings, thereby reducing the need for trained onsite staff. AI algorithms also may assist with glaucoma diagnosis, providing support for staff members who may not have as much formal medical training.

In order to realize the full value of new diagnostic technologies, it may be informative to consider populations that have higher likelihood of having glaucoma. For example, the risk of developing glaucoma is higher in patients of African, Asian, or Hispanic heritage; those with family history of glaucoma; those of higher age; those with systemic comorbidities such as diabetes, hypertension, and migraines; and those with ocular comorbidities such as severe myopia or hyperopia, eye injury, or thin corneas. Diagnostic technologies could be used earlier and more proactively in these patients, such as with screening programs that target specific races or age groups. Portable IOP testing or fundus photography could also be employed in primary care settings for family members of glaucoma patients, with subsequent referral to an ophthalmologist if results are concerning.

Newer diagnostics also may be particularly useful for populations that pose difficulties with diagnosis via traditional methods. For example, patients with normal-tension glaucoma (NTG) often remain undetected with traditional single-point IOP testing, given that their IOP is in the normal range. Such patients may benefit from using a home-based home tonometer or contact-lens IOP sensor, which could detect diurnal fluctuations in IOP that could cause visual field damage. Virtual reality headset perimeters also may enable more frequent VF testing, which could further assist with detecting any VF changes in NTG patients.

Glaucoma diagnostic techniques and technologies must and will evolve, as witnessed by the myriad of options now available or on the horizon. The emergence of new diagnostic modalities has the potential to circumvent the limitations of traditional diagnostic methods, proving these new technologies indispensable moving forward. They may streamline clinic efficiency, which is increasingly imperative given the impending demographic challenges[83–86] and the need for reliable and efficient means of identifying patients who need treatment. It also may improve patient experience, reduce costs, and increase the frequency and feasibility of obtaining valuable glaucoma data for disease detection, ultimately preventing blindness. Such clinical information is central to adopting a targeted approach to patient care and treatment, with the goal of maintaining and improving the vision and quality of life of patients with glaucoma.

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Consent for publication

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Author contributions

Ticiana De Francesco: Conceptualization; Data curation; Investigation; Methodology; Writing – original draft; Writing – review & editing.

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