Preserflo MicroShunt: A New Approach to POAG

WRITER Dr Nathan Kerr

New subconjunctival filtration procedures promise to predictably lower intraocular pressure (IOP) while reducing risks and accelerating recovery of patients with primary-open angle glaucoma (POAG).

Glaucoma affects over 60 million people worldwide and is the leading cause of irreversible blindness, responsible for bilateral blindness in over eight million people globally.[1] In Australia, glaucoma is one of the most commonly encountered ophthalmic conditions, affecting over 300,000 people.[2,3] Because glaucoma is often asymptomatic in the early stages, over 50% of cases are undiagnosed.[2] Due to an ageing population, the prevalence of this condition is expected to increase substantially over the coming decades.[4]

The goal of management is to prevent vision loss from glaucoma in a patient's lifetime and to maintain or enhance quality of life. Lowering IOP remains the only treatment proven to prevent vision loss from this disease.[5,6,7,8]

For patients where IOP remains uncontrolled despite maximum tolerated medical therapy, and/or glaucoma progression necessitates surgery, trabeculectomy has been the most frequently performed procedure.[9] While trabeculectomy is effective at lowering IOP, the degree of IOP reduction can be unpredictable, visual recovery may be prolonged, multiple post-operative visits and/or interventions are required, and serious adverse events such as hypotony, bleb leak, and endophthalmitis can occur.[10]

Fortunately, advances in glaucoma surgery now promise more consistent and predictable outcomes in a shorter procedure with faster recovery and an improved safety profile. An understanding of these new interventions, and where they fit in the treatment paradigm, is important in providing the highest-level of patient care for people with glaucoma.

Important studies have shown that new subconjunctival filtration procedures coming to Australia have proven efficacy and safety. These procedures promise to predictably lower IOP while reducing risks and accelerating recovery, thereby enabling patients to have surgery at an earlier stage before significant vision loss has already occurred.

WHEN GLAUCOMA EYE DROPS ARE NOT ENOUGH

While selective laser trabeculoplasty (SLT) is now recommended as first-line therapy for open-angle glaucoma,[11] daily glaucoma eye drops are a treatment for many patients. Medical treatment usually consists of a prostaglandin analogue; however, not infrequently a second, third, or even fourth medication is required.[12] Studies show that up to 59% of patients continue to progress despite medical therapy.[13] In some cases, this is due to non-adherence, which leads to faster progression and puts patients at greater risk of visual loss.[14,15] In one study, 45% of patients used their drops less than 75% of the time, despite knowing they were being monitored.[16] Common reasons for non-adherence include forgetfulness, difficulty with drop administration, and medication schedules that require multiple drops per day.[17] However, even when adherence with medical therapy is excellent, progression is more likely to occur in medically-treated patients compared to those treated with selective laser trabeculoplasty, minimally invasive glaucoma surgery (MIGS), or conventional surgery.[11,18–20] This is likely due to greater diurnal fluctuation in medically treated patients that results in optic nerve damage.[21] In our study comparing medical therapy with SLT, we found better diurnal IOP control and reduced IOP fluctuation with SLT in patients with open-angle glaucoma.[22]

In addition to failure to control disease progression, glaucoma eye drops may be associated with local and systemic side effects, ocular surface disease, and reduced quality of life. We surveyed over 2,500 patients with glaucoma or ocular hypertension to assess patient satisfaction with topical ocular hypotensives.[12] We found that symptoms such as redness, grittiness, burning, tearing, and blurred vision were present in up to 50% of patients.[12] When respondents were asked if they would prefer an alternative to eye drops, 47% indicated they would.[12] Concerningly, long-term use of topical glaucoma medications and/or toxic preservatives cause local inflammation

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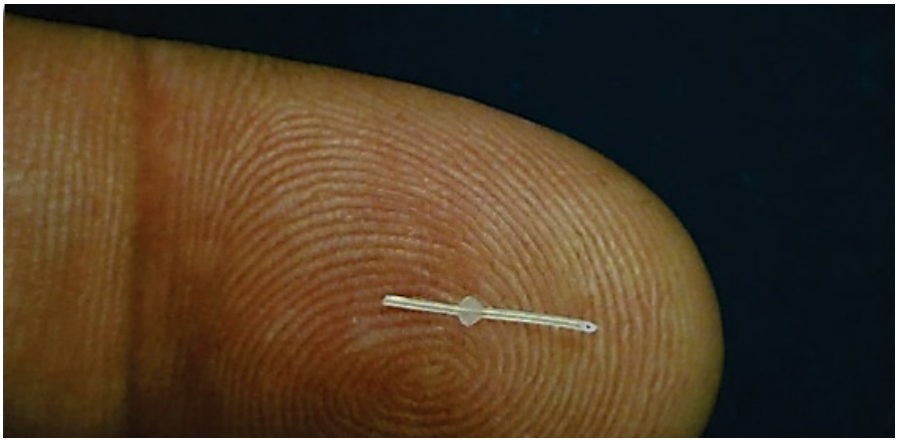

Figure 1. The Preserflo MicroShunt.

Figure 2. Eye one month after Preserflo MicroShunt implant.

in the conjunctiva[23] and increase the risk that glaucoma surgery will fail.[24] Fortunately, the introduction of minimally invasive glaucoma surgery (MIGS) is enabling a greater number of people with glaucoma to reduce or eliminate their need for glaucoma eye drops. Recently, the iStent inject was the first MIGS device shown to significantly improve Vision Related Quality of Life (VRQoL).[25] These improvements relate to improved eye comfort as a result of being medication free with improvements in ocular surface symptoms and vision-related acitivites.[25]

WHEN IS SURGERY INDICATED?

For patients where IOP remains uncontrolled despite medical therapy and laser treatment, surgery can be considered. The choice of procedure depends on the patient's type and stage of glaucoma, age and ocular co-morbidities, risk of complications, ability to attend follow-up, and preferences. The choice is individualised to each patient and surgery will follow a detailed discussion of the risks and benefits.

For patients with mild-to-moderate POAG not responsive to medical therapy and/or SLT, or where medical therapy is not tolerated due to side effects, the most appropriate procedure is minimally invasive, such as iStent inject, Hydrus, or iTrack. With minimal risk, a MIGS procedure may reduce or eliminate the need for glaucoma medications, lower the risk of visual field progression, and reduce the need for future invasive surgery such as trabeculectomy.[26] These procedures are performed via an ab interno approach, reliably reduce IOP, provide rapid recovery with minimal post-operative follow-up, and preserve the conjunctiva for future filtration procedures if required. For patients with visually significant cataract, these procedures can be combined with cataract surgery. However, for patients who have already undergone cataract surgery, or do not have visually significant cataract, these procedures can now be performed as a standalone procedure. Medicare rules stipulate that standalone procedures must be performed by a specialist, with training in micro-bypass glaucoma surgery, who has been recognised by the conjoint committee.

For patients with moderate-to-severe glaucoma, trabeculectomy has been the most commonly performed filtration surgery. However, it can be associated with vision-threatening complications such as hypotony, choroidal effusions, suprachoroidal haemorrhage, and endophthalmitis.[10] These complications can occur even years after surgery. Therefore, many surgeons reserve trabeculectomy for eyes with severe glaucoma or those with progressive normal tension glaucoma who require a very low IOP.

THE PROBLEMS WITH CONVENTIONAL FILTRATION SURGERY

Trabeculectomy bypasses the eye's natural outflow pathways, creating an alternative route for aqueous to exit the anterior chamber.[27] This procedure was described in the 1960s but is based on procedures described in the 19th century.[28] While still the most common type of filtration surgery, the number of trabeculectomies being performed each year has been steadily declining.[9] In trabeculectomy, a hole or fistula is created into the anterior chamber underneath a partial thickness scleral flap. This allows aqueous humour to drain from the anterior chamber into the space between the sclera and Tenon's capsule, forming a subconjunctival reservoir of aqueous humour known as a bleb.

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FREQUENT INTERVENTIONS

While effective at lowering IOP, trabeculectomy requires intensive post-operative follow-up and frequent interventions, such as releasable suture removal, laser suturelysis, injections of 5-fluorouracil (5-FU) anti-scarring medication, bleb needling, or injections of viscoelastic into the anterior chamber to adjust IOP in the early postoperative period. In a study of trabeculectomy, 78.2% of eyes required a post-operative intervention.[29]

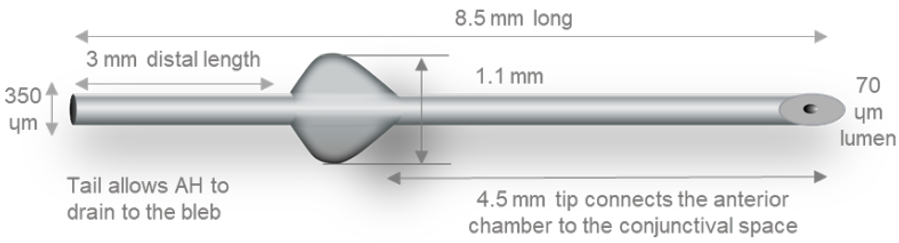

Figure 3. Dimensions of the Preserflo MicroShunt.

DELAYED VISUAL RECOVERY

During the period after surgery, visual recovery can be slow and vision may be blurred for six weeks to three months.[30] Additionally, trabeculectomy can create significant surgically induced astigmatism, necessitating glasses or a change in prescription.[31] This is due to the need to cut and then suture the sclera, as well as tightly close the conjunctiva to prevent bleb leak.

VOLATILE AND UNPREDICTABLE RECOVERY

There are many factors that can affect the flow of aqueous, including the size of the fistula, the dimensions and thickness of the scleral flap, the tension of the scleral flap sutures, elasticity of the patient's sclera, aqueous production, and resistance in the subconjunctival space. This can cause unpredictable outcomes, even with experienced surgeons. Over-drainage and hypotony is a potentially serious problem that can cause shallowing of the anterior chamber, choroidal effusions, hypotony maculopathy, and an increased risk of suprachoroidal haemorrhage. This is especially a risk in high myopia, uveitic glaucoma, aphakic glaucoma, and in eyes that have undergone vitrectomy. Hypotony can occur months or years after surgery. In a large multicentre study of trabeculectomy, 7.2% of eyes developed late onset hypotony.[32]

FREQUENT COMPLICATIONS

Patients undergoing trabeculectomy are at risk of both early and late post-operative complications. In a landmark clinical trial, early post-operative complications occurred in 37% of patients and late complications developed in 36%.[33] Alarmingly, nearly one in five patients required a return to theatre for re-operation after trabeculectomy.[33] While many complications are transient and self-limited, others may be permanent and sight-threatening.[33]

THE PRESERFLO MICROSHUNT ADDRESSES UNMET NEEDS

While trabeculectomy has been the standard for lowering IOP, it is far from perfect. The Preserflo MicroShunt (Figures 1 and 2) is a new device that provides significant IOP reduction with a much better safety profile and improved predictability. The Preserflo has been used widely in Europe since receiving CE marking in 2012, and has recently been approved by the Australian Therapeutic Goods Administration (TGA) for lowering IOP in patients with POAG. By improving safety and reliability, treatment can be performed earlier to preserve vision, reduce or eliminate glaucoma eye drops, and improve ocular surface disease.

DESIGNED TO PREVENT OVER-DRAINAGE AND HYPOTONY

The dimensions of Preserflo have been carefully selected to regulate flow and prevent hypotony. At 8.5mm in length with an internal lumen of 70µm in diameter (Figure 3), the device will provide sufficient resistance to aqueous outflow to prevent IOP falling below 6.5mmHg at normal rates of aqueous production (2.5µL/min).[34,35] These dimensions are based on the Hagen-Poiseuille equation which enables calculation of the resistance to flow of liquid through a cylindrical tube. This provides safety against hypotony, a serious and unwanted complication after trabeculectomy. In a pivotal head-to-head trial comparing Preserflo to trabeculectomy, transient hypotony was significantly higher in the trabeculectomy group (49.6% versus 28.9%; P<0.01).[36] While small enough to prevent over-drainage, the device is sufficiently large to not be blocked by small cells or blood. The bevelled tip avoids occlusion by the iris.

LESS INVASIVE AND FASTER VISUAL RECOVERY

The procedure is significantly less invasive than trabeculectomy (Figures 4, 5 and 6).

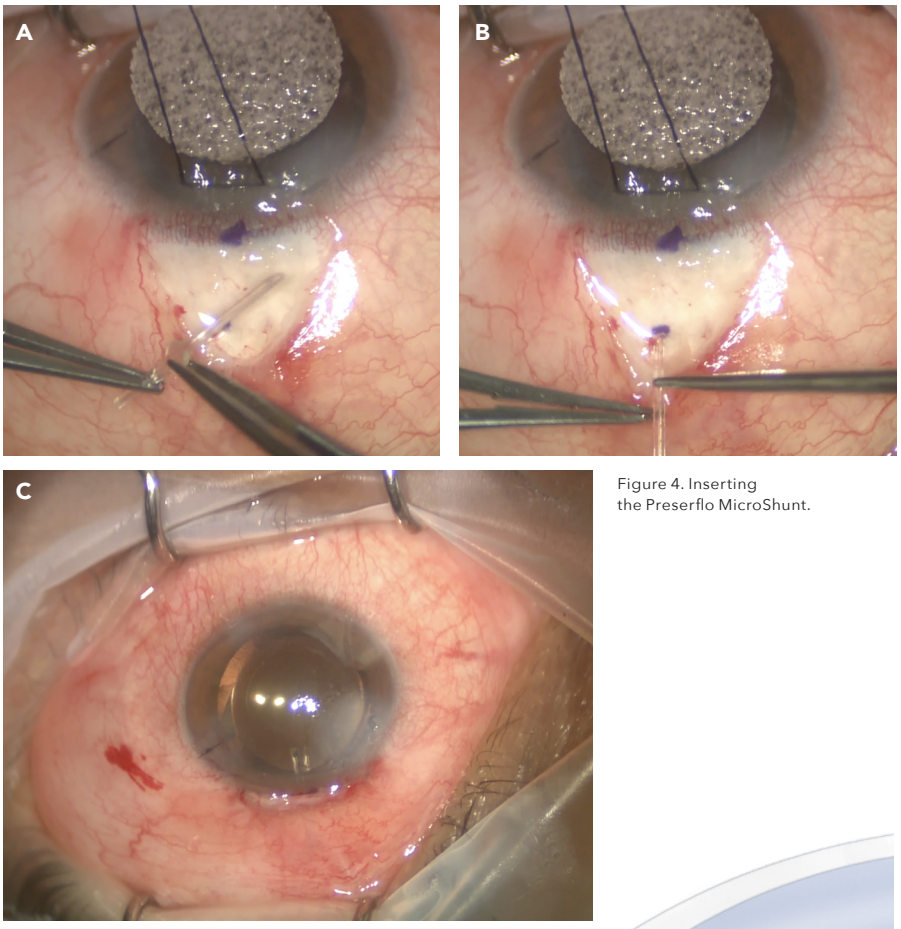

Figure 4. Inserting the Preserflo MicroShunt.

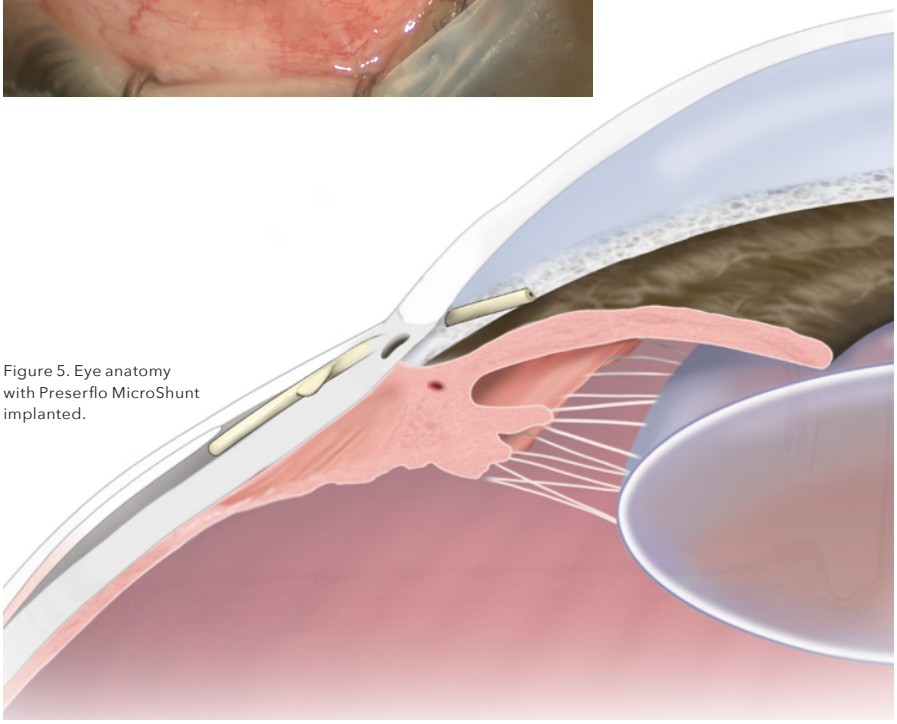

Figure 5. Eye anatomy with Preserflo MicroShunt implanted.

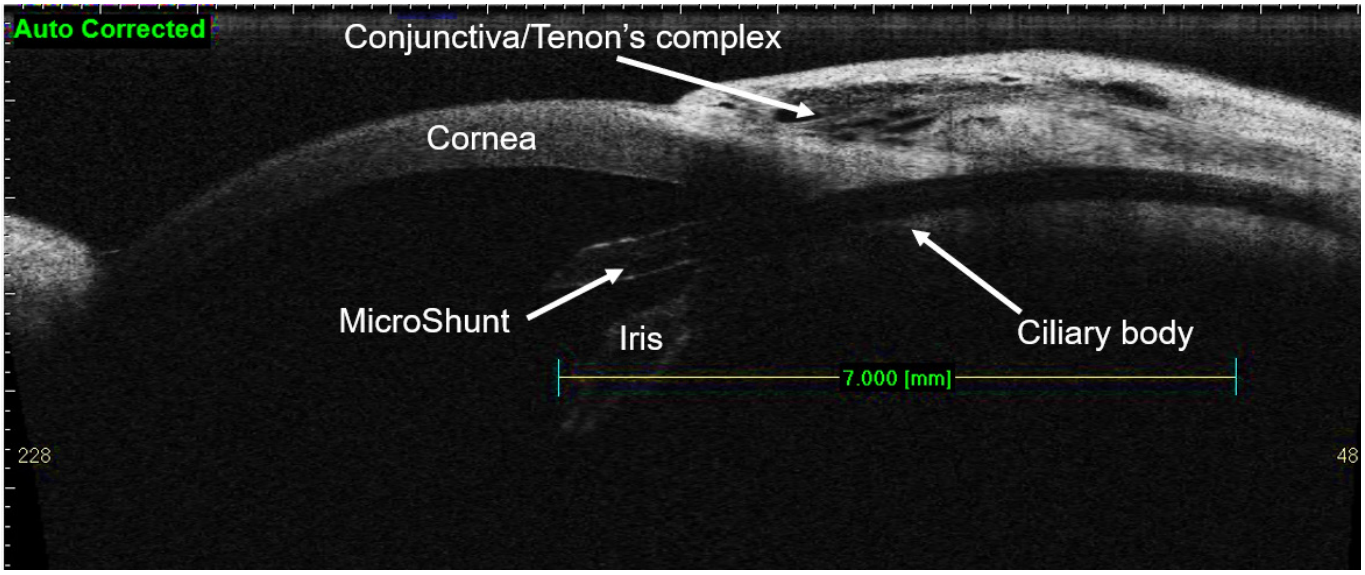

Figure 6. Optical coherence tomography depicting the Preserflo MicroShunt in place.

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It is not necessary to perform a scleral flap, sclerostomy, or iridectomy; all of which are essential steps for trabeculectomy. This results in a shorter and more gentle procedure with faster visual recovery. I first performed Preserflo in 2016 as an investigator at Moorfields Eye Hospital in London as part of the pivotal randomised controlled trial. It was clear that the patients treated with Preserflo had a more predictable post-operative course and faster recovery, frequently returning to baseline visual acuity within one week of the operation.

BETTER AND MORE COMFORTABLE BLEBS

The ideal and most comfortable bleb is posterior, low, and diffuse. Because the Preserflo is 8.5mm in length, and sits approximately 6mm back from the limbus, it directs fluid posteriorly to encourage low and diffuse blebs. This provides for a comfortable bleb with less risk of blebitis or bleb discomfort/dysaesthesia. Because flow is directly away from the limbus, the risk of bleb leak is reduced. In the head-to-head comparison, the rate of bleb leak was 8.9% in the Preserflo group and 14.5% in the trabeculectomy group, although this difference did not reach statistical significance.[36] As the Preserflo is covered by both the conjunctiva and Tenon's capsule, the risk of erosion or exposure is low.

MINIMISES INFLAMMATION

Most trabeculectomies fail because of fibrosis or scarring.[37] The Preserflo is made of an ultrabiocompatible material called poly(styrene-block-isobutylene-block-styrene) or SIBS. This material has been used in millions of cardiac stents[38] and induces less inflammation and fibroblast proliferation than silicone, a material commonly used in other types of glaucoma drainage device.[35,39–41]

PREDICTABLE IOP LOWERING AND MEDICATION REDUCTION

Both patients and surgeons desire predictable and consistent outcomes. In the pivotal trial, mean (± standard deviation) IOP reduced from 21.1 ± 4.9mmHg to 14.3 ± 4.3mmHg. One year after surgery, 94.5% of patients were on fewer medications compared to before surgery, and 65.5% were medication-free.[36] This is a benefit that many patients enjoy, providing them with greater freedom from eye drops and a reduction in ocular surface disease symptoms. There are studies showing sustained reductions in IOP and medication for up to five years after Preserflo surgery.[42] In one study, IOP reduced from 23.8 ± 5.3mmHg to 12.4 ± 6.5mmHg at five years.[42] Over the same period of time, medications reduced from 2.4 ± 1.0 prior to surgery to 0.8 ± 1.3 mmHg at five years.[42]

STREAMLINED POST-OPERATIVE RECOVERY

Patients desire rapid recovery with few interventions and visits. Because the Preserflo regulates flow from the moment it is inserted, it does not require suture removal or laser suturelysis to lower IOP in the post-operative period. In the pivotal trial, only 6% of patients who received Preserflo required a post-operative intervention compared to 49% of patients who underwent trabeculectomy.[36] This resulted in less frequent post-operative visits for patients receiving Preserflo.

SAFETY

The pivotal trial confirmed the favourable safety profile of Preserflo. Reassuringly, endothelial cell counts were the same between Preserflo and trabeculectomy groups.[36] Vision-threatening complications were infrequent. With any filtration procedure, it is important the surgeon is experienced and able to manage bleb leak, bleb-related infections, shallow anterior chamber, choroidal effusions, and malignant glaucoma. Fortunately, these events occur in 1% or fewer of patients.

CONCLUSION

To help preserve eyesight, it is essential that optometrists and ophthalmologists carefully monitor glaucoma to detect when the disease is uncontrolled or continues to progress, despite medical therapy, so that surgery can be offered in

"By regulating flow, the Preserflo provides for a faster recovery with fewer post-operative interventions and a lower risk of hypotony compared to conventional trabeculectomy surgery"

a timely fashion. Newer surgical procedures now mean that surgery can be offered earlier, before significant vision loss has occurred. The Preserflo's unique design and less invasive approach combines the benefits of subconjunctival filtration with the advantages of minimally invasive surgery. By regulating flow, the Preserflo provides for a faster recovery with fewer post-operative interventions and a lower risk of hypotony compared to conventional trabeculectomy surgery. By using novel materials and innovative design, the Preserflo addresses many of the unmet needs in glaucoma surgery, providing predictable IOP-lowering and enhanced safety. Ultimately, this helps us to achieve our goal of preventing vision loss from glaucoma and maintaining or enhancing the quality of life of our patients. mi

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Dr Nathan Kerr is a fellowship-trained glaucoma subspecialist in Melbourne. Dr Kerr specialises in minimally invasive glaucoma surgery (MIGS) and completed a prestigious glaucoma fellowship at Moorfields Eye Hospital in London where he trained in MIGS under the world-renowned surgeon Mr Keith Barton. Dr Kerr was one of the first Australian surgeons to perform the PreserFlo MicroShunt and he has been invited to teach MIGS surgery in the United Kingdom, Switzerland, France, and Australia. Dr Kerr serves as a Glaucoma Section Editor for *Clinical and Experimental Ophthalmology* and is Principal Investigator in Glaucoma at the Centre for Eye Research Australia. Dr Kerr is a consultant ophthalmologist at the Royal Victorian Eye and Ear Hospital and consults privately at Eye Surgery Associates in East Melbourne, Doncaster, and Vermont South. doctorkerr.com.au

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