TELEGLAUCOMA: READY TO GO?

N G Strouthidis,1,2 G Chandrasekharan,3 J P Diamond,4 I E Murdoch3

ABSTRACT
Telemedicine technologies and services allow today’s ophthalmic clinicians to remotely diagnose, manage and monitor several ophthalmic conditions from a distance. But is this the case for glaucomas? There has been a proliferation of telemedicine friendly devices in recent years that improves the capabilities of the clinician in managing glaucomas. The existing instruments still need to align themselves with accepted industry standards. There are successful programmes running in several areas of the world. The safety and efficacy of these programmes needs further exploration. The inability of a single device or test to diagnose glaucomas satisfactorily has also hampered progress in remotely diagnosing these conditions. There is, however, significant potential for telemedicine-friendly devices to remotely monitor the progress of glaucoma and, thereby, reduce some of the workload on an overstretched health service.

INTRODUCTION
Telemedicine, or telehealth, refers to the practice of medicine at a spatial and/or temporal distance by exchanging medical information via electronic communications.1 The key aspect in the development of telemedicine is the constantly evolving interaction between medicine and information and communication technology (ICT). Given that ICT can support data collection and exchange, this can enable improved communication and integration of clinical services. Radiology has been at the vanguard of telemedicine; electronic transfer of digital images between radiological departments is now standard practice because the images do not diminish in quality with transfer.

Telemedicine principles have already been successfully applied within ophthalmology in the National Health Service Diabetic Retinopathy Screening Programme and retinopathy of prematurity screening. A ‘store and forward’ approach is used whereby images/data acquired at one site are transferred to a remote grader who views these images at a different time. Alternative approaches include remote monitoring and interactive telemedicine where self-testing allows clinicians to monitor a patient, and real-time interaction may occur between the clinician and the patient.

Glucoma management increasingly involves use of devices that are perceived to be ‘telemedicine-friendly’. Automated perimetry, tomometry, corneal pachymetry, imaging of the optic disc, nerve fibre layer and anterior segment, may all generate digital outputs that can be transferred electronically and viewed remotely.

This review outlines the validity of remote review with current technology and work reported to date using remote technology in glaucoma detection and management. Papers included in this review were identified through pubmed searches using the keywords ‘teleophthalmology’, ‘teleglaucoma’, ‘glaucoma imaging’, ‘glaucoma screening’, ‘glaucoma case detection’, ‘glaucoma progression’ and ‘IOP measurement’; references in English were included.

TECHNOLOGY: STANDARDISATION AND INTEGRATION
For any telemedicine/telehealth system to be implemented it is vital that open information exchange standards are used. Table 1 illustrates the principal standards and associated organisations that exist in this field.

While some glaucoma devices can already be configured to automatically upload data in a standardised format, others cannot (eg, older Goldmann applanation tonometers and corneal pachymeters). Standardised digital interfaces for most monitoring devices are awaited, and until such point, manual data entry into the electronic patient record will be required.

POLITICAL CLIMATE AND RATIONALE FOR TELEGLAUCOMA
In general, regulatory, legal and financial issues are all barriers to adoption of telehealth. The political momentum in the UK supporting ‘telehealth’ is strong, with the prime minister, David Cameron, pledging that up to 3 million people with chronic conditions will be managed using telehealth technology, funded through the government’s Life Sciences Strategy.15 The principal cited reason was the success of the Whole Systems Demonstrator (WSD) trial. This was a cluster randomised trial conducted in 3230 people with diabetes, chronic obstructive pulmonary disease and heart failure.16 Subjects randomised to the telehealth arm underwent home self-monitoring during allotted sessions using instruments, such as glucometers, pulse oximeters, weighing scales and symptom questionnaires. This approach led to a lower 12-month admission rate and mortality at 12 months. Recently, however, doubts have been raised as to whether the strategy was cost effective when compared with standard care.17

Primary open-angle glaucoma (POAG) is a chronic condition with a prevalence of 2% in people over 40 years of age,18–22 rising to over 10% in some populations over 80 years of age.22,23 There is a significant burden of disease, with up to 10% of UK blind registrations being attributable to glaucomas.24 Hospital eye services are considerably challenged by the influx of new glaucoma referrals, while continuing to monitor existing stable patients. There is, therefore, an argument to try and minimise hospital visits by reviewing stable glaucoma patients outside the hospital clinic setting.

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Received 5 August 2013
Revised 22 January 2014
Accepted 16 March 2014
Published Online First
10 April 2014

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Depending on the requirements of the telemedicine system, both these standards can coexist. Several clinical information systems have adopted HL7 and other standards are in the process of conversion but there needs to be wider acceptance to ensure complete interoperability.

### Table 1  Summary of the current healthcare technological integration strategies and standards

<table>
<thead>
<tr>
<th>Standard/organisation</th>
<th>Nature</th>
<th>Purpose</th>
<th>Detail</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL7 (Health Level 7)²</td>
<td>International non-profit organisation</td>
<td>Involved in developing international open health informatics standards</td>
<td>Develops messaging, clinical document and other health informatics interoperability standards to enable exchange of healthcare information depending on the requirements of the telemedicine system, both these standards can coexist.</td>
</tr>
<tr>
<td>HL7 V2.X, V3.0, CDA³</td>
<td>HL7 V2.X, V3.0 and Clinical Document Architecture. These standards developed by HL7 enable information exchange and structuring of clinical documents</td>
<td>V2.X and 3.0 are messaging standards and can be used when real-time transfer of information is needed. HL7 V3 CDA allows representation and processing of clinical documents that makes it machine and human readable. The CDA document can include free text, images and other multimedia content. Telemedicine consultations can involve clinicians or patients sending patient summaries, referral letters or other clinical documentation between multiple entities and the CDA document can ensure interoperability even in the presence of legacy systems.</td>
<td></td>
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<tr>
<td>DICOM (Digital Imaging and Communication in Medicine)⁴</td>
<td>Administered by the Medical Imaging and Technology Alliance, a division of the National Electrical Manufacturers Association (NEMA)</td>
<td>International standard developed to ensure interoperability between imaging systems. DICOM has existed as a standard since 1993, and this has been one of the key developments in enabling the communication of radiological tests.</td>
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<tr>
<td>ANSI (American National Standards Institute)⁵ H.32x</td>
<td>Private non-profit standards development organisation</td>
<td>H.32x is a standard that enables video conferencing and allows clinicians and patients to communicate with each other regardless of the video conferencing hardware used, and are needed where real-time telemedicine video-conferencing applications are required.</td>
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<tr>
<td>Continua Health Alliance⁷</td>
<td>Non-profit open industry alliance of leading healthcare technology companies and device manufacturers. The alliance consists of fitness/wellness device and chronic disease personal health management device manufacturers</td>
<td>Members of this alliance select appropriate standards and establish strict interoperability guidelines that allow these devices and home monitoring systems to share information. Personal health and home monitoring devices which have undergone the Continua Certification Process should collect and exchange the health and wellness information with other certified devices in an efficient manner.</td>
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<tr>
<td>IHE¹⁰</td>
<td>Integrating the healthcare enterprise. International consortium of clinicians, vendors and health informatics professionals</td>
<td>Promotes the use of existing standards (DICOM, HL7, web services, etc.) IHE working group formulates technical framework specifications called IHE Profiles which allow vendors to independently develop solutions that meet requirements of this framework. These profiles address common yet difficult interoperability issues affecting healthcare information exchange and interoperability. IHE also participates in testing and validation of these profiles and vendor implementations so that they work in real-life scenarios, and actively promotes their use. IHE accelerates adoption of Electronic Health Records and allows exchange of information between disparate clinical environments and information systems and helps address the problem of information silos.</td>
<td></td>
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</table>

CDA, clinical document architecture; IOP, intraocular pressure.
Most reported teleglaucoma schemes have been used in remote areas where specific glaucoma expertise is not available. The number of staff at a remote site can be minimised, with potentially a ‘dedicated’ technician overseeing tonometry, imaging and perimeter at each testing station. Any potential teleglaucoma scheme’s management team will need to devise a specific training programme and competency assessments (along with continuing education and appraisal) for any staff undertaking testing at a remote site.

TELEGLAUCOMA-FRIENDLY TECHNOLOGY

Intraocular pressure measurement

Therapies for glaucomas are predominantly focused on lowering intraocular pressure (IOP), hence, this is a crucial element of any follow-up assessment. For detection of disease, IOP measurements above 21 mm Hg have a reported sensitivity of 47% and specificity of 92% for detecting POAG, and this does not improve when confined to high-risk groups.28

Goldmann application tonometry (GAT) is now available with a digital output (AT 900D, Haag-Streit International, Koeniz, Switzerland). Non-contact tonometers (NCT), rebound tonometers (iCare, Helsinki, Finland) and hand-held applanation tonometers (Tonopen, Reichert, Depew, New York, USA) have the advantage that less skilled operators can use them effectively, and they are portable. Repeated measurements with GAT are, however, more reproducible than automated methods of IOP measurement.29 Non-contact methods may be subject to systematic bias (rebound tonometry was found to overestimate IOP by a mean of 2.3 mm Hg up to 3.4 mm Hg compared to GAT) non-systematic bias (there is a tendency for tonopen to underestimate IOP at high IOP levels) and other sources of bias (pneumotonometry and rebound tonometry are prone to overmeasurement with increasingly thicker corneas). They identified the need for further evaluation of the performance of time domain OCT (TDOCT) in discriminating between normal and glaucomatous eyes.59

HRT and optical coherence tomography: glaucoma ‘classification’

The pre-eminent imaging modalities in glaucoma are confocal scanning laser ophthalmoscopy (CSLO, as performed using the HRT) and optical coherence tomography (OCT). A third modality, scanning laser polarimetry (GDx and its derivatives, Carl Zeiss Meditec, Dublin, California, USA), is as effective in terms of glaucoma ‘classification’ as HRT and OCT, but has largely been superseded by OCT technology in terms of clinical practice and in active research.

HRT uses two classification algorithms—the Moorfields Regression Analysis (MRA) and the Glaucoma Probability Score (GPS). MRA is based on the understanding that rim area varies with disc size, may decline with advancing age and may narrow in any sector of the disc in glaucoma. Very large and very small discs confound MRA. Atypical optic nerve head (ONH) morphology may lead to such discs falling outside the normative range without necessarily being glaucomatous. Sensitivities of 58–84% and specificities of 81–96% have been reported depending on inclusion and cut-off criteria.

GPS uses a mathematical model of ONH shape to discriminate between normal and glaucomatous eyes. The method is operator-independent as it does not require contour line placement. GPS does not confer any advantage over the MRA in terms of sensitivity and specificity. There is a dependency on disc size for MRA and GPS classification.

Several studies have demonstrated the performance of time domain OCT (TDOCT) in discriminating between normal and glaucomatous eyes. Comparisons between TDOCT, CSLO and scanning laser polarimetry have failed to identify a significant advantage of one device over another. A comparison between the retinal nerve fibre layer (RNFL), ONH and macular thickness parameters of the STRATUSOCT (Carl Zeiss Meditec) found that RNFL thickness and optic nerve head parameters had similar performance in differentiating between healthy and glaucomatous eyes and both outperformed macular thickness parameters. In all these studies, performance was
assessed using well-defined case controls with established repeatable glaucomatous visual field defects, a scenario that is much more clear-cut than is usually encountered in the normal clinical setting.

A large number of studies have now assessed the ‘diagnostic’ capability of the more recently available spectral domain OCT (SDOCT) devices, and most of these have made a comparison with the performance of TD-OCT. In all cases, SDOCT has been found to have a good diagnostic capability but no major advantage over TD-OCT.

The macula contains approximately 50% of all retinal ganglion cells, hence macular thickness may be useful for glaucoma diagnosis. The RNFL, the ganglion cell layer and the inner plexiform layer together make up the ganglion cell complex (GCC). GCC has significantly higher diagnostic power than macular thickness as measured by SDOCT or TD-OCT, and the best performing GCC parameters have been found to be equivalent to mean RNFL thickness as measured by TD-OCT.

OCT technology is now also used widely for the assessment of the anterior segment, and this could potentially be used as a proxy test for gonioscopy. OCT cannot pick up features, such as peripheral anterior synchiae, neovascularisation or pigmentation that are detectable by gonioscopy.

HRT and OCT: monitoring change

The current HRT3 software features two progression algorithms, trend analysis and topographical change analysis (TCA). Interpretation of the trend is empirical and a ‘rate’ of change cannot be generated. The importance of estimating a rate of change is highlighted by the results of the CSLO Ancillary Study to the Ocular Hypertension Treatment Study. A five times faster rate of rim loss was identified in eyes converting to glaucoma than those that did not. TCA assesses progression by measuring changes in the height of superpixels generating a ‘change probability map’ with red pixels representing significant height depression. TCA tends to identify more subjects as progressing than stereophotographic assessment. TCA has also been shown to be predictive of future visual field damage.

The rapidity by which OCT technology is evolving means there are a few longitudinal studies investigating progression. In teleglaucoma, it may therefore be preferable to employ stereophotographs and a semiautomated imaging technology. Stereophotographs are largely ‘future-proof’, but they lack automated quantification and progression algorithms, of which HRT TCA is the most mature and well established.

Functional testing

Static automated perimetry (SAP) is the most widely accepted functional test for the evaluation of glaucoma. SAP invariably requires a degree of patient learning for reliable performance and it is time consuming, even when using the Swedish Interactive Thresholding Algorithm (SITA). Ideally, for teleglaucoma purposes, a functional test should be easy to use and quick in order to maintain a high throughput. Objective (electrodiagnostic) perimeter would, therefore, be impractical. Frequency doubling technology (FDT), however, may offer a realistic alternative to SAP Studies report sensitivities for FDT of between 35% and 93% in early to moderate glaucoma, greater than 97% in severe glaucoma, with a specificity of 90% for early glaucoma and greater than 97% for advanced disease. FDT may detect glaucomatous visual field loss earlier than SAP but learning effect remains a problem in subjects without prior perimetric experience. Despite these advantages, SAP’s smaller test-retest variability and larger dynamic range make it currently the optimal choice for monitoring glaucomatous visual field progression. Some newer perimeter techniques, such as the Moorfields Motion Displacement Test, are being developed for use on multiple computer monitor platforms. It is conceivable that perimetry will become available for use in the domiciliary setting.

Clinicians are much better at detecting field progression when their decision making is augmented by using a computer algorithm. Event analyses ascribe progression when a predetermined threshold has been achieved. The native event analysis for the Humphrey Field Analyser (HFA, Carl Zeiss Meditec, Dublin, California, USA), Guided Progression Analysis (GPA), is based on the strategy used in the Early Manifest Glaucoma Treatment study. Trend analyses monitor the behaviour of a specific parameter over time, allowing a rate of change to be calculated. A ‘global’ trend analysis, that monitors change in the visual field index (VFI) over time, is included in the GPA package. An alternative approach is to perform pointwise linear regression analysis which is the technique adopted by PROGRESSOR (Medisoft, Leeds, UK). Trend analyses provide better receiver operator characteristic curves than event analyses. From a teleglaucoma perspective, there is a good argument for adopting external software, such as PROGRESSOR, as analysis is performed on a different computer from the perimeter following data transfer. This overcomes the issue of lack of Digital Imaging and Communication in Medicine (DICOM) compatibility when using older perimeters.

TELEGLAUCOMA IN PRACTICE

In glaucoma management and case detection, the outcome of most interest is the number of false negatives, that is, the number of those who are true cases or are progressing cases that are not detected. Detection of false negatives is a major challenge. Both outcomes are relatively rare. The normal methodology to approach such a scenario is to undertake studies determining the sensitivity and specificity using an enriched population. Sensitivity and specificity are independent of prevalence, therefore, improved estimates may be obtained by having large proportions of outcomes of interest in the study group. There is a notable lack of such assessments, meaning that there is a risk of accepting an unsafe system. If glaucoma has a prevalence of 2%, screening 6000 would yield 120 cases. Were only 80 cases detected, the system could be hailed a success, and yet, there are 40 cases undetected. A major factor in favour of decreasing false negatives in chronic disease screening is the opportunity for a ‘second bite at the cherry’ with repeat screening over time. All these issues are, as yet, inadequately explored. The proportion of false positives is also of interest, but much more easily determined.

Regular monitoring

There are a few published reports of teleglaucoma applied to routine care. The first reported teleglaucoma pilot study was undertaken in Finland, a country where large remote areas have had a chronic lack of ophthalmologists. The study used a video slit lamp, an automated perimeter and a non-mydriatic fundus camera, with real-time videoconferencing. A group in Canada has recently described a strategy to service people with, or at risk of, glaucoma in the rural setting and living near the university eye centre. The authors describe four main components to their service: enthusiastic staff, secure reliable software, appropriate hardware (a minimum of retinal camera, IOP central corneal thickness and either FDT or HFA), and national guidelines for glaucoma management. Huatala and colleagues
describe a teleophthalmology mobile unit that provides diabetic retinopathy screening and follow-up of stable glaucoma patients in Northern Finland.27 Patients undergo visual field testing using HFA and digital fundus photography. A nurse measures IOP and compares the measurement to a preset target. Images and visual fields are assessed offline by the glaucoma specialist. Online help is available by telephone. A similar approach is being applied within the UK in urban and rural centres. The Newmedica glaucoma service began at Bristol Eye Hospital in 2007 and has provided nearly 100,000 glaucoma review appointments to date from eight mobile sites. The service uses a proprietary electronic medical record software called Electronic Medical Management Application (EMMA), which allows online virtual reviewing over a secure internet connection. An optometrist and two technicians man each mobile clinic. The patient has visual acuity and HFA data collected. The optometrist then takes a history, examines the patient (including pachymetry and GAT), and acquires a dilated fundus photograph (monoscopic) or HRT image. All data are uploaded into EMMA including archive fields and disc images. At the end of the consultation, the optometrist provides a provisional management outcome made final within five working days after review of the data online by a glaucoma specialist working online in a virtual clinic. Once the outcome has been decided, the clinic software automatically writes to the patient and their general practitioner, and the next appointment is booked.

Detection of new cases
A systematic review of diagnostic tests for glaucoma failed to identify a particular advantage of a single test for the purposes of glaucoma screening.90 Indeed, a Health Technology Assessment suggested that screening for open-angle glaucoma would not be cost effective although targeted screening of subjects in high-risk groups (eg, family history, black ethnicity) might be worthwhile.100 A number of groups have tried to apply a targeted approach to glaucoma screening using teleglaucoma.

In Rotterdam, 10 community optometric practices were equipped with GDXs, and patients considered ‘at risk’ were offered imaging.101 The images and clinical details were transferred to the eye hospital for assessment. From 1729 patients screened, 467 (27%) were called to the hospital and 80 new cases of glaucoma were identified giving a positive predictive value of only 18%. In a study undertaken in Tasmania, visual acuity, autorefraction, SARS IOP measurement using the Tonopen and stereo disc photographs were all acquired at remote sites then amalgamated into a summary PDF file that was transferred electronically to a glaucoma specialist.102 First-degree relatives of patients with a confirmed diagnosis of glaucoma were screened and one new case of glaucoma was identified for every 19 participants. There was, however, a very low take-up of the scheme among subjects at risk.

Glaucoma data archiving
Managing glaucoma patients via a remote clinic necessitates the electronic archiving of historic clinical data, including visual fields and images. Visual field data and images can be electronically assimilated into the teleglaucoma notes relatively easily. However, archiving paper notes can present a significant problem where the patient population has been under the care of a clinic for many years, and where paper notes are commensurately bulky. Three potential methods for incorporating historic notes into a paperless teleglaucoma clinic include:

- To make historic paper notes available for the first few visits to the teleglaucoma clinic to allow an overlap, whereby the teleglaucoma notes progressively replace the paper notes (which are eventually archived).
- To make a full electronic copy of the paper notes and incorporate that archive into the teleglaucoma notes (usually in the form of PDF documents).
- To manually transcribe a summary of the salient events from the paper history into the electronic notes.

Each approach represents a compromise. Even the option of scanning the old notes in their entirety can overload the teleglaucoma clinic with data which can be hard to identify and is often of minimal value.

Postoperative review
Another area where telehealth may be useful is in postsurgical management. Crowston et al103 assessed the interobserver agreement for clinical signs in post trabeculectomy eyes when evaluated by real-time video images compared with face-to-face consultation. Remote assessment provided high levels of agreement for bleb vascularity, anterior chamber depth, and the existence of a bleb leak; it was much more variable for bleb height and bleb wall thickness. More recently, a Japanese group has similarly shown images acquired using a remote controlled slit lamp to be of use in postoperative management.104

CONCLUSIONS
Glucomas remain enigmatic conditions in which a diagnosis cannot consistently be made using a single test, or indeed a battery of tests. The proliferation of teleglaucoma-friendly devices, for IOP measurement and quantitative disc assessment have not necessarily increased our ability to detect glaucomas in the absence of a face-to-face consultation. In that regard, teleglaucoma is perhaps not yet ‘ready to go’. These technologies are, however, likely to be useful in the monitoring of patients with an established diagnosis of glaucoma, and it is in this context that a few teleglaucoma schemes have already become successfully established. Given the increasing age of the population, and the constraints upon already stretched hospital eye services, it is likely that reliance on teleglaucoma will increase. This may be despite the fact that the diagnostic and monitoring capabilities of currently available technologies will not necessarily meet the ambitions of the teleglaucoma schemes from the outset. There is a strong case for further robust studies investigating the positive and negative predictive power of all systems of glaucoma detection and monitoring.

Acknowledgements
NGS acknowledges a proportion of his financial support from the Department of Health through the award made by the National Institute for Health Research to Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology for a Biomedical Research Centre for Ophthalmology. The views expressed in this publication are those of the authors and not necessarily those of the Department of Health.

Contributors
NGS provided critical revision, original draft, interpretation, oversight and final draft. GC provided original draft, concept revision, oversight and final version. JPD provided critical revision, draft oversight and final draft. IEM provided concept, revising several drafts, oversight and final version. He is guarantor.

Competing interests
NGS has received lecture fees from Heidelberg Engineering and MSD as well as author and lecture fees from Allergan. He is an unpaid medical adviser to Moorfields Pharmaceuticals. JPD is Medical Director of New Medical Systems Ltd (Newmedica) which provides Glaucoma follow-up via Virtual Clinic service.

Provenance and peer review
Not commissioned; externally peer reviewed.

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Br J Ophthalmol 2014 98: 1605-1611 originally published online April 10, 2014
doi: 10.1136/bjophthalmol-2013-304133

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