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Portable hardware & software technologies for addressing ophthalmic health disparities: A systematic review

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Abstract

Vision impairment continues to be a major global problem, as the WHO estimates 2.2 billion people struggling with vision loss or blindness. One billion of these cases, however, can be prevented by expanding diagnostic capabilities. Direct global healthcare costs associated with these conditions totaled $255 billion in 2010, with a rapid upward projection to $294 billion in 2020. Accordingly, WHO proposed 2030 targets to enhance integration and patient-centered vision care by expanding refractive error and cataract worldwide coverage. Due to the limitations in cost and portability of adapted vision screening models, there is a clear need for new, more accessible vision testing tools in vision care. This comparative, systematic review highlights the need for new ophthalmic equipment and approaches while looking at existing and emerging technologies that could expand the capacity for disease identification and access to diagnostic tools. Specifically, the review focuses on portable hardware- and software-centered strategies that can be deployed in remote locations for detection of ophthalmic conditions and refractive error. Advancements in portable hardware, automated software screening tools, and big data-centric analytics, including machine learning, may provide an avenue for improving ophthalmic healthcare.

Keywords

Portable, vision, machine learning, blindness, digital health, prevention, chronic disease, vision screening, eye exams, global health, eyecare access

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Introduction

Three key factors contributing to global disparities in access to vision care are per capita income, healthcare coverage, and geographic location.[1] Current estimates suggest that 89% of those currently affected by visual impairment live in low- and middle-income countries, making affordable care a widespread global health issue.[2] In West Africa, a study of uveitis cases linked to the Ebola outbreak showed that, due to inadequate access to comprehensive care and timely treatment, 40% of affected individuals developed severe complications of this treatable eye condition resulting in blindness.[3, 4] The outcomes were attributed to the inability to access vision screening in time.

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Vision care disparities related to lower screening rates within the United States have led to Hispanic women receiving disproportionately lower cataract care than their white counterparts.[5] Furthermore, African American individuals have a lower rate of dilated fundus examinations despite a higher risk for diabetic retinopathy. They are twice as likely to develop preventable blindness from diabetic retinopathy than their white counterparts, with the gap increasing.[6]

Another important aspect of vision care is continuous monitoring of progressive ophthalmic conditions, such as glaucoma and macular degeneration, to identify gradual changes and hasten interventions.[1, 7, 8]

Many endeavors have been made to achieve universal eye care by expanding equipped vision facilities, hiring more trained personnel, and purchasing more vision screening tools to increase patient throughput.[9] Chou *et al*. argue that system-wide differences and disparate coverage across states should force policymakers and physicians to look for new interventions and provide relief to areas with the most need.[10] The overall capital cost to battle the need for more refractive error centers, including education and training, in the region of Americas is approximately $4.1 million, where $374,595 is a one-time cost of establishing and equipping new facilities with bulk-purchasing of refractive, ocular health screening, ocular dispensing, and business tools.[11, 12]

Integrating portable, low-profile technologies, such as those depicted in Figure 1, presents a promising solution for overcoming vision inequities, thereby improving vision care in marginalized communities.[13] Several healthcare facilities, including generalist locations, have initiated the adoption of these technologies with early success in the identification and treatment of diabetic retinopathy and pediatric vision deficits.

In this review, "portable" refers to technologies that are entirely handheld, whereas "semi-portable" refers to technologies that are partially handheld and tethered to mobile components such as a wheeled stand or table.

Portable hardware ophthalmic solutions

Aberrometers

The demand for portable and quantitative refractive error measurement in mobile healthcare settings has propelled the field towards smaller and more automated devices.

Netra (EyeNetra Inc., Cambridge, MA) is a smartphone-based subjective refraction system with variable lenses and a binocular-style headset.[12] The refractometer relies upon Scheiner principles, which is the concept that refractive error can be determined using double pinhole apertures with a Shack-Hartmann wavefront sensor.[14] Through its binocular fixation system, *Netra* measures both eyes simultaneously and can calculate interpupillary distance. With the help of verbal instructions from the device, the patient is tasked with aligning red and green lines oriented at different angles, eliminating the need for literacy. *Netra* measures sphere from -12 to $+5.5$ diopters in 0.25 diopter increments, cylinder from -7 to 0 diopters in 0.25 diopter increments, and axis to 1°.[14]

In a cross-sectional study of 87 subjects (152 eyes) that compares *Netra* with subjective refraction, Jeganathan *et al*. found a mean relative difference in spherical equivalent of -0.27 diopters.[14, 15]

The *SVOne* (Smart Vision Labs, New York, NY) is a portable Shack-Hartmann wavefront aberrometer that attaches to a smart phone to measure ocular aberrations and refractive error of each eye independently.[16] By taking the required images and averaging five measurement readings over a five-second period, the device uses Zernike decomposition to convert the wave aberration data into conventional sphere, cylinder, and axis measurements, measuring refractive errors within a range of ± 10 diopters and ± 5 diopters of sphere and cylinder, respectively.

In a prospective study on 50 subjects, Ciuffreda *et al*. investigated the *SVOne*'s use as an objective autorefractor in a comparison with retinoscopy, subjective refraction, and two commercially available autorefractors, *Topcon KR-1W* wavefront analyzer (Topcon Corp, Tokyo, Japan) and *Righton Retinomax-3* handheld autorefractor (Righton Opthalmic Instruments, Tokyo, Japan).[16] The *SVOne* measurements were not significantly different across all instruments.[16] Rubio *et al*. found in a study of 54 patients an average mean difference between *SVOne* and subjective refraction of -0.43 diopters, which was not statistically significant.[17] In a pediatric analysis of 40 subjects between 5 and 17 years old, Rosenfield *et al*. showed no significant difference between the spherical equivalent refractive error measured by the *SVOne* and autorefractive techniques.[18]

In an analysis of astronauts comparing *Netra* and *SVOne*, Masterova *et al*. found that *SVOne* had a tendency toward better intrasession repeatability, likely because the *SVOne* device has no subjective aspect of measurement.[19] Furthermore, *SVOne* captured measurements significantly faster than *Netra*, completing autorefraction in approximately 6 min compared to 12 min for *Netra*.[19] One drawback for the *SVOne* was that it consistently provided more negative refractive errors compared to the clinical autorefractor, while the *Netra* produced measurements better aligned with the clinical autorefractor.[19] *SVOne* was also compared to *Retinomax-3, WAM-5500* (Grand Seiko Co. Ltd, Hiroshima, Japan) and *Topcon KR-1W* autorefractors in pediatric and adult populations, with one cycloplegic subgroup, alongside subjective refraction, showing no difference in refractive assessment.[16, 18] Overall, subjects reported that the *SVOne* was preferred to *Netra* because of its easy-handling, audio feedback, and user confidence in their ability to make correct measurements.[19]

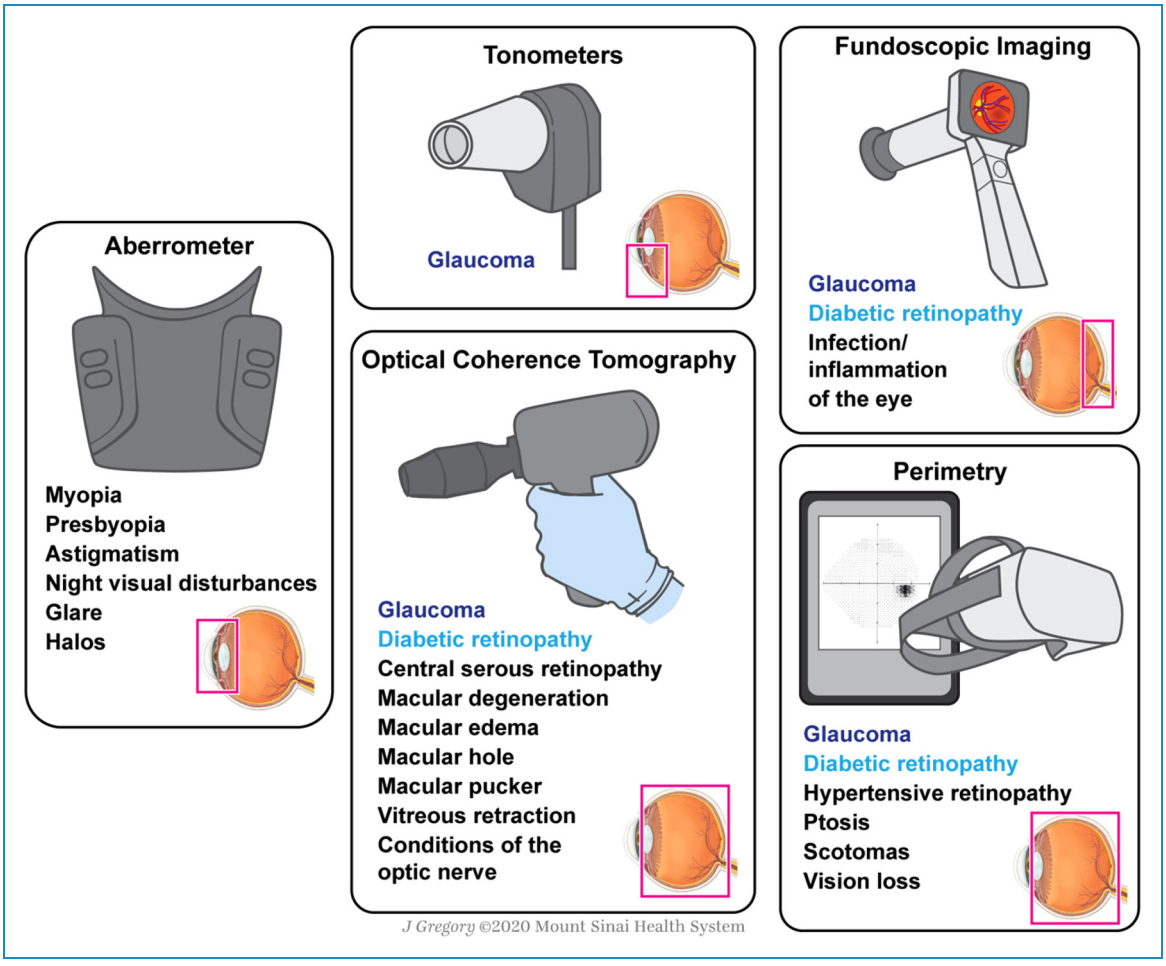

Figure 1. A schematic of a portable diagnostic vision care landscape with examples described in each respective section.

The *QuickSee/e-see* or *QuickSee* (PlenOptika, Cambridge, MA) is a novel handheld wavefront autorefractor that is independent of a laptop or smart device, implementing an open-view wavefront aberrometer that eliminates the use of relay lenses.[17] With a larger measurement range, the device uses optimized image processing to produce real-time refractive error measurements and includes a pupillary distance adjustment mechanism, controlled with a thumb wheel on the side of the device. The current model uses a 785 nm laser that delivers less than 40 μW of power to the eye, allowing for measurement of spherical and cylindrical refraction error of ±10 diopters and ±6 diopters, respectively.[17] Wavefront images are processed at eight frames per second using a customized algorithm that tracks patient-device alignment and accommodation. The device then synthesizes these dynamic measurements through a proprietary statistical algorithm and presents the final refractive measurement to the user.[17] Though the device has a binocular design, it records monocular measurements. Measurement in the opposite eye requires the device to be inverted. The device has been recently released in India and surrounding countries at one-third of the cost of commercial desktop autorefractors.[17] The console's compact design and portability make it an enticing tool for clinicians in need of a mobile, easy-to-use diagnostic tool for refractive error.

In a comparison of the *QuickSee* and desktop autorefraction followed by subjective refraction, the spherical equivalent and the cylindrical components of the power vectors measured with the *QuickSee* agreed within 0.25 diopters of the subjective refraction.[17] Visual acuity achieved by *QuickSee* was not significantly different; compared to *Netra* and *SVOne*, the *QuickSee* produced significantly smaller deviations from subjective refraction, undercorrecting by 0.09 diopters.[18]

Fundoscopic imaging

Damage to the retina and optic nerve is the basis of many leading causes of vision loss, including diabetic retinopathy, macular degeneration, and glaucoma.[20] This section focuses on portable fundoscopy cameras that are stand-alone and adaptable to smartphones (Table 1).

The *SmartScope* (OptoMed, City, Finland) is a handheld digital fundoscope with a non-mydriatic camera. Mydriatic and non-mydriatic versions of this technology demonstrated non-inferiority when compared against a mydriatic *TRC-50DX* (Topcon, Tokyo, Japan) table-top.[21] *Smartscope* is overall highly gradable; however, the presence of vitreous hemorrhages or advanced cataracts significantly decreases gradeability, necessitating ophthalmic experience to determine the quality of images.[22]

The *3nethra neo* (Forus Health, Bengaluru, India) is a mydriatic, wide-field digital fundoscope that is semi-portable by being tethered to a central module connected to a laptop. The study showed that *3nethra neo* was well tolerated for ROP screening, with comparable view to the *RetCam3* tabletop on initial cases (Natus Medical, Pleasanton, CA).[23]

Pictor (Volk Optical Inc., Mentor, OH) is an FDA-approved portable, non-mydriatic camera that permits posterior pole imaging with a 40° field view as well as non-contact anterior segment imaging using a cobalt blue LED to detect dry eye syndrome and corneal trauma. A prospective study in which non-ophthalmologists used this technology to screen infants resulted in successful identification of type 1 ROP.[24]

The *NM-200D* (Nidek, Hiroishi, Japan) is another example of a semi-portable handheld, non-mydriatic fundus camera. This device successfully generated normative data for cup-to-disc, a common metric for detection and monitoring of glaucoma, and arteriole-to-venule ratios in a pediatric population used in monitoring microvascular disease.[25]

The *Retinal Plenoptoscope* (Queensland UoT, Queensland, AU) is a non-mydriatic fundus camera that utilizes novel image rendering against corneal backscatter to achieve high-depth resolution. This strategy allowed for a higher degree of stereopsis (3D retinal renderings by imaging via two slightly modified pupilar light paths) and improved, glare-free image quality that has been a challenge with other portable fundoscopic devices.[26] Stereopsis is regarded as an advantage of slit lamp fundoscopy and is relied on for assessment in glaucoma and macular edema as a gold standard.

Several successful models of smartphone add-ons have recently been introduced to digital fundoscopy. Russo *et al*. demonstrated that non-mydriatic smartphone fundoscopy using the *D-Eye* add-on (D-EYE S.r.l., Padova, Italy) was not significantly different from dilated slit-lamp fundoscopy in detecting macular edema, although limitations with smartphone imaging emerge in patients with small pupil size and cataracts.[27]

According to Ryan *et al*., pairing smartphone with a diopter condensing lens without additional hardware has low sensitivity in detecting diabetic retinopathy in mydriatic eyes when compared to the *FF450 Plus* (Carl Zeiss Meditec, Dublin, CA).[28] However, comparing mydriatic slit-lamp microscopy to mydriatic smartphone imaging with a *D-Eye* add-on produced 85% accuracy.[27] *D-Eye* is able to intentionally reduce the magnitude of reflection from retinal structures that occurs during image acquisition, enabling improved non-mydriatic imaging. Some of its shortcomings include a single-image retinal view of 20°, requiring iterative imaging to achieve 90°.[29]

RetinaScope (University of Michigan, MI) adapted a handheld ophthalmoscope apparatus to a smartphone, capturing 50° of retina within a single image. Individual images are automatically stitched on the smartphone to generate a 100° field of view. Patel *et al*. recently demonstrated a 96% agreement rate in the identification of pediatric retinal disorders such as retinoblastoma and optic nerve hypoplasia when interpreting images captured with the *RetinaScope* versus the *RetCam3* (Clarity Medical Systems, Pleasanton, CA) and the *Optos 200Tx* (Optos, Marlborough, MA).[30, 31]

Finally, *RETeval* (LKC Technologies, Gaithersburg, MD) is a portable, non-mydriatic version of an electroretinography (ERG) that allows for evaluation of achromatopsia, cone receptor dysfunctions, retinitis pigmentosa, choroidal dystrophy, autoimmune retinopathy, and juvenile macular degeneration.[32, 33] The device also showed promising results in detecting vision-threatening diabetic retinopathy.[34] While earlier generation ERG devices were semi-invasive and required the use of special contact electrodes on the surface of the eye, *RETeval* uses skin-contact electrodes placed on the lower orbit.

Perimetry

In examining visual function, the most common method of quantitative, functional assessment are visual fields (VFs), which allow for static and dynamic targets to determine pattern and degree of vision loss. The current in-office gold standard is the *Humphrey Visual Field Analyzer (HVFA)* (Carl Zeiss Meditec, Dublin, CA), a table-mounted technology that uses proprietary algorithms to provide a detailed map of VF perimetry, as well as reliability metrics such as fixation deviation. HVFA is entirely reliant on a technician to run the test, making it susceptible to subjective technician bias and patients may find the machine overall uncomfortable.[35] Recently, several tablet- and virtual reality (VR)-based adaptations of perimetry examinations have emerged, introducing the possibility of vision screening in non-vision specialist locations including rural clinics or the home. These technologies are essential for longitudinal monitoring of diseases like diabetic retinopathy, glaucoma, and macular degeneration, particularly in regions where vision care is limited.

Several studies have demonstrated a high degree of comparability between tablet-based perimetry (TBP) and the *HVFA*. Prea *et al*. and Kong *et al*. found that the *Melbourne Rapid Fields (MRF)* (M&S Technologies,

Table 1. Comparison of clinically meaningful characteristics between discussed portable fundus cameras.

Name of device	Field of view	Non-mydriatic	Smartphone attachment	Glare reduction	Condition tested	Clinical use paper without comparison to gold standard	Comparison to tabletop fundus photography	Comparison to slit lamp or indirect ophtalmoloscopy	Clinical outcome for comparison to gold standard
Retinal Plenoptoscope (Queensland UoT, Queensland, AU)	32°				Healthy controls	*	*	*	*
SmartScope (OptoMed, Oulu, Finland)	45°				Diabetic retinopathy	*	×	*	Vision threatening diabetic retinopathy (VTDR)
3nethra Neo (Forus Health, Bengaluru, India)	120°				Retinopathy of prematurity	*	× - case study	*	Safety for infant
Pictor™ (Volk Optical Inc., Mentor, OH)	45°				Retinopathy of prematurity	x	*	*	*
NM-200D (Nidek, Hiroishi, Japan)	30°				Glaucoma, diabetic retinopathy	×	*	*	*
RetinaVue 100 (Welch Allyn, Skaneateles Falls, New York)	45°				*	*	*	*	*
D-Eye Smartphone Attachment (D-Eye)	20°				Cup-to-disk ratio, diabetic retinopathy	*	×	×	Vertical cup-to-disk ratio, diabetic retinopathy clinical diagnosis, VTDR
RetinaScope (CellScope, Berkely, CA)	50°				Pediatric opthalmological conditions, diabetic retinopathy staging	*	*	×	Diabetic retinopathy staging, referral-warranted diabetic retinopathy×

**RWDR = moderate NPDR or greater severity OR presence of macular edema.

Niles, IL) app on an *iPad* (Apple, Cupertino, CA) was equal in speed to the *HVFA* 24-2 SITA-fast algorithm and significantly faster than the 24-2 SITA-standard algorithm without sacrificing accuracy or longitudinal repeatability in a glaucomatous patient population.[36, 37] MRF showed higher fixation loss compared to the *HVFA* 24-2 SITA-standard.[38]

Similarly, Jones *et al*. demonstrated that *Eyecatcher* (UCL Institute of Ophthalmology, London, England), another TBP, was reliable in terms of mean deviation scores and concordance between identified locations of VF loss when compared to the *HVFA* 24-2 SITA-standard.[39] Anderson *et al*. discovered that home glaucoma monitoring with *MRF* TBP can allow for the identification of rapid field loss with an 80% sensitivity, 18 months faster on average than 6-month clinic testing, even when accounting for moderate at-home compliance.[40]

In a study of the *Visual Fields Easy* (George Kong SOFTWARE, Melbourne, Australia) iPad app in rural Nepal, early VF loss was not consistently detected due to a high false positive rate, although most cases of moderate and advanced VF deficits were concordant with 24-2 SITA standard HVFA findings.[41]

TBP continues to evolve in speed, accuracy, and interactivity. The *PERformance Centered Portable Test* (*PERCEPT*) (University of California, San Diego, CA) is an interactive TBP that dynamically increases visual task difficulties in order to identify central and peripheral VF losses. Rosen *et al*. demonstrated that this app was able to detect glaucoma and accurately predict one's previous history of motor vehicle crashes or falls based on traumatic impact that resulted in characteristic visual deficits.[42]

Recently emerging VR advancements allow for unique vision screening opportunities. VR offers eye-tracking, allowing to measure degrees from fixation due to the potential for insertion of convex lenses or the manipulation of test software to create "virtual spheres." Erichev *et al*. used the latter approach for the *P-VRD* (Total Vision, Russia), allowing for a screening range of 30° from fixation, with similar outputs to that of a *HVFA* 30-2.[43] VR perimetry also allows for unique methods of unbiasing examinations, such as a randomized presentation of stimuli to either eye without occlusion and thus inability of the patient to know which eye is being tested. Matsumoto *et al*. found high comparability between the *imo* head-mounted perimeter's binocular random single eye test (CREWT Medical Systems, Tokyo, Japan) and *HVFA* 30-2 SITA standard in the detection of glaucomatous VF losses.[44]

VR can also be used for alternative forms of perimetry, such as Frequency Doubling Technology (FDT) perimetry that is based on creating a flickering counterphase sinusoidal grate at low spatial and high temporal frequencies, which results in a double-grate appearance due to nonlinear perception of a magnocellular retinal layer, thereby assessing retinal health.[45, 46] Alawa *et al*. used a smartphone-based head-mounted display (BoboVR, Shenzhen, China) with *Mobile Virtual Perimetry* FDT on patients with new-onset or chronic primary open angle glaucoma and found no significant difference in VF loss reliability, false positive, and false negative scores compared to the *Humphrey Zeiss FDT* (Carl Zeiss Meditec, Dublin, CA).[47]

As portable perimetry is mobilized in generalist locations or patient homes, one potential drawback is the need for additional efforts to ensure that the obtained data is appropriately communicated with vision specialists to plan for comprehensive evaluation once abnormalities are identified. These in-person sessions enable physicians to obtain a complete clinical picture by performing thorough retinal and optic nerve head exams, intraocular pressure (IOP) tests, and retinal nerve fiber layer (RNFL) assessments.[48]

Optical coherence tomography

Optical Coherence Tomography (OCT) uses low-coherence near-infrared light scatter to visualize a cross-section of the retina, allowing for analysis of the retina's thickness and fine anatomical structures. The technology has, until recently, been limited to expensive tabletop devices with costs of up to $150,000.[49] However, the important role of OCT in making definitive diagnoses has driven adaptation toward more portable and cost-effective devices that cost as low as $7200.[49]

Song *et al*. published a study utilizing an early iteration of the semi-portable *QQ Labscope* (Lumedica, Durham, NC) OCT that demonstrated a contrast-to-noise ratio comparable to the tabletop *Spectralis OCT* (Heidelberg Engineering, Heidelberg, Germany).[48, 50]

iVue + iStand (Optovue, Fremont, CA), a semi-portable spectral-domain OCT (SD-OCT) was able to identify fine retinal signatures, such as foveal contour, that are predictive of successful ROP management with bevacizumab (an anti-VEGF therapy). Interestingly, Rothman *et al*. used the *Envisu* semi-portable SD-OCT system (Bioptigen, Research Triangle Park, NC) to successfully identify macular edema within infant eyes as a predictive measure for future visual or central nervous system deficits.[51]

Another study in ROP patients showed that handheld OCTA can capture retinal structures that can screen for disease severity. This included peripapillary and foveal microvasculature, epiretinal membrane (ERM), hyperreflective punctate vitreous opacities, and tractional vitreous bands.[52]

Maloca *et al*. demonstrated an intersection between sparse OCT and telemedicine with the *MIMO_02* prototype (MIMO AG, Bern, Switzerland).[53] In this study, the authors demonstrated a potential for increased test speed and portability if one sacrificed high resolution. Despite this loss in functionality, *MIMO_02* had central retinal thickness measurements comparable to the *Spectralis OCT*, a key parameter for monitoring AMD progression. The device may therefore allow for at-home monitoring of retinal disorders.

Recently, a standard SD-OCT device has improved in portability and accommodation of different examination positions with the introduction of the *Spectralis Flex* (Heidelberg Engineering, Heidelberg, Germany), although the device is still likely limited to in-office use due to its integration with a wheel-based stand. However, even with these adjustments, the *Spectralis Flex* was able to detect retinoblastoma through identification of hyperreflective vitreous opacities in a recent case study.[54]

Tonometry

Tonometry involves either physical or non-contact perturbation of the eye in order to measure IOP and is critical for evaluating patients at risk of glaucoma.[55]

Goldmann applanation tonometry (GAT) is considered the gold standard for IOP measurements,[55, 56] although it has several limitations that include requiring the use of fluorescein dye, topical anesthetics, and a slit-lamp arrangement, thus requiring a trained provider to operate it and to calibrate monthly.[57] However, there are numerous commercially available portable tonometers. These products range from contact devices, requiring topical anesthesia for direct corneal contact, as well as non-contact tonometers (NCTs) that measure IOP over the eyelid, with air puffs or other methods.[58] It is important to note that portable tonometers uniformly overestimate IOP measurements compared to GAT.

The *Schiotz tonometer* (Medical Technologies, New Dehli, India) was the most widely used portable tonometer due to its lower cost and not requiring batteries, until GAT took over in the last quarter of the 20th century.[59, 60]

The *iCare* contact tonometer (Tiolat Oy, Helsinki, Finland) is a portable rebound device that correlates metallic probe deceleration against the eye with IOP.[56, 61] Conversely, the *Pulsair* (Keeler, Malvern, PA) is a semi-portable NCT that determines IOP based on air applanation of the cornea, which may be more ideal for use with non-vision specialist locations and does not rely on topical anesthetics.[56] Prabhakar *et al.* demonstrated that the *Pulsair* showed better agreement with the *Perkins Applanation Tonometer* (*PAT*) and excellent comparability with GAT.[56, 62]

Accordingly, the *PT100* and *Tono-Pen AVIA* (Reichert, Depew, NY) are fully portable tonometers with a reported high ease of handling that is particularly suitable for facilities that lack trained individuals.[57, 62, 63] Hubanova *et al.* demonstrated a weaker agreement of *PT100* with GAT readings in hypertensive patients compared to the *Pulsair Intellipuff*.[62]

Software-based technologies

As portable ophthalmic technologies become more widely utilized, particularly in settings without specialists who can interpret test results, and as the adoption of teleophthalmology practices has been slow to gain momentum, machine learning (ML) shows promising potential to provide fast and reliable clinical information in the near future (Figure 2).

Deep learning (DL) models, a subset of ML involving the computation of multi-layer neural networks, use OCT data for algorithm training in the detection of glaucoma and/or prediction of its progression. The high accuracy of DL approaches in predicting glaucomatous eyes makes it a promising avenue for robust, scalable, and cost-saving diagnosis of glaucoma and other ocular abnormalities.

OCT- & Fundus image-dependent machine learning applications for unstructured data

Most ML applications in ophthalmology use high-dimensional data, such as imaging, to predict ocular health and function. In particular, DL methods applied to data from OCT and fundus imaging have been shown to be high performing.

Thompson *et al.* employed an algorithm that leveraged SD-OCT data to predict glaucomatous neuroretinal damage through the measurement of the minimum rim width relative to Bruch's membrane opening (BMO-MRW) on fundus images. This parameter has been shown to correlate well with glaucomatous VF loss.[64] The BMO-MRW model predictions from all optic disc photographs in their test set were highly correlated with the observed values from SD-OCT (Pearson's $r = 0.88$; $R^2 = 77\%$).[64]

Alternatively, studies quantified glaucomatous structural damage on optic disc photographs using RNFL thickness by initially training with SD-OCT data.[65, 66] Ultimately, the RNFL model was able to infer RNFL values from optic disc images that correlated strongly with SD-OCT-retrieved RNFL values (Pearson $r = 0.832$; $R^2 = 69.3\%$).[65] Similarly, Asaoka *et al.* strongly correlated RNFL and ganglion cell complex layer thickness with early-stage glaucoma, showing sensitivity and specificity of 82.5% and 93.9%, respectively.[67]

In comparing various ML classifiers and algorithm types, Silva *et al.* found that a random forest model produced the most accurate prediction of glaucomatous eyes based on SD-OCT and standard automated perimetry data.[68]

Furthermore, the area under the receiver operating curve (aROC) curve, an indication how accurate a model's classification is, for differentiating glaucomatous eyes from healthy ones was greater than or equal to 0.94 in all models previously described.[64–68]

Some examples of successful DL models include the detection of ERM, detection of pathologic lesions including intraretinal fluid, subretinal fluid, pigment epithelial detachment, and subretinal hyperreflective material, estimation of

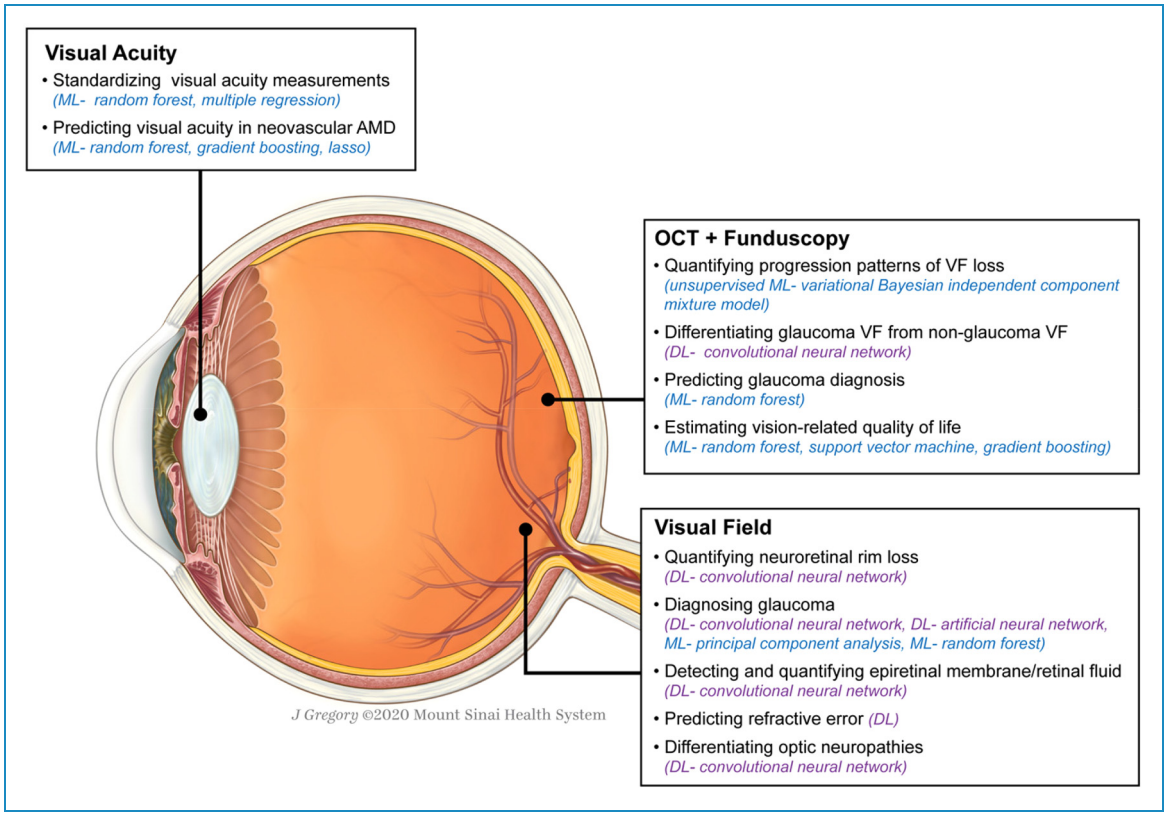

Figure 2. Machine learning (ML) integrations across different aspects of a comprehensive vision screening exam.

refractive error, estimation of visual acuity, and drusen quantification from OCT imaging.[69–75] Additionally, DL had enabled the extraction of accurate estimations of refractive error and visual acuity.[70, 74]

A DL algorithm trained on fundus photographs in a retrospective cohort of ROP patients demonstrated variability between and within clinician grading in assigning ROP severity scores.[75] This points toward the need of looking at other objective clinical features for identifying plus disease that could play a role in influencing treatment decisions.

ML has also been used to accurately differentiate between optic neuropathies and pseudopapiledema by using fundus photography.[76]

Deep learning-based techniques using structured data: EHR, visual field, and other sources

In addition to imaging, a number of ML applications in ophthalmology also leverage the growing amount of structured data from electronic health records (EHR) and VFs. In these applications, ML models use structured data to predict progression of disease and to classify diagnoses.[77] For example, Wen *et al*. used unfiltered real-world data sets to develop a DL model that generated predictions for future Humphrey VFs by up to 5.5 years.[78]

Some examples of successful models include neural networks that differentiate between glaucomatous from non-glaucomatous VFs, unsupervised ML detection of VF deterioration in glaucoma, and a random forest ML model of glaucoma diagnosis using RNFL and VF.[79–83]

DL models that do not use VF in differentiating glaucoma status have also been explored. Oh *et al*. designed an artificial neural network with nine non-categorized factors including IOP, vertical cup-to-disk ratio, sex, and age, that was able to predict open angle glaucoma with relatively high accuracy (84%), sensitivity (78.3%), and specificity (85.9%).[84] Scanning laser polarimetry-variable cornea compensation measurements have also been used to improve the differentiation between glaucomatous and normal eyes using an artificial neural network with high accuracy (aROC = 0.95).[85] Kalman filtering, a type of ML technique, forecasted accurate mean deviation values of IOP for patients with normal tension glaucoma.[86]

Bach *et al*. used an ML approach to achieve comparable or better accuracy for visual acuity.[87] In another study, Rohm *et al*. implemented ML algorithms to successfully predict visual acuity at 3 and 12 months in patients treated for neovascular age-related macular degeneration.[88] Finally, Gramatikov *et al*. created an artificial neural network to classify retinal birefringence scanning data in the pediatric diagnosis of amblyopia with comparable results to classical statistical methods.[89]

Non-machine learning-based computational techniques: statistical models, glaucoma progression analysis

Using a variety of statistical analyses, combined VF and OCT methods were found to have a more accurate and faster identification glaucoma progression than VF-only ones.[90] Serial analysis of combined wide-field OCT maps for detection of structural progression in early glaucoma showed strong agreement between glaucoma specialists (wide-field OCT thickness map: $\kappa = 0.649$; wide-field OCT deviation map: $\kappa = 0.833$).[91] However, a comparison of *Glaucoma Progression Analysis* (GPA, Carl Zeiss Meditec, Dublin, CA), a proprietary software analysis tool, showed only a fair level of agreement upon initial review ($\kappa = 0.52$) and re-evaluation ($\kappa = 0.62$).[92]

In order to address the subjectivity of characterizing ocular pathology, Castro *et al*. developed a freeware program, Halo v1.0 software that measures and calculates a visual-disturbance index, a parameter used to quantify the discrimination capacity of peripheral stimuli in the presence of visual disturbances like age-related macular degeneration or keratitis.[93] The Halo v1.0 software used the Strehl ratio, a measure of overall optical quality, to show that the pathologies previously mentioned had greater ocular scattering compared to healthy eyes.[93]

Non-machine learning, non-computational based techniques: smartphone applications, mobile games, computer programs, web applications

The visual nature of many ophthalmic exams makes them optimal for the use of smartphones, computer tablets, and web applications.

The *Nintendo 3DS PDI Check* (Nintendo, Kyoto, Japan) is a novel near vision screening game capable of assessing visual acuity, color vision, and stereopsis. Though studies were limited by their sample size, the *PDI Check* was associated with faster testing times compared to conventional testing and had a high specificity.[94, 95]

A visual acuity Snellen chart (gold standard) and Arabic figures that were administered on an *iPad* (Apple, Cupertino, CA) showed no significant difference from the logMAR visual acuity.[96] Additionally, the *Mobile Assessment of Vision by intERactIve Computer (MAVERIC)* system, which uses a computer tablet and software that collects touch responses from patients to measure low or high contrast visual acuity, exhibited similar high reliability and agreement.[97] However, mobile applications like *SightBook* produced discrepant visual acuities compared to clinic chart acuities.[98]

Mobile applications for vision screening have also incorporated an assessment of color vision. Portable games with chromatic contrast sensitivity, tablet versions of Ishihara plates for dyschromatopsia screening, and a web-based color vision test for color vision defects in optic neuritis have all demonstrated high levels of repeatability and comparability with established tests.[99, 100]

Discussion

As the global demand for ophthalmic care continues to grow, with current estimates suggesting 5% compound annual growth rate over the next 5 years, portable technologies have become increasingly important in addressing the needs of patients in resource-limited and resource-rich communities[101]. The increased demand for early detection and treatment is one of the key drivers of the market, indicating a clear need for more equitable, accessible, sustainable, comprehensive, and portable vision screening.[1] Early detection can be longitudinally more cost-effective according to a study that used a Markov simulation model on 1000 patients who received tonometry screening irrespective of glaucoma risk factors.[102]

Portable solutions can allow for increased sustainability and scale of impact given lower capital investment and feasibility of adaptation. One example of large-scale implementation is GoCheckKids (GoCHeck, USA), which is a smartphone photo screening platform for amblyopia detection that has been adopted by 6500 pediatricians as of May 2020.[102] Such tools allow for increased triage at the level of primary care and early referral identification. Furthermore, the adoption of the SPOT Vision Screener (Welch Allyn, USA) in 19 pediatric facilities resulted in increased screening implementation, from 65.3% to 86.5% of patients just 12 weeks after implementation.[13]

In addition to improving overall screening, these technologies have potential benefits for school vision screenings, nursing homes, and homeless shelters, where convenience and user-friendliness are highly important. Changes in healthcare policy and insurance models that are increasingly recognizing telehealth and mobile medicine models will certainly prompt further development of these technologies. These models are particularly important in the times of a COVID-19 pandemic with increased efforts for remote access and telemedicine for long-range delivery of medical care.

Some barriers to the adoption of portable technology are low levels of eye disease awareness in patients since early, disease-related changes are functionally subtle in most cases. Further barriers to the adoption of novel technologies into existing workflows include deeply ingrained technician or physician habits and strict billing systems. This is especially relevant for vision specialist offices, where a lot of expensive machinery has already been purchased and engrained into clinical practice.

This review has examined the literature that evaluates portable aberrometers, fundoscopy, and OCT and discussed the principles behind their design as well as clinical

validation, highlighting specific benefits and drawbacks that were identified.

In addition to technologies that are used for structural assessment of the eye, VFs are heavily relied upon for a functional component of the exam. This included adaptations of TBP and VR, both of which show promising results with a difference in fixation-measurements due to VR's biconcave structural advantage. Additionally, FDT has been considered as a promising tool for testing vision perimetry on a VR platform.

In light of the available portable hardware and software solutions, ML has been considered as the next step in unifying delivery of remote and more frequent eye care. Through the use of both structured and unstructured data that can be collected with portable advancements, the algorithm models can provide disease state predictions and propose recommendations that are non-inferior to those of trained specialists.

Although recent developments are making it possible to monitor vision remotely, there is a need for more cost-benefit analyses to show how access to portable technologies improves outcomes.[95] Recent studies demonstrate that automatic retinal image analysis is a cost-effective solution in primary care settings given a 23.3% reduction in costs after 5 years.[103] One study in South Africa calculated a cost-saving effect of $1206 per blindness case averted due to primary care integration of mobile fundus cameras. In finding ways to implement portable screening tools, it is also essential to identify a platform that can unify the structural screening aspects such as fundoscopy, tonometry, and OCT with functional components of a comprehensive exam like VFs, contrast sensitivity, and visual acuity.[104] This platform can be used to store and collect data to then actively build predictive models by using the established potential of ML, resulting in refer, non-refer recommendations, and ensuring longitudinal patient care. Such improvement in patient outcomes combined with the reductions in cost further encourage efforts toward a value-based and quality-driven eyecare system.

Conclusion

This systematic review analyzed the portable technologies landscape for ocular vision screening that compares most recently clinically tested software, hardware, and machine/deep learning. Given the medical field's fragmented status and steps towards coupling with tele-health and tele-ophthalmology, portable and remote ophthalmic testing is paramount to the continuity of quality care within our communities. This paper highlighted the most recent advancements and achievements in the last 10 years in the aforementioned topics for a comprehensive review. Professionals should continue monitoring and staying engaged with technologies penetrating the healthcare market while staying informed regarding clinical validity and adaptation of these products.

Literature search

Review articles retrieved in the systematic search are referenced along with any relevant primary literature. Filtering assumptions limited literature searches from the last 10 years, with the search entered on 21 January 2020. From this search, 1166 total articles were screened from PubMed.gov, and 90 were manually selected based on the inclusion criteria of English language, relevance to global vision frameworks and our criteria for portable and semi-portable devices. Since then, we incorporated additional articles to cover the breadth of newly emerging evidence until the beginning of 2021. The introduction section was not restricted to the systematic analysis approach as it describes a broader framework, making a total of 108 publications on portable technology that emerged within the past 10 years.

For the Introduction section, the search terms ("Vision Tests"[Mesh] OR (Vision AND ("screening" OR test* OR "care"))) AND ("Health Status Disparities"[Mesh] OR "Healthcare Disparities"[Mesh] OR (((health* OR economic OR sex OR ethnic OR gender OR racial) AND (disparit* OR inequal*)) OR at-risk OR underserved))). Additionally, the filters "Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Review, Systematic Reviews" were applied. Supplemental searches were added to include quantitative measures of global vision impairment (e.g. economic burden of treatment) as well as information about teleophthalmology.

The Tonometry section included search terms "((portable AND ("Vision Tests"[Mesh] OR vision)) AND (hardware OR tonometry OR pressure) AND (ocular hypertension OR optic disc OR retina OR Cataracts OR Macular degeneration OR Retinopathy OR Retinitis OR Glaucoma OR Strabismus OR Color blindness OR Macular edema OR keratoconus OR Retinal detachment OR Uveitis OR Low vision OR Blindness)." Supplemental studies related to pricing of each device as well as gold standard technologies were added. Finally, information about portable tonometry devices was acquired from Google Patents to determine the landscape of available patents worldwide.

In the Hardware section, we searched (portable AND ("Vision Tests"[Mesh] OR vision)) AND (hardware OR OCT OR optical coherence tomography OR fundoscopy OR infrared) AND (optic disc OR retina OR Cataracts OR Macular degeneration OR Retinopathy OR Retinitis OR Glaucoma OR Strabismus OR Color blindness OR Macular edema OR keratoconus OR Retinal detachment OR Uveitis OR Low vision OR Blindness).

For the Software section, the following search terms were used: (((((("Vision Tests"[Mesh])) AND (software

OR machine learning OR artificial intelligence OR deep learning OR neural networks) AND (ocular hypertension OR optic disc OR retina OR Cataracts OR Macular degeneration OR Retinopathy OR Retinitis OR Glaucoma OR Strabismus OR Color blindness OR Macular edema OR keratoconus OR Retinal detachment OR Uveitis OR Low vision OR Blindness))). Publications not retrieved from the systematic approach were used for the purposes of providing technological background in each section.

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Contributorship: Margarita Labkovich outlined the study, helped with organizing literature review research, worked extensively on introduction and portable hardware solutions sections, and brought the rest of the sections together, including discussion and conclusion. Megan Paul was responsible for sorting through the global health literature and helping draft introduction and tonometry sections. Eliott Kim, Shreyas Lakhtakia, and Aly A. Valliani focused on the software section. Eliott Kim also identified literature and organized the section that discussed aberrometers. Dr Zhou and Aashay Patel researched literature for the fundoscopy and perimetry sections. Andrew Warburton contributed by organizing citations, editing the aberrometry section, and providing suggestions for the entire manuscript. Randal A. Serafini assisted with organizing and editing the manuscript. Drs. Sklar, Chelnis, and Elahi reviewed the entire manuscript and provided their contributions and ophthalmologic expertise by citing additional technologies and bringing their physician perspectives.

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