

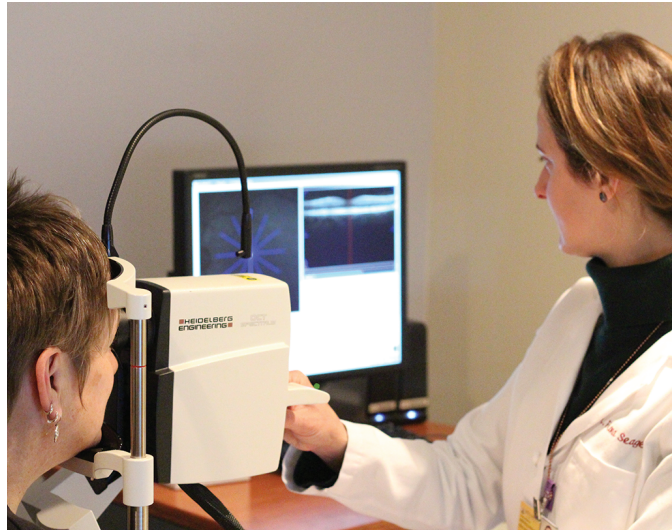


Painless OCT Scans Offer Valuable Insights

New methods to visualize the layers inside the eye are revolutionizing how Wilmer doctors diagnose both open angle and angle closure glaucoma initially, and how they tell if patients are continuing to maintain their vision. Patients who have been with Wilmer's Glaucoma Center for several years may remember the bright "flashbulb" photographs that were taken of the optic nerve in the past. While these gave a good idea of how much glaucoma had damaged the eye, they did not provide quantitative information about patient status, and they were uncomfortably bright—leaving vision flashed out for several minutes.

Investigators from MIT and Tufts University developed an improved method for imaging that uses much dimmer lights and processes the information somewhat like a CT scan used by radiologists. Not only is it perfectly safe, it is comfortable and provides pictures and numerical data immediately for Wilmer's glaucoma doctors. This technique, called spectral domain optical coherence tomography (SDOCT), has been in use in Wilmer's Glaucoma Center for more than five years. Its latest versions are now offered in two of the center's exam suites and are providing superior data with which to judge patient safety.

Glaucoma Center investigators are conducting two unique sets of research using the SDOCT instruments made by two companies. In one project, researchers are



Using an innovative method of imaging known as spectral domain optical coherence tomography (SDOCT), Wilmer researchers are gaining new information that will aid in more accurately diagnosing and treating glaucoma.

taking images and matching them with the visual field test data from the same patients at the 60 or so tiny places inside the eye that are tested in both machines. The hope: By combining the data from the two approaches, one showing the eye's structure and one showing its function, doctors will be able to provide a better diagnostic assessment of each eye's glaucoma process.

In another SDOCT-based project, nearly 100 Wilmer patients participated by drinking two standard

bottles of water as quickly as they could. This so-called "water-drinking test" has been known for 50 years to cause eye pressure to increase over the hour after rapid water intake. Wilmer researchers confirmed that pressure goes up five or more points by 30 minutes after chugging. The take-home lesson: Drink all the fluids you wish, but do so slowly sip by sip, not all at once.

This research project was intended to show why the pressure goes up, and in fact by imaging the layer of the eye called the choroid with SDOCT, researchers showed that, in general, it is not swelling inside this layer that causes the pressure rise, but rather narrowing of blood vessels that carry fluid from the eye back to the heart.

Perhaps most importantly, researchers had suspected that people with angle closure glaucoma would be different and their choroid would swell after water drinking. This proved to be true and will next be used as a diagnostic test in another form to decide which angle closure patients need treatment with a laser and which do not.

Identifying a New Drug Target in Glaucoma

Blindness in glaucoma is caused by the death of retinal ganglion cells (RGCs), the nerve cells inside the retina that transmit visual images from the eye to the brain. RGCs transmit visual information along a specialized cellular structure called an axon—it's a long, delicate, wire-like extension that travels in the optic nerve, much like the individual copper wires in an electrical cable. Unfortunately, if the axon is damaged, as might happen when the eye pressure is elevated, an “injury signal” is generated that instructs the RGC to die by “committing suicide.” And as a result, since the connection to the brain is lost, vision loss ensues.

An appealing therapeutic strategy for glaucoma is to develop drugs that would specifically interfere with the axonal injury signal, and thereby promote the survival and health of RGCs. However, the development of such “neuroprotective” drugs (drugs that prevent or reduce RGC death following injury) is difficult because the molecular mechanisms that signal optic nerve injury are not well understood. Now Dr. Donald Zack and Dr.

Derek Welsbie have developed a novel and powerful approach to identifying and characterizing the genes that mediate optic nerve injury.

Their new method, which uses robotic microscopes and RGCs grown in culture, has allowed them to screen through hundreds of genes in order to identify those that are important components of the injury signal. They have recently identified one, known as DLK, which seems to be critical for RGC cell death. Indeed, not only are DLK-deficient RGCs highly resistant to cell death in response to optic nerve injury, but in many regards they behave as if they have never been injured.

Perhaps even more exciting, Dr. Zack, Dr. Welsbie, and Dr. Harry Quigley have shown that drugs that target DLK can protect RGCs in animal models of human glaucoma. The labs are currently working to optimize these neuroprotective molecules, with the goal of creating a new class of glaucoma drugs that will aid in doctors' ability to help patients maintain and enjoy their vision.

A Familial Link to Angle Closure Glaucoma

The simplest and easiest “cure” for glaucoma is to make sure it never happens in the first place. A preventive approach is particularly effective when dealing with a form of glaucoma known as “angle closure.” Angle closure glaucoma is less common than open angle glaucoma (the most common form), but causes nearly half of the blindness due to glaucoma worldwide. The good news: Blindness from angle closure glaucoma is unnecessary since a safe, simple, office-based laser procedure can prevent the disease with near certainty—assuming the procedure is done at an early stage of the disease.

Unfortunately, screening everyone for angle closure glaucoma is not practical or cost effective. So how do physicians know which individuals to screen? Wilmer's Dr. Pradeep Ramulu has demonstrated a highly effective approach: screening family members. In collaboration with the Aravind Eye Institute in India, he evaluated 400 pairs of siblings for angle closure glaucoma. Brothers or sisters of angle closure patients had a nearly 40 percent chance of having angle closure themselves—more than 15 times the chance of a sibling of someone without angle closure.



Screening is vital for siblings of angle closure glaucoma patients, concludes Dr. Pradeep Ramulu, since they have a significantly increased risk of angle disclosure themselves.

“So if you have angle closure glaucoma, make sure your brothers, sisters, and children are checked for the disease,” says Ramulu. “Chances are high that your words can help them save their sight.”

Networking to Improve Treatment

By Michael V. Boland

The National Eye Institute is currently not funding any large-scale clinical trials related to glaucoma. This situation is unfortunate because such trials conducted over the past two decades have shaped our approach to glaucoma treatment today. There are likely many reasons for the current lack of large clinical studies but one of them is almost certainly the very high cost of establishing and maintaining the infrastructure needed to carry out such studies. In the traditional model, these costs are borne each time a new study is undertaken as the “coordinating center,” for each study is typically housed at a new institution. This approach is inherently inefficient and results in even less of the already limited federal funds for glaucoma research being available for actually learning new things about the disease and its management.

To make glaucoma clinical research more efficient and lower the barriers to initiating new studies, Dr. David Friedman, Dr. Henry Jampel, and I have submitted a proposal to the National Eye Institute to support the Glaucoma Research Network (GRN). It is worth noting that the preliminary data used to support the

application were only possible because of the generous support of grateful patients and their families. The GRN will include the infrastructure needed to carry out clinical studies of glaucoma, including Web-based data collection, data storage, and administrative support for operational, financial, and regulatory issues. The long history of the Wilmer Glaucoma Center of Excellence in both coordinating and participating in clinical studies makes it the perfect place to house this new approach to research.

Once established, the GRN will make it much easier for other investigators to propose new clinical studies while focusing on important scientific questions, rather than having to devote considerable effort to administrative issues. The other important change made possible by a research network like the GRN is that patients can then be recruited from any practice that wants to participate in research. This degree of collaboration within the glaucoma community not only means that the final results of the studies will be more applicable to glaucoma patients across the country, but that more glaucoma specialists will be able to truly collaborate on finding answers to the most important questions in our field.

Gaining a Better Angle on Glaucoma

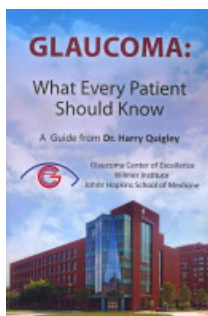
About 1 in 5 people in the United States who have glaucoma suffer from angle closure glaucoma, according to Wilmer’s Dr. David Friedman. Yet, he notes, when making a diagnosis, “Doctors are not routinely looking to see if the angle is closed.”

He and his colleagues recently probed the Medicare database to better understand the care provided to people with glaucoma. They documented that clinicians in some parts of the country diagnose glaucoma much more frequently than others, and that diagnosed angle closure glaucoma is rare. Failure to detect angle closure, Friedman notes, leads to inappropriate treatment. “At Wilmer, we are studying new technologies that might improve detection of angle closure,” he says.

Friedman and his colleagues are also analyzing how much it costs Medicare to treat glaucoma and assessing the drivers of that cost. “We will identify where savings are possible and will highlight variations in treatment practices. These analyses will also provide estimates of the future growth in expenses if we do not change how we take care of persons with glaucoma.”

“This research,” Friedman predicts, “will spur greater interest in developing new models of care.”

Glaucoma Book Goes Viral



Glaucoma: What Every Patient Should Know, written by Dr. Harry Quigley and collaborators from the Glaucoma Center of Excellence, has been available in book form and as a Kindle version for more than a year. It is approaching 1,000 copies sold and has received 5-star reviews on Amazon.com. It can be ordered online at www.hopkinsmedicine.org/wilmer/gce/book.html. Royalties from the book are donated to glaucoma research being carried out at the Glaucoma Center, so those buying it are not only learning about glaucoma, they are making a charitable donation.

Calculating the Right Time to Start Treatment

Many patients in the Glaucoma Center of Excellence are not being treated for glaucoma by lowering the eye pressure, but are simply being monitored without treatment. Most of these patients have either elevated eye pressure without any damage to the optic nerve (ocular hypertension) or have optic nerves that are suspicious for possible glaucoma damage. A question that arises in these situations is, “When does an eye that is under observation become one that should have a lower eye pressure?”

Clearly, if the optic nerve is determined to be worsening, the doctor will start treatment to lower the eye pressure. However, if the optic nerve is unchanged, but the eye pressure seems to be increasing, when is it time to start treatment? Dr. Henry Jampel and Dr. Michael Boland have used data from the Ocular Hypertension Treatment Study (OHTS) to help answer this question. The OHTS was a highly influential government-funded multicenter trial, in which many patients in the Glaucoma Center of Excellence participated. Drs. Boland and Jampel have modified the “risk calculator” from OHTS to help determine when it is time to start treatment.

To use this new on-line calendar (depicted in figure) the doctor and patient would first determine what level of risk of early glaucoma damage over the next five years would be acceptable (for example, a person who really doesn't want to use eye drops might accept a 50 percent, five-year risk, while a person who wanted to do everything to prevent any vision loss might only accept a 2 percent risk). The doctor would then enter the patient's

Ophthalmologic Informatics Lab

This calculator provides an estimate of the IOP that would result in a particular level of risk for developing glaucoma. Please enter values for your patient's age, pattern standard deviation, central corneal thickness, vertical cup-disc ratio, and for your desired risk of conversion to glaucoma in 5 years.

Age	<input type="text" value="67"/>	years (40-90)
Pattern Standard Deviation	<input type="text" value="2.0"/>	dB (0.50-4.00)
Central Corneal Thickness	<input type="text" value="562"/>	microns (450-700)
Vertical Cup to Disc	<input type="text" value="0.6"/>	0 to 0.9
Threshold for 5-year risk of progression	<input type="text" value="10"/>	Percent

Estimated threshold to initiate treatment mmHg

By using this risk calculator developed by Dr. Henry Jampel and Dr. Michael Boland, doctors will be able to provide highly individualized plans of care for patients being monitored for glaucoma.

“tolerance of risk,” along with specific details about the patient's eyes into the calculator. The calculator will then provide an estimate of the eye pressure at which the benefit of starting treatment outweighs the risks, cost, and inconvenience.

“We think that this type of individualized medicine will be good for our patients, and we plan to share the calculator via an open access website with our colleagues across the world,” say Jampel and Boland.

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CureGlaucoma is published once a year by the Wilmer Eye Institute at Johns Hopkins Hospital.