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The use of retinal photography in non-ophthalmic settings and its potential for neurology

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Abstract

Background—Ocular fundus examination is an important element of the neurological examination. However, direct ophthalmoscopy is difficult to perform without pupillary dilation and requires extensive practice to accurately recognize optic nerve and retinal abnormalities. Recent studies have suggested that digital retinal photography can replace direct ophthalmoscopy in many settings.

Review Summary—Ocular fundus imaging is routinely used to document and monitor disease progression in ophthalmology. Advances in optical technology have made it easier to obtain high-quality retinal imaging, even without pupillary dilation. Retinal photography has a high sensitivity, specificity, and inter-/intra-examination agreement compared to in-person ophthalmologist examination, suggesting that photographs can be used in lieu of ophthalmoscopy in many clinical situations. Non-mydriatic retinal photography has recently gained relevance as a helpful tool for diagnosing neuro-ophthalmologic disorders in the emergency department. Additionally, several population-based studies have used retinal imaging to relate ophthalmic abnormalities to the risk of hypertension, renal dysfunction, cardiovascular mortality, subclinical and clinical stroke, and cognitive impairment. The possibility of telemedical consultation offered by digital retinal photography has already increased access to timely and accurate subspecialty care, particularly for underserved areas.

Conclusion—Retinal photography (even without pupillary dilation) has become increasingly available to medical fields outside of ophthalmology, allowing for faster and more accurate diagnosis of various ocular, neurologic and systemic disorders. The potential for telemedicine may provide the additional benefits of improving access to appropriate urgent consultation in both clinical and research settings.

Keywords

direct ophthalmoscopy; retinal photography; fundus camera; telemedicine

Introduction

Examination of the ocular fundus is a fundamental component of the neurologic examination, providing the only opportunity for non-invasive, direct observation of neurologic tissue and its microvasculature.¹ Abnormalities of the optic nerve, retina, and choroid can offer clues to the etiology of neurologic disorders, as well as alert the

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neurologist to underlying systemic diseases that may be contributing to a patient's neurological condition.^{1, 2} Indeed, misdiagnosis or diagnostic uncertainty is reported in over one-third of neurological consultations in the emergency department,³ and the funduscopy examination often helps identify those serious conditions that would have been missed using only other aspects of the physical examination.⁴

Although direct ophthalmoscopes are widely available in most medical settings, its usefulness is limited by several practical difficulties. First, direct ophthalmoscopy requires substantial practice for the examiner to be able to view the retina and optic nerve. Even intensive, focused medical student training programs show a rapid decline in direct ophthalmoscopy skills without regular practice.^{4, 5} Second, the direct ophthalmoscope has a limited field of view (about 5°-10°), requiring the examiner to have a thorough understanding of retinal anatomy and excellent motor skills to venture away from the optic disc to adequately examine the retinal vessels, fovea, and macula (Figure 1).⁴ In addition, the narrow field of view requires the examiner to mentally reconstruct an overall view of the ocular fundus from the small frames gathered while scanning over different regions of the posterior pole of the eye, making identification of many abnormalities more difficult. Finally, it is very difficult to examine the optic nerve and the posterior pole without pupillary dilation, a procedure uncommonly performed outside of an eye clinic because of the additional 30 minutes of patient evaluation, the loss of ability to follow pupillary reactivity in neurological and neurosurgical patients (even the short-acting drops may have an effect up to 6 hours), and the very low, but nevertheless concerning, risk of precipitating acute angle-closure glaucoma.^{5, 6} The recognition of the importance of ocular fundus examination combined with consideration of these difficulties in using the direct ophthalmoscope, has recently led investigators to propose that non-mydratic (without pupillary dilation) retinal photography may be a promising alternative for the visualization of the ocular fundi of neurologic patients.

Retinal photography as a diagnostic tool

Technical aspects

Since 1886, when Jackman and Webster published the first human fundus photograph, imaging has been essential to the field of ophthalmology.^{7, 8} Early photographs allowed visualization of the optic nerve, but corneal reflections obscured the rest of the fundus. Over the next half-century, the techniques gradually improved, but were still limited by long exposure times and less than ideal light sources. Ultimately, the widespread use of electronic flashtubes and the convenient 35 mm film format ushered in a new era of retinal imaging.⁷

More recently, digital photography has generated another revolution in retinal photography. Digital images, rather than requiring a lengthy development process, can be displayed immediately after they are taken, allowing for real-time adjustments in composition, focus, and flash intensity to maximize quality. Without film there is essentially no incremental cost of obtaining additional images; quick, exact duplicates can be made, which can then be easily archived and transmitted to remote locations.⁹

During the same period, advances in optics have increased the field of view of ocular fundus cameras, typically to 30 degrees, even without pupillary dilation (i.e., non-mydratic). In addition, many models combine several useful photographic and diagnostic modalities in a single package (e.g., red-free photography, fundus autofluorescence, stereo photography, fluorescein angiography, and choroidal imaging).⁷

Advantages of retinal photography over ophthalmoscopy

Several studies have established the capabilities, even advantages, of digital retinal imaging to detect ocular fundus pathology compared to funduscopic examination. For example, studies on diabetic retinopathy screening (the most extensively evaluated area of retinal imaging) have found that retinal photography has higher sensitivity, specificity, and inter-examination agreement than ophthalmoscopy, even among ophthalmologists.^{10, 11}

Unlike direct ophthalmoscopy, non-medical personnel can readily obtain high-quality retinal photography after a short training process. In one study,¹² the quality of dilated and non-dilated digital images taken by three photographers with different levels of photographic training was evaluated. A trained ophthalmic photographer (20 years experience) and two non-professional photographers (one with 2 days and the other with 1 hour of training) did not have statistically significant differences in image quality based on the ratings of the photographs by two retina specialists. These findings concur with the recent Fundus photography vs. Ophthalmoscopy Trial Outcomes in the Emergency Department (FOTO-ED) study, in which nurse practitioners obtained photographs of diagnostic value in 97% of patients after only 15–30 minutes of training on a non-mydriatic digital fundus camera.^{13, 14}

It is particularly difficult to examine the ocular fundus of young children. Even with patient pupillary dilation, experienced ophthalmologists can have difficulty visualizing the fundus of young, uncooperative subjects. Non-mydriatic fundus photography also shows promise in this area. In one recent study,¹⁵ the use of a non-mydriatic digital fundus camera allowed for the acquisition of fundus photographs of satisfactory quality in children over the age of 3 years and in some children as young as 22 months, without pupillary dilation.

Additionally, the ease of transmitting digital images has also made digital imaging the preferred method for both telemedical use and for population-wide screening in which images can be sent reliably to reading centers for manual review or automatic screening.⁹

Retinal photography in ophthalmology

Imaging is an invaluable tool in ophthalmology where it is used extensively to diagnose, document, and monitor ocular disease.^{7, 16} In particular, it is now routinely used as an important screening tool for treatable, sight-threatening eye diseases in at-risk populations. In the case of diabetic retinopathy, there is level I evidence that single-field fundus photography can identify patients with diabetic retinopathy who require referral for ophthalmic evaluation and management.¹⁷ Likewise, fundus photography has also been demonstrated to have high reliability and accuracy in detecting referral-warranted retinopathy of prematurity, a potentially blinding eye disease among premature infants.¹⁸ Retinal photography has also been studied for the telemedical diagnosis of cytomegalovirus retinitis in HIV-positive patients in under-served countries with a high HIV burden.¹⁹ These retinal photography techniques are quite easy to use, convenient, and well-liked by patients; much research is ongoing to evaluate their cost-effectiveness.^{17, 18}

Retinal photography in non-ophthalmological settings

Not surprisingly, retinal imaging has become increasingly common outside the confines of ophthalmology. In recent years, it has shown promise in various clinical and research settings within internal medicine and neurology, as well as emergency medicine departments.

Internal Medicine

Retinal microvascular abnormalities and cardiovascular disease—An area in which retinal photography has proved useful in internal medicine has been the determination of cardiovascular risk. Extensive data from clinical and population based-studies show strong and consistent associations between elevations in blood pressure and the presence of retinal changes. The converse is also true: the presence and development of new hypertensive retinal findings is strongly related to elevated blood pressure.^{20–22}

These retinal findings are generally divided into two categories: those that directly involve the retinal arterioles, such as generalized and focal arteriolar narrowing and arteriovenous nicking, and those that include the retina itself, including hemorrhages, cotton wool spots, microaneurysms, macular edema, and exudates.²³ Generalized retinal arteriolar narrowing and arteriovenous nicking appear to be markers of cumulative long-term hypertension damage, and are independently linked with blood pressure levels measured 5–8 years before the retinal assessment.²¹ In contrast, focal arteriolar narrowing, retinal hemorrhages, microaneurysms, and cotton-wool spots reflect acute blood pressure changes, and are associated only with concurrent blood pressure measurements.^{21, 24} Retinopathic changes, but not vasculopathic ones, have been associated with twice the risk of incident congestive heart failure, even among otherwise low-risk individuals.^{25, 26} The presence of hypertensive retinopathy also doubles the risk of left ventricular hypertrophy and increases the risk of renal dysfunction and cardiovascular mortality.^{24, 27} For example, sub-analyses of the Beaver Dam Eye Study have found that individuals with retinal microaneurysms and retinal hemorrhages are twice as likely to die from cardiovascular events as those without these signs.²⁸ Furthermore, there is an increased risk of ischemic heart disease mortality related to arteriolar narrowing and decreased retinal arteriolar tortuosity.²⁹

Neurology

Retinal microvascular abnormalities are also predictive of cerebral microangiopathy, and the role of retinal photography in the investigation of microvascular disorders of the brain is an ongoing area of investigation.³⁰ As with hypertensive retinal changes, arteriolar and non-arteriolar changes have different implications for the risk of neurologic disease. By far, the non-arteriolar findings tend to be most associated with the increased risk of subclinical and clinical stroke and cognitive impairment, likely because they result from acute fluctuations in blood pressure, rather than chronic changes.^{24, 31}

Cognitive impairment—Cerebrovascular cognitive impairment represents 20% of all causes of dementia and is typically due to small vessel disease with resultant white matter lesions and lacunar infarctions. Retinal arteriolar abnormalities correlate with MRI signs of cerebral white-matter lesions, and retinal exudates correlate with the presence of lacunar infarction.³² The large, middle-aged, population-based Atherosclerosis Risk in Communities Study (ARIC) investigated the relationship between retinal microvascular abnormalities and cognitive impairment in a stroke-free population and found that the presence of retinal microvascular abnormalities (retinopathy, microaneurysms, retinal hemorrhages, and exudates) was independently associated with lower cognitive function.^{32, 33}

Microaneurysms and retinal hemorrhages were the most consistent findings linked to diminished cognitive function, and these same retinal findings have been associated with incident stroke.^{32, 34} The ARIC investigators also found that retinopathy and arteriovenous nicking on photography obtained at baseline were independently associated with 10-year cerebral ventricular enlargement, but not 10-year sulcal widening, suggesting a microvascular etiology for subcortical, but not cortical cerebral atrophy.³⁵

Stroke—Hypertension and diabetes are important risk factors for stroke and both conditions lead to changes in the retinal microvasculature.³² It is therefore not surprising that numerous studies have related retinal microvascular anomalies to stroke.^{31, 36} However, the ARIC Study found retinal microvascular anomalies, particularly microaneurysms and soft exudates, predicted subclinical strokes independent of the patient's hypertensive and diabetic status.³⁷ Other investigators have also found a similar relationship between hypertensive retinopathy and silent brain infarction in patients without a history of stroke or transient ischemic attack, independent of the patient's current hypertensive status.³⁸ Likewise, multiple population-based studies, including the Cardiovascular Health Study,²⁴ the Beaver Dam Study,³⁹ and the Blue Mountains Study⁴⁰ similarly found a relationship between retinal microvascular changes and stroke, after controlling for traditional stroke risk factors.

Emergency Department

Examination of the ocular fundus is particularly important in patients presenting with a variety of acute medical and neurologic conditions to the emergency department. Not surprisingly, funduscopy examination is only rarely performed in the emergency department for the reasons discussed earlier. Indeed, in the FOTO-ED study, only 14% of the 350 patients enrolled with a presentation warranting examination of the ocular fundus (chief complaint of headache, acute focal neurologic deficit, or visual change; or a diastolic blood pressure 120 or greater) had a funduscopy examination by the emergency physicians. Disturbingly, none of the 12.6% of these 350 patients who had a finding that would potentially alter the course of their emergency department management were detected by the emergency department physicians' direct ophthalmoscopy examination.^{13, 41} However, non-mydriatic fundus photography identified over 80% of the previously unknown relevant findings that were missed during routine emergency department evaluations. Non-mydriatic fundus photography in the ED has the potential to assist with the diagnosis of conditions such as optic disc edema (Figure 2), optic atrophy, retinal vascular occlusions, and grade III/IV hypertensive retinopathy (Figure 3). In several cases, non-mydriatic fundus photography resulted in the recall of patients to the emergency department and admission to the hospital.

Nurse practitioners participating in the FOTO-ED study received about 15–30 minutes of training followed by observation by the study staff until they felt comfortable obtaining photographs independently (generally after about 5–10 patients).¹⁴ The nurse practitioners were able to obtain photographs of diagnostic value in nearly all patients and 83% of the patients had at least one high-quality photograph.^{13, 14} The ease, comfort, and speed of non-mydriatic fundus photography were given high marks (an average 8.7 for all measures on a 10-point scale) by both patients and staff. Photography sessions required only a minimal portion of the total time that the patients spent in the emergency department: a median of 1.9 minutes, less than 0.5% of the emergency department visit.¹³

Taken together, the FOTO-ED study shows that non-mydriatic photography can play a useful role in the clinical evaluation of patients in the emergency department and that it can be feasibly incorporated into the emergency department workflow. Ongoing studies are evaluating the abilities of emergency department physicians to use the photographs themselves during clinical encounters as an alternative to direct ophthalmoscopy.

Telemedicine

A major advantage of retinal photographs is their ability to be easily transmitted for remote interpretation and consultation. Telemedicine is distance consultation among health professionals or between health professionals and patients via telecommunications technologies.⁴² There are two primary methods of performing telemedicine: (1) *synchronous*

by video tele-conferencing equipment, which enables real time communication between physician and patient, and (2) *asynchronous* by a store-and-forward method where consultation is completed at a later time.⁴³

Telemedicine helps eliminate barriers to patient care related to physical distance and can improve access to medical services that are inconsistently available in remote, or underserved communities. It has been suggested that telemedicine may provide faster, more accurate and cost-effective diagnosis compared to traditional methods, especially for patients with limited access to specialized care.^{44–46}

Visually-oriented disciplines, such as ophthalmology, commonly use telemedical approaches. The accuracy of telemedicine systems has been studied in many image-based specialties, including ophthalmology.^{19, 44, 47, 48} For instance, comparisons of retinal image-based diagnosis with the gold standard of in-person ophthalmic examination have shown high intra- and inter-rater reliability.^{19, 44, 48} Recently, telemedicine has become more commonplace in neurology, particularly when brain-imaging is involved.⁴⁹ Indeed, the use of telemedicine in acute stroke has increased rapidly over the last decade and has facilitated the safe and effective delivery of thrombolysis in a more efficient and widespread manner.⁵⁰

Nonetheless, there are substantial barriers to overcome in the regulatory, financial, and cultural domains surrounding telemedicine.⁵¹ There are additional risks to patient privacy and confidentiality, as well as concerns about control and ownership of electronic health records, all of which need to be addressed.⁵² Physicians assume increased medico-legal risk when they assess patients with potentially limited clinical data and no personal patient-physician relationship. Restrictive licensure laws in the United States also typically require a physician to obtain a full medical license in any state in which they provide care, increasing the time and financial barriers required to provide telemedical care across state lines.⁵³

Rapid changes in technology may help to reduce the start-up costs for new telemedical programs, improve the photographic quality, increase the portability (and thus useable range) of devices, and facilitate the exchange of the information obtained. Several new, portable devices for retinal photography, such as EyeQuick (Eye Quick, El Paso, TX), iExaminer (Intuitive Medical Technologies, Shreveport, LA), and Pictor (Volk Optical, Mentor, OH) have the potential of providing many of these advantages (Figure 4).^{54–56} However, these rapid changes can also require continual, potentially prohibitive, capital expenses to remain at the cutting-edge of telemedical consultation.

Conclusions

Non-mydratic retinal photography allows easy, reliable and reproducible imaging of the optic nerve and retina in non-ophthalmologic settings. Fundus photography is already widely used to tele-screen for sight threatening ophthalmological diseases, but its potential within internal medicine, emergency medicine, and neurology, as demonstrated by a growing body of literature, will likely result in its use outside ophthalmology. This tool provides invaluable information for patients with headaches, hypertensive crisis or acute neurological deficits, particularly in the emergency setting. There is no doubt that we will see numerous clinical applications of retinal photography in neurology in the next decade. Constant improvement in technology and the potential for telemedicine will likely contribute to a widespread use of this technology in numerous specialties.

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Figure 1. Non-mydriatic fundus photography allowing visualization of the entire posterior pole of the ocular fundus, including the optic nerve, the macula, and the major retinal vessels. As a comparison, the insert shows the typical view of the conventionally used direct ophthalmoscope which only shows part of the optic disc and requires active exploration of the fundus.

Figure 2. Severe bilateral papilledema in a patient presenting to the emergency department taken with a non-mydratic fundus camera.

Figure 3. Grade IV hypertensive retinopathy, with optic disc edema (star), arterial attenuation (circle; arteriovenous ratio of about 1:2, normal arteriovenous ratio is 2:3), cotton wool spots (arrow), and retinal hemorrhages (diamond).

Figure 4.
iPhone 3 (Apple, Cupertino, CA) displaying non-mydriatic fundus photograph.