

## Endoscopic Cyclophotocoagulation: An Overview and Asian Perspective

E-Shawn Goh,<sup>1,2</sup>*MRCOphth, MMed*, Boon-Ang Lim,<sup>1,2</sup>*FRCS, FAMS*, Leonard Yip,<sup>1,2</sup>*FRCS, FAMS*

### Abstract

**Introduction:** Surgical treatment of glaucoma has traditionally been classified as cyclodestructive (reducing inflow) or filtering (increasing outflow). Cyclodestructive procedures have traditionally been reserved for eyes with poor visual prognoses and refractory glaucomas including post-trauma, aphakia, congenital and developmental glaucoma. Since Uram described the first use of endoscopic cyclophotocoagulation (ECP) in 1992, short- and long-term outcomes for ECP have been promising. **Methods:** PubMed search and review of published English literature on ECP and comparison with limited results in a single Singapore ophthalmic tertiary hospital. **Results:** Safety and efficacy of ECP and combined phacoemulsification-ECP procedures in treatment of paediatric and adult glaucomas of various aetiologies and severities is reported. Local, short-term unpublished results from a single Singapore tertiary ophthalmic service are reported and concur with previously published results. **Conclusions:** Published reports and current experience with ECP have demonstrated that ECP with direct visualisation of the target tissues avoids the complications associated with “blind” trans-scleral cyclophotocoagulation by applying optimum energy to target tissue ciliary epithelium with endoscopic visualisation and infrared laser wavelength application. Significant financial barriers exist to introducing this service. It is safe and effective in controlling intraocular pressure and reducing reliance on anti-glaucoma medications. Wide-spread acceptance and use of this technique awaits large-scale randomised controlled studies.

Ann Acad Med Singapore 2007;36(Suppl):50-5

**Key words:** Combined cataract-glaucoma therapy, Cyclodestruction, Refractory

### Introduction

The heterogeneous group of conditions resulting in glaucomatous optic neuropathy have been treated with a combination of medical and surgical therapies. The advent of anti-glaucoma medications has reduced the requirement for surgical procedures in glaucoma.

Surgical treatment of glaucoma has traditionally been classified as cyclodestructive (reducing inflow) or filtering (increasing outflow). Filtering procedures have been the procedure of choice and, in an Asian context, are increasingly performed with the use of adjunctive anti-metabolites including mitomycin-C and 5-fluorouracil due to the increased propensity for scarring as well as early and late bleb-failure in individuals of pigmented races.<sup>1</sup> Trabeculectomy performed alone or in combination with small-incision cataract surgery is the most commonly performed surgical procedure for glaucoma in Singapore. This is due

to its efficacy and relative predictability.<sup>1</sup> However, trabeculectomy is not without issues or problems, as it may require frequent clinic visits and multiple interventions to ensure long-term bleb survivability. In addition, early or late bleb failure and bleb-related complications, ocular hypertension or hypotony may further complicate the post-surgical course of trabeculectomy.<sup>2</sup>

Cyclodestructive procedures have traditionally been reserved for eyes with poor visual prognoses and refractory glaucomas including post-trauma,<sup>3,4</sup> aphakia,<sup>5</sup> congenital/developmental glaucoma,<sup>5,6</sup> and glaucoma associated with previous penetrating keratoplasties,<sup>7</sup> as well as eyes with scarred conjunctiva not suitable for filtering procedures.<sup>3</sup> The reticence with the use of cyclodestructive procedures is related to the blind nature of trans-scleral procedures, and the high incidence of post-procedure inflammation, hypotony, cataract formation and treatment failure.<sup>8</sup> The

<sup>1</sup> Department of Ophthalmology, Tan Tock Seng Hospital, Singapore

<sup>2</sup> Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Address for Correspondence: Dr E-Shawn Goh, Department of Ophthalmology, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433.

Email: shawn\_goh@ttsh.com.sg

earliest cyclodestruction methods were performed by surgical excision, diathermy, cryotherapy, light coagulation, and eventually laser.<sup>4</sup> Laser cyclophotocoagulation may be performed with an Argon laser through a contact lens via the transpupillary route for aphakic eyes. More commonly, trans-scleral cyclodestruction is performed through a non-contact or contact probe. Initial experience using the ruby laser was subsequently superseded by the neodymium:yttrium-aluminium-garnet (Nd:YAG) laser which demonstrated improved scleral penetration.<sup>4</sup> Further developments in laser technology led to the employment of the compact and portable 810 nm wavelength semiconductor diode laser which offers improved melanin absorption and hence selectivity, over the Nd:YAG.

The principles of trans-scleral cyclophotocoagulation remain identical, regardless of method of delivery. Laser delivery is blind, and requires transmission of laser energy through the sclera, ciliary body and ciliary vessels, before final absorption by the target tissues of ciliary epithelium.<sup>9</sup> Histopathological changes of different modalities of trans-scleral cyclophotocoagulation are identical, demonstrating moderate to severe disorganisation of ciliary processes with fibrosis and atrophy of stroma, as well as non-pigmented and pigmented ciliary epithelium.<sup>10,11</sup>

Trans-scleral cyclophotocoagulation has been demonstrated to be effective for treating severe end-stage glaucoma in which other surgeries have failed or potential vision is limited. Within the limitations of varying definitions of success for this procedure, overall success rates vary between 34% and 81% of patients achieving target intraocular pressure (IOP) with or without concomitant use of anti-glaucoma medications, over a mean follow-up period of 30 months.<sup>12-15</sup> This procedure is also associated with a significant incidence of serious complications and postoperative discomfort.<sup>15</sup> In addition, due to the blind nature of treatment delivery, use of trans-scleral cyclophotocoagulation is conventionally limited in eyes with disorganised anterior segments.

Uram<sup>4</sup> initially developed and described a novel method to directly photocoagulate the ciliary body under endoscopic guidance, termed endoscopic cyclophotocoagulation (ECP). He was the first to incorporate a diode laser emitting pulsed continuous wave energy at 810 nm wavelength, coupled with a 175W xenon light source, helium-neon laser aiming beam and a video camera for imaging whilst recording. These functions were housed in a 0.88-mm (20-gauge) probe which offered a 70° field of view (Endo Optiks, Little Silver, NJ). All elements of the probe are transmitted via fibreoptics. Initial descriptions of the endoprobe were performed in vitreous surgery,<sup>16</sup> although the applications to anterior segment cataract and glaucoma surgery followed.

ECP has been gaining increasing popularity; however,

concerns still linger about the inherently ablative nature of this therapy, as well as the requirement for intraocular access to perform this procedure.

### Performing Endoscopic Cyclophotocoagulation

Endoscopic cycloablation is performed through an 18-gauge (1.2-mm diameter probe with viewing angle of 110°) or 20-gauge (0.88-mm diameter probe with viewing angle of 70°) probe inserted intraocularly. Depth of focus varies from 1 to 30 mm for the 18-gauge probe, and 0.5 to 15 mm for the 20-gauge probe.<sup>3,4</sup> Laser power (maximum of 1.2W) and duration are adjusted on the console. The actual duration of each treatment is determined by the period of pedal depression.

ECP may be performed in any patients including phakic, pseudophakic or aphakes. Due to the requirement for intraocular access in order to perform ECP, this procedure is frequently performed in conjunction with other intraocular procedures, most commonly with phacoemulsification cataract surgery.

Anterior segment and glaucoma surgeons routinely perform endocycloablation through their choice of preferred clear cornea/scleral tunnel incision. If combined with cataract extraction, the preference is for extracapsular phacoemulsification and posterior chamber lens implantation. Following placement of the intraocular lens into an intracapsular position, the posterior chamber between the posterior surface of the iris and the anterior leaf of the anterior capsule is insufflated with ophthalmic viscoelastic device (OVD). The straight or curved tip endoprobe is oriented outside of the eye, and inserted through the incision and directed toward the posterior chamber. The ciliary processes are photocoagulated under direct visualisation, with energy settings commencing between 40 and 60 mW and adjusted accordingly to achieve shrinkage and whitening of the ciliary processes whilst avoiding an audible “pop” (with bubble formation), indicating excess energy is administered. Energy delivered is minimised to avoid significant breakdown of the blood-aqueous barrier and excessive inflammation. Initial photocoagulation is directed at the raised processes without affecting the “valleys” of non-displaced ciliary epithelium. A minimum of 270° to a maximum of 360° is treated. A single incision is adequate to perform 180° of photocoagulation with a straight probe, whilst a similar incision is adequate to perform treatment over 270° for a curved probe. At the conclusion of the procedure, remaining OVD is removed from the anterior chamber by irrigation with balanced salt solution, and the wound is closed in the usual manner.

A posterior approach may be indicated in certain clinical conditions including aphakia or severe posterior synechiae limiting ciliary sulcus access. This is performed via standard

3-port pars plana vitrectomy with limited anterior vitrectomy. This would allow safe and adequate access to all ciliary processes. Treatment parameters and endpoints are identical to the anterior segment approach. Wound closure is in the usual manner for posterior segment surgery.

At the conclusion of surgery, an appropriate anti-inflammatory and antibiotic regime is administered as per routine cataract surgery. Cycloplegics, non-steroidal anti-inflammatory drugs (NSAIDs) and routine glaucoma medications are administered. The exceptions include miotics and prostaglandin analogues which may theoretically exacerbate intraocular inflammation and its attendant sequelae. Oral acetazolamide is administered post-procedure in patients with advanced glaucomatous damage for prophylaxis against intraocular pressure spikes due to inflammation, or retained OVD. Glaucoma medications are expected to be continued for 2 to 4 weeks until the clinical effects of ECP suggest tapering of glaucoma medications are appropriate. Hollander and Lin<sup>7</sup> described an isolated case of delayed-ECP effect 3 months following treatment for penetrating keratoplasty-associated ocular hypertension. This suggests that delaying ECP re-treatments in medically controlled glaucoma for patients with good visual potential may result in late treatment benefit, whilst offering the benefit of avoiding over-treatment. Topical antibiotics are administered for a minimum of 1 week, whilst steroids, NSAIDs and cycloplegics are tapered as inflammation subsides. Glaucoma medications are removed as clinically dictated.

### Clinical Results of Endoscopic Cyclophotocoagulation

Clinical experience with ECP has been expanding rapidly. Literature review was performed using a Pubmed search with the key words “endoscopic” and “cyclophotocoagulation” This returned a total of 15 published reports in the English language, between the years 1992 and 2007.

The first description of ECP was reported by Martin Uram in 1992.<sup>4</sup> The initial reports for ECP included a retrospective case series of 10 eyes with recalcitrant neovascular glaucoma treated with ECP for treatment areas of between 90° and 180°. After a mean follow-up of 8.8 months, the eyes demonstrated a mean reduction of 28.3% and a significant reduction in requirement for systemic and topical anti-glaucoma medications. Subsequently, Uram described a larger case series of 143 patients with intractable neovascular glaucoma, that demonstrated a dramatic IOP reduction of 67.6% from baseline, with a similar reduction in requirement for systemic and topical anti-glaucoma medications. There were no reports of serious intraoperative complications.

Following these initial descriptions of ECP, subsequent studies evaluated the safety and efficacy of ECP in the

treatment of other forms of refractory glaucomas.<sup>3,5,9,17-20</sup> The majority of studies described retrospective case series or poorly designed prospective studies. There was a predominant problem of the lack of a uniform definition for success which makes comparison between studies difficult.

Several reports retrospectively describe case series of ECP in the treatment of recalcitrant glaucomas.<sup>3,18</sup> Uram<sup>4</sup> was the first to describe the effects of phaco-ECP against phacoemulsification alone.<sup>4</sup> Chen et al<sup>19</sup> reported their series of 68 patients with diverse forms of refractory glaucoma which had failed prior treatment on maximal medical therapy and previous filtration/cyclodestructive procedures. Mean IOP reduction of 34% was reported after an average follow-up period of 12.9 months, with a corresponding decrease in requirement for anti-glaucoma medications. No significant intraoperative complications were described, with the exception of postoperative inflammation, transient choroidal detachment and a single case of malignant glaucoma.

Berke<sup>21</sup> was the first to report a randomised series of sufficiently large cohort and length of follow-up comparing combined phaco-ECP patients against phacoemulsification alone. He reported a series of 626 eyes, with mean follow-up of 30 months, of patients with moderately severe glaucoma. He compared in a randomised, non-blinded fashion patients treated by 5 surgeons with combined phaco-ECP against phacoemulsification alone. Treatment endpoints included mean IOP reduction and mean reduction in anti-glaucoma medications. With regard to the primary endpoints, there was no statistically significant difference for the phacoemulsification group alone, whilst the combined phaco-ECP group demonstrated mean reduction of IOP from 19.13 ( $\pm 4.14$ ) to 15.73 ( $\pm 3.00$ ) mm Hg ( $P < 4.48 \times 10^{-72}$ ), and reduction in mean number of anti-glaucoma medications from 1.53 ( $\pm 0.89$ ) to 0.65 ( $\pm 0.95$ ) ( $P < 1.23 \times 10^{-85}$ ). Berke et al<sup>21</sup> concluded that phaco-ECP effectively lowered IOP as well as reduced the number of anti-glaucoma medications required after 2 years, which translated into effective cost-savings for the patient and the medical community. Combined phaco-ECP did not increase the potential for developing cystoid macular oedema postoperatively, nor was it associated with an increased risk of serious complications such as endophthalmitis and visual loss compared to phacoemulsification alone. Rates of cystoid macular oedema were slightly lower in the combined phaco-ECP group (0.8% versus 1.2%) compared to the phacoemulsification group alone, although this difference was not statistically significant.

Gayton et al<sup>22</sup> published the only randomised controlled trial to date comparing combined cataract-glaucoma surgery (phaco-trabeculectomy) versus cataract-ECP. In their study, 58 eyes in 58 patients with combined cataract and

progressive glaucoma requiring surgery were randomised into treatment arms of combined phaco-trabeculectomy versus phaco-ECP. These patients were followed up for 2 years and the main outcomes measured were postoperative inflammation and IOP. Treatment failure was defined as IOP control requiring subsequent surgical intervention. Study results showed that IOP reduction was greater immediately postoperatively in the trabeculectomy group; however, both groups were equivalent at 1 month follow-up. In the immediate postoperative period, less inflammation was observed in the ECP group. However in general, the overall IOP reduction was greater in the trabeculectomy group, and less anti-glaucoma medications were required at all time points during follow-up. Trabeculectomy patients achieved target IOP control without medications in 42% of cases, compared to 30% for ECP patients. For patients achieving IOP control with medications, this was 54% for trabeculectomy versus 65% for the ECP group. Overall success rates for IOP control with or without medications were identical. Most significantly, there were no cases of post-treatment hypotony in either group. ECP was demonstrated to be effective in reducing IOP, was less invasive, caused less inflammation and has potentially less complications than traditional trabeculectomy filters.

Lima et al<sup>17</sup> described 34 patients in a prospective series comparing refractory pseudophakic glaucoma versus Ahmed tube implantation. Similar to previous studies, the ECP patients demonstrated significant reductions of 66.2% (average of 27.54 mm Hg) and mean reduction of one anti-glaucoma medication after a mean follow-up of 21.29 months. The ECP group reported an overall higher success rate of 73.53% (IOP <21 mm Hg) with or without anti-glaucoma medications. Most importantly, there were no serious complications associated with ECP, were simpler and less time-consuming to perform than Ahmed tube implantation.

ECP efficacy in treatment of paediatric glaucomas has also been demonstrated in several retrospective case series.<sup>5,6,23</sup> Neely et al<sup>23</sup> treated 36 eyes of 29 patients with childhood glaucomas of differing aetiologies. Treatment strategy varied between 180° and 270° (mean of 260°). The mean follow-up period of 19 months demonstrated that 34% eyes were successfully treated with a single treatment (mean reduction of 30%), and 43% achieved target IOPs with >1 treatments (average of 1.42 procedures). The most significant complications occurred in 4 aphakic eyes which included 2 eyes with retinal detachments, 1 eye with chronic hypotony and 1 experiencing severe visual loss (hand movement vision deteriorating to no perception of light). Neely et al concluded that ECP was moderately effective for the management of difficult paediatric glaucomas, with aphakic patients having an increased risk of significant postoperative complications.

Local experience has been limited, with initial results trending towards general agreement with previously published results. Yip et al reported unpublished early results of 23 eyes in 22 patients treated with ECP in a single tertiary centre in Singapore between October 2004 and April 2005. Eighteen eyes had combined phacoemulsification-ECP for moderate to severe glaucoma of various aetiologies. They reported overall success rates of 78.3% of eyes achieving target IOP of 22 mm Hg or lower with or without anti-glaucoma medications. There was a mean reduction in IOP (from 20.96 ± 4.63 mm Hg to 17.83 ± 6.19 mm Hg) which was statistically significant ( $P = 0.003$ ) and the number of anti-glaucoma medications required from (2.0 ± 0.8 to 1.0 ± 1.1). Both treatment endpoints demonstrated statistical significance ( $P = 0.003$ ). No serious postoperative side-effects were observed; however, 3 (13%) patients reported moderate visual loss (VA loss >10 ETDRS letters).

## Conclusion

Published reports and current experience with ECP has demonstrated that this novel technique of treatment delivery with direct visualisation of the target tissues avoids the complications associated with “blind” trans-scleral cyclophotocoagulation by applying optimum energy to target tissue ciliary epithelium with endoscopic visualisation and infrared laser wavelength application. Table 1 summarises the major studies in the English language examining the safety and efficacy of ECP in the management of moderate-to-severe glaucomas in eyes with good to poor visual prognoses. Across all aetiologies, disease severity and age groups, ECP has been demonstrated either in isolation or performed in combination with phacoemulsification, to effectively lower IOP in a sustained fashion and reduce the number of anti-glaucoma medications required to achieve target IOP in a cost-effective manner. Literature review in the previous 15 years suggests that the total reported short-term complication rates are less than 25% for severe inflammation, cataract or hyphema formation, and long-term complication rate of reduced vision for any reason is <16% in any individual study related to ECP treatment. Overall review of reported numbers for all glaucoma types and severities treated with ECP suggests that the long-term complication rate is less than 4.6%.

The use of ECP has had strong support in certain sections of the ophthalmic community in which glaucoma management is a significant part of their practice. One of the reasons for its relatively low take-up rate in the majority of centres, especially in most parts of Asia, is the prohibitive start-up costs of ECP equipment versus traditional filtering surgery equipment. As a surgical adjunct, ECP widens the choices available to glaucoma specialists in managing

Year	Author	Age group	n	Glaucoma type	Procedure type	Mean reduction (mm Hg)	Mean reduction topical anti-glaucoma med	Success rate (with or without medication)	Significant complications
1992	Uram	Adult	10	neovascular glaucoma	ECP	28.3	not reported	90%	hypotony 2 with chronic RRD
1995	Uram	Adult*	10	combination cataract - uncontrolled POAG	phaco-ECP	17.9 (57.0%)	not reported	unknown	vitreous Hb 1
1995	Uram	Adult	143	neovascular glaucoma	ECP	32.7 (67.6%)	2.8	unknown	transient visual loss (number unknown)
1997	Mora	Adult	8	moderate-severe glaucoma	ECP	unknown	not reported	unknown	Nil
1997	Chen	Adult	68	refractory glaucoma	ECP 56, Combined 12	10.7 (38.6%)	1	90% (IOP <22)	fibrin 16 (24%), hyphaema 8 (12%), CMO 7 (10%), VA loss 4 (6%), choroidal 3 (4%), malignant glaucoma 1 (1%) vitreous haemorrhage 2
1999	Gayton	Adult	29	IOP >30 mm Hg, progressive cupping/field loss	phaco-ECP	16 (64.5%)	not reported	95% (IOP <19)	chronic inflammation >1 month n = 2
2001	Neely	Paediatric	36	pediatric glaucomas	ECP	11.43 (32.6%)	not reported	34% (IOP ≤21)	sig cx: RRD 2, chronic hypotony 1, VA loss 1
2004	Lima	Adult	34	pseudophakic glauc vs ahmed	ECP	27.54 (66.2%)	1	73.52% (IOP <21)	VA loss 16%
2004	McFarland	Adult	180	moderate glaucoma	phaco-ECP	8.0 (44.4%)	90% reduction in use	unknown	Nil
2005	Lin	Adult	68	refractory glaucoma	ECP/combined	10.7 (34%)	1	90% (IOP <22)	Nil
2006	Berke	Adult	626	moderate glaucoma	phaco-ECP	3.4 (17.8%)	0.88	90%	Nli
2007	Carter	Paediatric	34	childhood glaucomas	ECP	9.7 (29.8%)	not reported	53% (IOP <23, >15% reduction)	sig cx: RRD 2
unpublished	Yip	Adult	23	moderate glaucoma	ECP/combined	3.1 (14.9%)	not reported	78.3% (IOP <22)	VA loss 3 (13%). All PXF cases treatment failure

CMO: cystoid macula oedema; ECP: endoscopic cyclophotocoagulation; IOP: intraocular pressure; POAG: primary open angle glaucoma; RRD: rhegmatogenous retinal detachment; VA: visual acuity

refractory glaucomas, particularly in clinical situations with limited visibility of the anterior segment or failed trans-scleral endocyclophotocoagulation. It has demonstrated safety and efficacy in retrospective and small randomised trials in controlling IOP for all aetiologies of glaucoma, reducing dependence on anti-glaucoma medications, as well as delaying progression to filtering trabeculectomy shunt procedures.

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