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Conventional trabeculectomy has so far remained the gold standard for glaucoma surgery, despite its potential vision-threatening complications.2,5 efforts are being made to develop a new surgical approach to overcome the limited success rate and safety issues of the traditional trabeculectomy. the pioneering work of Krasnow2 and the various modifications that succeeded it25 led to the development of a filtration procedure known as non-penetrating deep sclerectomy (npds). npds is known to have a higher safety profile compared with trabeculectomy but one of the main drawbacks of the procedure is its technical difficulty.11 a frequent complication of manual npds2 is inadvertent perforation into the anterior chamber (ac), necessitating conversion to a penetrating filtration procedure. Insufficient tissue dissection, which is another common problem related to technical difficulties, prevents effective fluid percolation and intraocular pressure (iop) reduction.23

Albert Einstein established the theoretical foundations for the laser in 191710 and the concept was further developed over the years. there is a great interest in using lasers for glaucoma treatment. theoretically, laser-assisted filtration surgery offers the potential advantage of improved accuracy, repeatability and safety.10 the main disadvantage is the potential collateral damage induced by scattered energy at the filtration site, which may lead to enhanced scarring, and may be detrimental to the long-term success of the filtering procedure.15 using a laser with high water absorbance and low light scattering may reduce the extent of collateral thermal damage and improve the long-term surgical success.5

CO2 laser was one of the earliest gas lasers to be developed.16 CO2 laser characteristics include photodissociation of dry tissue and coagulation of bleeding vessels, and effective absorption of laser energy by any water or aqueous present, even if only in a minimal amount. Assia and colleagues suggested using the CO2 laser for the treatment of patients with open-angle glaucoma and called the filtration procedure CO2 laser-assisted sclerectomy surgery (class).13,14 the procedure includes manual creation of a superficial scleral flap followed by progressive CO2 laser ablation of the scleral tissue. the ablation ceases when aqueous percolation is achieved as fluid absorbs the laser energy and prevents penetration through the remaining thinned scleral wall.

Preliminary studies of class in animals and in human cadaver eyes,26 and pilot clinical studies of class with the first model of the CO2 laser system (ot-133),11 have demonstrated its efficacy in achieving fluid percolation with significant IOP reduction and a low perforation rate. class using the ot-133 was found to be a safe and relatively simple procedure, but there were also several drawbacks, such as excessive charring and tissue coagulation around the treated area. Clinically, it was evident that failure had occurred in some cases because of early adhesions and synchiae formation. A second-generation system was then developed, iOptiMate™ (IOPtima Ltd, Ramat Gan, Israel) using a higher power laser and an advanced beam manipulator and scanner. Increasing the laser power and decreasing the beam dwell time resulted in increased control of the ablation process while decreasing residual momentary heating and tissue coagulation.
The objectives of the following trials were to evaluate the safety and performance of the IOPMate system in performing CLASS in a preclinical trial followed by a clinical trial.

Materials and Methods

Surgical Procedure

Following fornix-based superior peritomy and removal of the tenon capsule, a half-thickness rectangular limbal-based 5 mm x 5 mm scleral flap was dissected at the limbus into the clear cornea. A red laser (HeNe, ~200 μm spot size) aiming beam was used to mark the scanning area boundaries (Figure 1). Scleral ablation was performed with the CO₂ laser system (Adc, Lumenis, Yokneam, Israel). The laser beam was focused and applied on the treated eye using a beam-manipulating system attached to an ophthalmic microscope. The IOPMate system consists of a scanner, used to control the shape, size, and scanning parameters of the focused laser beam, a micromanipulator that attaches the system to the ophthalmic microscope and accurately positions the laser-scanned pattern on the desired ablation area, and a focusing assembly. Operation of the scanner is regulated by a control unit and the operating parameters are presented on a control panel. Scan dimensions (width and length) could be changed within the range of 1-4 mm. Initially, a wide scan area (e.g., 2.4 x 2.0 mm) was used to repeatedly remove layers of sclera until the percolation zone could be readily identified by the clear signs of percolation. The ablation area was then reduced and adjusted to target Schlemm’s canal in human eyes, or the plexus area in pig and rabbit eyes. The CO₂ laser was repeatedly applied with intervals of two to three seconds between applications to allow percolation to take place and be detected. Residual charred tissue was wiped away with a BSS damp Weck-Cel sponge and ablation was continued until sufficient percolation was achieved along a region of at least 3 mm in length (Figure 1). The scleral flap was repositioned and secured with two interrupted 10-0 nylon sutures.

In the living eyes, a high-molecular-weight ophthalmic viscosurgical device (Healon® 5, Abbott Medical Optics, Santa Ana, California, USA) was applied beneath the flap, the conjunctiva was adequately secured with 2-10-0 nylon buried sutures, and the eye was patched with antibiotic and steroid ointments. Living rabbits were anaesthetised using intramuscular ketamine (35 mg/kg) and xylazine (5 mg/kg) whereas patients with glaucoma were operated under subconjunctival anaesthesia with 2.5 % lidocaine without epinephrine. All living eyes were treated postoperatively with topical steroids and antibiotic drops.

Mitomycin C (MMC) was not used in the preclinical phase, whereas the application of MMC and its concentration were left to the surgeon’s discretion in the clinical trial.

Preclinical Phase

The preclinical trial, as previously described by our group, included an ex vivo (enucleated porcine and human cadaver eyes) and an in vivo model (12 New Zealand white healthy male rabbits). Aqueous percolation sufficiency and rate of perforations during scleral ablation were assessed. Histological examination included evaluation of the scleral crater formed at the ablated sclera, assessment of the dimensions and integrity of the remaining trabeculo-Descemet’s membrane, and grading of the mechanical and thermal damage to treated and adjacent tissues. Assessment of in vivo results focused on the inflammatory reaction, thermal damage at the ablated site, and the healing process.

Clinical Phase

This was a prospective, non-randomised, non-comparative, multinational, multicentre clinical study. The trials were carried out in Mexico City (Dr. Corrales and Turati), in Madanapalle, India (Dr. Thomas and Naveen), in Moscow, Russia (Dr. Annianova), in Ancona, Italy (Dr. Mariotti) and in Valencia, Spain (Dr. G. Muñoz).

Eligible participants were men and women, aged 18 or older, phakic or pseudophakic, with primary open-angle glaucoma (POAG) or pseudoxfoliative glaucoma (PXFG). The clinical diagnosis was based on findings of glaucomatous optic neuropathy and reliable and reproducible evidence of visual field defects typical of glaucoma. Primary filtration surgery was indicated in each participant, all of whom were on maximal tolerated hypotensive medications and had an IOP in the study eye of 18 mmHg or higher, as measured with a Goldmann applanation tonometer during three consecutive visits over a 90-day period prior to enrollment. The inclusion and exclusion criteria, follow-up schedule and assessments performed at each study visit have been fully described by our group. Follow-up duration was 12 months. Intraoperative and postoperative complications were classified according to severity and their relationship to the studied device. Also recorded was the incidence of intraoperative macro-perforations, defined as perforations accompanied by iris prolapse and/or AC shallowing.

"Complete success" was defined as Sc IOP < 18 mmHg measured at the six-month visit and 12-month endpoint, and IOP reduction ≥20 % compared with baseline without additional hypotensive medications or repeat filtration surgery. The same finding, but also including patients who required hypotensive medications postoperatively, was defined as 'qualified success'. Failure was defined as an IOP value <5 mmHg and >18 mmHg, IOP reduction of less than 20 % compared with baseline, severe loss of vision, or the need to undergo additional glaucoma surgery. Gonipuncture and needling were not considered to be failures or adverse events as both are commonly used as accepted and common postoperative interventions that are required to maintain or augment the operative results of glaucoma surgeries.
Surgery

Figure 2: Tissue Histology of a Porcine Eye

Tissue histology demonstrated a funnel-shaped scleral crater with a thin residual corneal-scleral layer in the deeper aspect.

Figure 3: Average Intra-ocular Pressure as Measured at all Study Visits (± SD)

Clinical Phase

The first 37 patients (from Russia, India and Mexico) have completed one year of follow-up and their results are presented. Twenty-five patients were later recruited in two additional sites (Spain and Italy). The one-year data are being collected and will be published once analysed.

Safety Analysis

Safety analysis revealed no device malfunctions and there were no device-related infectious perforations. Four cases of minor perforation were recorded. The AC remained deep and stable in all cases. Postoperative procedure related complications occurred in eight patients (21.6%): peripheral anterior synechiae (2), choroidal detachment (2), wound leak (2), diffuse (1) and hyphema (1). All but one complication were graded as mild and resolved spontaneously or with conservative treatment within month after surgery, and none was attributable specifically to the laser treatment. One patient developed choroidal detachment one week postoperatively and was treated using drainage with complete recovery.

Performance Analysis

The mean baseline IOP in rabbits eyes was 16.6 ± 2.8 mmHg (mean ± SD). The IOP dropped to 14.4 ± 3.4 mmHg at six months and 14.3 ± 3.1 mmHg at 12 months postoperatively (Figure 3), yielding average IOP reductions of
Discussion

Manual NPDs achieves IOP reduction by facilitating outflow of aqueous humor through the thin trabeculo-Descemet's membrane. The procedure is relatively safe but the surgical technique demands a high level of proficiency, with controversial efficacy relative to that of trabeculectomy.38,39

Theoretically, laser-assisted glaucoma surgery offers the potential advantage of improved accuracy, repeatability and safety. An increasing number of different radiation sources were examined for penetrating36,37 and non-penetrating36,37 glaucoma surgery with various success rates.

CO2 laser is commonly used in laser-assisted operations.38 Inherent characteristics of the CO2 laser make it suitable for a simplified non-penetrating filtration surgery, in particular its effective photodisruption of dry tissues as well as its effective absorption by any amount of water or aqueous present. CLASS procedure uses the CO2 laser as a radiation source for gradual removal of scleral tissue layers, leaving the thin trabeculo-Descemet's membrane through which aqueous percolates. The percolating fluid readily absorbs the laser energy, protecting the remaining tissue from further ablation and undesired perforation leaving the trabeculo-Descemet's membrane intact.

The feasibility and safety of CLASS using the early prototype (OT-133) were studied in experimental models40 and in pilot clinical studies.38 The OT-133 was superseded by the design of the IOPiMate system, implementing a revised beam-manipulating system, which was designed to improve and refine control of the ablation process and further decrease residual laser-induced thermal damage to the tissue.

IOPiMate was proved to have a high safety profile in preclinical and clinical studies. No technical complications related to the intraoperative device were recorded. There was no intraoperative or postoperative evidence of damage to adjacent tissues (sclera, cornea, iris base, ciliary body). There were no cases of persistent hypopyon during follow-up and no inflammatory reaction was recorded in the adjacent tissues, the AC or the vitreous cavity. No device-related macro-perforations were observed whereas micro-perforations occurred in both experimental and clinical models using the IOPiMate system. Small holes that are not associated with loss of AC depth and/or iris prolapse may improve aqueous drainage and do not necessitate conversion to penetrating trabeculectomy.38 Some surgeons indeed advocate purposeful micro-puncturing of the canal roof with a needle to improve fluid flow. We do not recommend this practice, but at the same time we do not regard micro-perforation as harmful. Postoperative complications were not considered serious and were mostly mild and transitory.

The main drawback of using lasers for filtration procedures is the potential collateral damage induced by the scattered energy. Collateral thermal damage adjacent to the sclerostomy site is believed to be detrimental to the long-term success of the procedure. Using a laser with high water absorbance and low light scattering reduces the extent of collateral damage and improves the long-term success. Thermal damage is an integral effect of CO2 laser and was believed to be a major limiting factor in the success rate using the OT-133 laser system. The IOPiMate system provides faster scanning, higher power focused laser beam, evenly distributed over the scanned area with some beam overlap to ensure uniform, effective ablation with minimal coagulative thermal damage to adjacent tissues. The energy is deposited using a scanner, which rapidly scans the focused laser beam across the treatment zone. The scanner is designed to move the focused beam such that the dwell time of the focused beam at each point is less than the thermal relaxation time, the characteristic heat conduction time constant in the tissue. Histological sections of experimental models showed minimal thermal damage at the lateral walls of the craters with no such damage at the bottom percolating zone, ensuring that the IOPiMate system involves reduced heat damage.

The IOPiMate system evaluated in laboratory models demonstrated precise scleral ablation with adequate percolation at the drainage area. The short- and intermediate-term efficacy of the CLASS procedure found in patients with open-angle and pseudoxfoliative glaucoma was at least comparable to that reported in a meta-analysis of the results of manual NPDs.31 The meta-analysis calculated a mean IOP<21 mmHg at a mean follow-up of 31.3 months, achieved by 48.6% of patients without any implant or antimetabolite medications, by 68.7% of patients with an implant and by 67.1% of patients upon use of antimetabolites. The convenience of micro-dissecting under direct microscopic observation and the simplicity of performance are appealing advantages. CLASS obviates the prolonged learning curve characteristic of manual NPDs. The surgeon does not need to manually dissect layers of sclera or locate the orifice of the Schlemm's canal, as in manual NPDs techniques. Instead, the surgeon gradually ablates an area which is easily identified by the use of simple landmarks (aiming dots of the scan pattern positioned on the surgical limbus). Once fluid is seen percolating, the natural drainage apparatus is clearly visible and the emerging fluid prevents further damage and perforation of the remaining thinned tissue.

Higher success rates may be achieved by augmenting the technique with implants or antimetabolites. Longer-term follow-up is required to evaluate the safety and long-term efficacy of CLASS, and to assess its usefulness in a wider spectrum of indications.

In summary, the use of laser technology to improve surgical accuracy is a highly appealing option. The feasibility and safety of CLASS using the IOPiMate system were successfully demonstrated in all investigated models by the achievement of percolation with no evidence of device-related macro-perforation.
Long-term Results of a Novel Minimally Invasive High-frequency Deep Sclerotomy Ab Interno Surgical Procedure for Glaucoma

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Abstract

High-frequency deep sclerotomy (HFDS) glaucoma surgery is a new ab interno procedure to lower the intraocular pressure in open-angle glaucoma. Using high-frequency energy, six small pockets are formed which significantly reduce the outflow resistance for aqueous humour. This article presents the impressive results of a long-term study about the HFDS glaucoma procedure and demonstrates its efficacy and safety. The operation technique and the devices used for a successful HFDS glaucoma intervention are described step by step.

Keywords

Open-angle glaucoma, high-frequency deep sclerotomy (HFDS), ab interno Glaucoma Tip, minimally invasive, intraocular pressure, surgical procedure, diathermy probe

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Purpose

The aim of this study was to demonstrate the efficacy and safety of a new surgical procedure termed high-frequency deep sclerotomy ab interno (HFDS) (formerly STT) for the treatment of primary open-angle glaucoma and juvenile glaucoma.

Patients and Methods

The main inclusion criterion for this study was an insufficient response to medical treatment of intraocular pressure (IOP). Data were documented according to a prospective study protocol. Fifty-three HFDS procedures ab interno in 53 patients with primary open-angle glaucoma and five with juvenile glaucoma were carried out between 1 April 2002 and 31 July 2002.

High-frequency Diathermic Probe

The high-frequency diathermic probe (ab interno Glaucoma Tip, Oertl Instrumente AG) consists of an inner platinum electrode, which is isolated from the outer coaxial electrode. The platinum probe tip is 1 mm in length, 0.3 mm high and 0.6 mm wide and is bent posteriorly at an angle of 15° (see Figures 1). The external diameter of the probe measures 0.9 mm. Modulated 500 kHz current generates a temperature of approximately 130°C at the tip of the probe. The set-up provides high-frequency power dissipation in the close vicinity of the tip. As a result, heating of tissue is locally very limited and is applied as a rotational ellipsoid.

Surgical Procedure

A clear corneal incision (1.2 mm wide) was placed in the temporal upper quadrant using a diamond knife. A second corneal incision was performed 120° apart from the first, followed by injection of Healon GV®. The high-frequency diathermic probe (ab interno Glaucoma Tip) was inserted through the temporal corneal incision. Visual inspection of the target zone (opposite the iridocorneal angle) was observed by a four-mirror gonioscopy lens. The high-frequency tip penetrates up to 1 mm nasally into the sclera through the trabecular meshwork and Schlemm's canal (see Figure 2), forming a deep sclerotomy (i.e., 'pockets') 0.3 mm high and 0.6 mm wide (see Figure 3). This procedure was repeated four times within one quadrant. Healon GV was evacuated from the anterior chamber with binarional irrigation/aspiration.

Results

The mean age of patients with open-angle glaucoma was 72.3 ± 12.3 years (range 15–92 years). Seventeen patients (32 %) were female and 36 patients (68 %) male. The mean age of patients with juvenile glaucoma was 9 ± 1.4 years (range 7–11 years). One patient (20 %) was female and four patients (80 %) male. In 25 cases (47.4 %) of open-angle glaucoma the right eye, and in 28 cases (52.6 %) the left eye, was treated. In three cases (60 %) of juvenile glaucoma the right eye, and in two cases (60 %) the left eye, was treated. Decentralised Snellen visual acuity was 0.7 ± 0.3 (range 0.1–1.0) for open-angle glaucoma and 0.58 ± 0.3 (range 0.1–0.8) for juvenile glaucoma, pre-operatively. For all patients the follow-up was 72 months.

Mean pre-operative IOP in the study population of 53 patients with primary open-angle glaucoma was 25.6 ± 2.3 mmHg (range 18–48 mmHg) and in the study population of five patients with juvenile glaucoma was 39.6 ± 2.3 mmHg (range 34–46 mmHg). Mean IOP after