Health Policy Advisory Committee on Technology

Technology Brief

EyeOP1®: Ophthalmic high intensity focussed ultrasound for glaucoma
February 2013

HealthPACT
emerging health technology
Technology, Company and Licensing

Register ID         WP 137
Technology name     EyeOP1®: Ophthalmic high intensity focussed ultrasound (HIFU) for glaucoma
Patient indication  Treatment of glaucoma to replace or augment current therapies (e.g., drugs, eye drops, lasers or surgery) that may not provide a satisfactory outcome and are accompanied by limitations, e.g., low compliance, dependence on the operator and disease progression.

Description of the technology

EyeOP1 is a non-invasive, therapeutic medical device that uses high-intensity focussed ultrasound (HIFU) to reduce intraocular pressure (IOP) via partial destruction of the ciliary body of the eye. The ciliary body produces aqueous humour (a watery fluid that fills the space between the cornea and the lens). Finely focused HIFU beams are directed into the ciliary body through miniature transducers in a ring-shape probe. The beams pass through eye tissue without disruption and reach the target area through the focal point, which has a volume of less than 0.3 mm.¹

The device consists of a console and a disposable probe. The probe is made up of two parts: the cone, which is used to position, centre and fixate the beam; and the therapy probe that generates the beams.¹ The use of HIFU therapy for glaucoma was trialled in the 1980s and 1990s but abandoned at that time due to device limitations. This newer device has been miniaturised to overcome the issues experienced with the earlier devices.

Figure 1    HIFU procedure with the EyeOP1 device.² Used with permission from EyeTechCare.
Company or developer

EyeTechCare, Rillieux-la-Pape, France

Reason for assessment

A new device with the potential to be a quicker and more cost-effective treatment for glaucoma when compared to current technologies.

Stage of development in Australia

☐ Yet to emerge ☐ Established
☐ Experimental ☐ Established but changed indication or modification of technique
☐ Investigational ☐ Should be taken out of use
☐ Nearly established

Licensing, reimbursement and other approval

CE Mark May 2011. Not yet approved by the US Food and Drug Administration (FDA).

Australian Therapeutic Goods Administration approval

☐ Yes ARTG number (s)
☒ No
☐ Not applicable

Technology type

Device

Technology use

Therapeutic

Patient Indication and Setting

Disease description and associated mortality and morbidity

Glaucoma is a group of eye conditions that cause damage to the optic nerve. Glaucoma can cause a gradual, irreversible vision loss and ultimately lead to blindness. Risk factors for glaucoma include elevated IOP, a family history of glaucoma, African descent, age over 50 years and myopia. Elevated IOP is the only treatable risk factor.\(^2\)

The ciliary body of the eye normally secretes aqueous humour into the eyeball and the fluid flows out of the eye via the trabecular meshwork (drainage tubes). Changes to this process can cause IOP to increase. Theories as to why increased IOP leads to glaucomatous changes include reduced optic nerve blood flow and mechanical compression of the axons causing death of the cells by trophic insufficiency.\(^2\) The most common form of glaucoma is primary open-angle glaucoma.\(^3\)
Number of patients

Glaucoma is the leading cause of irreversible blindness worldwide. According to Glaucoma Australia, one in ten Australians over the age of 80 years will develop glaucoma. An estimated 50 per cent of people with glaucoma have not been diagnosed with the disease. Glaucoma is the fourth leading cause of vision loss in Australia (after uncorrected refraction errors, cataracts, and age-related macular degeneration), affecting about 27,000 Australians in 2009. It is the second leading cause of blindness, affecting about 10,500 Australians in 2009. About 2.5 per cent of Australians over the age of 50 years have glaucoma. Of note, glaucoma is rare in Aboriginal and Torres Strait Islander populations.

Speciality Ophthalmology

Technology setting Ambulatory Care (Specialist Clinic)

Impact

Alternative and/or complementary technology

The Therapeutic Ultrasound for Glaucoma (TUG) is an alternative medical device which uses low power ultrasound to treat glaucoma. The device is under development by Eye Sonix (Long Beach, California). Although little information is available, the Eye Sonix website indicates that the treatment has the potential to gently decrease IOP, and could be used as an alternative or adjunct to drug therapy. The device was patented in 2011 and research to date has included in vitro; in vivo; and limited human, institutional review board-approved, clinical studies.

Current technology

All treatments for glaucoma aim to reduce IOP by one of two means:

- reducing aqueous humour production through the partial destruction or medical inhibition of the ciliary body; or
- facilitating the evacuation of aqueous humour from the eye.

Current treatments include drugs/eye drops, laser treatment and surgery.

People newly diagnosed with early or moderate chronic open-angle glaucoma, who are at risk of significant vision loss, may be prescribed pharmaceutical eye drops, usually as a lifelong treatment. The drops influence the production and/or outflow of aqueous humour. Additional treatment may involve laser trabeculoplasty (under local anaesthesia) which uses a laser to open up the blocked trabecular meshwork. An alternative laser treatment (cycloiodide laser treatment) involves inactivating some of the ciliary body. The main drawbacks to these treatments are that they are non-selective, often resulting in damage to adjacent structures; and they have an unpredictable dose-effect relationship that prevents accurate prediction of the treatment effect.
If surgery is indicated, the most common procedure is trabeculectomy which involves creating a flap valve in the eye to allow aqueous humour to drain. The procedure is performed under either local or general anaesthetic and takes about an hour. The therapeutic procedures listed for the treatment of glaucoma on the Medicare Benefits Schedule (MBS), along with a description of their fees and utilisation in 2012 is below (Table 1).

**Table 1: Therapeutic procedures for the treatment of glaucoma listed on the MBS.**

<table>
<thead>
<tr>
<th>Item number</th>
<th>Description</th>
<th>Fee</th>
<th>Benefit</th>
<th>No. of procedures*</th>
</tr>
</thead>
<tbody>
<tr>
<td>42746</td>
<td>GLAUCOMA, filtering operation for, where conservative therapies have failed, are likely to fail, or are contraindicated (Aaes.) (Assist.)</td>
<td>$955.00</td>
<td>75% = $716.25</td>
<td>1,605</td>
</tr>
<tr>
<td>42749</td>
<td>GLAUCOMA, filtering operation for, where previous filtering operation has been performed (Aaes.) (Assist.)</td>
<td>$1195.70</td>
<td>75% = $896.80</td>
<td>363</td>
</tr>
<tr>
<td>42752</td>
<td>GLAUCOMA, insertion of drainage device incorporating an extraocular reservoir for, such as a Molteno device (Aaes.) (Assist.)</td>
<td>$1338.45</td>
<td>75% = $1003.85</td>
<td>238</td>
</tr>
<tr>
<td>42755</td>
<td>GLAUCOMA, removal of drainage device incorporating an extraocular reservoir for, such as a Molteno device (Aaes.)</td>
<td>$165.45</td>
<td>75% = $124.10, 85% = $140.65</td>
<td>16</td>
</tr>
<tr>
<td>42770</td>
<td>CYCLODESTRUCTIVE procedures for the treatment of intractable glaucoma, treatment to 1 eye, to a maximum of 2 treatments to that eye in a 2 year period (Aaes.) (Assist.)</td>
<td>$294.80</td>
<td>75% = $221.10, 85% = $250.60</td>
<td>174</td>
</tr>
<tr>
<td>42782</td>
<td>LASER TRABECULOPLASTY, for the treatment of glaucoma. Each treatment to 1 eye, to a maximum of 4 treatments to that eye in a 2 year period (Aaes.) (Assist.)</td>
<td>$451.10</td>
<td>75% = $338.35, 85% = $383.45</td>
<td>28,310</td>
</tr>
<tr>
<td>42783</td>
<td>LASER TRABECULOPLASTY, for the treatment of glaucoma. Each treatment to 1 eye - <em>where it can be demonstrated that a 5th or subsequent treatment to that eye (including any treatments to which item 42782 applies) is indicated in a 2 year period</em> (Aaes.) (Assist.)</td>
<td>$451.10</td>
<td>75% = $338.35, 85% = $383.45</td>
<td>1</td>
</tr>
</tbody>
</table>

*Number of procedures taking place between January 2012 and January 2013 in the private sector.*

In Australia, recent comprehensive clinical guidelines for the screening, prognosis, diagnosis, management and prevention of glaucoma were published by the National Health and Medical Research Council.6

**Diffusion of technology in Australia**

There has been no identified use of this technology in Australia or New Zealand.
International utilisation

<table>
<thead>
<tr>
<th>Country</th>
<th>Level of use</th>
<th>Trials underway or completed</th>
<th>Limited use</th>
<th>Widely diffused</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>✓</td>
<td></td>
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<td></td>
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<tr>
<td>Israel</td>
<td>✓</td>
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<td></td>
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<tr>
<td>Italy</td>
<td>✓</td>
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<tr>
<td>Spain</td>
<td>✓</td>
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<tr>
<td>Switzerland</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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</tr>
<tr>
<td>United Kingdom</td>
<td>✓</td>
<td>✓</td>
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</tr>
</tbody>
</table>

Cost infrastructure and economic consequences

The cost of glaucoma to the Australian health care system in 2005 was $342 million, with a total annual cost estimated at $1.9 billion in 2005, rising to an estimated $4.3 billion by 2025.\(^4\) Information about the cost of the device was requested from the manufacturer but was not made available. The administration of the device appears to be simple using a rapid, one-step, reproducible treatment.\(^2\) According to the manufacturer, the procedure can be provided on an ambulatory basis, under local anaesthesia, and it takes about two minutes.\(^10\) If the procedure proves to be safe and effective, it may offer an appealing glaucoma treatment. Its potential advantages include short procedural time, outpatient setting, suitability for patients who are not candidates for surgery, and reduced need for long-term medications. Potential savings would be balanced by the cost of the console, disposable probes and service contract, and the cost of staff training.\(^3\)

Ethical, cultural or religious considerations

No specific considerations were identified.

Evidence and Policy

Safety and effectiveness

Only one small, non-comparative study in humans has been published (level IV intervention study).\(^11\) Several larger studies are underway (see Ongoing Research).

Aptel et al\(^11\)

An industry-funded, prospective, non-comparative pilot study at three academic glaucoma centres in France examined the results of an early version of EyeOP1 in 12 patients with treatment-resistant glaucoma. The study’s purpose was to assess the safety of the device and to determine its effectiveness in reducing IOP; in particular, to assess ‘HIFU cyclo-coagulation by a miniaturized annular device containing six piezoceramic transducers.’

Study participants had refractory primary or secondary glaucoma with at least one previous incisional glaucoma surgery (primarily trabeculectomy), an average baseline IOP ≥ 21 mmHg
on maximally tolerated medical treatment, best-corrected visual acuity < 20/60, and specific visual field defects. The mean patient age was 55 years (range 25 to 84), and 75 per cent of patients were women.

Each patient had one eye treated; most patients (83%) received general anaesthetic. Patients 1–4 (group 1) had six treatments lasting three seconds; patients 5–12 (group 2) had six treatments lasting four seconds. The mean follow-up was 6.5 months (range 1–13). The main outcome measures were complications and IOP reduction.

Safety

No major intra-operative or postoperative complications occurred. Minor postoperative corneal complications developed in four patients with previous corneal abnormalities: superficial punctate keratitis (n=3) and central superficial corneal ulceration (n=1). All four patients were successfully treated with artificial tears and vitamin A.

Effectiveness

Surgical success (defined as IOP reductions of 20% and an IOP of 5 mmHg) was achieved in 10 out of 12 (83%) patients. A mean IOP reduction of 34 per cent was achieved at the last follow-up (mean 6.5 months); IOP reduction was significantly greater in the group treated with the higher dose (Table 2). Ultrasound showed the ciliary body had shrunk in nine of the 12 patients (75%).

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline IOP in mmHg</th>
<th>Post-operative IOP in mmHg (% relative reduction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
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<tr>
<td>Group 2</td>
<td></td>
<td></td>
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<tr>
<td>All patients</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Month 1</th>
<th>Last follow-up*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>27.9 ± 5.7 (22.0%)</td>
<td>27.3 ± 3.2 (22.8%)</td>
<td>28.0 ± 8.1 (20.1%)</td>
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<tr>
<td>Group 2</td>
<td>26.9 ± 15.1 (-33.8%)</td>
<td>24.2 ± 9.2 (-38.2%)</td>
<td>23.0 ± 8.6 (-40.8%)</td>
</tr>
<tr>
<td>All patients</td>
<td>27.3 ± 12.4 (-29.8%)</td>
<td>25.2 ± 7.7 (-33.1%)</td>
<td>24.7 ± 8.5 (-33.9%)</td>
</tr>
</tbody>
</table>

IOP: intraocular pressure

* Mean follow-up was 11.5 ± 1.5 months for Group 1, 4 ± 2.5 months for Group 2 and 6.5 ± 4.3 months for the whole group

The study authors noted that, as this was an early study, safety was the primary concern. This led to conservative parameters for treatment and surgical success criteria that could be seen as not too stringent. They acknowledged their small sample size and relatively short follow-up, and noted that a multicentre study evaluating the long-term efficacy and safety of the procedure in patients with less advanced glaucoma is in progress. They also noted the need for future prospective, comparative, randomised clinical trials.

Economic evaluation

No cost information or economic analyses were identified.

Ongoing research

Two studies of interest were located:
• **EyeMUST, NCT01338467**: This industry-sponsored, non-comparative, open-label study has enrolled 60 patients at nine centres in France.\(^\text{12}\) Participants have one of three types of glaucoma (primary open angle, pseudo-exfoliative or pigmentary), have an IOP > 21 mmHg, and have failed conventional intraocular glaucoma filtering surgery. Enrolment commenced in April 2011 and the study is expected to end in June 2013. The primary efficacy outcome is an IOP change from baseline to 6 months after HIFU treatment. Preliminary results were presented at a June 2012 workshop organized by Eye TechCare at the European Glaucoma Society Congress in Copenhagen: 83–90 per cent of patients, across all trial sites, responded to treatment with an average reduction in IOP of 42–49 per cent. Tolerance and durability were good, with no major side effects reported.\(^\text{13}\)

• **EyeMUST2, NCT01592955**: An industry-sponsored, post-marketing study is planned for 12 sites in six countries (Germany, Israel, Italy, Spain, Switzerland and the United Kingdom), with planned enrolment of 100 patients. The primary efficacy outcome will be the success or failure rate at one year (success defined as an IOP reduction > 20% vs baseline or an IOP < 21 mmHg). Study completion is stated for December 2013 (primary data collection completed in December 2012).\(^\text{14, 15}\)

• **EyeMUST3, NCT01791673**: An industry sponsored, non-comparative, open-label study enrolling 30 patients across five centres in France. Those eligible for inclusion had one of three types of glaucoma (primary open angle, pseudo-exfoliative or pigmentary), had IOP > 21 mmHg and had no previous conventional intraocular glaucoma filtering surgery. Enrolment commenced in November 2012 and the study is expected to end in April 2014. The primary efficacy outcome is the proportion of eyes that achieve an IOP of > 5 mmHg and < 21 mmHg or an IOP reduction > 20%.\(^\text{16}\)

A further comparative clinical trial of EyeOP1 versus trabeculectomy is planned but no information on this trial was located.\(^\text{13}\)

**Other issues**

All studies completed or underway are industry-sponsored.

**Summary of findings**

Only one small, non-comparative pilot study of EyeOP1 has been published and three multicentre, single arm studies are underway. A comparative study (EyeOP1 versus trabeculectomy) is planned, but no information on this study was found.

The aim of the EyeOP1 treatment is to reduce IOP in patients with glaucoma and the preliminary results are promising, with minimal adverse effects. In addition, the procedure has been reported to be very quick and can be administered in an ambulatory setting. Long-term follow-up is limited at present, extending to about one year for some patients. Costs are currently unknown, particularly the prices of the console disposable probes and service contract, as well as the cost of staff training.
HealthPACT assessment

New treatments for glaucoma are needed due to the increasing incidence of the disease, particularly modalities that allow for selective treatment so that damage to adjacent structures in the eye is limited. From the limited evidence base available the EyeOP1 device does not appear to provide any additional benefits for patients with glaucoma over current treatment alternatives. As such, no further research is warranted at this time.

Number of studies included

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

Total number of studies 1
Total number of Level IV intervention studies 1

References


**Search criteria to be used (MeSH terms)**

MeSH: Glaucoma/therapy*, Ultrasonic Therapy/instrumentation*

Other: EYEOP1, cyclo-coagulation