Heralding Change in Glaucoma

Leading Thinkers Explain How Recent Breakthroughs Can Be Put into Practical Use

Proceedings of the Sixth Annual Scientific Meeting of the Optometric Glaucoma Society

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INTRODUCTORY REMARKS

We are excited to bring you the proceedings from the Sixth Annual Meeting of the Optometric Glaucoma Society (OGS), held in Tampa, Florida on October 23, 2007. This year’s meeting honored the many accomplishments of Paul Kaufman, MD. Professor Kaufman discussed how the eye ages, and in particular how aging changes impact upon aqueous outflow. In his Honoree lecture, Dr. Kaufman described changes in glaucoma therapy that may occur in the future. These include the possibility of gene therapy and neuroprotection being avenues that clinicians may have available. Other speakers included Thomas Freddo, OD, PhD, Douglas Anderson, MD, Michael Sinai, PhD, William Swanson, PhD, Richard Parrish, MD and Steven Gedde, MD. The President's lecture was given by David Greenfield, MD and the Travel Award recipient was Subha Venkataraman, BSOPTOM.

The meeting’s first session dealt with Blood Flow and Normal Tension Glaucoma. Dr. Anderson described a process by which optic nerve blood flow may be compromised as well as possible therapeutic avenues. Dr. Greenfield in his talk on Normal Tension Glaucoma, describes a condition felt to be in part due to compromised blood flow and the controversies surrounding its management. The second session dealt with the structural and functional assessment of the eye. Dr. Swanson described the issues behind perimetric testing, and why the concept of a functional reserve may not be valid. Dr. Sinai in his presentation talked about imaging as part of the structural assessment. With the recent introduction of Fourier Domain (Spectral) Optical Coherence Tomography, the future is upon us as these new instruments provide resolution not previously available. And in the last of the morning sessions, Dr. Thom Freddo described recent research exploring the concept of aqueous outflow resistance and how we may have been looking at the wrong place. Dr. Freddo’s hypothesis is that herniations may occur within the collector channels that add resistance to aqueous outflow, leading to elevated intraocular pressure.

The afternoon session included the President’s lecture, given by Dr. David Greenfield. He described a paradigm shift that is occurring within glaucoma diagnosis, and how new instrumentation is leading this charge. The final sessions dealt with the future of glaucoma treatment. Dr. Parrish described where we are going in regards to medical therapy and Dr. Gedde discussed new surgical approaches.

I would like to thank the speakers who took time from their busy schedules to share their wisdom with OGS members and guests. I would especially like to thank John Flanagan, MCOptom, PhD who was the program chair and John McSoley, OD the meeting chair. I would also like to thank Mike Patella, OD who as secretary has worked tirelessly on behalf of the OGS.

The “Proceedings of the Sixth Annual Scientific Meeting of the Optometric Glaucoma Society” were developed by Frank Celia, our medical writer who has the ability to take a difficult subject and distill pages of information into simple, understandable concepts. Finally, I would like to thank Pfizer, Inc. and its team of Karen Fixler, Jill Burdge and Dennis Kowalski for their support of the OGS and in particular, providing an unrestricted grant that allowed us to produce this supplement.

Please visit the OGS website, www.optometricglaucomasociety.org and check out our quarterly e-journal that is published to one’s email account free of charge. I hope you enjoy this supplement and find it useful.

Murray Fingeret, OD
Executive Vice-President, Optometric Glaucoma Society
Editor, Proceedings of the Sixth Annual Scientific Meeting of the Optometric Glaucoma Society
BY SUBHA VENKATARAMAN, BS/OPTOM

As the eye care world learns more about vascular dysregulation and its relationship with glaucoma, there has been a push to investigate what effects anti-glaucoma drugs may or may not have on ocular blood flow. Dorzolamide (Merck) is the medication most often associated with such a benefit. While some studies show dorzolamide increases ocular blood flow, others find it has no vascular effect. Our team at the University of Waterloo sought to shed light on this issue, and at the same time develop a more in-depth way of looking at vascular dynamics in the eye.

Most studies in this field confine their assessment of glaucoma drugs to measuring homeostatic blood flow; that is, how much blood makes it to the retina and ocular nerve head. A potentially more robust indicator of vascular function is vascular reactivity, which can be defined as the magnitude of change in any hemodynamic parameter between a baseline measurement and a subsequent response to induced physiological provocation.

In a paper published in 2006, we described a novel method of provoking a physiological response to a hypercapnic stimulus (increased concentration of carbon dioxide in the blood)1, and applying this to the assessment of retinal arteriolar vascular reactivity. This is not as easy as it sounds, since our goal was “pure” isoxic hypercapnia, or an increase in arterial concentration of CO2, without a concomitant change in arterial O2 levels. The difficulty is increasing CO2 causes variable hyperventilation, which disturbs arterial oxygen saturation. But we appear to have succeeded, and this method produced a significant and measurable increase in retinal arteriolar diameter, blood velocity and blood flow in young, healthy patients.

So we then turned our attention to investigating how isoxic hypercapnia might impact retinal arteriolar and ocular nerve head (ONH) vascular reactivity in untreated POAG patients and those with progressive POAG, measured against age-matched controls. Additionally, we looked at the effect of a two-week regimen of dorzolamide 2% in patients in the untreated glaucoma group.

Along with 17 controls, 9 patients with untreated glaucoma and 17 patients with progressing glaucoma (defined as a recent optic disc hemorrhage) underwent study. We used the Canon Laser Blood Flowmeter to measure vascular reactivity.

Isoxic hypercapnia caused mean retinal arteriolar diameter to increase in all the groups, but significantly more so in the control group. The same was true of mean arteriolar blood velocity and blood flow. The magnitude of change in the retinal arteriolar vascular reactivity was smallest in patients with progressing glaucoma.

After treatment with dorzolamide, the arteriolar vascular reactivity in patients with untreated glaucoma demonstrated an 18 percent increase in blood velocity and a 26 percent increase in blood flow above baseline measurements.

Though the improvements with dorzolamide might look impressive, they can hardly be viewed as conclusive, since the increased vascular reactivity may simply be a side effect of drug’s main purpose: lowered intraocular pressure.

Still, these results do add to the clinical understanding of the drug, and one hopes future research will benefit from this new methodology.

Reference:

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More Evidence of Ischemia’s Central Role in Glaucoma

Blood flow is challenged by high IOP, but failure of autoregulation to overcome the challenge may be needed to produce glaucomatous nerve damage.

BY DOUGLAS R. ANDERSON, MD

Overwhelming evidence indicates high intracocular pressure contributes to the development of glaucoma. For example, elevated IOP correlates with greater prevalence of open angle glaucoma (OAG). If IOP rises secondary to trauma, uveitis, angle blockage, etc., the optic nerve head (ONH) sustains damage. When we raise intracocular pressure in animals, they get glaucoma. All this is beyond dispute.

And yet another factor (or factors) must be at work here. Only a small portion of eyes with abnormal IOP develop glaucoma. Depending on the degree of elevation, perhaps as many as 80 percent of ocular hypertensives go their whole lives without developing nerve damage, or at least enough damage to be of consequence. I have followed patients with pressures in the 40s mmHg for years whose visual fields never changed a bit. Then there is normal tension glaucoma to consider. Thirty percent of all glaucoma patients show no abnormalities in IOP, yet their optic nerves collapse, deteriorate and cup just like patients with high pressures. The unavoidable conclusion is that elevated IOP works in concert with something else, something likely even more integral than increased pressure.

In the past, we were taught that any elevation of IOP will reduce blood flow to the optic nerve head. This idea has been around for years, and I am sure many practitioners still believe it to be a universal consequence of elevated pressure. On paper it makes sense. If pressure in the vein that exits the eye were not at least slightly higher than the intraocular pressure, the vein would collapse. This extra pressure should come at the expense of pressure levels in the supporting arterial venous system, thus inducing ischemia in those areas. But, in fact, among normal, healthy patients, something called “autoregulation” prevents this.

Autoregulation alters blood flow by a mechanical or chemical physiologic process that changes the tone of the blood vessel wall, thereby changing resistance to flow. Because the term autoregulation is not well defined, it is important to note the process discussed here is entirely localized (local conditions influence local blood flow through local mecha-
nisms), and occurs independently from the regulation of blood flow in response to systemic conditions. It is not autonomic regional or whole body neuronal control, nor is it hormonal control. Autoregulation, as it is discussed here, occurs independently of such well known regulators.

Autoregulation responses vary from person to person. A few years ago I was involved in a study that measured autoregulation of the ONH in 10 healthy subjects. In eight, the autoregulation response was sufficient to maintain circulation up to intraocular pressures of about 40 mmHg, but in two subjects' blood flow began to suffer at 20 mmHg. One cannot help but observe this is the same percentage of ocular hypertensives that go on to develop glaucoma.

This led to our desire to better understand autoregulation in the ONH. But here things get trickier, because most vascular physiologists believe the mechanisms of autoregulation are confined to the pre-capillary arterioles, and for the most part, the ONH is arteriole free. A few feeding arterioles project into the optic nerve tissue, but capillaries are the predominant vessels in the ONH. After many years of study, we believe conventional thinking on this score to be erroneous. We postulate that capillaries play an active role in the mechanics of autoregulation.

At the crux of our theory lies a cell type known as a pericyte. Abundant in the retina and ONH, these cells bear a strong resemblance to vascular smooth muscle. They have the same receptors and contractile machinery used by vascular smooth muscle to control arterial tone, and they respond to many of the same stimuli. Pericytes have other functions, such as nutritional ones, but we have concentrated on their potential role in autoregulation.

After developing a method of growing and studying these cells in isolation in culture, we found that pericytes in vitro react in three ways that would facilitate autoregulation inside the eye. First, oxygen tension affects the contractile tone of the pericytes. Oxygen modulates pericyte relaxations induced by 3-morpholino-sydnonimine (SIN-1), which produces nitric oxide. However, in the absence of nitric oxide stimulation, oxygen has no effect on pericyte cells, hypothetically because superoxide associated with higher oxygen levels inactivates nitric oxide and its effect on vessel relaxation.

Secondly, the presence of carbon dioxide affects the contractile tone of pericytes, causing them to relax. Such reactions appear to be mediated by carbon dioxide’s influence on the extracellular pH. When carbon dioxide was introduced in a manner that changed extracellular pH, but kept steady in the extracellular pH, cell relaxations failed to occur. Again, these results reinforced our belief that in vivo pericytes can alter blood flow by responding to local metabolic conditions.

Finally, pericytes relax in the presence of adenosine, a substance known to accumulate under ischemic conditions, when adenosine is not consumed by the synthesis of ATP (adenosine triphosphate). This relaxation is caused through activation of the adenosine A2 receptor.

It is interesting to note that outside factors can influence these processes. For example, we know angiotensin II, a vasoconstrictive peptide, influences the response of pericytes to carbon dioxide. In our study, angiotensin (at concentrations that do not cause vascular constriction) reduced the amount of cell relaxation caused by carbon dioxide and the amount of time the relaxation lasted. However, a 10-minute pretreatment with saralasin, the competitive angiotensin II receptor antagonist, reversed this effect. Thus do we have a specific example of how an autoregulatory response to carbon dioxide might be made inadequate, and a suggestion that therapy aimed at the cause of the reduced regulatory response might be effective.

Glaucoma The Many Challenges of Normal-Tension Glaucoma

BY DAVID S. GREENFIELD, MD

One of the few certainties regarding normal-tension glaucoma (NTG) is the beneficial nature of lowering intraocular pressure. This was demonstrated by the Collaborative Normal-Tension Glaucoma Study (CNTGS), in which 60 percent of patients who did not receive intraocular pressure (IOP) lowering treatment progressed over a five-year period, while only 20 percent of those treated progressed. In this report, I will summarize the results of the CNTGS and identify what we know and don’t know about NTG.

I. The effectiveness of intraocular pressure reduction in the treatment of normal-tension glaucoma

The Collaborative Normal-Tension Glaucoma Study Group (CNTGS)

References:

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provides detailed information regarding the effect of aggressive IOP reduction on the pathogenesis of normal-tension glaucoma. Visual field progression was measured with and without therapeutic intervention for up to 7 years. Funded by the Glaucoma Research Foundation, this comprehensive research initiative has yielded valuable findings regarding the importance of IOP reduction for prevention of optic nerve damage and visual field progression.

**Study objective**
- To determine the effectiveness of 30% IOP reduction on progression of visual change in normal-tension glaucoma.

**Design**
- 24-site multicenter, prospective study

**Methods**
- One eye per each of 145 subjects with normal-tension glaucoma was randomized either to 30% IOP reduction or no treatment (control)
- Randomization criteria included documented progression of field defects, new disk hemorrhage, or field defects that threatened fixation
- **Treatment for IOP reduction**: medication (excluding beta blockers or alpha-2 adrenal receptor agonists due to concerns of vasoactivity), ALT, or filtration surgery
- **Survival analysis**: Time to visual field progression

**Findings**
- At 5 years, treated patients showed overall survival of 80% compared to 40% in controls (P = .0018)
- The beneficial results of IOP reduction were only found when the impact of cataracts on visual field progression (caused mainly by filtering surgery) were removed
- Therefore, lowering IOP without producing cataracts is desirable

**Clinical Pearls**
- Therapeutic intervention (30% IOP reduction) helped prevent visual field progression. However, one must adjust for the development of cataracts, which occur commonly after filtration surgery, to detect the therapeutic benefit of IOP reduction.
- 30% IOP reduction was achieved in 57% of patients receiving medical therapy with or without ALT, which underscores the importance of conservative therapy. Since beta blockers, alpha-2 agonists, and prostaglandin analogues were not used in the study, currently available medical agents may achieve IOP reduction in a greater percentage of patients.
- Approximately 50% of eyes without a history of progression did not progress by 7 years when untreated. However, if progression has been documented in the past, future progression is highly likely, and IOP reduction is recommended.
- Confirmatory visual fields are essential for verifying suspected progression. For both visual function as well as structural tests, it is important to confirm suspected progression.
- Disc hemorrhage is a strong, negative prognostic sign; other risk factors include migraine and female gender.

**II. Ancillary Diagnostic Testing**

**A. Neuroimaging**
- Anecdotal reports of occult intracranial mass lesions exist that simulate NTG. Stewart and Reid reported compressive intracranial lesions in 2 of 53 patients (3.8%) referred for evaluation of NTG. In another study, 8 of 141 subjects (5.7%) suspected of having glaucoma by optic nerve screening were found to have intracranial lesions. In a series of glaucoma patients who underwent neuroimaging between 1985 and 1995, none were found to have evidence of anterior visual pathway compression. We recommend neuroimaging in atypical patients characterized by young age, reduced central vision, vertically aligned visual field defects, and eyes with optic disc atrophy exceeding cupping.

**B. Carotid Blood Flow and Laboratory Evaluation**
- Referral to a vascular laboratory to exclude clinically significant carotid occlusive disease has been suggested in the evaluation of patients with NTG. Laboratory testing has been proposed to rule out anemia, hyperviscosity syndromes, diabetes, hyperlipidemia or cranial arteritis. Pilot data from 20 patients with NTG and POAG who underwent carotid Doppler ultrasonography, serum laboratory testing (erythrocyte sedimentation rate, complete blood count, VDRL, FTA-ABS) and scanning laser Doppler flowmetry demonstrated no differences among these two groups of patients. Sedimentation rate should be performed in older patients with a history of abrupt visual loss or other symptoms suggestive of cranial arteritis; carotid studies are warranted in patients with symptoms of transient visual loss or ocular signs of embolic phenomenon or ocular ischemia.

**III. Intraocular Pressure and Visual Field Asymmetry in NTG**

Cartwright and Anderson performed a retrospective review of 14 patients with untreated NTG and asymmetric IOP (≥1 mmHg). A masked assessment of disc photos & visual fields showed damage was worse in the eye with greater IOP. Crichton et al found that 13 of 47 (28%) patients with asymmetric visual field loss had a corresponding asymmetry in IOP. Other retrospective studies have found that 22% to 66% patients with untreated LPG demonstrate a significant correlation between asymmetric visual field loss and mean IOP. In contrast, prospective data from 190 subjects enrolled in LoGTS demonstrates no relationship between baseline IOP asymmetry and VF asymmetry suggesting an unclear pathogenic relationship between IOP and NTG.

**IV. Conclusions**
- In summary, younger age, reduced central vision, abnormal color vision, optic disc pallor disproportionate to the degree of cupping, and vertically aligned visual field defects represent risk factors for compression intracranial lesions. There is insufficient evidence to suggest that patients with NTG should undergo routine neurodiagnostic, vascular, or serum laboratory examination. A comprehensive history and ocular examination will assist the clinician in targeting persons in whom such testing is warranted.
The Future of Perimetry
Low spatial frequencies should reduce test-retest variability.

BY WILLIAM H. SWANSON, PH.D.

Introduced late last year, the new Heidelberg Edge Perimeter—in addition to its many other advantages—offers an open software platform. This provides unprecedented freedom of choice in the stimuli we are able to present patients. With so wide a range of options now available, the question naturally arises: what do we want from perimetry and by what means can we best achieve it?

Having studied this matter for a number of years, I think it can be narrowed down to three basic needs. First, we want low between-subject variability, which will aid in determining who is abnormal. To achieve this, the derogatory effects of blur, pupil size, and the aging lens must be minimized.

Second, when establishing visual field defects, we want low variability between tests and retests. Excessive variability in a visual field defect once it is determined remains one of the principal challenges of long-term glaucoma management.

And finally, the Holy Grail of functional testing, we want a superior ability to detect ganglion cell damage. In the past, there has been great concern that conventional perimetry is not up to this task.

So, how to accomplish these goals? Avoiding blur is fairly straightforward: use a low spatial frequency, such as seen in Frequency Doubling Technology (FDT) perimetry. A 2007 study comparing between-subject (uncorrected ametropes and age-matched emmetropes) and within-subject FDT results found no differences in FDT parameters (mean deviation, pattern standard deviation, central threshold, and mean sensitivity) or in the contrast sensitivity estimates between the central and peripheral test locations.1 However, the downside is that FDT produces a high normal between-subject variability, partly because it uses 20 decibels per log unit rather than 10 decibels per log unit used in conventional perimetry.

Frequency Doubling Technology perimetry also employs a high temporal frequency. In all ages of subjects, there is a wide range in pupil sizes, anywhere from 3–7 mm. Variations in pupil size affect sensitivity, and this factor has more impact on FDT than Contrast Sensitivity Perimetry (CSP), though not because of the above-mentioned 20 decibels per log unit. Variations in pupil size have less effect on CSP because CSP employs a slower temporal presentation. The same holds true of the aging lens. Thus, low temporal and spatial frequencies should reduce between-subject variability.

Defect variability in visual field results presents a major challenge. A -6 dB loss may test normal at the subsequent visual field test, and on the third test it could shoot up to -30 dB. Unpublished data have shown that low spatial frequencies reduce variability in defects for both high (FDT) and low (CSP) temporal frequencies. Low spatial frequencies ought to solve many of our variability problems.

When discussing how to better assess ganglion cell loss through visual field results, the glaucoma world has labored under the false belief that a significant amount of ganglion cell loss precedes damage becoming detectable by visual fields. The threshold was thought to be around 50 percent of ganglion cell loss. In other words, it was once believed a patient could lose 40 percent of his or her ganglion cells and still not demonstrate visual field defects.

More recent data suggest this is not the case, that noise produced by the differences in measuring structure and function skewed these conclusions. The problem is we measure visual field loss on a logarithmic scale, and structural defects on a linear one. This apples-to-oranges dynamic means the relationship between the measurements is curvilinear, not linear. When researchers corrected for this artifact, they found that in many cases perimetry loss occurs prior to observable structural defects—the exact opposite of conventional wisdom. A major take-home message of this finding is that perimetry as a diagnostic tool has more clinical value than once thought.

In other words, we are getting good data from perimetry; we just need to analyze it better. My suggestion: instead of performing regression analysis on perimetry data, use Bland-Altman analysis, a widely excepted statistical method for allowing clinicians to compare two different measuring techniques. We have demonstrated this approach

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References

Heidelberg Edge Perimeter (HEP)
in several recent studies.²⁻⁴

In summary, FDT and CSP have shown the value of using sinu-
soids on monitors instead of circles on a dome. And it is probably a
good idea to use lower temporal frequencies than those provided by
FDT. Such improvements should get us one step closer to finding
those very small visual field changes so vital in managing and diag-
nosing glaucoma.

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The Future of Structural Imaging
What advances lie ahead for imaging devices?

BY MICHAEL J. SINAI, PH.D.

Assessing structure via computer-based retinal imaging devices has
become an indispensable tool in glaucoma management and diagnosis.
Studies show imaging results have a high positive- and negative-predict-
itive power for detecting glaucoma, and images compare favorably to
high-quality stereo-photographs. The World Glaucoma Association
(WGA) recommends use of scanning laser imaging in routine examina-
tions, and pre-perimetric glaucoma diagnosis based on structural im-
ages alone is now common. Not only does imaging augment clinical
examinations, it also plays a vital research function by shedding light on
disease pathogenesis itself.

For many years, a trio of technologies has dominated this field: 1.)
scanning laser polarimetry (GDx VCC), which measures light retardation
caused by birefringence of the retinal nerve fiber layer (RNFL) structure;
2.) confocal scanning laser ophthalmoscopy (CSLO), usually known as
HRT, which creates three-dimensional images based on reflected light;
3.) optical coherence tomography (OCT), which provides cross-sectional
views of the retina, retinal nerve fiber layer and optic nerve based on the
echo time delay of back-scattered light.

Each possesses strengths and weaknesses. Scanning laser po-
larimetry’s major contribution is providing RNFL thickness information,
an important indicator of early glaucoma. It also works from a large data
base, is easy to use and interpret, and has software to analyze progres-
sion. On the other hand, interference in the birefringence patterns can
affect the accuracy of the results in some individuals. Also, when the re-
tardation measurement is converted into thickness estimates, the device
assumes a uniform birefringence around the optic nerve head, which
studies show may not exist. Additionally, as valuable as RNFL data is,
other important structures, such as the contours of optic nerve head, are
not evaluated in the analysis. Finally, the data have yet to be made
backwards-compatible with prior versions.

To overcome the atypical pattern of birefringence, a newer version
will be available shortly that includes a software-based algorithm, known
as enhanced corneal compensation (ECC), that corrects for this artifact.
Initial studies prove this version more accurate.

The strengths of the HRT-3 include its accurate depiction of optic
disc morphology; sophisticated progression analysis; a large ethnic-spe-
cific database; backwards compatible data (so the HRT-1 and HRT-2 do
not become obsolete); a corneal microscope attachment; and some reti-
nal capabilities—for example, it can measure retinal edema.

Retinal Layers with RTVue & Histology

On the downside, HRT-3 does not evaluate the RNFL as well as
some other instruments. Then there is the much-discussed necessity of
manual contour line drawing, in my opinion not as burdensome as its
reputation suggests, but I include it for the sake of comprehensiveness.
Finally, the reference plane from which the neuro-retinal rim and cup are
determined, is fixed on the surface height of the temporal side of the op-
tic disc, a height that may change during the course of the disease, po-
tentially distorting results.

A remarkable area of CSLO research involves retinal cell markers.
M. Francesca Cordeiro, MD, at Moorfield’s Eye Hospital and Institute of
Ophthalmology in London, has developed a technique that employs reti-
nal markers to image dying ganglion cells. The technique causes gan-
glion cells to light up as they undergo apoptosis, a process of
programmed cell death. Experiments are still in the early stages, but
such images from humans in vivo could provide enormous research and
disease management benefits.

Strong points of OCT include: cross-sectional imaging (which helps
detect retinal pathologies, where edema, fluid buildup, lesions, etc., of-
ten lurk beneath the surface); calculating RNFL thickness; and providing
high quality—albeit mixed—ethnicity-database comparisons.

On the other hand, OCT pixel numbers are relatively low, which limit
its data somewhat; no progression analysis is offered; RNFL results de-
depend on keeping the scan ring centered on the optic nerve head, and
the slow scan speed permits eye-motion artifacts; and finally the optic
disc measurements are not always reproducible.

The latest advance in OCT technology is Fourier domain OCT, also
known as Spectral domain OCT. Mine is one of seven companies cur-
rently offering this type of imaging, which seeks to address some basic
weaknesses in previous instruments. Resolution and speed have been
greatly improved, affording more detailed images, increased data collec-
tion and diminished eye-motion artifacts.

Theses images can provide extremely comprehensive layer-by-layer
assessment, not only RNFL analysis but cup and rim information and di-
rect ganglion cell data. Some systems offer fundus imaging features,
and there is potential for anterior imaging as well.

How does Fourier domain provide these improvements? The higher
resolution comes from the usual source, a wider bandwidth lightsource.
But the quicker scan speed took more ingenuity. In conventional OCT, a light beam is directed into an interferometer, where it is split in two, one beam going into the eye and the other onto a reference mirror which moves back and forth. The distance of this mirror’s movement determines the depth of the information in the A-scan. Both light beams are re-combined and the interference pattern between them creates the A-scan. The movement of the reference mirror takes time, as the A-scan is created one pixel at a time in depth.

In Fourier domain, the reference mirror remains stationary, and the A-scan is created in a different way. Again, the light from the eye and from the reference mirror are combined in the interferometer, but this time it is split up by wavelength, each of which undergoes analysis by a spectrometer. This “spectral interferogram” is then converted by a Fourier transform into a typical A-scan. This occurs all at once, instead of one pixel at a time, greatly increasing the scan speed.

The high speed and high resolution allow more data to be captured in less time. Furthermore the technology opens the possibility of directly assessing ganglion cell layers in the macula region and examining whether their loss occurs early in the development of glaucoma. In the past, researchers investigated conventional OCT’s ability to do this, but found few promising results. OCT’s accuracy appeared confined to the peripapillary RNFL region around the disc. But with Fourier domain OCT, the improved layer by layer detail allows the possibility to segment out the ganglion cell complex for analysis. This complex is made up of all layers associated with the ganglion cells, including the ganglion cell axons (RNFL), the cell bodies, and the ganglion cell dendrites, (the inner plexiform layer, IPL).

It should be noted that though these advances hold great promise, they have yet to prove out in clinical validation studies. Nevertheless, I think it safe to predict the near future will bring many well received improvements in structural assessment.

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OGS Honoree Lecture
The Aging Anterior Segment and Glaucoma
Might the biomechanics of aging contribute to the disease?

BY PAUL K. KAUFMAN, MD

With age comes wisdom, but unfortunately almost everything else that comes with it is unpleasant, glaucoma not least among them. We expend great effort lowering intraocular pressure because it is the one risk factor we know of that can be modified, but the real villain here is the passage of time. Aside from race, advanced age arguably constitutes the most substantial risk factor for the disease.

Many things happen to an aging eye, one of the most noticeable being loss of accommodation. By the time we reach 35, we have lost two-thirds of our accommodative amplitude. Right around the time we lose accommodation completely, the incidence curve of glaucoma begins to ascend. If you superimposed a line chart with the age of complete accommodative loss against the age of glaucoma development, the upward curve would be almost identical. Is this a coincidence?

Here I put forth a theory that it is not a coincidence, that in fact the two are related. It is highly speculative and like most theories probably wrong, but it certainly looks worth studying. The pieces of this puzzle fit too snugly to be ignored completely. Based on what is known about the biomechanics of an aging eye, a plausible argument can made that age-related aqueous outflow obstruction, in conjunction with certain aspects of presbyopia, is responsible for the development of open-angle glaucoma.

Although IOP tends to rise with age, the body’s production of aqueous humor changes little, declining only about 2.5 percent per decade over the course of 30 or 40 years—roughly the same rate as in monkey models. There is also a decline of aqueous outflow facility, which is roughly analogous to that in monkeys, decreasing about 40 percent over 40 human years.

The number of cells in the trabecular meshwork (TM) also declines, and when compared to age-matched normal patients, this number is lower in glaucoma patients of all ages. The TM also exhibits a build up of extra-cellular material at the entrance of the uveoscleral pathway.

In the case of uveoscleral outflow, we have for many years labored under the misconception that primate and humans differ considerably. The conventional thinking says monkeys’ uveoscleral outflow is much higher than humans’. This is probably not true, having been based on a 35-year-old study that compared young, healthy animals to older humans, many of them with ocular tumors. Moreover, the belief that humans have low uveoscleral outflow has led to a lack of research interest in the possibility that reduced uveoscleral outflow plays a role in glaucoma. In fact, more recent studies have found that human uveoscleral outflow is robust but declines with age, as in monkeys. Thus, if aqueous production remains the same, and uveoscleral outflow declines, TM outflow must rise to make up the difference. But, in order to explain the concurrent rise in IOP, TM resistance must also have risen, and this also appears to be the case. This scenario is the accepted version of how the eye ages, and is supported by tonographic studies in humans and perfusion studies in monkeys.

Meanwhile, the lens and ciliary muscle undergo their age-related changes. Presbyopia occurs from loss of lenticular elasticity. There is also a decline in the forward movement of the ciliary muscle in primate models. In a young monkey, the muscle contracts right up to the level of the scleral spur. By the time the monkey loses its accommodation com-
BY THOMAS F. FREDDO, OD, PH.D.

For many years, researchers have searched in vain for the location of the aqueous outflow resistance in normal human eyes. Equally uncertain is the location of the added resistance seen in eyes with Primary Open Angle Glaucoma (POAG). Still more frustrating, we do not know whether the POAG-related resistance consists of an added resistance at the normal site, or of a separate resistance occurring at a different site in the eye, or of a combination of both. The most widely suspected area has been the trabecular meshwork (TM). Decades have been invested studying the trabecular meshwork for clues to resistance. I feel as though I have spent half my life wandering from the ciliary body to the meshwork, all to no avail—until now.

The seminal findings described here make me wonder whether we have been looking in the wrong place for a long time. (Credit for this discovery goes principally to one of my associates, Haiyan Gong, MD, Ph.D., an assistant professor of ophthalmology at Boston University School of Medicine.)

Since the 1950s, it has been assumed that the primary materials causing resistance in the TM are due to the accumulation of glycosaminoglycans (GAGs), and that GAGs increased with age, which sometimes resulted in glaucoma. However, this theory has not held up well. For example, we now know the concentration of GAGs in almost every other body tissue declines with age, and there is no reason to suggest it does otherwise in the TM. Also, after removing GAG hyaluronate from the TMs of animal models, we saw no decreases in IOP. Research in the early 1990s conducted with a microprobe suggested the main site of resistance in the normal eye might lie within 14 microns of the inner wall of Schlemm’s canal and the juxtanaculcular (JCT) region.1 But how these tissues regulate outflow resistance and contribute to the development of POAG remains unknown.

After looking at this study and the other literature in this field, one can conclude that (depending on which data you accept) up to half the resistance associated with glaucoma is located somewhere other than the TM, perhaps at multiple locations.

Traditionally, in histopathological studies of the TM, we usually section the eye in the sagittal plane. Under normal circumstances, sectioning the eye this way does not provide a clear look at the collector channel ostia. But by sectioning the eye tangential to Schlemm’s canal, we were able to overcome this problem, allowing examination of long expanses of Schlemm’s canal and its multiple collector channels. This sectioning technique led to our discovery. In POAG eyes, both human and animal models, we found a significant amount of tissue partially or completely obstructing the opening into the collector channel canal. It looked as though the inner wall of Schlemm’s canal and the JCT tissue had collapsed into the aperture of the collector canal. We termed such collapses “herniations.” As IOP was increased, the percent and degree of these herniations also increased. In healthy eyes, herniations were partially or completely eliminated after we reduced IOPs to normal levels. In contrast, herniations in eyes with POAG remained when the IOP was 0 mmHg.

Thus we hypothesize that in POAG a process involving normally reversible herniations of the TM into collector channel ostia may become irreversible, leading to progressive elevation of IOP as increasing numbers of herniations become permanent. It may be that this herniation process constitutes a second resistance, added to whatever produces...
the resistance in normal, healthy eyes. Our hypothesis might explain why canaloplasty, a novel surgical procedure invented by South African physician Robert Stegmann, MD, works so well. Canaloplasty may rupture existing hemiations, clearing collector channels, and by leaving the suture behind, also reduce the risk of future collapses.

References:

President’s Lecture
Glaucoma Diagnosis and Monitoring
Paradigm Shift

DAVID S. GREENFIELD, M.D.

Examination and documentation of the optic disc and retinal nerve fiber layer (RNFL) is essential in the diagnosis and monitoring of glaucoma. Yet in a recent chart review of almost 400 patients with glaucoma, approximately 50% of patients did not have an optic disc drawing or photograph. Ocular imaging technologies provide automated, objective and quantitative measurements of the optic disc and RNFL. Such assessments are highly reproducible and show good agreement with clinical estimates of optic nerve head structure and visual function. This presentation will review available technologies for RNFL imaging in glaucoma diagnosis and monitoring. New advances in various ocular imaging technologies will be presented.

Ocular Imaging Technologies

The gold-standard for assessment of structural glaucomatous damage is a stereoscopic photograph of the optic disc. The RNFL may often be visualized using either red-free photography or standard optic disc photography. Glaucomatous RNFL atrophy is generally diffuse but may also be visualized as a wedge shaped focal area of loss. True RNFL defect should be at least as wide as a retinal vein and contact the border of the optic disc.

Confocal scanning laser ophthalmoscopy (CSLO), a technology embodied in the Heidelberg Retinal Tomograph (HRT, Heidelberg Engineering, Heidelberg, Germany), enables the operator to evaluate three-dimensional characteristics of optic nerve head topography quantitatively.2 3 Up to 64 coronal sections of the optic nerve head are acquired over a depth of approximately 3.5 millimeters, and a color-coded topographic map of the optic nerve head is generated.

Scanning laser polarimetry (SLP, GDx-VCC, Laser Diagnostic Technology, San Diego, CA) uses a confocal scanning laser ophthalmoscope with an integrated polarimeter to quantitatively evaluate RNFL thickness. Due to their arrangement in parallel bundles, axonal microtubules exhibit form birefringence resulting in a net change in retardation of passing light which is proportional to RNFL thickness.4 5 The most recent commercial device incorporates a variable corneal compensator to neutralize the confounding influence of corneal polarization axis and magnitude. Variable corneal compensation has been reported to increase the discriminating power of this technology for glaucoma detection.6 10 As compared to fixed corneal compensation, recent data has shown that GDx-VCC provides increased correlation with visual function,10 greater discriminating power for glaucoma detection,9 and greater correlation with RNFL assessments obtained with optical coherence tomography (OCT).11

Optical coherence tomography (Stratus OCT, Carl-Zeiss Meditec, Dublin, CA) is a noninvasive, noncontact, transpupillary imaging technology which can image retinal structures in vivo with a resolution of 8 to 10 microns.12 13 Cross-sectional images of the retina are produced using the optical backscattering of light in a fashion analogous to B-scan ultrasonography. The anatomic layers within the retina can be differentiated and retinal thickness can be measured.14 15

New Advances

HRT. The most recent advances in the HRT consist of utilizing discriminant functions and/or regression analyses to differentiate normal optic discs from abnormal and borderline ones with a high degree of discrimination. HRT also provides several automated analysis of change over time based on trend analysis of the global disc or of sectors of the disc, and on the topographic change analysis which does not require the drawing of the contour line around the disc border. Moreover new software is expected that includes a “reference plane free” longitudinal evaluation.

The CSLO Ancillary study to the Ocular Hypertension Treatment Study (OHTS)16 is the first to provide compelling evidence that CSLO topographic parameters are significantly associated with the development of glaucomatous optic disc or visual field damage in ocular hypertensive subjects. These data suggest that topographic measurements, when combined with other known predictive factors (CCT, IOP and age) could assist the clinician in assessing the likelihood of developing POAG. This is critical information in order to assess global risk for glaucoma and identify patients in whom treatment is beneficial.17

GDx-VCC. The GDx-VCC generates RNFL thickness assessments by neutralizing eye-specific corneal polarization axis and magnitude using the concept of the macula as an intracocular polarimeter. Compared with earlier commercial iterations, the GDx-VCC significantly improves the structure-function relationship in glaucoma, agreement with other imaging technologies, and discriminating power for glaucoma detection. Prospective studies18 have demonstrated that RNFL measurements using the GDx-VCC may predict progression in glaucoma suspects. Recent evidence suggests that atypical patterns of peripapillary birefringence have been observed in a subset of normal and glaucomatous eyes and commonly present as alternating peripapillary circumpapillary bands of low and high retardation around the optic nerve head. A modification of variable corneal compensation may reduce the prevalence of such artifact.

OCT. Recently, several investigators19 20 have reported high levels of reproducibility using the Stratus OCT. Budenz and colleagues21 reported a sensitivity and specificity using a criterion of ≥1 abnormal peripapillary quadrants at the <1% level of 83% and 100%, respectively. Using a criterion of average RNFL thickness normal at the <5% level, the sensitivity and specificity was 84% and 98%, respectively. Perhaps most significantly, recent studies have demonstrated that OCT is capable of RNFL change detection. Medeiros and colleagues22 reported a patient in...
whom progressive RNFL atrophy was detected using OCT 70 days following traumatic optic neuropathy. Wollstein and colleagues demonstrated that OCT was at least as sensitive as standard automated perimetry in detection of glaucomatous progression among 64 eyes with POAG followed for a mean of 4.7 years. Prospective studies have demonstrated that thinner baseline RNFL thickness measurements in glaucoma suspects are predictive of conversion to primary open-angle glaucoma.

References:

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How Medications Could Be Improved

Would changes induce better compliance?

By Richard Parrish, MD

We do not treat glaucoma per se. We treat people with glaucoma, which is different. Our overarching goal should not be to lower IOP, but to prevent changes in function or structure. We believe that lowering IOP is a means of achieving our real goal, preservation of visual function, or to put it another way, preservation of the patient’s quality of life. But assessing a patient’s health-related quality of life (HRQOL) is difficult. For some of us involved in National Eye Institute-related studies, this has become a hot button issue. The HRQOL questionnaires used in these studies are designed to test across disease entities, and while useful for comparing general disease states, they lack specificity for assessing visual function.

There are vision specific questionnaires—or standard instruments, as these questionnaires are called—but most tend to put greater focus on central visual acuity. Attempts to develop glaucoma-specific standard instruments have been hampered by the fact that glaucoma patients are often unaware of any functional disability early in the course of the disease. Until recently, it was thought that developing metrics to assess the HRQOL in glaucoma was virtually impossible. This widely held opinion was contradicted by the recent findings of the Los Angeles Latino Eye Study (LALES). The investigation determined measurable HRQOL reductions in patients with relatively small amounts of visual field loss. These reductions were mostly related to driving skills and risk of falls. Another recent study also demonstrated that patients with only mild visual field loss are at higher risk for falls and motor vehicle accidents.

These studies notwithstanding, we lack agreed-upon metrics to track such issues, so we fall back to using the IOP level as de facto metric. All our therapies—medical, laser, and surgical—base their success or failure primarily on this criterion, and the “medical establishment,” such as Medicare, the FDA, and third party payors follows suit. Until we move beyond IOP reduction and assess how patients’ lives are impacted by this disease, our ability to measure real medication efficacy will remain in its current highly fragmented state. We need to know:

• What change in structure and function is real and measurable?
• How much change in structure and function is age related?
• How does structural change correlate with visually meaningful impairment or the likelihood of future visual impairment to the patient?
• How much visual field impairment is meaningful to the patient?

The Perfect Therapy

In a best case scenario, our medical therapies should lower IOP within the range of 10–12 mmHg, and maintain a flat diurnal curve. Studies have shown the importance of sustained IOP reduction that remains constant during the day and night. As stated above, the therapies should demonstrate preservation of structure and function. In addition to being safe and effective, the perfect medical therapy would have a high value-to-cost ratio, be minimally intrusive, and, as eminent physician George Spaeth, MD, said at the 2007 American Ophthalmological Society Meeting, it would be very important if patients could receive some intrinsic reward for complying with medical regimens. As it stands now, topical medications are perceived as a nuisance.
Solutions, suspensions and gels require frequent applications, are messy and sometimes sting. Oral medications carry the risk of systemic side effects. For example, oral acetazolamide is very effective, but has so many side effects that many patients cannot tolerate it. A possible solution is subconjunctival injections or insertions of medications that would serve as a depot for sustained release, but it is unclear whether patients would accept this option. We know retinal subspecialists are successfully administering intravitreal injections to patients once a month and sometimes less frequently. A major potential problem with subconjunctival injections is their lack of reversibility. Inhaled forms of drug administration have evolved considerably. Insulin can now be taken in this manner; however, I do not know if enough concentration of the drug could be inhaled to reach the eye. Finally, the idea of a subcutaneous sustained implant may be appealing because it could be extracted if adverse reactions occurred. Of the options discussed here, this last one seems to me to be the most viable.

However we achieve it, our goal should be to reduce the number of dosages the patient is responsible for. Research shows a direct relationship between number of applications and likelihood of taking the medication. The perfect therapy is useless unless the patient takes it, and we all know compliance rates among glaucoma patients are extremely poor.

Patients today want cures, not treatments that last a lifetime. We may never “cure” glaucoma, but less invasive surgical options such as selective laser trabeculoplasty (SLT) are a step in this direction. If we could develop a way of making patients feel better by complying with therapy, other than our just telling them they are doing a good job, I think that would bring us closer to achieving our ultimate goal.

References:

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The Future of Glaucoma Therapy
Options such as gene therapy are closer than you think.

BY PAUL L. KAUFMAN, MD

To general practitioners, some of this article may sound futuristic, overly optimistic, or just plain outside the realm of possibility, but, medically speaking, a great deal of it is closer than one might think. Delivering genes to rat and primate models by use of viral vectors has already occurred in a laboratory setting, as has the in vivo imaging of dying retinal ganglion cells (RGCs). Most people reading this will see in their professional lifetimes at least some of these innovations come to everyday practice.

Trabecular Meshwork (TM) Outflow Targets

It probably won’t be long before we see a trabecular meshwork (TM) therapy, other than our just telling them they are doing a good job, I think that would bring us closer to achieving our ultimate goal.

New targets

Neuroprotection. Much has been written about neuroprotection, so I will not belabor this topic other than to say our knowledge of the mechanisms of neuronal death and its prevention is sufficient to envision glaucoma therapy directed at preserving retinal ganglion cells and axons. But a related matter does deserve mention. From a desire to minimize side effects, we tend in the glaucoma field to favor local treatments over systemic ones. However, recent studies have suggested that glaucoma affects cells as far back as those in the lateral geniculate nucleus (LGN), the brain structure to which retinal ganglion send their signals, and even the visual cortex, where final processing occurs. If this is true, a neuroprotective agent localized to the retina, no matter how effective, may do patients little good. Hence systemic approaches may ultimately prove to be the smarter pharmacological strategy in diseases like glaucoma.

Stem cells. There are three main targets for stem cell therapy in glaucoma. Foremost is retinal ganglion cell replacement. Another target is the replacement of glial supporting cells in the optic nerve head, which may be involved in the pathophysiology of glaucoma. And finally replacing TM cells that are lost or malfunctioning due to age may help improve outflow physiology.

Gene therapy. My involvement with gene therapy is not so much in hunting for genes that cause problems, though this is certainly an important area of research. My interest is in using genes to reprogram cells, ordering them to do things medically desirable for the patient. One
of the ways we reprogram cells is by using viral vectors. There are dangers in vectorology: the duration of expression may not last long enough; viral toxicity may occur; immune/inflammatory responses may occur, among other potential problems. But viral vectors carrying inserted genes can effectively inhibit the rho cascade or myosin light chain kinase in the same way that drug therapies can. A 2003 study demonstrated the neuroprotective efficacy of viral vectors carrying a neurotrophin gene in a rat model of glaucoma. A modified adeno-associated viral (AAV) vector was used to over-express brain-derived neurotrophic factor (BDNF) in the RGCs of rats with simulated glaucoma. When compared to rats without neuroprotection, treated animals demonstrated a 40% increase in RGC survival.

Drug delivery

Drug delivery to the posterior segment continues to evolve, with potential impact on glaucoma. Using rabbit models, a 2003 study successfully injected nanoparticles into the vitreous, which were then phagocitized by retinal pigment epithelial cells. The nanoparticles were able to release a marker dye for a period of four months. This technique could conceivably be used to deliver medications to RGCs. Another innovation known as encapsulated cell technology (ECT) appears promising. These are implants consisting of cells genetically modified to produce a specific therapeutic protein. The cells are encapsulated in a semi-permeable, hollow fiber membrane that hangs in the pars plana, slowly releasing the protein to the target site. In a small cohort of patients, ECT was found to be safe. It is currently undergoing phase II clinical trials.

Diagnostics

Continuous monitoring of intraocular pressure ought to be a major priority among glaucoma researchers and device manufacturers. We strongly suspect that IOP fluctuation is a risk factor for the disease, independent from elevated IOP itself. Furthermore, the basic technology to achieve at-home monitoring currently exists. Probably the most viable approach would be an implantable ocular sensor of some kind that broadcasts results via radio frequency, either to a doctor’s office or to a monitor in the patient’s home.

Finally, in vivo visualization of RGCs as they undergo programmed cell death (apoptosis) is now within our grasp. In pioneering research by M. Francesca Cordeiro in the United Kingdom, individual nerve cells can be visualized while undergoing apoptosis. Annexin-5, a protein that usually resides within the cell, becomes externalized during apoptosis. This protein can be marked so that under confocal laser-scanning ophthalmoscopy the dying cell appears as a dot of light. Such a diagnostic tool would be invaluable to monitoring disease progression and therapeutic efficacy research.

In my opinion, before long all of these innovations and discoveries could play vital roles in glaucoma therapy. But, to end on a cautionary note, I’ll quote famous physicist Niels Bohr: “Prediction is very difficult, especially about the future.”

References:

The Future of Glaucoma Surgery
Where we have been, and where we are going.

BY STEVEN J. GEDDE, MD

Trabeculectomy continues to be the mainstay surgical option for glaucoma therapy, surpassing by far in number any of the other surgeries performed in this field. And yet, despite undergoing many improvements over the years, the popularity of trabeculectomy is in decline. Surgeons are increasingly opting to use drainage implants, and laser trabeculoplasty in the form of selective laser trabeculoplasty (SLT) is gaining ground. In addition, many new surgical approaches and implantable devices are on their way to the market.

In this article, I want to summarize these trends and review how they came about, plus delve into what the future might hold for glaucoma surgical options.

Trabeculectomy

Introduced in 1968, trabeculectomy continues to be the most frequently performed glaucoma procedure. Over the years, it was discovered that success rates improved with the adjunctive use of antifibrotic agents such as 5-fluorouracil and mitomycin C. However, it was also discovered, after long-term follow-up studies, that these adjunctive agents increased the complications associated with the procedure. In particular, the risk of late onset bleb leak and bleb related infections has prompted many surgeons to look for alternative surgical approaches.

Recent changes in trabeculectomy technique that have been adopted by some surgeons, myself included, are: 1.) a lower dosage of mitomycin C, and a more diffuse application of the drug; 2.) switching from limbus-based to fornix-based conjunctival flaps. These modifications seem to produce a more diffuse, low-lying bleb; one that is at lower risk for bleb leaks and infections, and is more comfortable for patients.

According to Medicare data, the number of trabeculectomies performed per year is in steady decline. From 1995 to 2004 the number of trabeculectomies fell from 51,690 per year to 24,178. Much of this decline is likely due to advances in drug therapy, but it also may be linked to a rise in the use of glaucoma drainage implants. In the same time period, implant surgeries climbed from 2,728 per year to 7,744.1

Drainage implants

Also introduced in 1968, drainage implants share a common design: a tube connected to a plate. Aqueous is shunted through the tube from the anterior chamber to the plate, which is located in the equatorial region of the globe. The aqueous fluid pools in the capsule that forms...
around the plate, and eventually, the fluid passes through the capsule by passive diffusion. Drainage implants differ in size, shape, and material of the plate. Some have valves and some do not. The valve stops flow through the device if the intraocular pressure becomes too low. When compared to trabeculectomy, the risk of long-term infection with drainage implants appears to be lower. However, implants have their own unique risks, such as diplopia and tube erosion.

A recent multi-center, randomized clinical trial compared the safety and efficacy of non-valved implant surgery to trabeculectomy. Both produced similar IOP reduction after one year of follow-up, but there was less need for supplemental medical therapy following trabeculectomy. However, drainage surgery was more likely to maintain IOP control and to avoid persistent hypotony and re-operation. Overall, trabeculectomies resulted in a greater number of postoperative complications, but when data were weighted for severity of the complications, no significant differences between the two procedures were found.

**Laser trabeculoplasty**

Laser trabeculoplasty has traditionally been viewed as a supplement to maximum tolerated medical therapy. It is also recognized as a useful option for patients with open angle glaucoma who are poorly compliant with medical therapy. In the early 1990s, a multi-center, randomized clinical trial called the Glaucова Laser Trial found that argon laser trabeculoplasty (ALT) was as effective and safe as medical therapy when used as a first-line treatment. But ALT never really caught on as an initial therapy. However, the recent introduction of Selective Laser Trabeculoplasty (SLT) has re-opened the debate over whether laser trabeculoplasty is suitable for primary therapy.

One of the problems with ALT is that its IOP lowering effect diminishes over time, by about 5 to 10 percent per year. After five years, only 50 percent of treated patients retain the beneficial effect. Because different types of lasers are used in SLT and ALT, it appears that the newer procedure generates less collateral damage to the tissue, and thus has more potential for repeatability. Though histology research supports this theory, the perceived advantage remains theoretical, because longitudinal data are not yet available. Both procedures work equally well, so the results of long-term studies will have a considerable impact on the future of SLT.

**New techniques, devices**

**Express Implant**: Stainless steel with an internal diameter of 50 to 200 microns, this device shunts aqueous from the anterior chamber to the sub-conjunctival space, and creates a perilimbal filtering bleb much like a trabeculectomy. Due to a high incidence of hypotony and hypotony-related complications, as well as erosion of the device, the initial experience with this device was disappointing. But after we realized it was best to place the implant under a scleral flap, these complications were markedly reduced. The device is FDA approved and offers a trabeculectomy-like results without the need for a sclerostomy and peripheral iridectomy.

**Trabectome**. This device, which consists of a handpiece with an I/A port and a electrocautery tip, ablates the trabecular meshwork and inner wall of Schlemm’s canal via an ab interno approach. It is FDA-approved, and one study found that an average pressure reduction from 28 to 16 mmHg was sustained for more than a year.

**Glaucosas Trabecular Bypass Micro-Stent**. Again, using an ab interno approach, this titanium, snorkel-shaped device is inserted into Schlemm’s canal. It is currently undergoing clinical investigation and is not approved by the FDA.

**Eyepass Glaucoma Implant**: This is a silicone Y-shaped device also designed to shunt aqueous into Schlemm’s canal. The proximal end is inserted into the anterior chamber and each arm inserted into Schlemm’s canal. It is not FDA approved.

**Canaloplasty**: This technique makes use of a microcatheter with a fiber optic tip, which is passed through Schlemm’s canal via an ab externo approach. Then Healon GV is used dilate the canal. After that, a 10-prolene is placed in the canal to keep it open. This technique has gained a great deal of acceptance, especially overseas, and is approved by the FDA.

**Miami-InnFocus Drainage Implant (MIDI)**: This implant is made of polyethylene-b-isobutylene-b-styrene (SIBS), the same material used in the coronary stents employed in angioplasty. This material has been shown to be biocompatible, and as a result causes less inflammation leading to a thinner capsule being produced. The inner diameter of this stent ranges from 70 to 150 microns, and this small size offers some resistance to early postoperative hypotony. MIDI is not FDA approved.

**Small-Diameter Aqueous Shunt (SAS)**: This device seeks to take advantage of Laplace’s law, which states that surface tension on the wall of the capsule is proportional to the bleb diameter. In other words, smaller diameters produce less tension. Reduced wall tension results in a thinner capsule, and thus lower IOP. This device is not FDA approved.

**Gold Micro Shunt**: Made from 24-karat gold, this flat device is inserted into the anterior chamber and the suprachoroidal space. A titanium sapphire laser can be used to titrate flow. Though available in Europe, it is not FDA approved.

**Excimer Laser Trabeculoplasty (ELT)**: This is another fiber optic probe system that delivers laser power to the trabecular meshwork, creating micro-perforations that connect the anterior chamber to Schlemm’s canal, without causing thermal damage to the trabecular meshwork. During the procedure, ten of these laser excitons are performed over 90 degrees of the angle. Though available in Europe, this device is not FDA approved.

Given the steady decline in the popularity of trabeculectomy, we should expect at least some of these procedures to move to the forefront of our options in the evolving world of glaucoma surgery.

References:

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The Optometric Glaucoma Society (OGS) was formed seven years ago with a mission to promote excellence in the care of patients with glaucoma through professional education and scientific investigation. The major objectives are to: promote education of the membership and other healthcare providers related to all forms of glaucoma; promote the acquisition of new knowledge about glaucoma, in part through the development of clinical research within optometry that is related to glaucoma; facilitate the dissemination of information about glaucoma to healthcare providers and the public and, establish collaborative relationships with other related organizations.

There are 66 members in the OGS, coming from several countries around the world. The OGS is equally divided between clinicians and scientists, with ODs, PhDs and MDs making up our membership. The OGS is a member of the World Glaucoma Association (WGA) with seven members on the faculty of the 2007 World Glaucoma Congress. Additional information including membership information and the application may be found on the OGS website at www.optometricglaucomasociety.org.

The OGS is involved in several programs that are related to improving optometric glaucoma education. We publish on a quarterly basis an electronic journal that is free of charge and available to anyone who wishes to subscribe. Individuals may sign up at the OGS website. We also publish a glaucoma handbook, produced yearly that is a review of glaucoma diagnosis and management. This is also available for free and distributed to 35,000 optometrists. Also, the OGS holds a glaucoma residents program each fall in which one new resident from each school participates. And finally, the OGS in collaboration with the American Optometric Foundation is funding an Ezell Fellowship in Glaucoma, which is intended to enhance the opportunities for post-graduate optometric glaucoma research.