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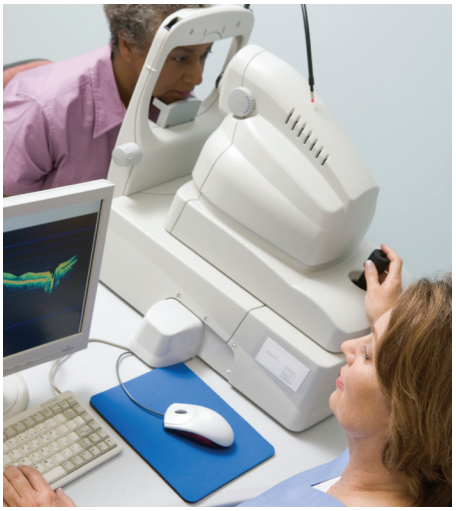
CLINICAL UPDATE

New Approach Improves Ability to Predict Which Glaucoma Patients Need Aggressive Treatment



One of the major challenges in the field of glaucoma has been reliably separating the patients who will progress rapidly—and thus need immediate and aggressive treatment—from those that will have a slow progression and may never lose vision. "We overtreat some patients and undertreat others," says Joseph Caprioli, MD, David May II Professor of Ophthalmology and chief of the Stein Eye Institute's Glaucoma Division. "This is not a reflection of our competence, but of our limitations in identifying which patients are most likely to lose vision and how quickly."

The problem with conventional approaches to predicting glaucoma progression, Dr. Caprioli says, is that they take the entire visual field into account—but, particularly in its early stages, glaucoma tends to inflict localized damage. "The nature of glaucoma damage is non-uniform progression," Dr. Caprioli explains. "When you take global measures, looking at the average of all visual fields, you miss out on the regional change." Adding to the imperative of focusing locally rather than globally, Dr. Caprioli notes, is the fact that the portion of the visual field that is affected is likely to decline at a much faster rate than parts of the field that have been relatively spared.

Dr. Caprioli and colleagues have developed a software-based approach designed to take into account these factors. The system analyzes a sequence of visual fields, pinpoints the areas that are progressing the most rapidly, and then uses the data to predict future visual field outcomes if there is no change in treatment. "The key is to divide visual fields into faster-progressing points and slower-progressing points," says Dr. Caprioli. "That enables you to detect the signal from the noise and identify patients who are at the greatest risk of losing vision."

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Discovery that Sagging Eye Syndrome May Indicate Adult-Acquired Strabismus Has Major Clinical Impact

A Stein Eye Institute researcher's discovery that ligament degeneration is a major cause of adult-acquired double vision due to strabismus is having a major clinical impact—from reducing unnecessary neurological testing to pointing the way toward corrective surgery that can eliminate the need for prism glasses in many patients.

"We have shown that it is simple to clinically diagnose strabismus caused by wear and tear on ligaments within the eye socket, and that this form of strabismus is highly associated with drooping eyelids that often require blepharoplasty surgery," says Joseph L. Demer, MD, PhD, Leonard Apt Professor of Pediatric Ophthalmology and chief of the Pediatric Ophthalmology and Strabismus Division. "This means doctors no longer have to feel obliged to order expensive neurological evaluations of these patients, and these patients no

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SteinEye

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Among the problems that Dr. Caprioli's approach addresses is that factors other than glaucoma—such as cataract formation or aging—can also produce deterioration of a visual field, although at a slower rate. Dr. Caprioli has found that the software system separates the effects of glaucoma from these other factors.

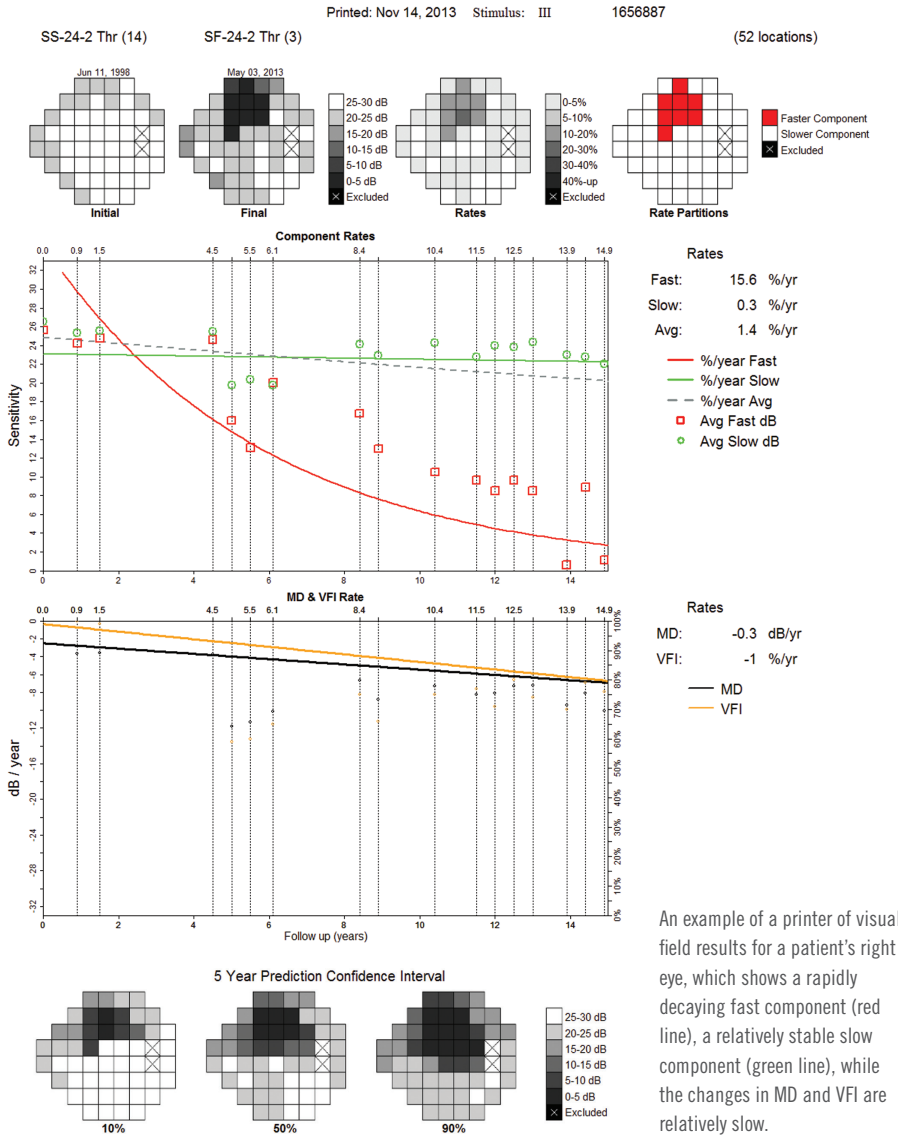
Dr. Caprioli says his system quantifies what experienced glaucoma specialists have intuitively done in clinical exams. "You try to look for an area that might be getting worse, and filter out the other measurements," he says. "But for a practitioner who doesn't do this every day, that qualitative process is much more difficult. This provides them with a tool that is like having an 'expert in a box.'"

Even for an experienced glaucoma specialist, the digital system can improve the ability to sift through the variable fields and accurately identify the most at-risk patients. In employing the approach with his patients, Dr. Caprioli says, he has been surprised at what he has been able to detect that he would have otherwise missed.

Dr. Caprioli's group has conducted multiple studies to validate the system's ability to separate patients who will progress rapidly from those who will progress slowly. The first study, focusing on patients with substantial visual field damage, found that forecasts correlated well with measured outcomes over six or more years of follow-up. Dr. Caprioli and colleagues then conducted a second study involving patients with much less glaucoma damage and found the new system to be equally adept at identifying earlier-stage patients at high risk of rapid progression. "The system is more sensitive than other predictive systems with early glaucoma patients and more specific than other systems with patients who have advanced glaucoma," Dr. Caprioli says.

Dr. Caprioli notes that his group has no proprietary interest in the software it developed and has made the technique available to anyone who wants to use or adapt it. As the system proves its value, he suspects the approach may be incorporated into commercial products. In the meantime, Dr. Caprioli is continuing to conduct research on the system, including using it to identify risk factors for those patients who appear to be getting worse the fastest. His group has also begun exploring other potential models to see if they can improve on the approach.

In an era of growing constraints on health care resources, it is becoming increasingly important to focus glaucoma treatment on patients at the greatest risk of losing vision—making prompt identification of the rapidly progressing patients critical. "It's a matter of applying limited resources appropriately," Dr. Caprioli says. "We want to treat those who really need it and spare patients who are getting worse at such a slow rate that they are likely to live out their lives with perfectly good vision. If we have a handle on the rate of progression and a sense of how much longer the patient is likely to live, we can make a better judgment about how aggressively that patient should be treated, if at all. We need to get the right level of treatment to the right patients at the right time. This approach can improve our ability to do that."



An example of a printer of visual field results for a patient's right eye, which shows a rapidly decaying fast component (red line), a relatively stable slow component (green line), while the changes in MD and VFI are relatively slow.

Sagging Eye Syndrome *continued from cover*

Patients with sagging eye syndrome frequently have blepharoptosis and superior lid sulcus defect, both of which are due to stretching and disinsertion of the levator tendon from the tarsal plate. This connective tissue degeneration mirrors changes in the ligament system supporting the extraocular muscle pulleys.

longer need to hear the alarming news that a stroke or brain tumor may be the cause of their double vision. In addition, we have shown that a simple and relatively painless operation can leave many of these patients free of spectacles."

Starting in 2009, Dr. Demer and an ophthalmology fellow in his lab, Zia Chaudhuri, MD, began a series of studies based on Dr. Demer's suspicion that adult strabismus might be caused by ligament degeneration. Their findings not only confirmed the suspicion, but also showed acute ligament rupture in symptomatic cases of sagging eye syndrome in older patients with strabismus, along with muscle elongation in other cases. Dr. Demer then refined surgical approaches for these cases that have proved effective.

Traditionally, Dr. Demer notes, double vision from sagging eye syndrome has been seen as a red flag for a stroke or other brain disorder, particularly if double vision came on suddenly. "It was previously not appreciated that acute strabismus could be due to a connective-tissue disease," he says. "Now we're quite confident of that."

Moreover, Dr. Demer explains that a good clinical examination, including looking for stretching and sagging of the eyelid tissues, is usually all it takes to make the correct diagnosis. "Instead of having to recommend costly and anxiety-provoking neurological investigations for patients, the eye doctor just looks the patient in the face and within a few seconds either sees these findings or doesn't," Dr. Demer says. "Once you understand the relationships, these are not subtleties."

Dr. Demer has found in studies of cadaver eyes that a particular ligament, called the LR-SR band, tends to weaken with age and will often spontaneously rupture, causing the double vision. His group has shown that symmetrical stretching—and especially rupture—of the LR-SR ligament causes horizontal double vision for distance, but not near, viewing. This problem is common among older drivers—it can be particularly dangerous, for example, if they are driving a car at night and have difficulty detecting whether the car coming toward them is safely on the other side of the dividing line. Dr. Demer's group has also found that asymmetrical stretching or rupture of the LR-SR ligament causes vertical double vision—resulting in often-intolerable depth-perception symptoms that can lead sufferers to close or wear a patch over one eye.

Beyond the anatomical studies, Drs. Demer and Chaudhuri were able to confirm the pathology of sagging eye syndrome thanks to the use of high-resolution MRI scanning of the orbits. Dr. Demer has received continuous funding support from the National Eye Institute for nearly 25 years to improve MRI technology for the eye muscles and surrounding tissues. Through the development of several techniques, Dr. Demer and colleagues have significantly improved the resolution of the scan, enabling them to visualize the ligaments in a way that would be impossible with a conventional MRI, and to correlate their changes with the strabismus that the patients developed.

Because the eye muscles in sagging eye syndrome become elongated, Dr. Demer has found that the surgical dose—the amount of repositioning of the muscle attachments to the eye—must be substantially greater than would be required in treating other forms of strabismus. "To get an appropriate change in the amount of crossing of the eyes, you have to do more surgery on the muscles than you would in muscles of typical length," he explains.

Based on knowledge gained from the biomechanical and anatomical studies his group has performed, Dr. Demer has developed a partial tenotomy surgery for a highly precise vertical alignment of the eyes. "This allows us to consider routinely doing surgery for small amounts of double vision that were previously believed to be untreatable by surgery," he says. In most cases, Dr. Demer notes, the minimally invasive surgery can be performed in an awake patient, under eye drop anesthesia.

For older adults who have previously undergone cataract intraocular lens operations, the surgical treatment of strabismus related to sagging eye syndrome can restore spectacle independence, freeing them from the need for prism glasses. "Surgeons operate on many patients at Stein Eye for cataract and in the process eliminate their near-sightedness, far-sightedness, and astigmatism," Dr. Demer explains. "The only remaining thing keeping these patients from going without glasses is double vision. The surgical techniques we have developed now can eliminate the need for prisms."

Dr. Demer has been sharing his knowledge within the ophthalmology field. His group published a paper in *JAMA Ophthalmology* that included a large series of quantitative MRI scans. Dr. Demer delivered the Leonard Apt Lecture on his findings at the annual meeting of the American Association of Pediatric Ophthalmology and Strabismus last March. "This concept has been well received by the international surgical community," Dr. Demer says. "New surgical techniques are being proposed and tested. This is a development that can benefit a significant number of patients."

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AARP The Magazine ranks Jules Stein Eye Institute as No. 3 in the country for complex eye-care referrals.

Calhoun Vision Light Adjustable Lens Clinical Trial

Kevin M. Miller, MD, is conducting a study to evaluate the safety and effectiveness of the light adjustable lens (LAL) for reducing spherical and astigmatic refractive errors and improving unaided visual acuity following cataract surgery. The study group will receive the LAL and undergo postoperative lens power adjustments using a light delivery device (LDD). The control group will receive a commercially available monofocal intraocular lens. The LAL device and LDD procedure are investigational. For more information, call (310) 206-1634, or e-mail shah@jsei.ucla.edu.

Jack Rootman, MD, Brings His Expertise to the Orbital and Ophthalmic Plastic Surgery Division

The Stein Eye Institute's Orbital Disease Center specializes in minimally invasive interdisciplinary approaches, including UCLA's world-renown interventional radiology service. Jack Rootman, MD, joined the Orbital and Ophthalmic Plastic Surgery Division in September and is participating in patient care activities as a senior consultant. Dr. Rootman brings unparalleled experience in orbital disease and is available to see complex national and international referral patients. For more information, call (310) 206-8250, or e-mail oculoplastics@jsei.ucla.edu.

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