

GLAUCOMA

**Appropriate
glaucoma medication**

Dr Brian Ang

**Do I need gonioscopy
when I have an OCT?**

Alex Petty

**Glaucoma and
chronic hypertension**

Dr Zheng He

Dr Christine Nguyen

Dr Bang V Bui

Dr James Armitage

Professor Algis Vingrys

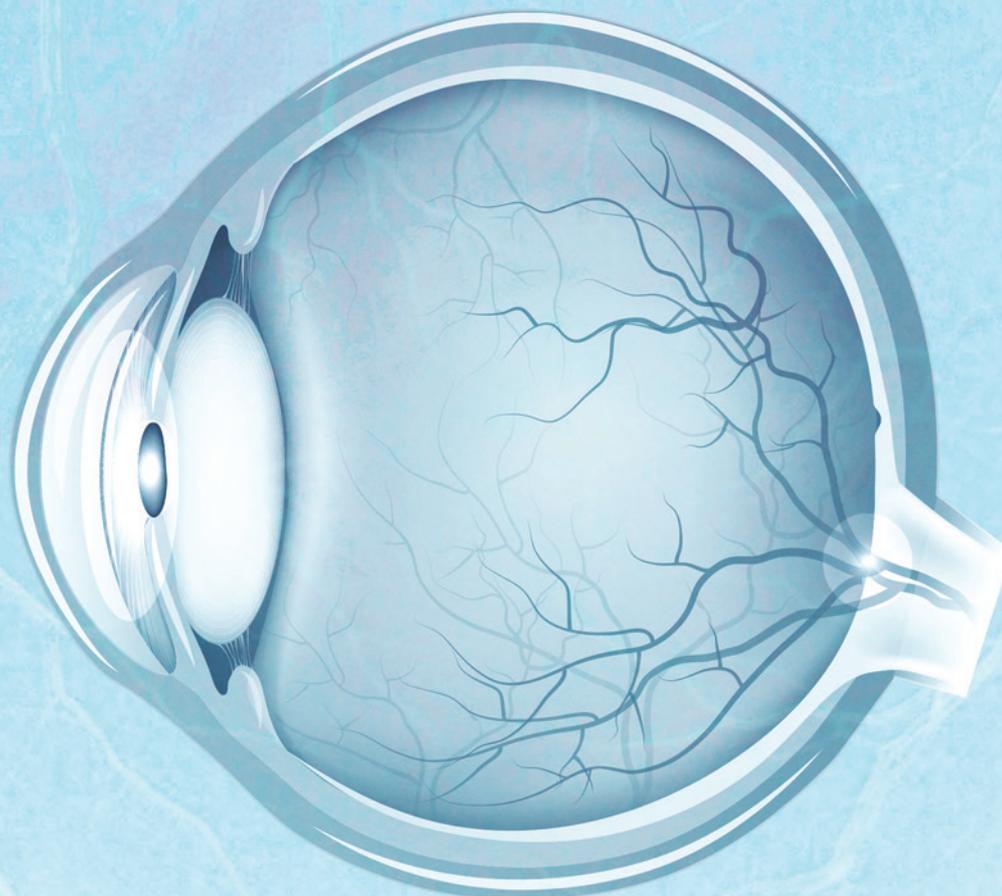
**Quality of life and
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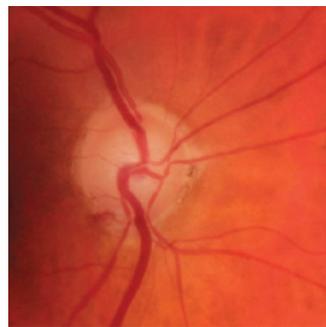
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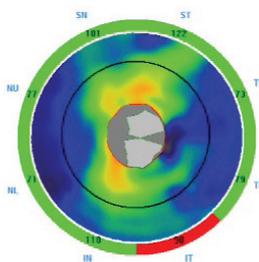
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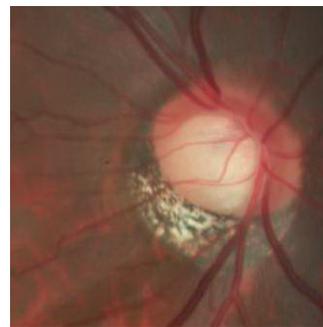
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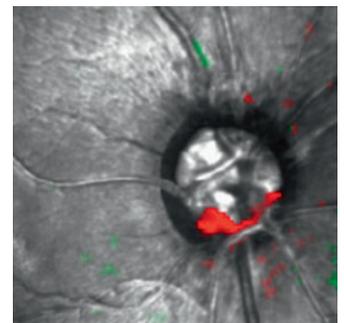
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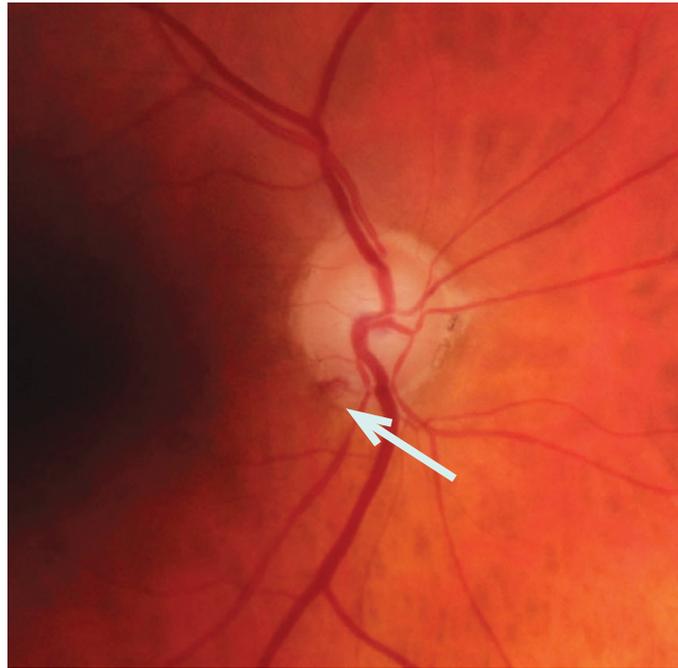
WHEN PATIENTS present with an eye problem, it is common not only to find the cause or causes but also discover other incidental ocular conditions.

Think back to the last few patients you saw recently and you may realise that most usually have more than one eye problem.

Given that we are initially guided by the patient's symptoms and medical history, one may be forgiven for looking for a single pathology and neglecting others, for example, focusing our attention on the retina in a patient who presents for a diabetic eye check. Part of the reason for this is that our learning is based on information sources (textbooks, conferences, publications and public health awareness programs) that are disease-specific and oriented. We are quick to focus on one area of the eye but what happens if a patient has more than one eye problem?

Patients usually present for an eye examination when they are experiencing symptoms related to their vision, ocular discomfort such as dry eye symptoms, when they are at risk of developing symptoms like diabetes or when they have family history of glaucoma. The prevalence of eye conditions increases with age, with 80 per cent of the world's blindness due to refractive error, cataract, glaucoma, diabetes and macula degeneration.

Given that many eye conditions are asymptomatic in the early stages, it is not uncommon for patients to have early signs of more than one of these conditions. Before deciding which treatment is best, one needs to determine whether their conditions are related. Remember that any chosen treatment can exacerbate other eye problems, for example: topical steroids and cataract.



▲ Figure 1. Optic disc showing damage inferiorly with a Drance haemorrhage Photo: Dr L Liu

Dry eye

As an example, let us look at glaucoma. It is defined as a progressive optic neuropathy where accelerated loss of retinal ganglion cells leads to changes of the optic nerve and retinal nerve fibre layer, usually leading to loss of the peripheral vision initially and then loss of the central vision later. There are many risk factors associated with the development and progression of glaucoma, but intraocular pressure is the only risk factor we can modify. Treatment includes topical IOP-lowering drops, laser procedures (iridotomy, trabeculoplasty, cyclodiode) or glaucoma filtering operation such as a trabeculectomy and aqueous drainage devices (such as tube surgery).

Glaucoma is a life-long condition that once diagnosed usually requires

ongoing treatment and monitoring. However, we know that up to 50 per cent of glaucoma is undiagnosed at the time of the consultation¹ so it is important to exclude glaucoma in all patients.

It has been shown that topical glaucoma treatments can cause or exacerbate dry eye symptoms. The latter is usually related to ocular surface disease (OSD) which can also be caused by blepharitis or rarely keratoconjunctivitis sicca. One of the main causes is related to the preservatives found in these drops, the most common being benzalkonium chloride.² The severity of the symptoms is related to the preservative load the patient receives: concentration, number of drops per day and exposure over time. These preservatives can either initiate or contribute to pre-existing OSD symptoms. Recently, non-preservative glaucoma drops have become available, which can be initiated in those with newly diagnosed glaucoma and pre-existing OSD, or substituted in those glaucoma patients who develop dry eye symptoms.

Cataracts

Other conditions may be present at the initial consultation or develop

subsequently. Cataract, the cloudiness of the natural lens in the eyeball, eventually worsens over time and may be accelerated by a number of conditions including diabetes, steroids and ironically, glaucoma treatments (drops, laser³ or surgery⁴). As the cataract worsens, the vision can become impaired either slowly or quickly, depending on the type of cataract. The ongoing enlargement of the lens can also lead to angle closure that can cause the IOP to rise or worsen glaucoma. Current technologies allow us to remove the cataracts successfully in 98-99 per cent of cases.

With increasing age, it is not uncommon for cataract and glaucoma to co-exist in the same patient although the severity of each condition may vary. There are various treatments available for glaucoma and cataracts; however, although there is usually vision improvement following cataract surgery, the vision loss from glaucoma is permanent. What is the role of cataract surgery in the glaucoma patient?

Cataract surgery

Traditional teaching has always been that we remove cataracts for vision reasons and perform glaucoma surgery

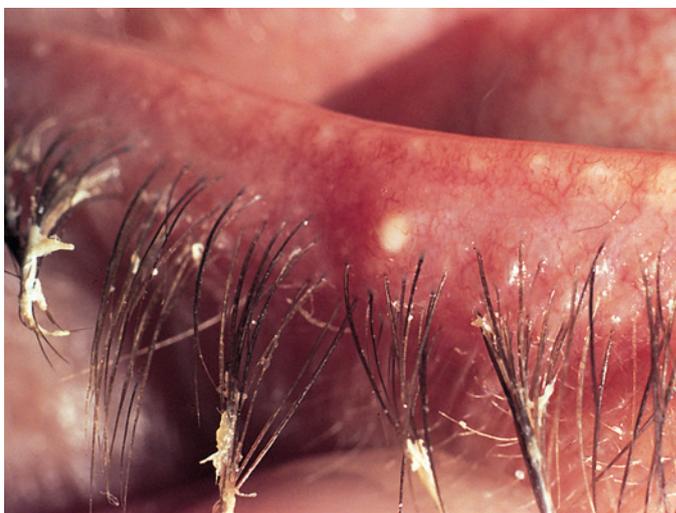
for glaucomatous progression. Once diagnosed, glaucoma is a life-long condition that requires ongoing treatment and monitoring. A cataract, on the other hand, progresses slowly over time—but may be accelerated by the treatments we have to stabilise the glaucoma—and usually requires surgical removal.

Does one wait until the vision is significantly impaired before removing the cataract or should this be removed earlier in the glaucoma patient's lifetime? It raises another issue: how does one define a cataract? Although we rely on the Snellen/LogMAR acuity test to determine the severity, cataracts can also affect refraction, colour discrimination and contrast sensitivity, depending on the pathologic type. We do not routinely test the latter two visual modalities,⁵ so a patient with a cortical cataract may complain of glare but the vision may be still 6/9.

From a glaucoma perspective, there has been a trend for early cataract surgery during the glaucoma patient's lifetime. Removing the cataract early can improve the patient's current level of vision, stabilise (compare: angle closure glaucoma patients) or lower the IOP slightly, allow easier clinical examination and monitoring of the glaucoma, and improve the imaging of the optic nerve and surrounding retinal nerve fibre layer.⁶

From a surgical perspective, glaucoma filtering surgery is easier when the patient is pseudophakic and in patients undergoing cataract surgery following a trabeculectomy, there is an increased rate of bleb failure. Earlier cataract surgery is technically easier in patients with pseudoexfoliation and may reduce the glaucoma risk in patients with angle closure.

There is a lot of anecdotal evidence to support the trend for early cataract surgery but we still await long-term prospective trials in this area.



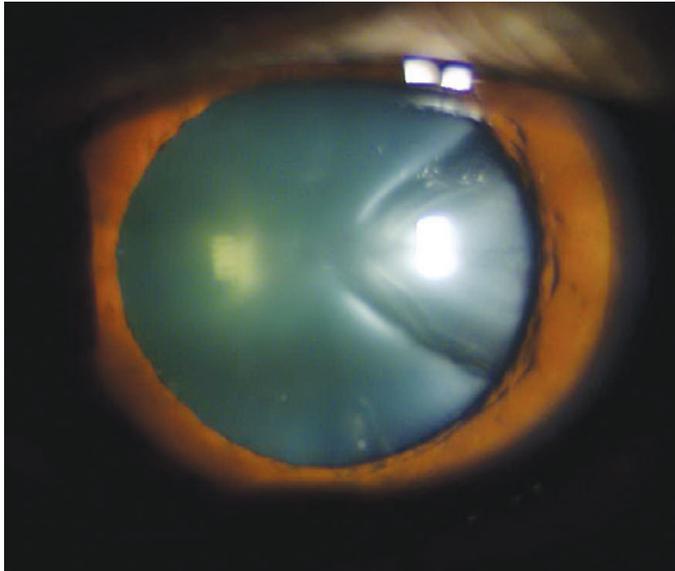
▲ Figure 2. Anterior blepharitis

Continued page 4

Glaucoma-related problems

From page 3

In the past, we have concentrated on the patient's main problem (usually the glaucoma) and tended to neglect the other eye problems the patient may have until it becomes visually significant. Given the high success rate of cataract surgery, there is a strong argument to consider this earlier in the glaucoma patient's lifetime to maximise their visual potential, improve the clinician's ability to monitor the disease and plan for any



▲ Figure 3. Cortical cataract Photo: Dr L Liu

future glaucoma procedures, if needed. This decision needs to take into account the severity of the glaucoma, the degree of cataract and the patient's perceived visual disability.

Other problems

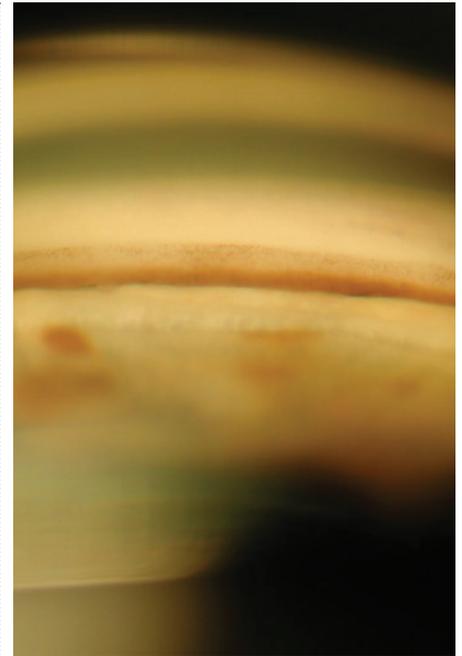
Then there are many patients who present with other non-glaucoma related problems such as early visual loss due to cataracts or sore, gritty eyes. It is important to exclude not only glaucoma in these patients, but also those who are at risk of developing this disease. The most common risk factors are age, IOP, a family history of glaucoma and the central corneal thickness.

Other risk factors for open angle glaucoma include ocular conditions, for example myopia, pseudoexfoliation and so on, systemic diseases such as hypertension and epidemiological causes. However, the risk factor for angle closure glaucoma is iridotrabecular contact, which is most commonly found in the dark when the pupil is physiologically dilated. Epidemiologically, it is more commonly found in patients with increasing age, females, and those patients of Asian origin, although it occurs in Caucasians too.

Anatomically, iridotrabecular contact is found in eyes that are hypermetropic, have shallower

anterior chambers and are smaller. Gonioscopy remains the gold standard in assessing the angle as one will miss between 25-50 per cent of angle closure if relying on the central anterior chamber depth, Van Herick⁷ and flash light tests. Therefore, gonioscopy needs to be performed to exclude angle closure or iridotrabecular contact.

Patients usually have multiple eye problems—some obvious, some in the early stages and some asymptomatic. Therefore, it is important to find the cause or causes of their presenting problem and then, one needs to look for other eye conditions. In the case of glaucoma, this includes performing



▲ Figure 4. Gonioscopy of angle Photo: Dr L Liu

gonioscopy to exclude angle closure and should be part of the routine eye assessment in all patients,⁸ regardless of their presenting eye problems.

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Glaucoma medications

Seven points to remember when
symptoms and treatments

Dr Brian Ang

FRCOphth FRANZCO

The Royal Victorian Eye and Ear
Hospital, Melbourne Eye Specialists

GLAUCOMA is a leading cause of blindness worldwide and a major public health concern. As intraocular pressure (IOP) is an important modifiable risk factor for the development and progression of glaucoma,¹⁻³ much of glaucoma management is focused on lowering IOP to reduce the risk of optic nerve damage and subsequent vision loss.

IOP control can be achieved via medication (Table 1), laser or surgery. The effect of laser trabeculoplasty is impermanent, and surgery is generally considered only if the IOP remains elevated or if the glaucoma continues to progress despite maximum tolerated medical therapy. The great majority of glaucoma patients can expect to be

on at least one topical IOP-lowering medication at some point in the course of their glaucoma management.

How difficult can it be to treat a glaucoma patient medically? In theory, it sounds easy. Prescribe the patient with a topical IOP-lowering medication and after four to six weeks, the IOP should be reduced. In reality, there are numerous important issues that need to be considered before deciding on the type of glaucoma medication to use, or indeed, even whether glaucoma medication is appropriate for that particular patient.

There are seven considerations that clinicians should address when managing a glaucoma patient medically.

● Confirm glaucoma and exclude other pathology

First and foremost, the patient should have the diagnosis of glaucoma confirmed before starting treatment. Not all optic disc cupping and visual field loss are due to glaucoma. Any clinical feature that does not seem typical for glaucoma—such as neuroretinal rim pallor, reduced

colour vision, or bilateral field defect that obeys the vertical meridian—needs to be investigated further. A misdiagnosis of glaucoma and consequent missed diagnosis of other ocular or neurological condition, which may coexist with the glaucoma, can be potentially disastrous for the patient.

● Exclude angle closure in all glaucoma patients

Originally thought to be a condition primarily affecting Asian populations, angle closure is now increasingly recognised as a significant cause of glaucoma in Caucasian populations as well.⁴ In patients with angle closure glaucoma, medication alone will be insufficient to lower IOP because the underlying cause of angle closure also requires treatment. Depending on the mechanism of angle closure, treatment options may include laser iridotomy, laser iridoplasty or cataract surgery.

It is essential that all suspected glaucoma patients be assessed for angle closure with gonioscopy and/or anterior segment optical coherence tomography imaging in dark conditions.

Class	Mechanism of action	Medications
Prostaglandin analogue	Increase aqueous outflow – uveoscleral pathway	Latanoprost 0.005% Travoprost 0.004% Bimatoprost 0.003% Tafluprost 0.0015%
Beta-adrenergic antagonist	Decrease aqueous production	Timolol 0.25% / 0.5% Betaxolol 0.25% / 0.5%
Alpha-adrenergic agonist	Decrease aqueous production	Brimonidine 0.15% / 0.2%
Carbonic anhydrase inhibitor	Decrease aqueous production	Dorzolamide 2% Brinzolamide 1% Acetazolamide (oral)
Muscarinic agonist	Increase aqueous outflow – trabecular meshwork	Pilocarpine 1% / 2%

▲ Table 1. Classes of intraocular pressure lowering medications

addressing signs,

- **Decide on appropriateness of eye-drops**

Once the diagnosis of glaucoma has been confirmed and angle closure has been excluded, the next issue to consider is the appropriateness of eye-drops as primary treatment. Selective laser trabeculoplasty (SLT) has been shown to be as effective as latanoprost in lowering IOP over a 12-month period,⁵ with repeat treatments reported to be safe and as efficacious as the primary treatment.⁶

Depending on personal or social circumstances, SLT may be more appropriate as primary treatment compared to topical medication for certain patient groups, such as pregnant women and arthritic patients who are unable to squeeze the eye-drop bottles.

- **Be aware of local and systemic side-effects**

All medications, even topical eye-drops, have the potential to cause local and/or systemic side-effects. Local side-effects include eyelash growth and periorbital skin pigmentation with prostaglandin analogues, allergic dermatitis with brimonidine, and corneal decompensation with carbonic anhydrase inhibitors.

Systemic side-effects include bronchospasm and postural hypotension with beta-adrenergic antagonists, respiratory depression with brimonidine, and confusion with pilocarpine. These effects can cause significant morbidity in elderly patients.⁷ Patients need to be asked and be made aware of the potential side-effects to reduce the risk of suffering medication harm.

- **Reduce risk of side-effects**

When patients are prescribed with glaucoma eye-drops, they are effectively being asked to experience potential side effects over the long term

to control a generally asymptomatic disease that may or may not result in blindness in their lifetime. By decreasing the side-effects, the likelihood of patient adherence to medication is enhanced.

Side-effects can be minimised by limiting the amount of eye-drops used, using lower concentration preparations, switching rather than adding drops, and using combination preparations where possible. Digital occlusion of the nasolacrimal ducts for one to two minutes following drop instillation can also decrease systemic absorption and side-effects.

- **Be aware of toxicity from preservatives**

Preservatives in eye-drops, such as benzylkonium chloride, are essential to prevent microbial colonisation; however, these preservatives also significantly worsen the symptoms of ocular surface disease commonly experienced by many glaucoma patients.⁸ The ideal would be to use preservative-free drops, such as tafluprost and preservative-free bimatoprost, where possible. Preservative toxicity can also be reduced by using preparations with gentler preservatives that do not contain benzylkonium chloride.

- **Emphasise importance of compliance**

Ultimately, the success or failure of treatment depends on whether the patient uses the glaucoma medications as prescribed. Poor compliance is associated with higher IOP, progressing glaucoma, unnecessary changes to treatment, and increased health-care costs.⁹ Regularly ask patients about how often they forget or neglect to use their eye-drops. If a patient is non-compliant with treatment, try to ascertain the underlying reason(s). These can vary from cost and medication side-effects to difficulty with the eye-drop bottle,

poor understanding of treatment, and plain forgetfulness. Strategies to deal with non-compliance should encompass acknowledging the patient's difficulties, explaining the importance and rationale for treatment (with the help of an interpreter or family member if necessary), clearly writing down the eye-drop regime, and working out a mutually acceptable solution.

Summary

The guiding principle when managing glaucoma patients should always be: First do no harm. Medical treatment has the potential to cause harm through wrong diagnosis, inappropriate choice of medication, and local and systemic side-effects, as well as under- and over-treatment.

It is up to the clinician to ensure that the risk of harm from glaucoma treatment is far outweighed by the risk of harm from the glaucoma itself.

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The link between chronic hypertension and glaucoma

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HIGH BLOOD pressure (> 140/90 mmHg) is probably the most common comorbidity in glaucoma patients presenting to optometry clinics. In Australia, the prevalence of hypertension is 28.6 per cent.¹ This number increases to 59.5 per cent in men and 70.0 per cent in women above the age of 70 years.² Chronic high blood pressure leads to structural remodeling in the small arteries and arterioles, increasing resistance in the peripheral blood vessels and promoting the risk of multiple end organ damage.

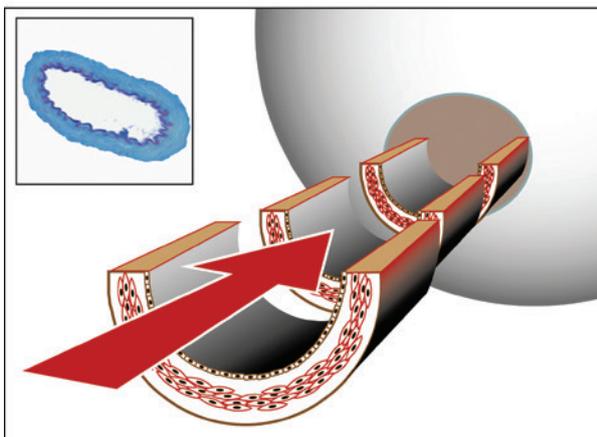
While chronic arterial hypertension is a well-documented risk factor for stroke, the link between hypertension and open angle glaucoma remains uncertain. The National Health and Medical Research Council guidelines for glaucoma (2011) state that the link between glaucoma and hypertension 'is likely to be a complex relationship as the patient's age and duration of systemic hypertension both impact upon the hypertensive state.'³

As the prevalence of both systemic hypertension and glaucoma increase with age, an association between the two diseases may merely be incidental. We need to consider whether there is a true interaction that modifies the risk of glaucoma in those suffering from systemic hypertension. For example, the difference between intraocular pressure and blood pressure determines ocular perfusion pressure. Any blood pressure reduction treatment will inadvertently reduce ocular perfusion pressure and may have the potential to produce detrimental effects for the optic nerve.

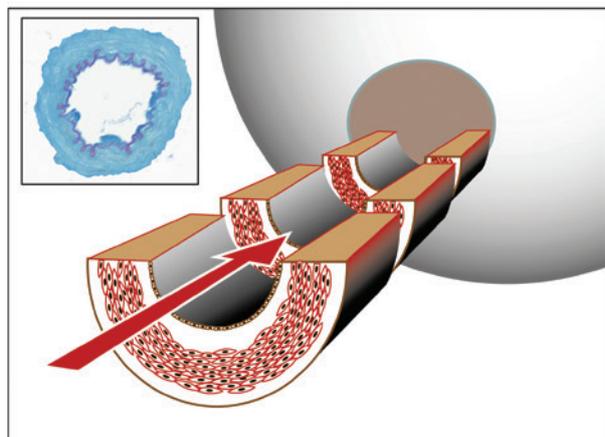
Short term vs long term systemic hypertension

The Baltimore Eye Survey⁴ (5,308 participants) compared young and older patients with hypertension and found that young patients with high blood pressure had less risk of glaucoma. Paradoxically, systemic hypertension in older subjects

A. Normal artery



B. Chronic arterial hypertension



▲ Figure 1. A schematic of the central retinal artery under normal conditions (A) and following changes of thickening, narrowing and impaired reactivity in chronic hypertension (B). These structural changes will compromise blood flow autoregulation and lead to partial ocular ischaemia. The insets show the experimental evidence for increased wall-to-lumen ratio of the ophthalmic artery in rats with chronic high blood pressure.

New study highlights the need to include blood pressure status in your patients' risk assessments

increases the risk of glaucoma.

A lower risk of glaucoma with hypertension is consistent with the idea that higher blood pressure provides better perfusion pressure to the eye. In contrast, in older patients with a longer duration of systemic hypertension and more severe vascular changes (thicker, narrower and more rigid arteries) the benefits of improved perfusion pressure are not apparent.

These data suggest that the way systemic blood pressure modifies the susceptibility of glaucoma depends on the patient's vascular status. As shown in Figure 1A, high blood pressure within normal arteries acts as a driving force for blood flow into the eye and therefore helps to counteract high intraocular pressure. However, as arteries become rigid and narrow with older age and long term hypertension, local blood flow to the eye can be compromised such that high blood pressure is no longer beneficial or protective against glaucoma (Figure 1B).

This idea is supported by our laboratory studies.⁵ We have found that rats with transient high blood pressure (one hour) can withstand acute intraocular pressure elevation better than those with normal blood pressure. However, the functional 'protection' afforded by improved ocular perfusion pressure was compromised when the duration of high blood pressure was extended from one hour to four weeks, which was associated with damage to the vascular walls.⁵

This finding is consistent with epidemiological data from the Los Angeles Latino Eye Study,⁶ which showed that the relationship between blood pressure and the prevalence of glaucoma is a 'J-curve'. That is, patients at both the high and low end of the blood pressure spectrum are at increased risk of glaucoma. This suggests that patients with hypotension can be at increased risk of glaucoma

due to insufficient ocular perfusion pressure, whereas those with long-term hypertension may suffer greater glaucoma risk due to structural vascular changes.

Hypertension and blood flow autoregulation

Our experimental data suggest that the association between chronic hypertension and increased risk for glaucoma is not merely incidental; the prevalence of the two independent entities do not simply increase in parallel with ageing. Chronic hypertension may compound the risk for glaucoma.

Ocular perfusion pressure shows normal physiological variation due to a host of factors such as circadian fluctuation (both in intraocular pressure and blood pressure), postural changes or physical activity. Despite such variation, retinal blood flow can be maintained relatively stable thanks to the intrinsic capacity of the small arteries and arterioles to adjust diameter and thereby buffer any changes in pressure or metabolic demand.⁷ This process, known as autoregulation, acts to ensure a constant supply of oxygen and nutrients to the retina.

In chronic hypertension, when atherosclerosis and arterial remodeling compromise the vascular elasticity and therefore the capacity to autoregulate, even a small reduction in ocular perfusion pressure can result in blood flow deficiency. Our recent study showed that in rats with chronic high blood pressure, the retina is less able to maintain blood flow during intraocular pressure challenge.⁵

These results highlight the need for primary eye care providers to not only screen for hypertensive retinopathy in patients with high blood pressure, but also to be mindful to include the blood pressure status in the glaucoma risk assessment along with other risk

factors. The Thessaloniki Eye Study has shown that while high blood pressure is detrimental, over-zealous treatment of blood pressure can also lead to increased risk of glaucoma.⁸ This latter finding suggests that the eye in hypertensive individuals becomes accustomed to higher 'ocular perfusion pressure' and that abrupt reductions in blood pressure do not give the eye enough time to adjust, leading to relative ischaemia.

Further studies are needed to develop an algorithm to optimise individual blood pressure ranges for patients with glaucoma and coexisting high blood pressure.

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A disc conundrum

Congenitally anomalous conditions can make it difficult to judge glaucomatous disc changes

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GLAUCOMA is defined as a primary optic neuropathy. We are all well aware of the acquired changes that occur to the optic nerve due to glaucoma, such as vertical elongation of the optic cup, focal neuroretinal rim damage, retinal nerve fibre layer (RNFL) defects, and the development of parapapillary atrophy and Drance haemorrhages.

These disc changes are easier to identify in patients with initially normal optic nerves. Much more daunting is diagnosing glaucoma in patients who have congenitally anomalous nerves to begin with.

Added to the fact that congenital optic disc anomalies can have visual field and RNFL abnormalities, diagnosing glaucoma in eyes with congenitally anomalous nerves is a conundrum.

Tilted disc syndrome

Tilted disc syndrome (TDS) is a unilateral or bilateral, unchanging congenital optic disc anomaly that can be discovered in patients of any age, with an incidence of two per cent in the general population.^{1,2} In TDS, the disc appears to be rotated about its axis with the long axis of the disc approaching the horizontal meridian in extreme cases, giving the disc a D-shaped appearance. The most consistently encountered finding is a conus in the inferior and inferior

nasal aspect of the parapapillary retina contiguous with the optic disc that can give the optic disc a pseudo-glaucomatous appearance. Visual acuity is unaffected in TDS; however, visual field loss is common. The most commonly encountered visual field abnormality is a superior temporal scotoma, though defects can occur elsewhere.^{3,4} Parapapillary RNFL abnormalities exist in eyes with TDS and can be confused with those occurring in glaucoma.⁴

CASE REPORTS

Patient 1

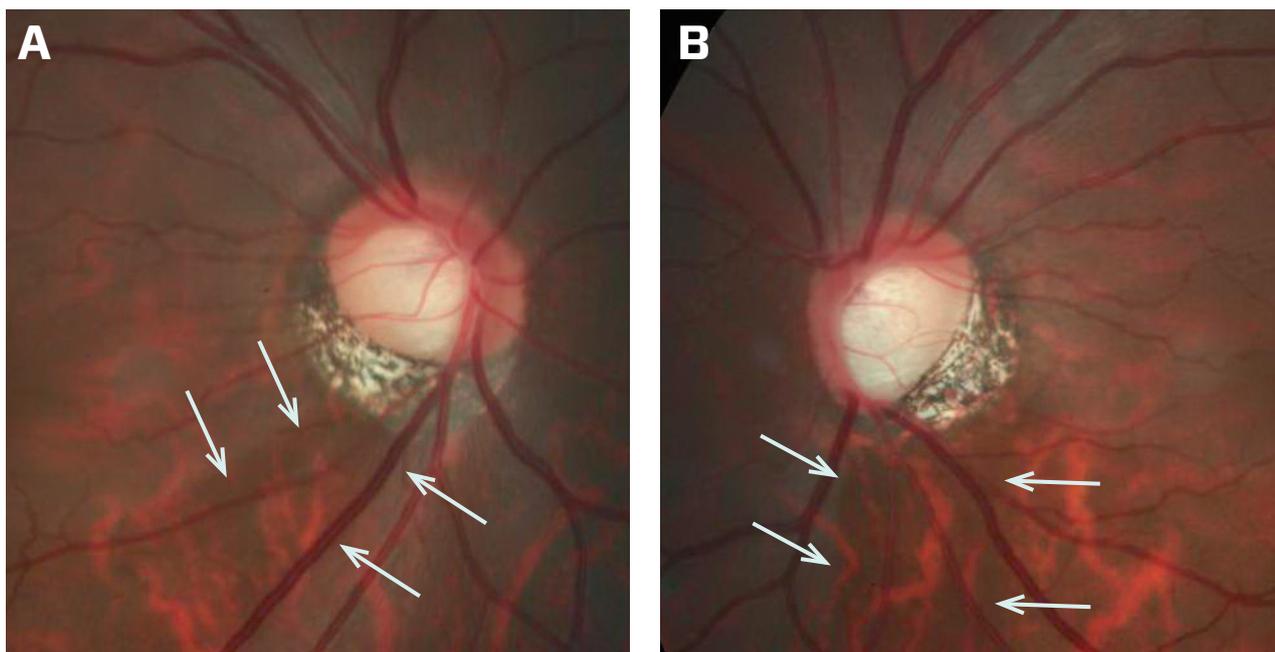
The first patient is a 79-year-old man who had long been treated for glaucoma and came for a second opinion. He was currently using timolol 0.5%, brimonidine tartrate 0.2%, and latanoprost in each eye. His best corrected visual acuity was



▲ Figure 1A. Patient 1. Right eye showed a marked coloboma of the retina and optic nerve.



▲ Figure 1B. Patient 1. Left eye demonstrated TDS.



▲ Figure 2A and 2B. Patient 2. Notable retinal nerve fibre layer abnormalities in each eye.

6/9 in each eye with a mildly myopic astigmatic correction. His intraocular pressure was 11 mmHg OU. A dilated examination revealed congenitally abnormal discs in each eye. The right eye showed a marked coloboma of the retina and optic nerve, while the left eye demonstrated TDS.

Clearly, it was not possible to discern glaucomatous rim changes or RNFL defects in either eye. Without knowing the visual field status of the patient or the pre-treatment IOP, a definitive opinion on his glaucoma could not be given. A disc haemorrhage, which doesn't occur from TDS, was seen in his left eye, making it highly suspicious that he had glaucoma as well as congenital disc anomalies. He was well educated about his conditions and to continue his medications, and instructed to return to the ongoing care of his previous doctor. (Figures 1A and 1B)

Patient 2

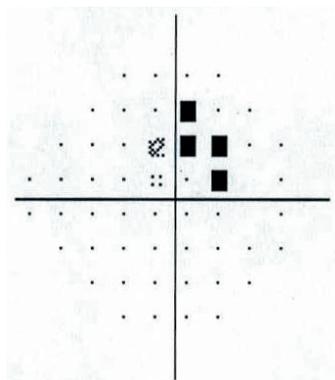
The second patient is a visually asymptomatic 45-year-old Japanese woman referred for ongoing glaucoma management. She had been seen by a local optometrist who diagnosed glaucoma based on optic disc appearance and a pre-treatment IOP of 17 mmHg OU. He placed her on

timolol 0.5% OU and referred her for further evaluation and ongoing care. Using timolol, her IOP was 14 mmHg OD and 13 mmHg OS. Uncorrected visual acuity was 6/6 in each eye and there was a relative afferent defect in the left eye. There were no biomicroscopic abnormalities and her anterior chamber angles were gonioscopically open OU. Pachymetry revealed a central corneal thickness of 554 microns in each eye. The dilated examination showed remarkably

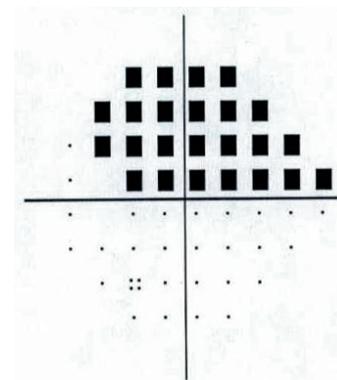
obliquely tilted optic discs in each eye with the right eye more extreme than the left. There were also notable RNFL abnormalities in each eye. (Figures 2A and 2B)

Threshold perimetry showed minimal visual field loss in the more anomalous right eye but extensive loss in the left eye with a significant threat to fixation. (Figures 3A and 3B)

Continued page 15



▲ Figure 3A. Patient 2. Threshold perimetry showed minimal visual field loss in the more anomalous right eye.



▲ Figure 3B. Patient 2. Extensive visual field loss in the left eye with a significant threat to fixation.

Glaucoma red-green disease

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GLAUCOMATOUS optic neuropathy is one of the leading causes of irreversible blindness in the Western world, with an increasing prevalence due to increasing and ageing population.¹

Although glaucoma is classically described as 'a bilateral but sometimes asymmetric optic neuropathy, with characteristic cupping, loss of the neuroretinal rim and nerve fibre layer, and corresponding visual field defect', its actual diagnostic criteria are vague.

Although landmark studies in glaucoma have often given a set of diagnostic criteria for their patients with glaucoma, these still vary widely and show that there is no single test that is adequate for the diagnosis or determination of progression of glaucoma. The use of various instruments or clinical signs to define glaucoma are inconsistent.² Even until the 1990s, there were studies that used intraocular pressure (IOP) as the criterion for the diagnosis of glaucoma, which we know may occur even in the presence of apparently 'normal' IOP.³

Another challenge in the diagnosis and management of glaucoma is pre-perimetric glaucoma. The classic glaucoma continuum described by Weinreb and colleagues begins at a stage when the eye is normal and progresses until total blindness.⁴

The pathological process in glaucoma is the acceleration of normal retinal ganglion cell apoptosis, and this progresses from an undetectable state to a state of apparent, clinical nerve

Over-reliance on imaging can yield false positives (red) and false negatives (green)

fibre damage, before it is detected by perimetric testing, and then finally functional impairment and blindness.

The stage where clinically apparent structural loss of the neuroretinal rim or nerve fibre layer is known as pre-perimetric glaucoma. With this clinical entity, clinicians become more dependent on structural measurements for assessing glaucoma.

Imaging techniques such as scanning laser polarimetry (GDx), confocal scanning laser ophthalmoscopy (HRT), and optical coherence tomography (OCT) allow eye-care practitioners to objectively detect, diagnosis and monitor changes to the optic nerve head.

Despite the usefulness of these imaging modalities in clinical practice, especially in the case of clinically earlier glaucoma,⁵⁻⁷ the United States Federal Drug Administration (FDA) lists only visual functions as endpoints for studies on glaucoma, and these include visual fields, colour vision, visual acuity and contrast sensitivity.⁸

The FDA states that in order for structural endpoints to be included, they need to demonstrate clinical correlation to current or predicted future visual function, since it is argued that functional loss is a better representation of the real world.

Another limitation of imaging techniques is that they are affected by patient factors such as age, disease severity, disc size and axial length. This is compounded by the limited range of patients in each instrument's normative database, which is used to compare a patient's result to determine whether they are range, borderline or abnormal.

These problems may result in false positives or false negatives, and this has been referred to as 'red' and 'green' disease. Red disease occurs when an instrument flags a nerve fibre layer as being 'red'—disease—but it is clinically normal, and green disease occurs when it is flagged as being 'green'—normal—but clinical examination suggests that it is actually pathological.⁹

The following four cases illustrate the need for careful clinical examination in the diagnosis and management of glaucoma, rather than relying solely on the measurements from the instrument.

CASE REPORTS

Red disease

Case 1

KK is a 24-year-old Asian male who presented for routine examination. Dilated fundus examination showed cup-disc ratios of 0.6 OD and 0.3 OS with a slightly thin inferior neuroretinal rim. Nerve fibre layer appeared intact on fundoscopic examination. Intraocular pressures were 16 mmHg OU. Central corneal thicknesses were 553 µm OD and 557 µm OS. Automated perimetry results were within normal limits. Baseline OCT testing showed inconsistent flagging of thin areas in right and left eyes in all three sector maps.

For example, the right eye 36 sector map flagged the 2 o'clock region as being borderline, while the four sector map flagged the inferior quadrant as

Continued page 14



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TGA approval date: 13th November 2013. **Reference:** 1. GANFORT PF 0.3/5 Approved Product Information.

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Eye Care

Red-green disease

From page 12

being borderline. However, with a fundoscopically normal nerve fibre layer, as well as an absence of wedge or focal defects with colour fundus photography, this patient was diagnosed with 'red disease' and was considered a glaucoma suspect. (Figure 1A)

Case 2

KP is a 30-year-old Asian female who presented for routine examination of high myopia and glaucoma suspect

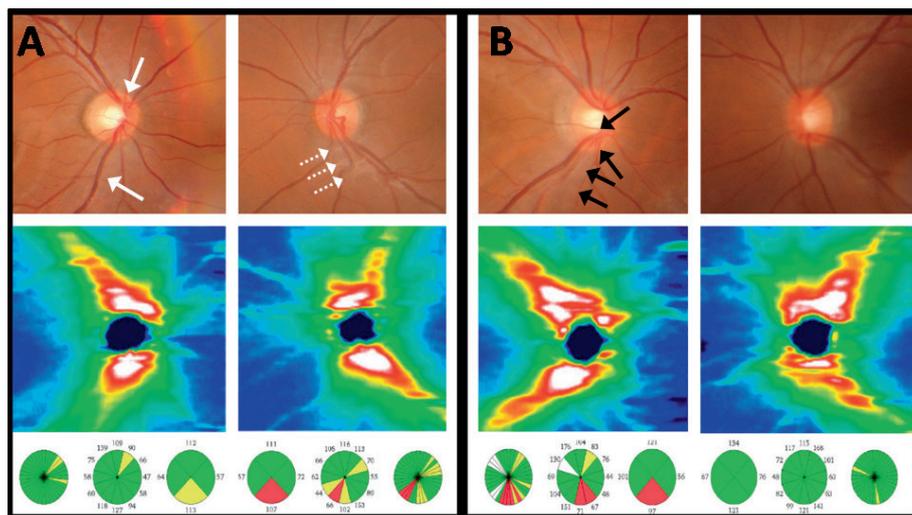
status. Dilated fundus examination showed cup-disc ratios of 0.7 OD and 0.6 OS with small and tilted discs OU due to high myopia of 7.00 D OU. The nerve fibre layer appeared intact in both eyes. Intraocular pressures were 16 mmHg OD and 17 mmHg OS. Central corneal thicknesses were 549 µm OD and 551 µm OS. Automated perimetry results were within normal limits. OCT imaging flagged the inferior sector as being outside normal limits in the right eye, with two adjacent sectors which were flagged as above normal limits. This was likely to have been due to a tilted disc configuration.

This patient was diagnosed with 'red disease' and continued to be monitored as a glaucoma suspect. (Figure 1B)

Green disease

Case 3

FT is a 64-year-old Asian female who presented for routine eye examination. Anterior examination showed heavy pigment deposition on the corneal endothelium and also on the trabecular meshwork and Schwalbe's line with gonioscopy. Dilated fundus examination showed cup-disc ratios of 0.3 OD and 0.5 OS. Neuroretinal rim was full and pink OD, and there was inferior pallor with associated nerve fibre loss OS. Intraocular pressures were 28 mmHg OD and 29 mmHg OS. Central corneal thicknesses were 573

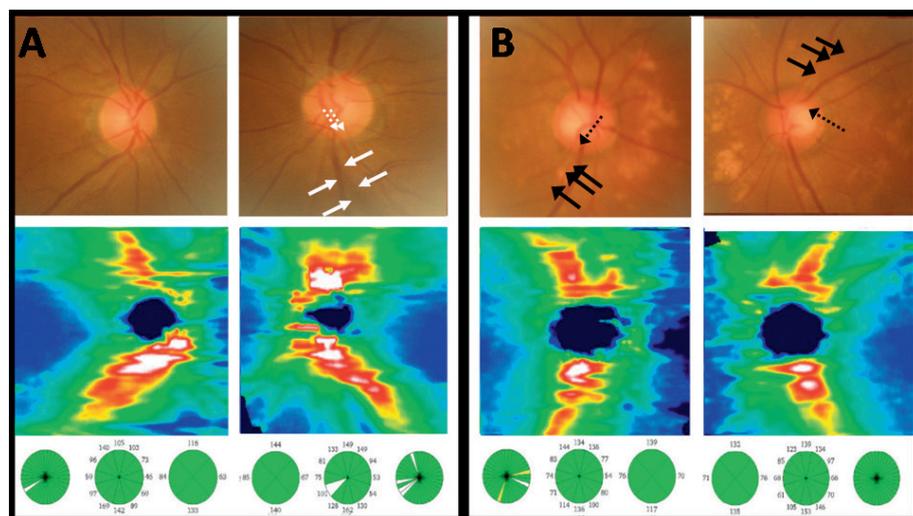


▲ Figure 1. (Top to bottom) Colour fundus photos, colour thickness map from OCT, sector RNFL thicknesses
 A: Case 1. Although the instrument flagged a superior sector and inferior quadrant in the right eye and inferior and superior sectors as outside normal limits, fundoscopic and photographic examination shows intact neuroretinal rim in the right eye (solid white arrows) and left eye (dashed white arrows)
 B: Case 2. The instrument flagged the inferior sector of the right eye as being outside normal limits, but the neuroretinal rim appears intact and there is no apparent nerve fibre layer defect (solid black arrow)

▲ Figure 2. (Top to bottom) Colour fundus photos, colour thickness map from OCT, sector RNFL thicknesses

A: Case 3. The instrument reported all sectors to be within normal limits or above normal limits; however, the fundus photo shows clear inferior wedge defect (solid white arrows) and thinning of the inferior rim (dashed white arrows)

B: Case 4. The instrument also reported sectors to be within normal limits, with only two sectors of the right eye being flagged as borderline; however, fundoscopic examination shows thinning of the neuroretinal rim in both eyes (dashed black arrows) and absent nerve fibre layers (solid black arrows)



µm OD and 549 µm OS. Automated perimetry results were within normal limits. OCT imaging showed all sectors to be within normal limits OU. However, fundoscopic examination and colour fundus photography showed clear inferior nerve fibre loss.

This patient was diagnosed with pigmentary glaucoma (green disease) and was commenced on timolol 0.5% mane to both eyes. (Figure 2A)

Case 4

HK is a 71-year-old Asian female who presented for routine eye examination. Anterior examination showed grade 3+ mixed cataracts in both eyes. Dilated fundus examination showed cup-disc ratios of 0.9 OU with deep cupping, and inferior and superior notching of the neuroretinal rim with associated nerve fibre loss OU. Intraocular pressures were 23 mmHg OD and 22 mmHg OS. Central corneal thicknesses were 503 µm OD and 509 µm OS. Automated perimetry results were unreliable OU. OCT imaging labelled the nerve fibre layer to be within normal limits in all quadrants OU. Once again, fundoscopic examination and colour fundus photography, despite dense cataracts, showed severe thinning of the neuroretinal rim.

The patient was diagnosed with primary open-angle glaucoma (green disease) and was commenced on timolol 0.5% mane to both eyes. (Figure 2B)

Conclusion

These four cases demonstrate that along with the suite of technologies available to clinicians, glaucoma remains a clinical diagnosis. OCT imaging is an excellent technology that provides an objective measurement of structure in ocular disease and allows clinicians to have a quantitative tool to monitor structural changes over time. However, there are limitations to these devices.

Clinicians must be aware of red disease and green disease, especially in the context of pre-perimetric glaucoma, and be cognisant of the overall clinical findings to arrive at a diagnosis and formulate the most appropriate management plan for each individual patient.

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Disc conundrum

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The anomalous optic discs made them difficult to assess for glaucomatous changes. It was felt that the visual field loss could be due to the disc anomaly or glaucoma, or both. Had the visual field abnormality been less extensive in the left eye, the patient would have been monitored closely over time without treatment, in order to determine if the field loss was unchanging and due to her anomalous discs or changing due to glaucoma.

However, the threat to fixation in the left eye placed the patient at risk of visual disability if she actually had progressive glaucoma, making treatment the most prudent option. She was taken off timolol temporarily to determine her IOP range. After several visits, her IOP never exceeded 16 mmHg in either eye. Several medications were tried over time and all were well tolerated, but most gave minimal IOP reduction. Eventually, bimatoprot 0.01% was found to lower IOP to 12 mmHg OU, which was the best response seen and she is being closely monitored on this treatment.

Congenitally anomalous conditions such as obliquely inserted nerves and TDS can confound glaucoma diagnosis because you cannot easily judge glaucomatous disc changes and RNFL, and visual fields are often abnormal. In these cases, we need to increase our emphasis on IOP, family history, corneal thickness and other risk factors to help guide decisions. If visual fields are only mildly abnormal, monitoring the patient for changes over time is a viable option. However, if field defects are extensive and the patient's vision is threatened, it is recommended to err on the side of caution and offer treatment in these instances.

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Do I need gonioscopy when I have an OCT?

Knowledge of the anterior chamber angle characteristics is essential

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TRADITIONALLY, the gold standard technique for examining the anterior chamber angle is gonioscopy. In the hands of a skilled practitioner the use of a gonioprism can quickly and accurately ascertain if an angle is open, narrow or closed and what other pathology may be present.

My personal observation is that some optometrists, young and old, are using gonioscopy less frequently and are less confident in their ability to interpret what they see when carrying out an examination.

Two possible explanations that may be drawn from this are that the time-restrictions placed on eye examinations makes gonioscopy impractical or that the information gained from gonioscopy is not deemed useful by practitioners as part of a comprehensive eye examination. A survey published in *Clinical and Experimental Ophthalmology* in 2008 has shown that only 56 per cent of ophthalmologists performed gonioscopy.¹

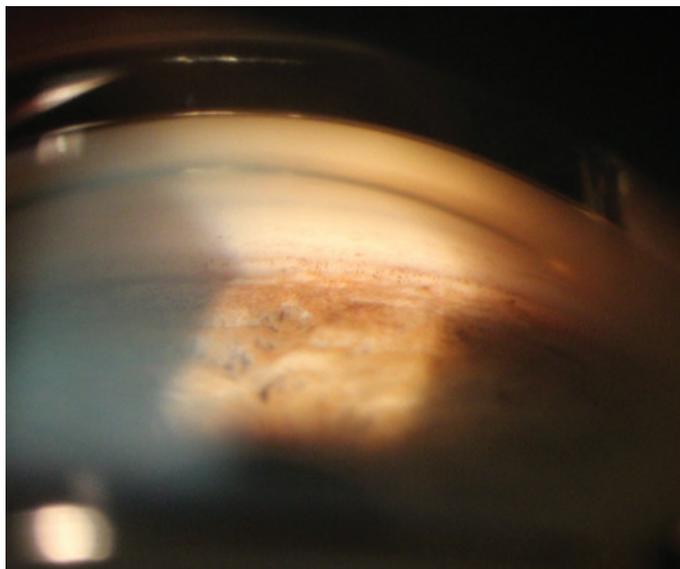
Both of these trends are concerning, given that the knowledge of the anterior chamber angle characteristics is essential when evaluating a patient with suspected glaucoma. The increased adoption of spectral-domain optical coherence tomography (SD-OCT) in general ophthalmic practices raises the question of whether anterior-segment SD-OCT can replace gonioscopy for anterior chamber evaluation in clinical practice or whether gonioscopy is

still an important technique that an optometrist or ophthalmologist should regularly use.

Gonioscopy has many advantages including its lack of expense, its reasonably short procedural time, the ability to dynamically see features across an entire angle quadrant and, when using a non-flange gonioprism, the ability to indent the cornea to differentiate between appositional and synechial angle closure.

Gonioscopy does have its shortfalls. It is a contact procedure that many patients find uncomfortable, its results are affected by factors such as examiner skill, patient co-operation, environmental light exposure and inadvertent corneal pressure, and it is a qualitative assessment, making comparison over time or between practitioners potentially unreliable.

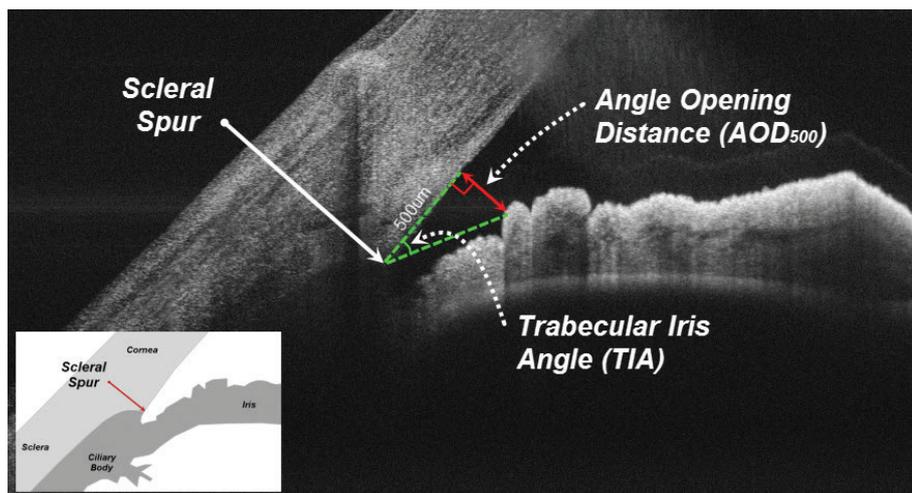
Other techniques to evaluate the



▲ Figure 1. Typical gonioscopic view of a wide open angle with light pigmentation



▲ Figure 2. Comparison of a narrow angle (< 0.2:1) in an older patient (left) and a young patient (right, respectively) as measured with Van Herick estimation of anterior chamber width to corneal width



▲ Figure 3. Useful landmarks and parameters when examining an ASOCT of an angle (Nidek RS3000)

anterior chamber angle include estimation of the Van Herrick anterior chamber to cornea ratio at the limbus with the slitlamp, ultrasound biomicroscopy and anterior OCT. Van Herrick is a technique often used by optometrists and ophthalmologists but is no substitute for angle visualisation due to its lesser ability to detect primary angle closure.^{2,3,4}

UB has been used since the early 1990s to look into anterior eye structures but these machines are rarely seen

outside ophthalmological centres. SDOCT is swiftly becoming commonplace in optometric practices and many of these machines have versatile anterior segment modules and analysis software, making imaging of the anterior chamber realistic. Some machines such as the Tomey Casia can even simulate a 3-D gonioscopic view from its scans.

The advantages of OCT for anterior chamber angle imaging include the speed and ease of image capture (which

could be carried out by a technician during pretesting), the ability to quantify the information with useful parameters such as the TIA (trabecular-iris angle, also used in the Schaffer and Spaeth gonioscopy grading scales) or AOD500 (angle opening distance), and the control of environmental light.

Disadvantages include the fact that angle structures are still altered by pupil size, accommodation and position of gaze, and when compared to ultrasound, structures such as the ciliary body and suprachoroidal space cannot be visualised. Anterior OCT is often used as a line scan to give a cross-section in a particular meridian and therefore, cannot show information across the entire quadrant without numerous scans, potentially missing areas of trabecular contact or peripheral anterior synechiae.

OCT will also not give information about coloured pathological features within an angle such as pigmentation or new blood vessels. (Figure 3)

There are several scenarios in which anterior OCT is particularly useful.

● **Evaluating lens vault**

Lens vault is defined as the distance measured between the anterior

Continued page 18

SCHEIE		SCHAFFER			SPAETH		
Classification	Findings	Classification	Findings	Angle Width (deg)	Classification	Finding	
Wide open	All structures visible	Grade 4	Ciliary body is visible	35 - 45	Iris insertion	A Anterior B Behind C In sclera D Deep angle recess E Extremely deep recess	
Grade I	Iris root not visible	Grade 3	Scleral spur is visible	20-35	Width of angle recess	0,10,20,30,40 degrees	
Grade II	Ciliary body not visible	Grade 2	Only trabecular meshwork is visible	20	Peripheral iris configuration	S Steep R Regular Q Queer	
Grade III	Posterior trabecular meshwork not visible	Grade 1	Only Schwalbe's line is visible	≤10	12 o'clock pigmentation	0 None 1+ Just visible 2+ Mild 3+ Moderately dense 4+ Dense	
Grade IV	None of the angle structures visible	Grade 0	Angle is closed	0			

▲ Table 1. Comparison of the three main gonioscopy grading scales

Gonioscopy

From page 17

surface of the crystalline lens and the perpendicular line connecting opposite scleral spurs. Foo *et al* 2012 showed that lens vault was one of the main predictors of angle closure.⁵ This value essentially relates to the bulk of the lens taking up space in the anterior chamber and is more predictive than just lens thickness, as thick lenses do not necessarily move the peripheral iris closer to the trabecular meshwork. Patients with lens vault as a dominant factor in their angle closure glaucoma may benefit more from cataract surgery, as it has been shown that the amount the angle opens corresponds to the drop in IOP following lens extraction.⁶ (Figure 4)

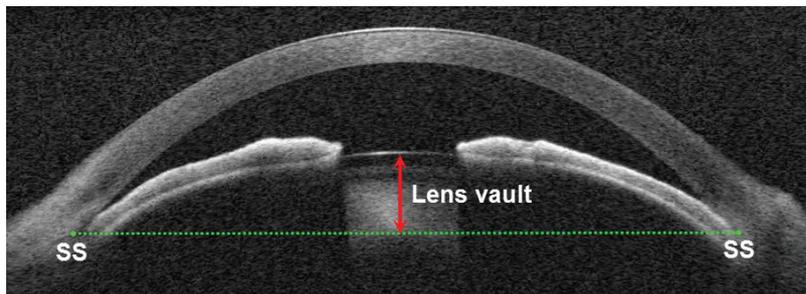
• Documenting narrow angles

Gonioscopic grading can be confusing as the three main scales are conflicting and can be laborious to master (Table 1). Being able to quantify the extent at which an angle is open and compare this value consistently over time and between observers potentially offers a more accurate method of angle assessment as reports suggest intra-observer variation in ASOCT analysis of the anterior chamber angle is low.⁷

Several studies have looked into how anterior segment OCT compares with the gold standard of gonioscopy. Sensitivity for detecting angle closure was shown to be as high as 98 per cent although specificity was lower at 55 per cent.⁸ Indeed, ASOCT has been shown to classify a higher proportion of eyes in the sample as having one or more closed quadrants (59 per cent) versus gonioscopy (33 per cent).⁹ Interestingly in this paper, the superior, inferior



▲ Figure 5. ASOCT showing the effect on anterior chamber angle opening when light is shone in the pupil. The image on the left has a penlight being shone in the fellow eye to simulate poor gonioscopy technique, whereas the right image is in a dark room (Nidek RS3000).



▲ Figure 4. Lens vault diagram in a closed angle eye (Tomey Casia)

and nasal quadrants appeared more frequently closed with ASOCT yet the temporal quadrant was more often closed with gonioscopy. (Figure 5)

Conclusion

OCT adds a very useful tool to the arsenal of the ophthalmic practitioner for anterior chamber angle screening and monitoring changes to these structures over time. Any test is more useful than no test, so for an individual not confident in their gonioscopic technique, OCT could provide a potentially more accurate result. However, do not forget that especially in glaucoma suspects and patients diagnosed with glaucoma, OCT in its current form cannot replace gonioscopy. If you individualise your procedures to use OCT as a screening tool and confirm your findings with darkroom gonioscopy on suspicious angles, then you can still provide excellent patient care while not disrupting your busy practice schedule.

The final point to make is that images in medicine are very powerful tools. Using the OCT scans to educate patients about their condition will reinforce their understanding in a way simply describing the gonioscopy

result cannot. If our patients are well educated during their consultations, they will become more compliant and recognise the importance of their routine eye examinations in the future.

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Cataract surgery and glaucoma

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THE INCIDENCES of both glaucoma and cataracts increase with age. This means that patients with both pathologies become increasingly common as we live longer, and with new technology we detect glaucoma earlier.

For a patient with glaucoma, a visually significant cataract that warrants surgery now opens up a multitude of treatments, benefits and potential complications that need to be explored.

Angle closure

The first and simplest case to discuss is primary angle closure glaucoma and phacomorphic glaucoma. If a patient still has a significant degree of iridotrabecular contact despite a patent peripheral iridotomy, then a lensectomy is the appropriate next step in their treatment. Removing the crystalline lens with a thickness of 4-6 mm and replacing it with an artificial lens with a thickness of approximately 1 mm opens up the angle significantly.

If there has been iridotrabecular contact for a prolonged period of time, then there may be peripheral anterior synechiae (PAS). These adhesions between the iris and trabecular meshwork create a physical barrier to aqueous outflow and in the longer term, cause scarring and failure of the trabecular meshwork.

In patients with PAS, goniosynechiolysis can be performed at the same time as the cataract extraction. This involves physically peeling the iris

off the trabecular meshwork using the surgical gonioscopy lens to visualise the angle. If the meshwork has not been scarred, then this may restore aqueous outflow and a normal IOP.

Cataract surgery as a treatment for glaucoma

Numerous studies have shown that cataract surgery alone may lower the IOP by up to 6 mmHg even when the angle is completely open prior to surgery. This effect can last for up to two years. The mechanism is unknown and unfortunately, we cannot predict which patients will have this IOP lowering effect. Nonetheless, cataract surgery alone may sometimes significantly improve a patient's IOP.

Micro invasive glaucoma surgery (MIGS) is an extremely promising new development in glaucoma surgery. The two different MIGS devices that are available in Australia are stents that bypass the trabecular meshwork and allow aqueous to flow straight into the canal of Schlemm. The stents therefore bypass the trabecular meshwork, which is the presumed barrier to the efficient outflow of aqueous.

The stents are less than 1 mm in cross section and can be seen only on gonioscopy. They can be inserted

when cataract surgery is performed. As the stents drain into the canal of Schlemm, their effect will be limited by the episcleral venous pressure. This means that unlike a trabeculectomy, they cannot lead to hypotony.

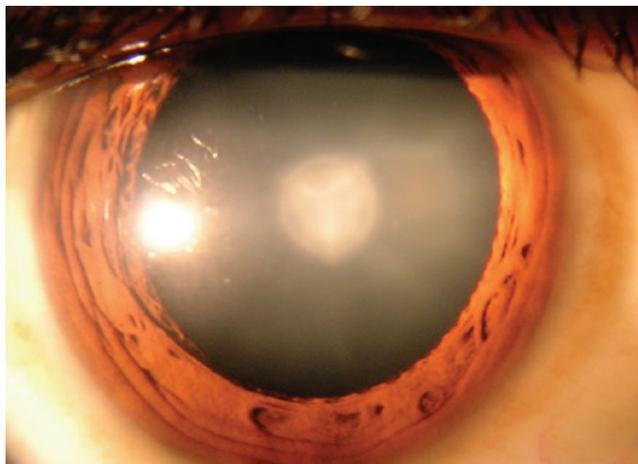
The outcomes of MIGS may be potentially better, safer and more predictable than those of traditional glaucoma surgery.

Specific issues for patients with glaucoma

The vast majority of patients on ocular anti-hypertensives use prostaglandin drops. Years ago, these were stopped in the peri-operative period as they were thought to increase the risk of cystoid macular oedema; however, this theory has been discredited.

Generally, all glaucoma drops with the exception of pilocarpine should be continued up to the day prior to cataract surgery. They should be continued post-operatively with the caveat that they may be stopped or modified if the cataract operation lowers the IOP.

Post-operatively, all patients will need to use steroid eye-drops. Although



▲ Figure 1. Cataract in human eye Image: Rakesh Ahuja MD

Cataract surgery

From page 19

the rate of steroid response is higher in patients with glaucoma, they are generally used only four times per day for one month, so a significant rise in IOP from the steroids is unlikely.

If the steroids drops are stopped too early and the patient develops cystoid macular oedema, then steroid drops may be required for many months. If the patient is a known severe steroid responder, then additional medications may be needed to control the increase in IOP over the short term.

Preserving the ocular surface is an important part of post-operative management in glaucoma patients. Many surgeons routinely use three different drops after cataract surgery: an antibiotic, a steroid and an NSAID such as Acular or Voltaren. Combined with the patient's glaucoma drops, both the medications themselves and their preservatives can damage the ocular surface quite significantly.

It is important to change the patient to preservative-free medications wherever possible to avoid causing unnecessary damage to the ocular surface. Even with non-preserved medications, many glaucoma patients will develop a moderate transient epitheliopathy. This should settle with non-preserved lubricants once the additional post-operative drops are ceased.

Cataract surgery in patients who already have a functioning trabeculectomy

With MIGS, selective laser trabeculoplasty and prostaglandin analogues, it is reasonably rare for a patient needing cataract surgery to have already had a trabeculectomy. Unfortunately, even a perfectly functioning trabeculectomy will sometimes fail after routine cataract surgery.

This is thought to be due to post-operative inflammation. Generally, the surgeon will administer a sub-conjunctival injection of the anti-metabolite 5-Fluorouracil at the end of the cataract surgery and use intensive

post-operative steroids to reduce the risk of these failures.

To avoid these complications, if there are no contra-indications, cataract surgery will often be combined with a trabeculectomy to avoid issues in later years.

Cataract surgery in end-stage glaucoma

Patients who have very severe or end-stage optic nerve damage are at risk of 'snuffing out' their vision after cataract surgery. The risk of this is particularly increased if there is a 'macular split' on the visual fields. There are multiple potential causes of this but the ultimate mechanism is further damage to an already perilously damaged optic nerve.

Intra-operative or post-operative IOP spikes, or damage from a higher intraorbital pressure (as opposed to intraocular) from a peri-bulbar anaesthetic may all be contributing factors. As with all patients with glaucoma, meticulous control of these factors is vital to ensuring a good outcome. These patients are often given oral acetazolamide for two to five days post-operatively to avoid pressure spikes. To reduce intro-orbital pressure spikes from the anaesthetic, topical or general anaesthesia may be needed for the procedure.

A patient with severe glaucoma may require a trabeculectomy or a glaucoma drainage tube in the future. The surgeon must take meticulous care of the conjunctiva intra-operatively to preserve it for any future surgery.

Conclusions

Cataract surgery alone may be very beneficial for patients with glaucoma; however, with MIGS, cataract surgery may have even more benefits. Despite the advantages of cataract surgery, it is vital that all of the potential complications are anticipated and avoided wherever possible.

Glaucoma patients need close monitoring post-operatively and even if their IOP drops enough so that they can stop drops altogether, they still require follow-up in the long term.

Talk to your

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DESPITE therapeutic advances, the global burden of glaucoma today is high and will continue to rise—60.5 million people suffered from glaucoma in 2010, and by 2020 this is predicted to reach 79.6 million.¹ Glaucoma impacts quality of life (QoL) for all patients with the disease.

QoL is a reflection of an individual's general well-being: one's ability to pursue a fulfilled and happy life.^{2,3} QoL is influenced by a number of dimensions, including mental health, physical ability, general health perceptions, social and workplace function and independence. Although the components of a good QoL are unique for each person, vision is consistently a key determinant.⁴⁻⁶

QoL: influential factors

Loss of visual function due to glaucomatous optic neuropathy (GON) is the major determinant of health-related QoL for glaucoma patients. This can impact venturing from home, driving, walking, seeing at night, reading, adjusting from dim to bright conditions and vice versa, judging distances, walking on stairs and seeing objects coming from the side.⁶⁻¹⁰ Motor vehicle accidents and injuries related to falls are potential serious consequences of glaucomatous vision loss.¹¹

Reduced health-related QoL begins

patients about their quality of life

Factor in their real-life concerns

in the earliest stages of glaucoma and deteriorates proportionally to visual field loss.^{12,13} Knowledge of the diagnosis only minimally influences the negative QoL effects: vision-related QoL is reduced even in individuals who are unaware that they have glaucomatous vision loss.¹³

The detrimental impact of loss of visual function is magnified when the vision loss is bilateral;¹²⁻¹⁴ however, the influence of the second eye may not be as great as originally thought. More recent data show that global visual field indices from the better eye are as influential on QoL as binocularly integrated visual field indices.¹⁵

Other ocular and visual factors distinct from GON influence QoL among glaucoma patients. It is important to identify and understand these factors, as unlike GON, many of these can be modified or corrected. Ocular surface discomfort, commonly exacerbated by topical glaucoma medications, contributes to the overall burden of disease.¹⁶ Cataract, frequently found among glaucoma patients,¹⁷⁻¹⁹ is a well-recognised cause of reversible vision impairment among glaucoma patients;⁹ it is also an important determinant of their QoL.²⁰

Psychological, social, cultural and emotional factors are important. As sight deteriorates, the psychological burden grows, together with an increasing fear of blindness, social withdrawal from impaired visual function and depression.²¹⁻²³ A patient's visual dysfunction may be influenced by other debilitating medical conditions, and psychological and social constraints. These factors interact in a complex manner and are difficult to measure; however, they can be reflected in holistic QoL assessment.

QoL: clinical perspective

In clinical practice, QoL assessment can be performed routinely for glaucoma patients, without questionnaires. QoL can be assessed by enquiring about the patient's general medical history, visual function,

		Does your vision give you any difficulty, even with glasses, with the following activities?				
		None	A little	Some	A lot	Severe
1.	Walking after dark	1	2	3	4	5
2.	Seeing at night	1	2	3	4	5
3.	Walking on uneven ground	1	2	3	4	5
4.	Adjusting to dim lights	1	2	3	4	5
5.	Going from light to dark room or vice versa	1	2	3	4	5
6.	Seeing objects coming from the side	1	2	3	4	5
7.	Walking on steps/stairs	1	2	3	4	5
8.	Judging distances of foot to step/curb	1	2	3	4	5
9.	Finding dropped objects	1	2	3	4	5

▲ Table 1. The Glaucoma Activity Limitation-9 Questionnaire

independence, well-being, mood and level of satisfaction with their care. A close therapeutic relationship between clinician and patient, characterised by active listening and a supportive, non-judgemental approach, leads to an accurate QoL assessment.

QoL is at the core of our role as clinicians—the goal of the therapeutic relationship with our patients is to maximise their QoL. Preventing glaucomatous vision loss is crucial to achieve this end. However, minimising the impact of treatment-related discomfort and treating other causes of visual morbidity are equally important strategies to improve QoL and visual function.

Clinicians often gauge the success or failure of glaucoma management by focusing on serial visual field testing and/or nerve fibre layer structural analysis as markers of progressive GON, yet this is only one aspect of the overall impact of glaucoma on a patient. Often the patient's main concerns are ocular surface discomfort, blurred vision (which is typically not due to GON), and the risk of going blind.^{16,23} By addressing QoL concerns, patient and clinician can together reorientate towards common, realistic goals resulting in better concordance with treatment programs, a more

harmonious relationship and greater patient satisfaction.²⁴

When making clinical decisions, QoL concerns should be considered foremost. For example, a common management dilemma is when patient and clinician are faced with three choices: to commence/add a topical medication, undertake a course of laser (for example, selective laser trabeculoplasty) or continue with the current treatment.

While the intraocular pressure, the severity and progression rate of GON, the mechanism of glaucoma and the relative success of the proposed treatment must be considered, so too must other factors. These include the implications for ocular surface disease, other causes of visual morbidity, general health issues, other disability, patient knowledge, beliefs and attitudes, and the suspected adherence to any proposed treatment plan. Such decisions first require proper patient education, open and realistic discourse, clear, informed choices for the patient to make, and a frank discussion of potential QoL impact.

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Quality of life

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QoL measurement for patients with glaucoma

● Patient reported outcome questionnaires

Formal QoL analysis typically involves questionnaires, also known as patient reported outcome (PRO) tools. A number of PROs is available for patients to systematically self-measure the effects of glaucoma on their QoL. Most PROs involve several items and each item is a question related to a specific functional ability. The respondent grades their answer reflecting the severity of the problem on a Likert scale. For example, see Table 1, the Glaucoma Activity Limitation-9 (GAL-9).

PROs typically used among glaucoma patients can reflect general health (for example, the 12-item Short Form Health Survey), broad visual function (for example, the 25-item National Eye Institute Visual Function Questionnaire [NEI-VFQ]) or can be glaucoma specific (for example, the GAL-9).²⁵ Our group has found the latter in particular useful in quantifying visual disability related to glaucoma.^{6,16,20,22}

● Item response theory: Rasch analysis

Increasingly sophisticated strategies for QoL analysis produce more fruitful results. In the past, QoL data analysis involved adding raw scores from each item of the PRO to create a combined QoL score; however, this approach is increasingly recognised as problematic.

For example, how can we assume that each PRO item has equal weight in reflecting QoL? Is each item equally valid, or are some items tangentially influenced by unwanted, confounding factors? Can we assume that a particular PRO is sufficiently matched for glaucoma patients of all severities, or is it sensitive only at one end of the glaucoma severity spectrum?

These problems can be addressed by Rasch analysis of the data. Rasch analysis is a type of Item Response

Theory initially developed by educational psychologists in the 1960s, and applied only recently to vision-related QoL research. In Rasch analysis, questionnaire summary scores are transformed into log score intervals to permit parametric analyses to be performed on the data.²⁶ Rasch analysis has led to improved PROs. For example, the GAL-9 is a Rasch analysed, refined version of the Glaucoma Quality of Life-15, with improved psychometric properties.²⁷

● Utility value assessment

Utility values are increasingly used as preference-based measurements of health-related QoL. Utility values are used to grade patient health experience from zero (death) to one (perfect health), or vision-specific experience zero (complete blindness) to one (perfect vision). Utility values are easily converted to quality-adjusted life-years (QALYs), which are critical to health economic analyses.^{28,29} As health resources are tightening, QALYs are important metrics for cost-utility analysis for the allocation of health funding.

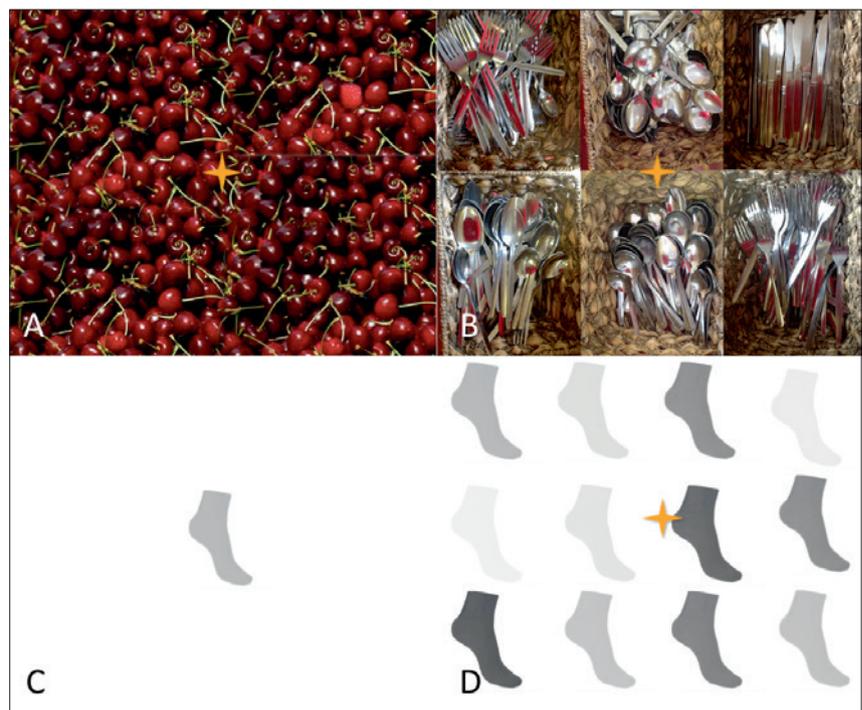
Future directions: clinical research guiding clinical practice

Our group has used a three-pronged research strategy to evaluate QoL among glaucoma patients.

First, in our recent research we have used only Rasch-analysed PROs and then performed Rasch analysis on our results, thereby refining the integrity of QoL information gained from clinical studies.

Second, we have systematically quantified the influence of key factors on QoL in glaucoma, some of which may be treatable or reversible. These include studies specifically evaluating the influence of depression,²² ocular surface disease,¹⁶ cataract²⁰ and age-related macular degeneration (AMD)³⁰ in patients with glaucoma.

That these factors influence QoL is unsurprising; however, each study has revealed additional important results with clear implications for clinical practice. For example, we demonstrated the relationship between deteriorating QoL and increasing daily



▲ Figure 1. Objective quality of life assessment: each image is projected onto a large screen requiring 30 degrees of visual field. Patients are asked to: A. find a raspberry among the cherries; B. find a fork among the spoons, and a spoon among the forks; and to correctly match the sock in C with one in D.

dose of drop preservative. We found that cataract density determined on slitlamp examination may be a better guide than visual acuity when deciding the optimal timing of cataract surgery in glaucoma patients. We found that patients with both AMD and glaucoma have a heightened self-perceived risk of falls compared to those with glaucoma alone. Other factors we are currently investigating include the influence of patient education and location of visual field deficit on QoL in glaucoma.

Third, we have designed a new objective QoL assessment tool. Questionnaires have their limitations and can be influenced by mood, recall bias and other non-clinical factors.³¹ These unwanted influences can be minimised by objective vision-related QoL assessment. Using computer-based simulations, this test evaluates patients' ability to perform visually demanding tasks under timed conditions. The test involves a series of screen images; each one reflects a real-life scenario, such as driving, matching socks, shopping at a supermarket, detecting people in a crowd or finding cutlery in a draw (Figure 1).

Each image has a central fixation point, therefore the patient is required to use their peripheral vision to locate the desired object. In a sense, the test is a hybrid of a visual field test and a functional assessment of activities of daily living. This test would be a useful glaucoma education tool for patients, clinicians and the public.

Conclusion

QoL research in glaucoma has made considerable progress over the past few decades, providing important insights into our patients' concerns, lifestyle and daily function in society. These insights have key implications for the way we undertake patient care. Whether explaining the nature of the condition, offering counseling for future risk, or empowering patients to make informed treatment decisions, QoL is a key ingredient for many dimensions of the patient-clinician relationship.

Understanding a patient's psychosocial background and QoL helps the health team (patient, optometrist, general practitioner, pharmacist and ophthalmologist) work together more effectively and tailor patient-centred

treatment strategies, leading hopefully to more successful glaucoma care. Continued efforts are needed to delineate better the ocular, systemic and psychological influences of QoL in glaucoma and to refine our methods of QoL assessment.

As therapeutic and diagnostic techniques in glaucoma improve, we must remember to focus on our patients as individuals, address their real-life concerns and understand the impact of glaucoma on their current and future well-being.

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ABSTRACTS

Retinal sensitivity is reduced in patients with obstructive sleep apnoea

Patients with obstructive sleep apnoea (OSA) have been shown to have reduced retinal sensitivity, as measured using standard automated perimetry (SAP), compared with age-matched, healthy control patients.

This study involved the prospective enrolment of OSA patients (n = 80) and age-matched controls (n = 111). Participants underwent at least one reliable SAP (Humphrey 24-2 SITA standard). Peripapillary retinal nerve fibre layer thickness (RNFL) was measured with spectral domain optical coherence tomography (SD-OCT). OSA patients were sub-classified into three groups based on the apnoea/hypopnoea index as having mild, moderate or severe OSA.

Mean visual acuity, central corneal thickness and RNFL thickness did not differ significantly between the OSA and control groups. The SAP mean deviation was higher in patients with OSA compared with controls (-0.23 ± 0.8 dB versus -1.74 ± 2.8 dB, p < 0.001). In patients with OSA, SAP threshold values were more depressed in the peripheral field. The apnoea/hypopnoea index was significantly correlated with the SAP indices (p < 0.001).

It is important for clinicians to be aware that OSA patients may have non-glaucomatous visual field abnormalities, which needs to be differentiated from glaucoma.

Invest Ophthalmol Vis Sci 2014; 55: 11: 7119-7125.

Motor vehicle collisions and central binocular visual field damage in primary open angle glaucoma patients

In this Japanese study, the number of self-reported motor vehicle collisions was found to not be related to the extent of central visual field abnormality in patients with primary open angle glaucoma (POAG).

POAG patients (n = 247) were surveyed about their motor vehicle collision history and driving habits. The relationship between motor vehicle collision history and 52 total deviation values of an integrated binocular visual field, better and worse visual acuities, age and gender were examined.

A total of 51 patients (20.6 per cent) reported a prior motor vehicle collision. There were significant differences between patients with and without a collision history for better visual acuities, a single total deviation value in the superior-right visual field and the average distance driven per week (p < 0.05). No significant relationship was evident between collision history and the mean visual field deviation. There was a significant positive relationship between collisions and the distance driven per week (p = 0.005).

Taken together, these data suggest a complex relationship between visual function and driving tasks in POAG. Careful consideration should be taken with regard to attempting to predict a patient's driving abilities from their central visual field findings.

PLoS One 2014; 9: 12: e115572.

Association between mitral valve prolapse and open-angle glaucoma

The presence of pre-existing mitral valve prolapse (MVP) has been found to be a significant predictor for the development of open-angle glaucoma.

This retrospective cohort study used a longitudinal health insurance database from the National Health Insurance program in Taiwan, consisting of more than one million individuals who were followed from 1996 to 2008. A total of 21,677 people had experienced MVP; 86,708 subjects without MVP were propensity-score matched and served as a comparison group.

The incidence of open-angle glaucoma in patients without MVP and those with a history of MVP was 10.2 and 16.1 per 10,000 person-years, respectively. The adjusted HR for open-angle glaucoma in the MVP group was 1.88 (95% CI: 1.58 to 2.23).

Heart 2014; ePub 11 December 2014.

Effectiveness of tele-glaucoma versus in-patient examination for glaucoma screening

Tele-glaucoma, involving the electronic examination of stereoscopic digital ocular images by an ocular specialist, has been shown to be an effective screening tool for glaucoma.

A systematic review and meta-analysis sought to both assess the usefulness of tele-glaucoma as a screening tool for glaucoma and to provide estimates of the diagnostic accuracy, diagnostic odds ratio and the relative percentage of glaucoma cases that were detected.

A total of 45 randomised controlled clinical trials were included. Meta-analysis showed that tele-glaucoma was relatively more specific (specificity: 0.790, 95% CI: 0.668 -0.876) and less sensitive (sensitivity: 0.832, 95% CI: 0.770 -0.881) than in-person patient examinations. It was reported that the relative odds of a positive screen test in glaucoma cases was 18.7 times more likely than a negative screen test in a non-glaucoma case.

This analysis demonstrates that tele-glaucoma can be used to screen for glaucoma. The findings suggest that more cases of glaucoma can be detected using this method than in-person examination.

PLoS One 2014; 9: 12: e113779.

Relationship between central corneal thickness and oxygen levels in the anterior chamber angle

An inverse correlation has been found between central corneal thickness and oxygen levels in the anterior chamber angle.

This prospective, cross-sectional study involved 124 patients undergoing cataract and/or glaucoma surgery. Prior to the surgical procedure, an oxygen sensor was used to measure anterior chamber oxygen levels at three

locations: near the central corneal endothelium, in the mid-anterior chamber and in the anterior chamber angle. Multivariate regression analyses were used to assess for correlation between oxygen levels and central corneal thickness.

The only significant relationship found was a correlation was between central corneal thickness and oxygen in the anterior chamber angle.

It was concluded that this finding could provide insight into the reason why a relatively thinner cornea could increase glaucoma risk. The authors hypothesised that exposure of the outflow system to higher oxygen levels may increase the risk of oxidative damage within the trabecular meshwork.

Am J Ophthalmol 2014; ePub 26 November 2014.

NTG and optic nerve head torsion

Optic nerve head torsion has been found to be a feature of normal-tension glaucoma (NTG).

Using two-dimensional optical coherence tomography images, this study compared optic nerve head tilt and torsion in eyes with NTG (n = 78) and primary open angle glaucoma (POAG, n = 78); eyes were matched according to age and axial length. Comparisons between the groups were made for the extent of horizontal, vertical and maximum optic nerve head tilt and torsion. Further comparisons were undertaken based on myopic status and visual field deficit location.

The degree of vertical and horizontal tilt did not differ between NTG and POAG eyes. NTG eyes had significantly higher degrees of torsion than POAG eyes (p = 0.022) did with matched axial length. In addition, NTG eyes showed a significant difference in the degree of maximum tilt and torsion, and the direction of vertical tilt and torsion by the location of the visual field defect.

Taken together, these data suggest that NTG is more prominently associated with optic nerve head torsion compared with POAG in eyes of similar axial length.

Invest Ophthalmol Vis Sci 2014; Nov 25; 56: 1: 156-163.

Uveitis a potential confounding factor for retinal nerve fibre layer thickness measurements

The presence of uveitis has been reported to be a confounding factor that may limit the accurate assessment of retinal nerve fibre layer (RNFL) thickness, using optical coherence tomography (OCT).

A comparative, retrospective pilot study involved consecutive uveitis patients who had undergone OCT RNFL measurements in an ophthalmology clinic. Included in the study were uveitic eyes without glaucoma (n = 76) and uveitic eyes with established glaucoma (n = 135). Global and sectoral RNFL thickness measurements were taken.

In non-glaucomatous uveitic eyes with active inflammation (n = 19), mean global- and sectorial-RNFL measurements were thicker than the normative 95th percentile.

The mean global RNFL measurement in these eyes was also greater than in the non-glaucomatous uveitic eyes without active inflammation (n = 57). In uveitic eyes (both quiescent and active) with glaucoma, the mean global RNFL thickness was found to be significantly greater than in eyes with a similar stage (moderate) of non-uveitic glaucoma.

It was concluded that these findings raise concern about the value of OCT RNFL measurements for detecting and monitoring glaucoma in eyes with uveitis.

Ophthalmology 2014; ePub 4 November 2014.

Relationship between iris surface features and anterior chamber angle width

An association has been described between irises with more surface crypts and a lighter colour and a wider anterior chamber angle, in Asian eyes.

In this prospective, cross-sectional study, subjects (n = 600) were recruited from a large population-based study in Singapore. Digital slitlamp photographs were used to assess iris surface features (that is, the number and size of crypts, the number and circumferential extent of furrows and colour). Anterior chamber width was measured using

optical coherence tomography images. Data from right eyes were used in analyses.

Included in the analyses were a total of 464 eyes, which had digital photographs of suitable quality for grading. Following adjustments for age, sex, ethnicity, pupil size and corneal arcus, it was found that a higher crypt grade was independently associated with a wider anterior chamber angle. Darker irises were associated with a narrower anterior chamber angle.

The authors concluded that these findings suggest that iris surface features may be a useful adjunctive measure to assess the risk of angle closure.

Invest Ophthalmol Vis Sci 2014; 55: 12: 8144-8148.

Swimming goggle wear is not associated with an increased prevalence of glaucoma

A recent Australian study has shown that frequent wearing of swimming goggles does not lead to an increased risk of glaucoma.

Regular swimmers (n = 231) and non-swimmers (n = 118) underwent comprehensive ocular examination, including the measurement of intraocular pressure, visual fields and retinal nerve fibre layer (RNFL) thickness using optical coherence tomography.

Based on intraocular pressure and visual fields, no new cases of glaucoma were detected in the participants who swam regularly. There were also no significant differences in RNFL thickness between swimmers and non-swimmers.

Br J Ophthalmol 2014; ePub 9 September 2014.

Pre-perimetric open angle glaucoma

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CASE REPORT

MRS A, a 60-year-old Caucasian female, was referred to the Centre for Eye Health for a glaucoma assessment due to large cupping in both eyes. The patient did not have any obvious historical risk profile for glaucoma apart from her age.

Entering visual acuities with habitual correction were 6/7.6 OD and 6/6 OS.

Corneal thicknesses were measured at 545 μm OD and 537 μm OS with ultrasound. IOPs were 22 mmHg in each eye at 11 pm. Gonioscopy showed open angles with no evidence of secondary glaucoma.

Stereoscopic optic nerve assessment (Figures 1 and 2) showed moderately large optic disc cupping in average-sized optic discs. There was no evidence of Drance haemorrhages, no significant Beta peripapillary atrophy and no evidence of retinal nerve fibre layer (RNFL) defects with red-free assessment. There was some undermining of the neuroretinal rim (NRR) in each eye with deep cupping, prominent but regular lamina pores but no evidence of focal thinning, pallor or notching in either eye.

RNFL analysis with the Cirrus OCT (Figure 3) classified all sectors as within or above normal limits compared to a normative database. The TSNIT graphs and quadrant analysis however showed an asymmetry inferiorly (right inferior RNFL reduced).

Ganglion cell thicknesses (data not shown) were all within or above normal limits in both eyes with minor asymmetries.

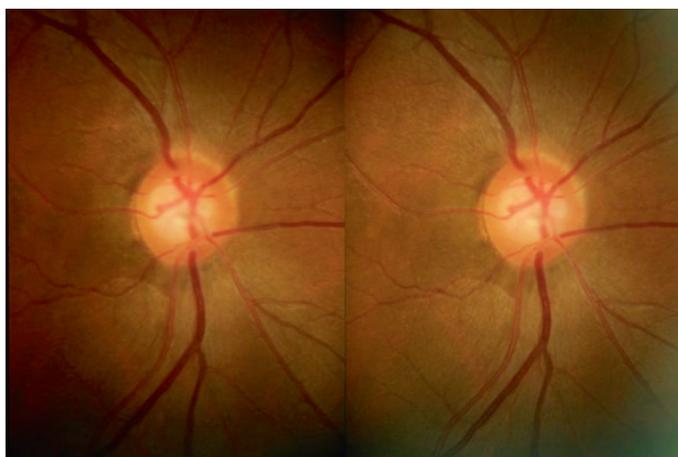
Heidelberg Retina Tomograph 3 (HRT3) (Figure 4) classified the NRR as outside normal limits in both eyes compared to a normative database (superior nasal OD and inferior nasal OS).

Visual field testing (data not shown) showed good reliability indices. There was a minor superior field defect in the pattern deviation plot for the right eye and Glaucoma Hemifield Test (GHT) was classified as outside normal limits. The left field was essentially clear.

Based on this initial set of results, the patient was advised to repeat the visual fields at the referrer's practice to confirm if the defect in the right eye was repeatable and assuming a clear result, be reviewed with repeat imaging annually.

Mrs A was referred back to the centre 18 months later, at which time there was no change in the historical risk profile and IOPs were 20 mmHg OD and OS. There were no notable fundoscopic changes in the NRR or RNFL, no marked changes in the HRT or OCT (three results are needed for instrument-based change analysis)

Continued page 28



▲ Figure 1A. Stereo photographic image of the right disc at the initial visit (best viewed with base out prism)



▲ Figure 1B. Stereo photographic image of the right disc at the third visit

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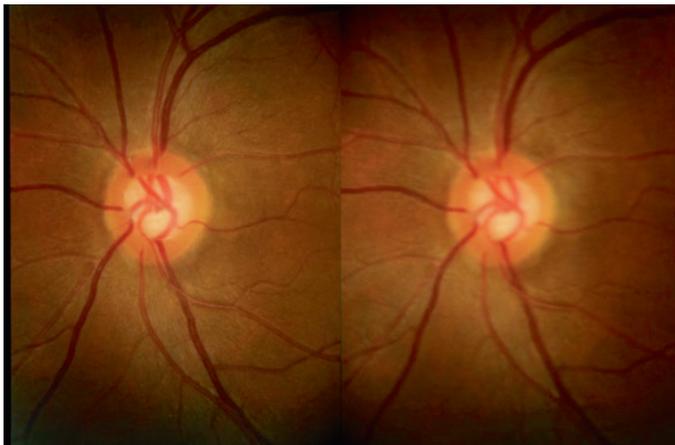
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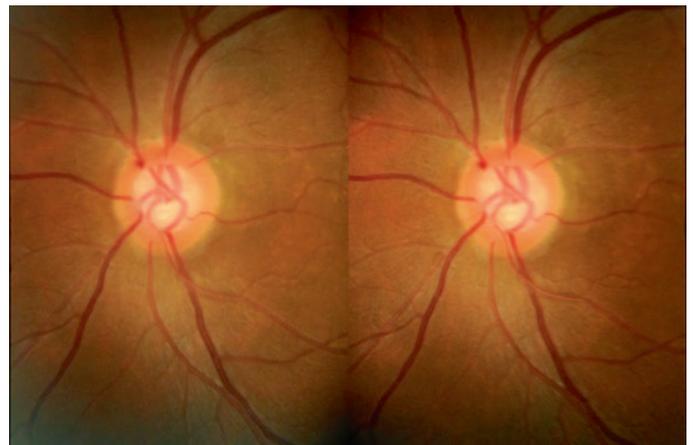
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▲ Figure 2A. Stereo photographic image of the left disc at the initial visit



▲ Figure 2B. Stereo photographic image of the left disc at the third visit

Pre-perimetric

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and the visual fields were essentially clear in both eyes. Annual review was recommended.

Mrs A was seen again at the centre 12 months later. Her historical risk profile and IOPs were unchanged from the previous visit.

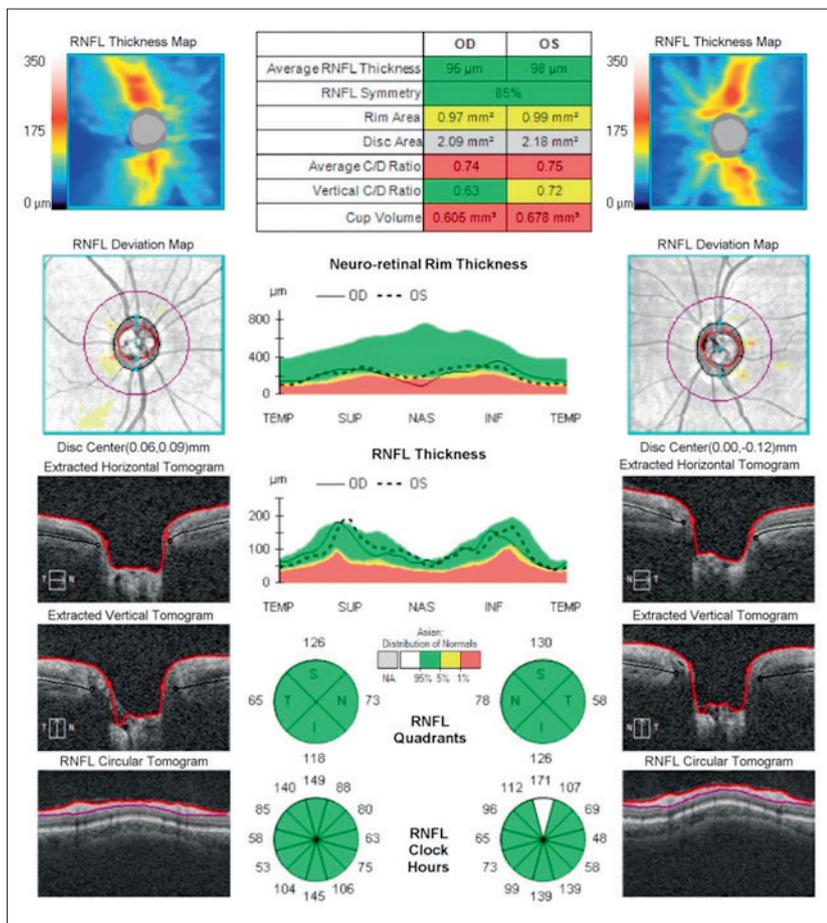
Comparative stereoscopic nerve evaluation (Figures 1A and 1B) showed a darkening of the inferior nasal RNFL extending from the disc in the right eye. There was also a change in contour of a blood vessel overlying the inferior temporal neural retinal rim correlating with a thinning of the rim in this location. There was no apparent change in rim of the left disc however a Drance haemorrhage was noted supero-nasally.

HRT3 topographical progression analysis (Figure 5) correlated with the disc appearance and showed a thinning of the inferior neural retinal rim in the right eye with no statistically significant changes in the left—a minimum area of 20 megapixels (small squares) is required to represent a significant area of change.

Cirrus OCT GPA (Figures 6 and 7) showed an area of possible thinning inferiorly on the deviation map, the RNFL thickness profile and inferior quadrant analysis of the right eye.

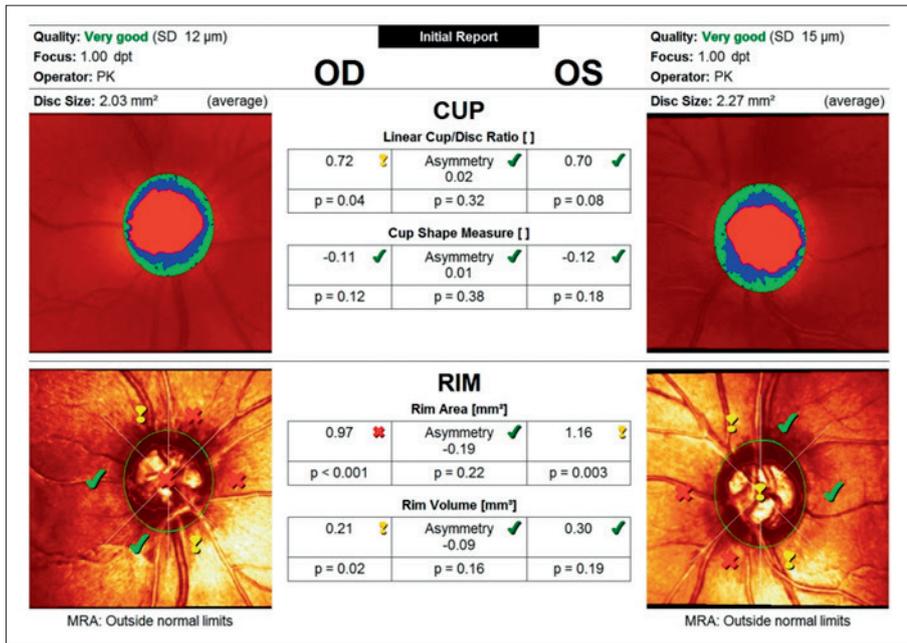
The left deviation map showed scattered areas of change with the average RNFL thickness, and the inferior and superior nasal regions in particular showed possible loss.

Progression analysis was not available on visual fields results; however, 24-2 testing (Figures 8 and 9) revealed mostly edge point defects in both eyes with no notable correlating defects reflective of the changes seen on imaging and the discs.



▲ Figure 3. Cirrus OCT optic nerve and RNFL analysis at the initial visit

Based on the changes seen in disc

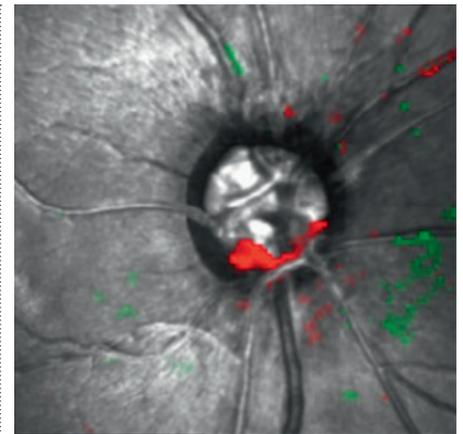


▲ Figure 4. Heidelberg Retina Tomograph 3 Moorfields Regression Analysis of the NRR at the initial visit

appearance which were supported by HRT and OCT results, particularly in the right eye, this patient was diagnosed with pre-perimetric open angle glaucoma and commenced on Xalatan drops which reduced the IOPs to 15mmHg.

Discussion

NHMRC guidelines note that advanced imaging of the optic nerve head can be valuable in diagnosing glaucoma.¹ This case highlights how imaging equipment can act as a supplementary



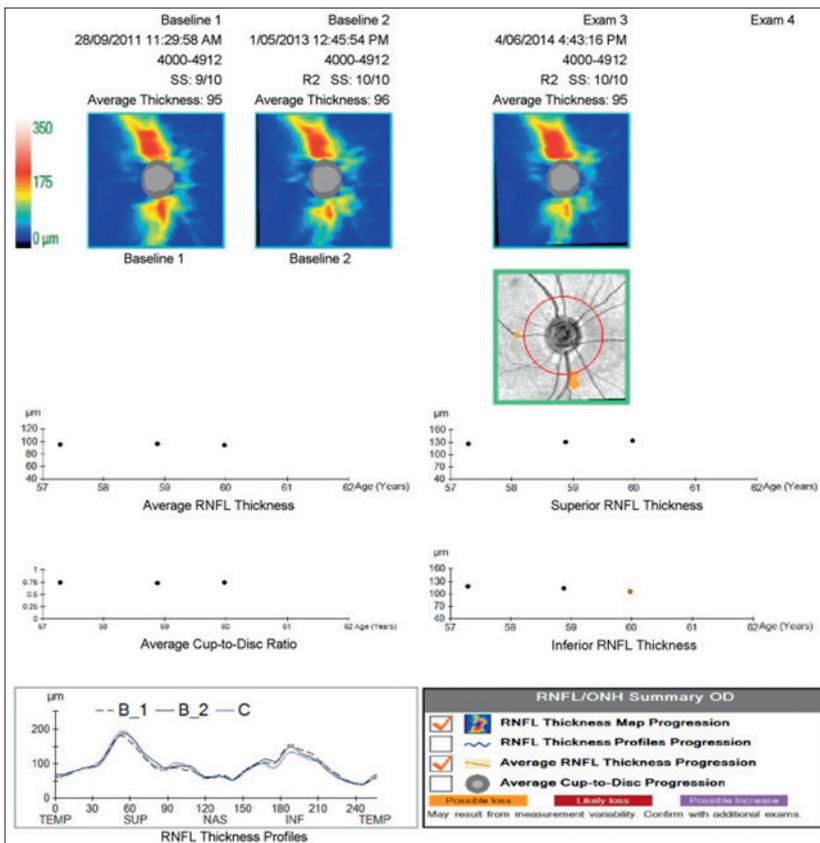
▲ Figure 5. Heidelberg Retina Tomograph 3 topographical change analysis of the right eye at the third visit

technique for detecting glaucoma conversion or progression. The HRT can provide an objective assessment of the NRR including topographic and parameter based change analysis.

OCT measurements are becoming an integral part of a structural glaucoma assessment and progression analysis, with new methods aimed at detecting the loss of neural tissue constantly being researched and developed.

The optic nerve haemorrhage and imaging results prompted further analysis of the NRR with flicker stereo photographs, with it unlikely that the subtle change in the right eye would have been otherwise detected.

The current gold standard of glaucoma diagnosis is still based on assessment of the optic nerve head and visual fields. In the Ocular Hypertension Treatment Study (OHTS), of the patients who converted to glaucoma, 35.2 per cent were diagnosed from visual field changes, 55.2 per cent from optic nerve changes and the remaining 9.6 per cent were diagnosed based on concurrent changes.² A variety of visual field changes can occur in glaucoma, with two or three examinations required to confirm the repeatability of a defect. Due to literature on progression analysis being currently available only for



▲ Figure 6. Cirrus OCT Guided Progression Analysis of the right eye at the third visit

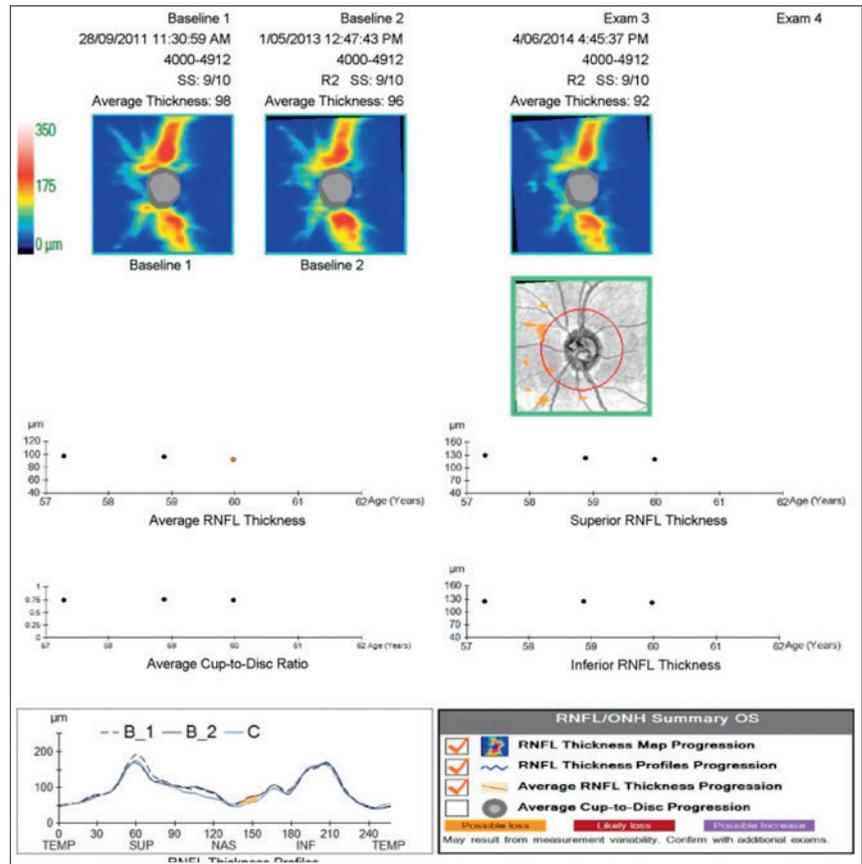
Pre-perimetric

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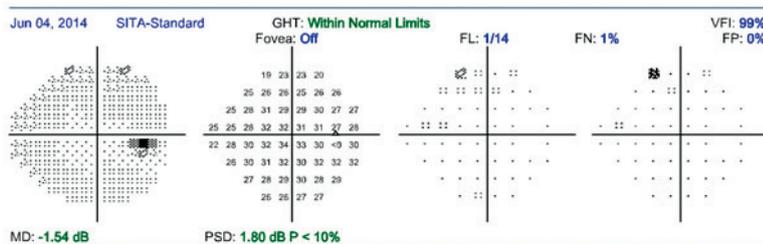
white-on-white SAP, it remains the gold standard for measuring progression.³

In this patient, the loss of structure precedes a detectable loss of function. This highlights the need for careful stereoscopic nerve examination, ideally with a comparison to previous stereo images to ensure early glaucoma diagnosis. Changes that can occur in glaucomatous progression of the NRR identified and utilised in the OHTS included:

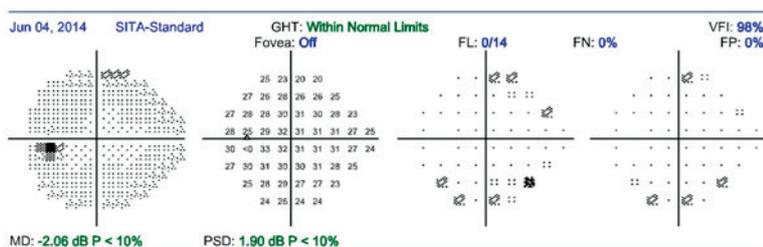
- A change in the position of the vessels greater than expected from a shift in the position of the eye
- The development of a notch
- The development of an acquired pit
- Thinning of the NRR
- Development of localised or diffuse pallor.



▲ Figure 7. Cirrus OCT Guided Progression Analysis of the left eye at the third visit



▲ Figure 8. Humphrey 24-2 SITA-Standard Visual Field Analysis of the right eye at the third visit



▲ Figure 9. Humphrey 24-2 SITA-Standard Visual Field Analysis of the left eye at the third visit

Other changes that should also be carefully considered include:

- Drance haemorrhages⁴
- Changes in Beta zone atrophy (the inner zone of chorioretinal atrophy around the disc)
- The development of, deepening or widening of localised wedge RNFL defects
- Changes in the visibility or shape of the Lamina Cribrosa pores.

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Overview of micro-invasive glaucoma surgery

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IN THE GLAUCOMA management ladder, the most common treatment paradigm for primary open angle glaucoma (POAG) and secondary open angle glaucomas would be initial topical antihypertensive drops, followed by laser therapy such as selective laser trabeculoplasty (SLT), then ultimately, surgery.

Several studies have suggested 360-degree SLT is as effective as initial topical medication such as prostaglandin analogues.¹ Further larger randomised controlled trials are being undertaken to confirm these findings or support the use of initial SLT therapy; for example, the LiGHT (Laser in Glaucoma and Ocular Hypertension) Study, Moorfields Eye Hospital, UK.

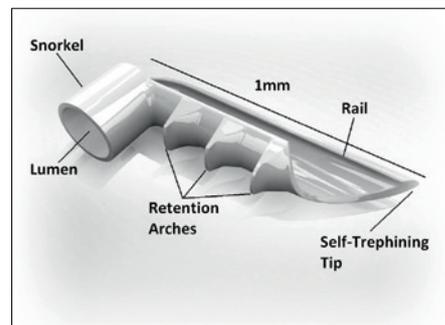
For a number of patients, surgery is still required despite the recent advances in glaucoma medical and laser therapy. Trabeculectomy, introduced by Cairns in 1968, still remains the gold standard

surgery for many types of open angle glaucoma (OAG). Although the Tube versus Trabeculectomy study supported the use of glaucoma drainage devices in lower risk cases other than refractory glaucoma,² glaucoma drainage devices use in primary cases is still being investigated.

Even though the techniques in performing trabeculectomy and glaucoma drainage devices have improved significantly since their introduction, they still carry significant risk profiles to cause patient concerns. For those patients with mild to moderate OAG requiring surgery, micro-invasive glaucoma surgery (MIGS) may be a safer option.

MIGS is a recently-coined acronym to include several modern operations or devices that cause minimal or no disruption to the conjunctiva and use an *ab interno* approach. Some *ab externo* incisional surgeries such as canaloplasty have also been included in MIGS.

In Australia, MIGS generally refers to operations that use a clear corneal incision that does not violate the conjunctiva at all, often performed at the time of cataract surgery. Currently, two MIGS devices are approved for use in Australia and they will be discussed



▲ Figure 2. iStent (first-generation)

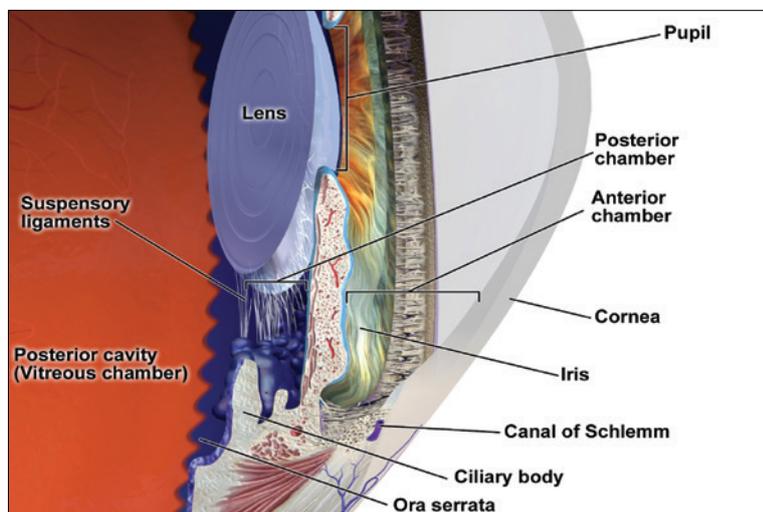
below. To insert these devices, a direct intraoperative gonioscopic view of the drainage angle is required, as they are designed to sit in the Schlemm's canal to bypass the trabecular meshwork. In other words, direct aqueous drainage from the anterior chamber into the Schlemm's canal and ideally the collector channels is made possible.

The basis for these trabecular bypass stents relies on the fact that in most OAG, the juxtacanalicular trabecular meshwork provided the majority of aqueous outflow resistance.⁴ Therefore, in theory, it is possible for these trabecular meshwork bypass stents not to work at all if the outflow resistance is located elsewhere beyond the trabecular meshwork/Schlemm's canal. Unfortunately, at present, it is very difficult to determine the site of outflow resistance clinically in individual glaucoma patients and this remains an area for further investigation.

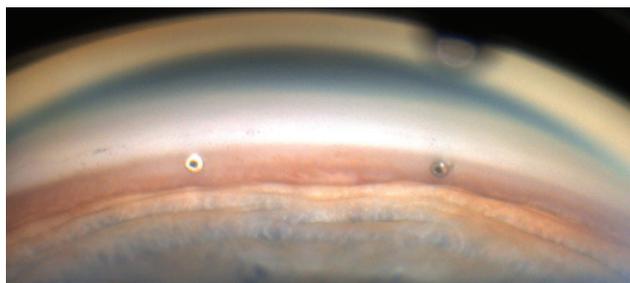
iStent

The iStent (Glaukos Corp, Figure 2) is an L-shaped heparin-coated titanium device that measures 1 mm in length and 0.3 mm in height. It is a first-generation trabecular bypass stent and one of the smallest implants ever used in humans. It is also the device with the most study data.

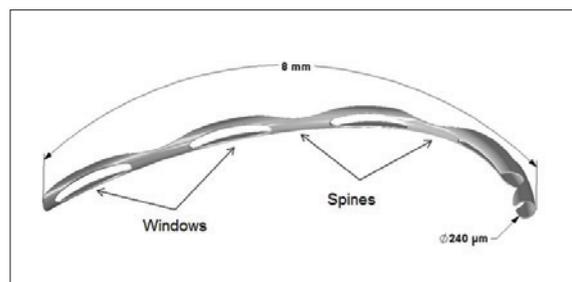
Generally, one iStent is inserted during cataract surgery in Australia. However, some surgeons insert more than one to



▲ Figure 1. Anterior eye, with Canal of Schlemm at lower right³



▲ Figure 3. Multiple iStent insertion
Image: www.ophtalmicphotography.info



▲ Figure 4. Hydrus Microstent

Micro-invasive

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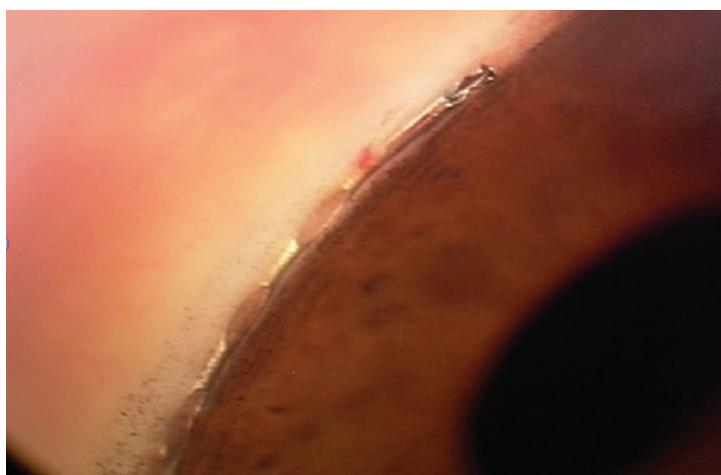
provide better aqueous drainage into Schlemm's canal, thereby increasing the likelihood of gaining collector channel access, to provide better IOP control (Figure 3). In fact, the second-generation iStent inject (not yet available in Australia) may come with an injector preloaded with two stents for this exact reason and early results of multiple stenting are encouraging.⁵

The largest study for first-generation iStent compared one iStent combined with cataract surgery versus cataract surgery alone in 240 eyes with mild to moderate OAG. At one year and two years, more patients in the iStent group achieved IOP ≤ 21 mmHg without medications (72 per cent vs 50 per cent at one year, and 61 per cent vs 50 per cent at two years).⁶

Hydrus Microstent

The Hydrus Microstent (Ivantis Inc, Figure 4) is a Schlemm's canal scaffold that bypasses the trabecular meshwork as well as dilating the Schlemm's canal through its entire length. It spans 8 mm in length or about three clock-hours when inserted into the drainage angle, hence, it targets more potential collector channels (Figure 5). The combined effect of trabecular meshwork bypass with Schlemm's dilatation may potentially or at least in theory provide more significant IOP lowering.

The Hydrus Microstent is made of nitinol, a highly biocompatible alloy that contains both nickel and titanium, and has high elasticity and shape-memory. Currently, there are many Hydrus studies near completion but the results are yet to be published; however, preliminary results have very promising. There is no published data comparing the safety and efficacy of Hydrus Microstent to the iStent but a head-to-head trial is currently underway.



▲ Figure 5. Gonioscopic view of Hydrus Microstent in the Schlemm's canal

The future of MIGS?

MIGS is still relatively new as a treatment. Apart from the aforementioned devices, there are many others being investigated or trialed. There are suprachoroidal space drainage devices such as the iStent Supra from Glaukos Corp, and Cypass from Transcend Medical; as well as those that access the subconjunctival/subTenon's space through an ab interno approach such as the Xen gel stent from Aquesys Inc.

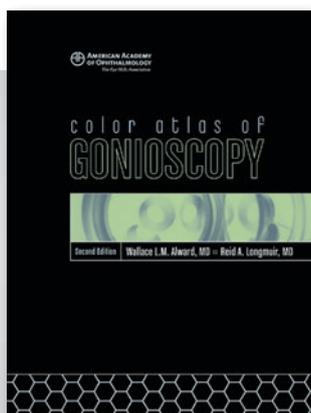
Currently, we don't have enough data to indicate the most efficacious device. Perhaps as more study data becomes available, we will be able to choose the best device to tailor for the individual eye and patient. Whether MIGS can have an expanded use in patients with advanced glaucoma remains to be studied. The impact from MIGS in terms of cost-effectiveness, quality of life, ocular surface disease and even IOP fluctuations may become better understood with future trials.

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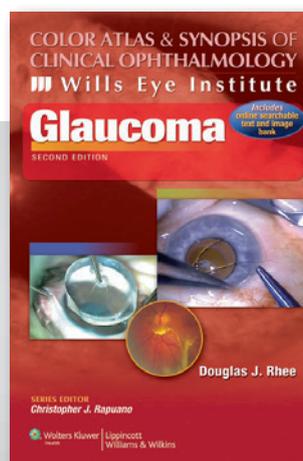


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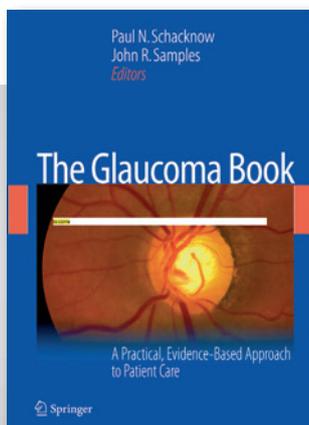
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*Please note changes in Product Information.

Reference: 1. EYLEA Product Information. [†]wAMD = Wet age-related macular degeneration



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