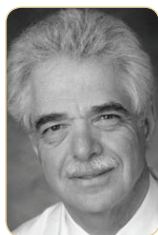# TELEMEDICINE IN OPHTHALMOLOGY

Numerous factors are driving a transition to remote screening.

BY CARL H. PARK, MD; EHSAN RAHIMY, MD; ABTIN SHAHLAEE, MD; AND JAY L. FEDERMAN, MD

Telemedicine is the remote diagnosis and management of patients using telecommunication technologies (eg, telephony, a local computer network, or the Internet). Telemedicine screening in ophthalmology usually involves the remote gathering of images, typically fundus photos, with subsequent analysis to identify patients who have a referral-warranted ocular disease. Screening programs exist for several ophthalmic diseases, including age-related macular degeneration, glaucoma, and hypertensive retinopathy. This article focuses on the use of telemedicine in screening for diabetic retinopathy (DR) and retinopathy of prematurity (ROP).

OPPORTUNITIES IN DR

DR is the leading cause of blindness in the working age population of the world.[1] To identify DR, there is a burden of effectively screening the more than 30 million people with diabetes in the United States each year.[2] This screening burden is expected to grow to close to 45 million patients with diabetes in the United States by the year 2030.[3]

At the same time, access to qualified eye care providers for traditional face-to-face exams is severely limited. In the developed world, it is estimated that 30% of patients with diabetes do not have ready access to eye care.[4] For the developing world, DR screening is severely limited and in many cases unavailable.

Portability

With rapid advances in camera technology, intelligent software, and cloud computing paradigms, the barriers to deploying an effective DR telemedicine screening platform have mostly been overcome. (*Note: For more on artificial intelligence in retina screening, see the March 2017 issue of* Retina Today, *where Peter A. Karth, MD, MBA, and Ehsan Rahimy, MD, discuss the use of a deep learning algorithm for automated detection of DR and diabetic macular edema in retinal fundus photographs.*[5]) Most DR screening programs currently utilize traditional tabletop fundus cameras, but, thanks to the development of smaller and cheaper camera sensors, portable fundus cameras are now a reality.

Several attachments have been developed for use with smartphone cameras to obtain fundus images. However, most of these systems have an awkwardness factor (eg, they require one to place a 28 D indirect ophthalmoscopy lens in front of the phone camera) or they have a narrow field of view. Newer smartphone camera attachments may overcome some of these limitations.

The ideal fundus camera for DR screening image capture will probably be a portable optical coherence tomography (OCT) scanning laser ophthalmoscope (SLO) system. Such systems are in development in the academic setting and may debut commercially in the near future.[6] There would be numerous advantages of such a system compared with traditional fundus cameras. First, the OCT-SLO technology would obtain widefield images through a small pupil. Second, image quality would not be compromised during image acquisition with dark fundus pigmentation. Third, the 3-D OCT information would be ideal in screening for diabetic macular edema, which is difficult to recognize reliably utilizing a nonstereo fundus image.[7]

AT A GLANCE

- Identification of referral-warranted DR is not enough; a successful telemedicine screening program should close the loop between effective screening and timely examination.
- Ideally, ROP telemedicine screening should be implemented via a custom platform designed to minimize errors and maximize accuracy of interpretations.
- The practice of medicine freed of borders, time zones, and personnel resources opens the door to economical and widespread screening for ophthalmic diseases.
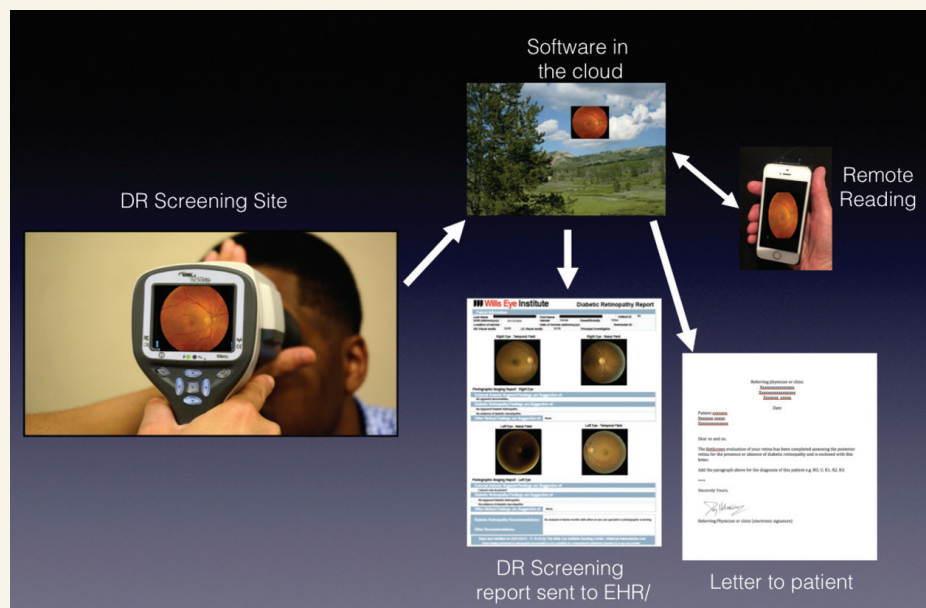
Figure 1. An example workflow of a DR screening software platform. A portable fundus camera is deployed to the screening site, where the captured images are securely transmitted to the cloud software platform for analysis. Image analysis can take place anywhere, given that the cloud software is web-based and can be accessed by any standard browser. The reading software automatically generates a report for the referral source and, in some cases, for the patient, which may facilitate compliance with follow-up examinations.

Telemedicine screening for DR has been subjected to numerous peer-review validation studies.[8-11] In 2014, the UK National Health Service established mandatory screening of all known patients with diabetes. DR is no longer the most common cause of blindness in the United Kingdom.[12] Other telemedicine screening programs have significantly reduced the incidence of blindness caused by diabetes.[13]

Compliance

Identification of referral-warranted DR is not enough. A study by the Centers for Disease Control and Prevention showed that only 30% of patients sought eye care after receiving a telemedicine-based determination of referral-warranted DR.[14] A successful telemedicine screening program for DR must close the loop between effective screening and timely examination by eye care specialists.

Centralized or local software platforms for storage and analysis are gradually being replaced by cloud-based software (Figure 1). A sophisticated cloud-based platform utilizing standard web-based protocols could coordinate image capture, image upload, data storage, and image analysis, either by an eye care specialist, a reading center, or an automated artificial intelligence–type platform. Analyzed image reports could then be forwarded, preferably electronically, to the intended recipient or recipients for further patient management.

Artificial Intelligence

There has been a surge in the use of artificial intelligence and machine learning within the medical field over the past several years to help improve pathologic detection of cancer and interpretation of radiology images. A deep learning algorithm developed by Google researchers was found to be capable of interpreting fundus photographs depicting various stages of DR at least as accurately as a cohort of ophthalmologists.[15,5]

Deep learning refers to a form of machine learning whereby an algorithm is able to program itself from observing a large set of labeled examples, removing the need to specify rules explicitly.[16] Drawing inspiration from the structure of the human mind, artificial neural networks can analyze large data sets to discover underlying patterns. One of the exciting aspects of deep learning is that "feature engineering" is not required.[17] Instead of researchers hand-coding instructions to the algorithm on what a microaneurysm, hemorrhage, or neovascular frond looks like, rather, they input an image labeled as *severe diabetic retinopathy* for example. With enough labeled data, the computer eventually learns what that is. While it is possible that the algorithm independently appreciates the same characteristic features of DR, it is also feasible that it may have identified its own pattern recognition of disease beyond the scope of how humans interpret the disease. Elucidating exactly what the machine "sees" is the subject of ongoing work.

Gulshan et al trained their deep learning neural network utilizing a reference series of 128,175 DR screening fundus images, graded multiple times by a group of ophthalmologists with assessment of degree of DR.[15] Once the human grading was completed, this development set was subsequently presented to the neural network algorithm for training. After the training, the investigators utilized two sets of new images (EyePACS-1 set = 9,963 images, and Messidor-2 set = 1,748 images) to "test" the algorithm against a reference standard of board-certified ophthalmologists' readings. In these validation sets, with the algorithm programmed for high sensitivity, it achieved 97.5% and 96.1% sensitivity and 93.4% and 93.9% specificity in each of the two sets, respectively. For comparison, guidelines for DR screening initiatives recommend at least 80% sensitivity and specificity. All together, these findings suggest that automated DR screening, even though in its nascent stages, may someday assist ophthalmologists in evaluating more patients in a more efficient manner.

OPPORTUNITIES IN ROP

Screening for ROP is a workflow process that is amenable to telemedicine. All accredited neonatal intensive care units (NICUs) in the developed world require screening for ROP.
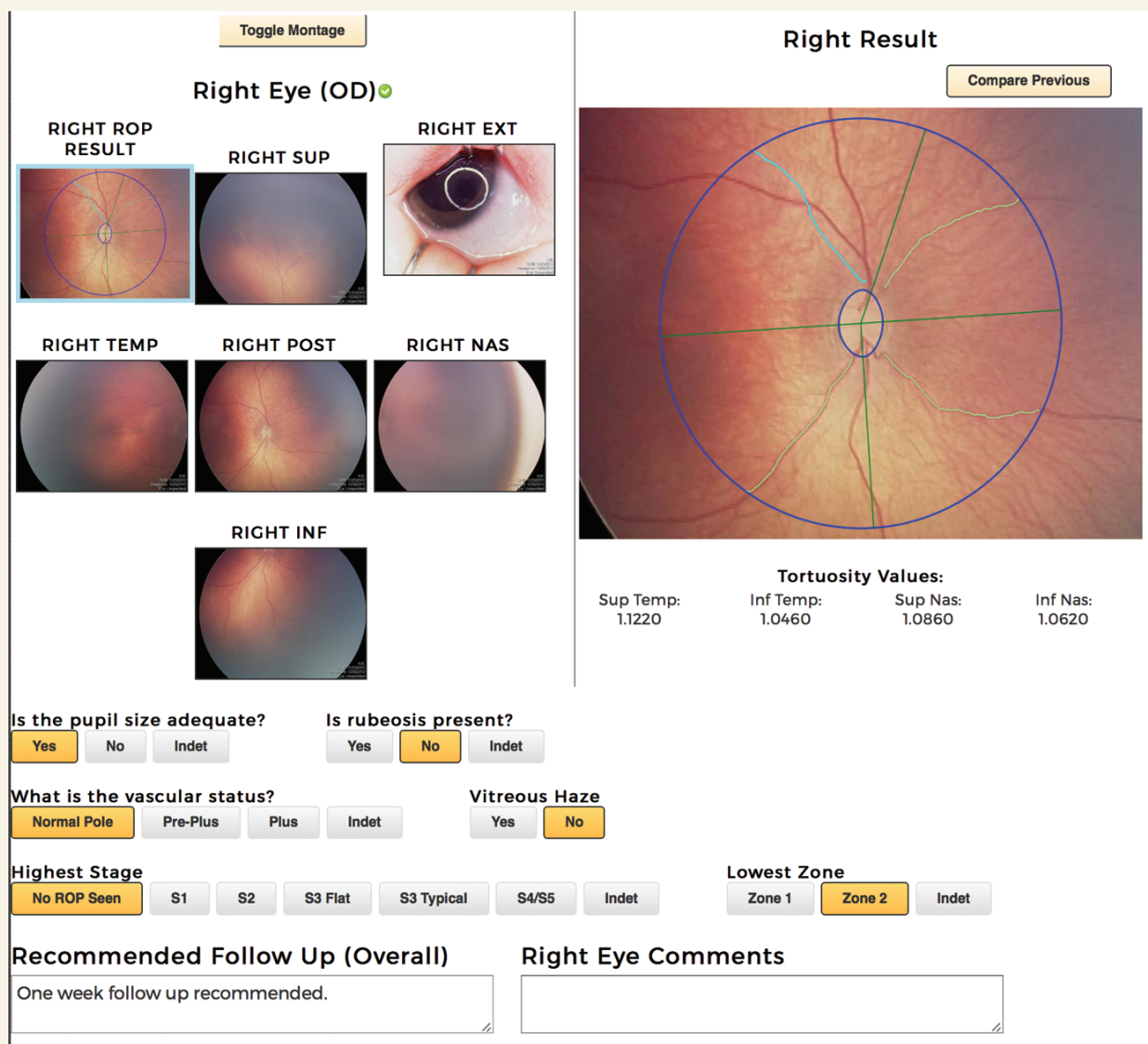
Figure 2. An example workflow screen capture from the FocusROP system (Interview Medical Systems) demonstrating the standard image sets for ROP photo screening (external, posterior, temporal, nasal, superior, and inferior). The recommendation for follow-up examination is automatically generated using a software algorithm. ROP screening platform may incorporate quantification of plus disease by measuring vascular tortuosity.

The relative lack of trained ROP experts and the heavy time, financial, and legal burdens of traditional bedside screening are driving the transition to remote ROP telemedicine screening.

Multiple prospective studies have demonstrated the effectiveness and relative equivalence of remote telemedicine screening for ROP versus bedside indirect ophthalmoscopy examination for detecting referral-warranted ROP (digital fundus findings of plus disease, zone 1 disease, and/or stage 3 disease or worse).[18,19]

Camera Specifications

Fundus image capture in premature babies presents a unique set of issues. Photography done without voluntary cooperation necessitates the use of a corneal contact camera system. For ROP screening, an imaging system should be relatively portable to allow its potential use across several NICUs to leverage the investment. The camera should offer a wide-field view of the fundus, with sufficient depth of focus to ensure that images are sharp from center to periphery. The camera should offer versatility in imaging eyes and fundi of different colors. Last, the camera should offer connectivity to enable the easy export of files in standardized medical image formats, such as DICOM, and offer secure connection to the Internet, allowing remote storage and interpretation of images.

RetCam imaging systems (Natus Medical) offer a relatively ergonomic contact camera handpiece designed for wide-field image capture (130˚) in the eyes of premature infants. However, the camera is showing its age in its relative low resolution (approximately 1 MP exported resolution), difficulties in capturing dark fundi, and lack of standardized connectivity. Recent expiration of key patents protecting the RetCam systems has sparked renewed interest in the development of pediatric contact fundus imaging systems. Closest to the market in the United States is the Icon camera system (Phoenix Clinical). It includes a handheld contact lens camera for pediatric use with high image resolution and a good

color profile in darker fundus photos. The Icon camera is also expected to include standard DICOM exports of image sets, which would allow easier integration with electronic health records and ROP management software.

Image Interpretation

Managing the workflow—from capturing the fundus images of premature babies to communicating the interpreted findings to the NICU—represents the critical aspect of telemedicine screening for ROP. ROP telemedicine screening must be implemented utilizing a platform designed to minimize errors and maximize accuracy of interpretations (Figure 2). Image transfers for remote interpretation should be performed using a secure, encrypted Internet connection. Images that are emailed using commercial email platforms (eg, Google or Yahoo) or transferred using a USB flash drive are not considered secure and could potentially result in catastrophic error, such as loss of images or mixing up of image sets. Once the image or images arrive for interpretation, there should be a standardized protocol for interpreting the image sets, with obvious attention paid to the presence or absence of plus disease, the highest stage and the lowest zone of ROP.

Follow-up Time

The biggest hazard to optimal management of ROP arises when an incorrect follow-up examination time for a given disease status is observed.[20] Improper timing of ROP screening follow-up can be avoided by incorporating a codified follow-up algorithm in the workflow software. Current guidelines suggest that type 1 ROP eyes be automatically referred for bedside exam, that type 2 eyes be automatically scheduled for repeat photo screening in 1 week, and that eyes with no ROP be photo screened every 2 weeks until final confirmation that no ROP is present. Telemedicine workflow for ROP should also include fail-safe mechanisms for dealing with untimely readings (eg, incorporation of an automated alerting system when photo interpretation is overdue) due to the time-critical nature of the disease process.

More Reasons for ROP in Telemedicine

Telemedicine screening for ROP provides optimal documentation of disease status with photographic evidence (as opposed to often crude drawings), improved temporal comparison of disease status (checking zone margins with serial comparison of photos), potential quantification of plus disease (Figure 2),[21] better management of physician time, and minimization of bedside exams until referral-warranted ROP is detected on photo screening.

BRIDGING GAPS

The practice of medicine without borders, time zones, and personnel resources opens the door to economical and widespread screening of ophthalmic diseases. It also suggests a future in which no region of the world is too remote or too poor to receive high quality medical care. The future for telemedicine in ophthalmology undoubtedly holds much promise. ■

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