

## **Title: Examining the ocular fundus in Neurology**

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## **Abstract**

**Purpose of review:** The fundoscopic examination can be a technically difficult, and often omitted, portion of the neurologic examination, despite its great potential to influence patient care.

**Recent findings:** Medical practitioners are often first taught to examine the ocular fundus using a direct ophthalmoscope, however, this skill requires frequent practice.

Nonmydriatic tabletop and portable fundus photography and even smartphone-based photography offer alternative and practical means for approaching examination of the ocular fundus. These alternative tools have been shown to be practical in a variety of settings including ambulatory clinics and emergency departments. Decreased retinal microvascular density detected with fundus photography has been linked to accelerated rates of cognitive decline. Research has also found optic disc pallor and retinopathy detected via fundus photography to be more prevalent in patients with recent stroke or transient ischemic attack.

**Summary:** Alternative methods of fundoscopic examination based on fundus photography have the potential to improve the ease of use, portability, and availability of funduscopy. Recognition of changes in retinal microvasculature has the potential to noninvasively identify patients at highest risk for cognitive impairment and cerebrovascular disease. However, further research is needed to determine the specific utility of measurements of retinal microvascular changes in clinical care. Innovative funduscopy techniques offer neurologists new approaches to this essential facet of the neurological examination.

**Keywords:** funduscopy, cerebrovascular disease, cognitive impairment

## **Introduction**

Neurologic examination findings, when detected and accurately interpreted, are important noninvasive tools that help clinicians optimally care for patients. However, the fundoscopic examination remains poorly and infrequently performed by non-ophthalmologists, including neurologists. [1] The fundoscopic examination is even discouraged by many medical student preceptors, which likely reflects growing unease in performing the skill by preceptors as well. [2\*] Nevertheless, waning skill and frequency in the performance of fundoscopic examinations due to technical barriers do not lessen the value of this singularly important portion of the neurologic examination. Nervous system diseases that threaten neurologic function, vision, and even life give clues in the ocular fundus that cannot be obtained in any other way, including optic disc edema, optic disc pallor, retinal hemorrhages, and evidence of vascular occlusion. The Accreditation Council for Graduate Medical Education has recognized the importance of funduscopy in its Milestones Project by recommending residents be able to identify papilledema prior to independent practice in Neurology. [3]

Recent research has also provided evidence that imaging of the ocular fundus may identify patients at particular risk for cognitive impairment and to stratify patients' risk for cerebrovascular disease. The urgency of solving the problem of reliably detecting ocular fundus findings has been magnified by decreasing clinician proficiency in funduscopy (via direct ophthalmoscopy), its persistent relevance in patient care, and the potential for information from funduscopy to impact the evaluation of neurologic diseases not directly related to vision, such as dementia and cerebrovascular disease. Advancements in technology have helped address some of the technical barriers of

direct ophthalmoscopy that hinder clinicians in performing a funduscopy examination. The advent of cameras that do not require pupillary dilation (nonmydriatic), some of which are even handheld, as well as smartphone-assisted devices for funduscopy has given hope to the dying art of ocular fundus examination. Case reports highlight the persistence of cases in which several missed opportunities for funduscopy in patients with unremarkable neuroimaging led to permanent vision loss that could realistically have been prevented with information from a timely funduscopy examination. [2\*] These stories emphasize the urgency of continuing to push forward in the pursuit of novel methods to examine the ocular fundus in a way that is easily performed, readily available, non-invasive, and inexpensive.

### **Tools for Funduscopy Examination**

A variety of tools now exist to assist medical professionals in performing an ocular fundus examination.

#### **Direct Ophthalmoscopy**

The direct ophthalmoscope offers its user a 5° view of the ocular fundus, which allows for a very detailed examination of a small area at one time with 15x magnification; the PanOptic™ [Welch Allyn Inc., Skaneateles Falls, NY] variety increases the field of view to 25°. [1] While the direct ophthalmoscope is ubiquitous, its availability is overshadowed by technical difficulty in its use, its small field of view, and the magnification of these disadvantages in patients who are poorly cooperative or have undilated pupils. [2\*, 4\*] Portable units must also be adequately charged. These disadvantages contribute to less than half of neurologists performing a funduscopy examination on patients being seen

for a chief complaint of a headache. [5] Only 14% of the 350 patients in the Feasibility of Non-Mydriatic Ocular Fundus Photography in the Emergency Department (FOTO-ED) study (all of whom had a headache, focal neurologic deficit, elevated diastolic blood pressure, or acute visual loss) had a funduscopic examination performed. Additionally, emergency department (ED) physicians in the study failed to identify 100% of relevant ocular fundus findings when using direct ophthalmoscopy. [6] Despite their disadvantages, direct ophthalmoscopes are widely available in emergency departments and ambulatory clinics and are portable enough to be taken to the bedside in any location. Direct ophthalmoscopes are also fairly inexpensive and can be used in poorly responsive patients. The direct ophthalmoscope is still a useful tool for clinicians who have overcome its technical barriers through regular use.

### Fundus Photography

While a direct ophthalmoscope only offers examiners a small field of view, fundus photography shows a much wider field, yielding a 45° field of view at a lower magnification. Fundus photography was invented in the 1880s, but refinement of the camera technology led to the development of nonmydriatic fundus photography in the 1970s and digital fundus photography in the 1990s. The more recent refinement of nonmydriatic fundus camera technology yields very good quality imaging, rivaling the quality of photographs obtained with pupillary dilation in many cases [Figure 1]. A major advantage of nonmydriatic fundus photography is the ability to obtain high quality images with a 45° field of view without pupillary dilation, which circumvents the technical difficulty of using a direct ophthalmoscope. [1] In addition, fundus photographs can be securely shared to obtain a second opinion, stored to track

abnormalities over time, used for teaching purposes, or serve as an aid in patient education. In the FOTO-ED study, the use of fundus photography did not decrease expediency of evaluation or treatment in the ED. The camera was found to be easy to use, and technicians were trained in only minutes. [6]

Obvious disadvantages of tabletop nonmydriatic fundus photography include device cost and the need for the patient to be in a location with the device with the ability to sit upright with their head still and follow simple commands, making it inaccessible for many critical care patients. [7\*\*]

#### Handheld Nonmydriatic Fundus Photography

As technology advances, medical devices have become smaller, lighter, and easier to use, and nonmydriatic fundus photography is no exception. Handheld nonmydriatic fundus cameras have recently become commercially available and provide many of the advantages of tabletop cameras while allowing for use of the device in poorly cooperative patients, as in critical care settings. In one Neurology residency, the handheld nonmydriatic fundus camera was heralded among residents for its portability, ease-of-use, and its association with less patient discomfort due to less of a requirement for light during the examination. [7\*\*] In one retrospective study, masked neuro-ophthalmologists were able to identify optic disc edema with greater than 70% sensitivity and 80% specificity through evaluation of optic disc photographs taken with a handheld nonmydriatic camera. [8\*] These handheld cameras have many of the advantages of portable direct ophthalmoscopy, while providing a larger field of view. The captured images can also be transmitted remotely, allowing interpretation by

specialists that may not otherwise be immediately available to examine the patient.

Disadvantages of handheld nonmydriatic fundus cameras include cost and inferior image quality in comparison with a tabletop device. Interestingly, however, one group showed that a handheld nonmydriatic fundus camera could be assembled from just a few, easily obtainable components; therefore, cost may become a less significant barrier in the near future. [9\*] Further research is needed to examine the impact of handheld nonmydriatic fundus photography on the frequency of fundus examination by clinicians, the accuracy of interpretation of abnormal findings, and patient outcomes.

#### Smartphone-based Fundus Photography

The widespread use of smartphone devices with built-in cameras has made them a ready target for inclusion among devices performing ocular funduscopy. Attachments that fit directly onto a smartphone device offer a particular advantage in availability, affordability, and portability. While various attachments are available, image quality has been a concern for some devices, and it can require considerable practice to use the devices effectively, not unlike direct ophthalmoscopy. [7\*\*] Smartphone-based fundus photography has shown some promise in detecting diabetic retinopathy when photographs were analyzed with artificial intelligence software. Using smartphone-based imaging, software was able to detect diabetic retinopathy with a sensitivity of greater than 90% and specificity of greater than 80%. [10\*]

See Table 1 for a review of some of the advantages and disadvantages of various devices used for ocular funduscopy. [1, 2\*, 4\*, 7\*\*]

## **Contribution of Funduscopy to Neurologic Research**

The prevalence of stroke and dementia increases with age and will predictably present an increasing public health problem as life expectancy also increases. A crucial step in addressing the growing health problems of stroke and dementia is identifying who is at risk as early as possible, when therapeutic targets may have the most potential to halt or even reverse disease progression. Novel, noninvasive screening tools are needed. Changes in retinal vascular caliber can be detected via fundus photography in an outpatient setting and may have the potential to identify patients with preclinical cognitive impairment. Research has shown that retinal microvascular findings may provide a window to similar changes in cerebral microvasculature, which could facilitate an earlier diagnosis of cerebrovascular disease, and provide a relatively inexpensive and non-invasive marker for disease progression.

### Cerebrovascular disease

The neurosensory retina and cerebrum are both parts of the nervous system and similarly vulnerable to systemic disease. As early as the 1940s, post-mortem histopathological evidence showed similarities between cerebrovascular disease in the basal ganglia and pons and fibrinoid degeneration in the retina. In current practice, magnetic resonance imaging can show small vessel disease, but fundus examination via retinal photography may decrease future dependence on more expensive neuroimaging studies. Retinopathy has been correlated with stroke incidence, but the mere presence of retinopathy is too non-specific to be useful in predicting stroke in individual patients. It remains to be seen whether earlier, reliable detection of more precise retinal changes can help facilitate a meaningful reduction in stroke incidence. [11\*\*]



In one study using nonmydriatic fundus photography, patients with recent minor strokes or transient ischemic attacks (TIA) were found to have a higher prevalence of optic nerve atrophy than healthy controls across nearly all age groups. Arteriovenous nicking was also found to be significantly more prevalent in individuals with a recent stroke.

[12\*] Remote transmission of ocular fundus photographs and their use in telemedicine also raises the possibility of its use as a novel screening tool for cerebrovascular disease in patients that may not otherwise have easy or reliable access to specialty medical care.

### Cognitive Impairment

Small vessel disease is associated with dementia. Worsened objective cognitive performance using neuropsychological testing has been correlated to changes in the retinal arteriovenous network such as arteriolar narrowing and venular dilation.

Decreased density of retinal microvasculature has also been shown to correlate to a similar loss of intracranial vascular abundance in patients with Alzheimer's disease.

[11\*\*] However, the ability of clinicians to reliably detect subtle changes in the retinal vasculature with photographs is unknown. If subtle retinal changes can be reliably detected using standardized protocols, further research will be needed to determine if a preclinical cerebrovascular disease state can be identified and treated.

One large prospective study (N=12317) found an association between retinopathy and acceleration of cognitive decline. Data from the Atherosclerosis Risk in Communities Study showed that retinopathy detected via nonmydriatic fundus photography was associated with accelerated rates of 20-year cognitive decline. The degree of retinopathy

was graded, and moderate to severe retinopathy was found in 2% of participants, 83% of which also had diabetes mellitus. Unfortunately, greater than 50% of subjects died prior to study completion or were lost to follow-up. Patients who did not complete the study were more likely to have had retinopathy (unspecified severity) or poorer cognitive performance. [13\*]

Other studies have been less conclusive in finding a correlation between cognitive decline and ocular fundus examination findings. In meta-analysis of 10 studies, most using nonmydriatic fundus cameras, the clearest association was a decreased fractal dimension—the complexity of vascular branching—with Alzheimer’s dementia. [14]

Identification of retinal changes may aid in the treatment of systemic diseases such as diabetes and hypertension before clinical signs of cognitive impairment exist. Type-1 diabetes has been correlated with a higher prevalence of cognitive impairment in age-matched controls. One study followed persons with type-1 diabetes with fundus photographs over an average of 17.56 years and neurocognitive testing, and found an association between progressive retinal arteriolar narrowing and clinically-significant cognitive decline. The caliber of vessels was calculated using software rather than an examiner’s eye. [15\*]

Other studies, once adjusted for potentially confounding risk factors, have found no statistically significant correlation between dementia and retinal caliber. Furthermore, no link between macular degeneration and cognitive impairment has been found. [14]

The factors contributing to both cognitive impairment and retinopathy are multifactorial,

and differences in the relative contribution of various risk factors may play a role in the inconsistency of results in across studies.

### Other Neurologic Conditions

The ocular fundus examination is useful for neurologists in both emergent and non-emergent settings. Identification of optic nerve head edema in the emergency department has the potential to save vision and avoid unnecessary delays in treatment by prompting further evaluation for and treatment of conditions such as venous sinus thrombosis and intracranial hypertension.

A cross-sectional study using FOTO-ED study data examined patients presenting to the ED with optic nerve head edema (ONHE). These data showed that 37 of the 1408 (2.6%) patients included in the study were found to have ONHE in at least one eye. The most common associated chief complaints included headache and vision loss. Patients in whom ONHE was discovered were more likely to be admitted to the hospital and to receive additional neuroimaging. As headache is the most common neurologic complaint in the emergency department, physicians have a real opportunity to improve patient care when ocular findings such as ONHE are recognized early. [16\*\*]

### **Future Directions**

Research has shown that there is a relationship between ocular fundus findings such as retinopathy and cognitive impairment and cerebrovascular disease. While these conditions share common risk factors such as hypertension, diabetes mellitus, cardiovascular disease, and tobacco use, further research is needed to determine how

ocular fundus findings may inform the care of patients with these conditions beyond the current standard of care. The association between retinal changes and dementia is complex, and weakens when controlling for confounding variables. [13\*] Nevertheless, further research into the association between ocular fundus findings and neurologic conditions such as cognitive impairment and cerebrovascular disease has the potential to offer earlier, noninvasive diagnosis of these conditions, with exciting possibilities that could introduce a novel therapeutic window in which intervention may slow, halt, or even reverse disease progression.

In the clinic, novel technologies that are being applied to the ocular fundus examination have the potential for an immediate impact in patient care. The rapid advancement of nonmydriatic digital fundus photography technology forecasts a trend toward smaller devices that are easier to use, cost less, and provide better image quality than their predecessors.

## **Conclusion**

The physical examination in neurology remains essential to the optimal diagnosis and management of neurologic disease. While neuroimaging technology such as magnetic resonance imaging (MRI) may assist in localizing a lesion, MRI access is limited in some areas and neuroimaging can be normal in patients with serious nervous system pathology. Evaluation of the ocular fundus, regardless of the method, is a vital part of patient-centered, individualized clinical care. The various devices available for ocular fundus examination are tools to facilitate this critical subset of the neurologic examination. Identification of retinal hemorrhages, cotton wool spots, optic disc edema,

and optic nerve atrophy help to deliver optimal neurologic patient care and funduscopy has the potential to assist in addressing the global health burden of cognitive impairment and cerebrovascular disease. Examination of the ocular fundus, regardless of the method, must therefore be encouraged by not only neurologists but by all medical professionals.

**Key Points:**

- The ocular fundus examination remains a vital part of the neurologic examination, though it is often omitted by neurologists and other non-ophthalmologists.
- Technological advancements in funduscopy have introduced new devices that perform funduscopy while avoiding some of the technical barriers inherent in the direct ophthalmoscope.
- Research suggests that fundus examination via photography can aid in the detection of cognitive impairment and cerebrovascular disease.
- Funduscopy has the potential to improve vision and neurologic outcomes by identifying signs of significant life or vision-threatening conditions.

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This important cross-sectional analysis of data from the FOTO-ED study found that 2.6% of patients that met the study's inclusion criteria (chief complaint of headache, vision loss, neurologic deficit, or elevated blood pressure) had optic nerve head edema, which influenced the patient's final diagnosis and disposition from the ED.

### **Figure legend:**

Figure 1: Actual example of a color fundus photograph of the right eye obtained through an undilated pupil using a tabletop nonmydriatic fundus camera. (Original)