Efficacy and safety of deep sclerectomy with uveoscleral implant plus collagen matrix implant overcoming the superficial scleral flap in glaucoma surgery

Jéssica Botella-García¹,²,³, Marta Balboa¹, Pau Romera-Romero¹,³, Theo Stijnen⁴, Adrián Sánchez-Fortún¹, Karl Mercieca⁵, Jordi Loscos-Arenas¹,³,⁶

¹Department of Ophthalmology, Hospital Germans Trias i Pujol, Badalona 08916, Spain
²International University of Catalonia (UIC), Barcelona 08017, Spain
³Department of Surgery, Barcelona Autonomous University (UAB), Barcelona 08035, Spain
⁴Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden 2333, The Netherlands
⁵University Hospitals Bonn Eye Clinic, Bonn, 53127, Germany
⁶Germans Trias i Pujol Research Institute (IGTP), Badalona 08916, Spain

Co-first authors: Jéssica Botella-García and Marta Balboa

Correspondence to: Jéssica Botella-García. Carretera de Canyet, s/n, Badalona 08916, Spain. jessicabotga@gmail.com; jbotellag.germanstrias@gencat.cat

Received: 2023-01-12          Accepted: 2023-08-16

Abstract

- **AIM:** To assess the efficacy and safety of non-penetrating deep sclerectomy (NPDS) with uveoscleral implant plus subconjunctival and intrascleral collagen matrix implant overcoming the superficial scleral flap lips (modified deep sclerectomy technique, DS) and minimal use of mitomycin C in glaucoma surgery.
- **METHODS:** A retrospective review of 47 consecutive glaucoma patients who underwent NPDS with DS between January 2017 and May 2018. Best-corrected visual acuity, intraocular pressure (IOP), post-operative need for glaucoma medications, visual field mean deviation (MD), re-interventions, needling revisions and laser goniopuncture were noted. Absolute success was defined as IOP≤18 mm Hg without topical medication. Relative success was defined as the same criteria but with the addition of any antihypertensive medication. IOP over 18 mm Hg on two consecutive follow-up visits was considered as a failure.
- **RESULTS:** Fifty-two eyes of 47 patients were evaluated. Mean preoperative IOP was 25.37±6.47 mm Hg, and decreased to 15.04±4.73 at 12mo and 12.21±4.1 at 24mo (all P<0.0001). Requirement for topical medications dropped from a mean of 3.06±0.25 per patient to 0.51±0.99 and 1.11±1.23 respectively after 12 and 24mo (all P<0.0001). No medications were required in 45.5% of patients after 24mo. Relative and absolute success rate at 24mo were 85.5%±5% and 48.5%±7.4%, respectively.
- **CONCLUSION:** DS is a safe and effective non-penetrating glaucoma surgery variation. It aims to retain the patency of all pathways created for aqueous humor drainage: the intrascleral bleb, the supraciliary space and the open communication between intrascleral and subconjunctival compartments.
- **KEYWORDS:** deep sclerectomy; glaucoma surgery; uveoscleral implant

DOI:10.18240/ijo.2023.11.11


INTRODUCTION

Glaucoma is a progressive optic neuropathy which can eventually lead to blindness due to retinal ganglion cell death. Intraocular pressure (IOP) is the only modifiable risk factor and IOP reduction remains the current main focus of glaucoma treatment[1-2]. Although trabeculectomy is widely regarded as the commonest surgical treatment for glaucoma, non-penetrating deep sclerectomy (NPDS) has been shown to be similarly effective with less complications, especially when it comes to the risk of post-operative hypotony[3-4]. In NPDS, the inner wall of the trabecular meshwork is preserved and acts as an outflow resistance point. Mermoud et al[5] have previously compared efficacy and postoperative complications of NPDS with intrascleral collagen implant versus trabeculectomy in primary open angle glaucoma (POAG). They reported no differences in IOP reduction but post-surgical
complications were significantly lower in the NPDS group. Absorbable and non-absorbable devices have been used and described in NPDS\(^{[6-8]}\). Muñoz\(^{[9]}\) described the technique for suprachoroidal T-flux implantation in NPDS creating a direct access of the aqueous to this space through the implant and obtaining a significant IOP reduction at 18mo follow up. Bonilla et al\(^{[10]}\) found a significant IOP reduction with the implantation of 2-hydroxyethyl methacrylate (HEMA) implant (V-2000, Esnoper\(^{®}\), AJL Ophthalmics, Álava, Spain) into the suprachoroidal space at one year follow up. There are other previous favorable results of NPDS with uveoscleral implant\(^{[6-8]}\).

The Esnoper Clip\(^{®}\) (AJL Ophthalmic S.A, Álava, Spain) is a non-absorbable HEMA implant (5.50×1.30×2.20 mm\(^3\)) which has two plates allowing aqueous humor drainage through intrascleral and suprachoroidal spaces preventing intrascleral lake collapse.

Unlike the Esnoper Clip\(^{®}\), Ologen\(^{®}\) (Aeon Astron Corporation, Taipei, Taiwan, China) is an absorbable implant made from lyophilized porcine collagen and cross-linked hyaluronic acid. It modifies surgery-induced fibrosis by acting on myofibroblast migration and is active in both the proliferative and remodeling phases of surgical wound healing\(^{[11-12]}\). Some comparative studies have shown greater safety and efficacy for trabeculectomy using collagen matrix, while others have not reported any advantage\(^{[13-16]}\). Collagen matrix could also be used in NPDS just acting as an intrascleral absorbable implant limited to intrascleral space or as in the modified deep sclerectomy (DS) technique, overcoming the sclera lips and keeping the connection between intrascleral and subconjunctival spaces open, but there is a paucity of evidence on the literature for this\(^{[17-18]}\).

The aim of this study was to analyze the two-year safety and efficacy outcomes of a group of patients undergoing NPDS with uveoscleral implant (Esnoper Clip\(^{®}\)) combined with collagen matrix (Ologen\(^{®}\)).

**SUBJECTS AND METHODS**

**Ethical Approval** The study process complied with the Helsinki Declaration and was approved by the Ethics Committee of the University Hospital Germans Trias I Pujol. All patients were informed of the research purpose and gave their written consent.

This is a single-center, retrospective, longitudinal, non-comparative cohort study of two-year outcome for 47 consecutive patients who underwent NPDS with the modified DS technique between January 2017 and May 2018 at the Glaucoma Unit of Hospital Germans Trias i Pujol (HUGTIP). A total of 47 subjects with glaucoma diagnosis were included in the study. All of them were patients over 18 years old with POAG or secondary glaucoma with poor IOP control despite the use of maximum tolerated glaucoma medication and progressive deterioration of the visual field (VF).

Patients who underwent a combined phacoemulsification plus NPDS procedure at the same time were not excluded. Exclusion criteria were the following: patients with angle closure, patients with any history of previous glaucoma surgery, including laser trabecuoplasty, or any form of intraocular surgery within six months of the NPDS procedure in the study eye, moderate or severe diabetic retinopathy, any cause of ocular neovascularization, active ocular inflammation, plateau iris syndrome, aphakia, history of malignant neoplasia, axial length <20 mm and >26 mm, pregnancy and unwillingness to participate.

The primary outcome was reduction in IOP in the postoperative stage up to and including the two-year post-operative timepoint. Secondary outcomes were number of topical glaucoma medications required post-operatively, best-corrected visual acuity (BCVA) and VF mean deviation (MD) changes, surgical re-interventions, rate of laser goniopuncture (LGP) and needle revision, at the 3, 12, and 24mo time points.

**Data Collection and Examination** Demographic and clinical data were extracted from a bespoke patient electronic database. Glaucoma sub-type, IOP, BCVA, number of glaucoma medications, MD in VF, and pachymetry (UP-1000\(^{®}\), Nidek, Japan) were collected from each patient, both pre-operatively and post-operatively when relevant. Follow-up visits were scheduled at 24h post-surgery, then at 3, 12 and 24mo post-operatively.

IOP was assessed by Goldman applanation tonometry (GAT). Glaucoma medications, were registered as the number of active ingredients, rather than number of drops or tablets. BCVA was quantified using a decimal scale test via projector on a white wall. All these measurements were documented for each visit, along with slit-lamp anterior segment examination findings, gonioscopy and fundus biomicroscopy. VF were measured using a Humphrey visual field analyzer; (Humphrey Zeiss, Dublin, CA, USA) with 24-2 SITA fast in a static perimetry mode. MD was annotated to compare pre-operative values with those at 12 and 24mo post-operatively. VF was considered unreliable when false-positive rates were over 15% or false-negative rates and fixation losses exceeded 20%. Patient’s demographic data are summarized in Table 1. IOP, number of glaucoma medications and BVCA were registered in all patients.

Post-surgical manipulations performed to enhance NPDS subconjunctival and trabeculo-Descemet’s window aqueous flow within the 24mo follow-up period were also annotated. These post-operative maneuvers to lower IOP further involved either a YAG LGP (Visulas\(^{®}\) YAG III Combi, Carl Zeiss Meditec Inc., Germany) or subconjunctival needling

---

\[1\] et al

\[2\] et al

\[3\] et al

\[4\] et al

\[5\] et al

\[6\] et al

\[7\] et al

\[8\] et al

\[9\] et al

\[10\] et al

\[11\] et al

\[12\] et al

---

1807
Postoperative management

All patients received topical ciprofloxacin 3 mg/mL (Alcon Cusi SA. El Masnou, Barcelona, Spain) three times a day for two weeks and topical dexamethasone 1 mg/mL drops (Alcon Cusi SA. El Masnou, Barcelona, Spain) six times a day, the latter being gradually tapered off over 24wk.

In cases where target IOP was not reached, LGP and/or bleb were performed. LGP was usually performed shortly after surgery when there was suspicion of insufficient percolation of aqueous humor through the TDW. When LGP was required at a later time (more than 6mo after initial surgery), a low filtration rate was assumed to be present as a result of fibrosis of the TDW. We did not consider LGP as a surgical failure as it was planned, the phacoemulsification was performed at the beginning of surgery with clear corneal temporal approach of 2.2 mm. It included standard phacoemulsification, intraocular lens insertion in the capsular bag (T ASPHINA 509M; Carl Zeiss Meditec Inc., Germany) and acetylcholine injection in the anterior chamber at the end of the NPDS.

The Esnoper Clip® implant is inserted into the intrascleral space allowing access to the supraciliary space. The two footplates of the Esnoper Clip® implant are sutured posteriorly with a nylon 10/0 loose stitch and the Tenon’s and conjunctival layers are sutured with two simple nylon 10/0 sutures.

In those patients where combined cataract and NPDS surgery was planned, the phacoemulsification was performed at the beginning of surgery with clear corneal temporal approach of 2.2 mm. It included standard phacoemulsification, intraocular lens insertion in the capsular bag (T ASPHINA 509M; Carl Zeiss Meditec Inc., Germany) and acetylcholine injection in the anterior chamber followed by corneal suture using a nylon 10/0 stitch to keep it closed and prevent accidental MMC entry into the anterior chamber which is removed after NPDS. We finished the surgery injecting 0.2 mL of ceftoxime in the anterior chamber at the end of the NPDS.

**Postoperative Management** All patients received topical ciprofloxacin 3 mg/mL (Alcon Cusi SA. El Masnou, Barcelona, Spain) three times a day for two weeks and topical dexamethasone 1 mg/mL drops (Alcon Cusi SA. El Masnou, Barcelona, Spain) six times a day, the latter being gradually tapered off over 24wk.
subconjunctival level, observing scleral lips sealed. This consists of reopening the surgical fistula, with a 25 G needle with the help of MMC at 0.2 mg/mL (0.02%) 0.1 mL.

**Statistical Analysis** Primary outcomes were taken as the decrease in IOP in the postoperative stage up to two years. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 26.0. Comparisons between the various follow-up time points and the preoperative one, as well as between pairs of follow-up points, were performed by simple paired t-tests (for approximately normal variables) or exact Wilcoxon signed rank tests (for non-normal variables). These analyses did not account for the correlation between the eyes of the five patients who were operated on both eyes. In order to correct for this correlation, we also analyzed the differences between times with a linear mixed model, using empirical standard errors where appropriate. Since these analyses led to the same conclusions, we have only presented the results of the simple analyses. Linear mixed models were used to study differences in IOP reduction between groups defined by baseline characteristics. All linear mixed models used unstructured covariance matrices. Success rates were studied using Kaplan-Meier analyses. P-values below 0.05 were considered statistically significant.

**RESULTS**

**Demographics** The study included 52 eyes of 47 patients with glaucoma aged between 43 and 87. The 88.5% of the patients presented POAG and 12% secondary glaucoma (uveitic glaucoma 1.9%, pigmented glaucoma 1.9%, angle recession 1.9%, elevated episcleral venous pressure 1.9% and glaucoma post-keratoplasty 3.9%). They underwent an NPDS between January 2017 and May 2018 in HUGTiP. All patients were followed for at least 12mo and 15% of visits were missing between the first and second year (8 eyes). Three surgeries (5.8%) were combined with phacoemulsification.

**Time Comparisons** Mean preoperative IOP was 25.37±6.47 mm Hg which was reduced immediately after surgery to 7.02±6.1, 15.35±5.7 at 3mo, 15.04±4.73 at 12mo and 12.21±4.1 mm Hg at 24mo postoperatively. Comparing with baseline IOP, all assessments showed a statistically significant reduction (P<0.0001 with the pairwise t-test) but there were no significant differences between IOP outcomes at 3, 12 and 24mo.

The mean number of topical anti-hypertensive medications at the preoperative visit was 3.06±0.25, with all patients being on at least one active medication. This number reduced to zero at 24h post-surgery but increased to 0.8±0.33 at 3mo, 0.51±0.99 at 12mo and 1.11±1.23 at 24mo. The percentage of patients on no glaucoma medications at 24mo was 45.5%. All pairwise differences were statistically significant (P<0.0001 with exact Wilcoxon signed-rank test). All data are shown in the Table 2. Kaplan-Meier survival curves for success criteria A and B were calculated as depicted in Figure 2. Absolute success rate (criterion A) was 48.5%±7.4% at 24mo and the relative...
success rate (criterion B) was 85.5%±5% at 24mo.
Mean BCV A (measured in decimal Snellen chart) changed marginally from 0.66 preoperatively to 0.64 at 3mo (\(P=0.32\)), to 0.68 at 12mo (\(P=0.88\)), and to 0.66 at 24mo (\(P=0.66\)). There were no significant differences in BCV A outcome between the scheduled visits.

MD in dB was used to measure VF function. MD was -13.71±9.26, 15.37±13.83, and -16.02±12.21 at baseline, 12mo and 24mo respectively. Changes in VF MD were not statistically significant.

The type and number of early postoperative complications were summarized in the Table 3. The most frequent complication was the presence of flare in the anterior chamber. All the complications described occurred in eyes with POAG, except for one eye with uveitic glaucoma who developed corneal edema and Descemet’s membrane folds.

A total of 34 interventions were performed at any postoperative stage, 95.9% of them being done in the first year. Postoperative interventions such as LGP, needling or re-operation are detailed in Table 4. By 24mo, five patients had required a needle revision with MMC (11.4%), 28 patients had received a LGP (63.6%) and 1 patient had required a re-operation (2.3%) which belongs to the group of POAG.

During the first year, 27 eyes (51.9%) required an LGP and one eye also underwent a second one. The mean time between surgery and LGP was 148.76d. In one case there was transient overfiltration with an IOP of 2 mm Hg. LGP produced an immediate mean IOP reduction of 31.1% (from 21.56±5 to 13.56±4.55 mm Hg). In Figure 3 the changes in mean IOP in LGP and needling cases respectively are shown.

Analysis of the association between demographic characteristics and IOP changes was performed using a linear mixed model corrected for baseline IOP. Considering the sub-types of glaucoma mentioned above, there were no statistically significant differences in IOP between groups (\(P=0.78\)). In relation to eye laterality, we saw that on average the left eye had a 2.1 mm Hg higher change of IOP compared to the right eye, which was statistically significant (\(P=0.015\)). Referring to gender and age (<60y, 60y to <80y, ≥80y), there were no differences (\(P=0.938\) and \(P=0.724\) respectively).

With regards to postsurgical procedures, the only statistically significant finding was a larger IOP reduction in eyes that had been treated with LGP by the 12mo follow-up mark (\(P=0.036\)).

**DISCUSSION**

This retrospective study showed that modified DS technique resulted in a 51% decrease in IOP from baseline sustained over 2y. The success with (relative) and without (absolute) antiglaucomatous medication was 85.5% and 48.5% respectively. The number of medications required to control IOP was reduced from a mean of 3.06 before surgery to 0.5 and 1.11 at 12 and 24mo respectively postoperatively. These results are mainly in concordance with other authors’ previous publications\[5,8,19-20\]. However, the success criteria were less
strict (21 vs 18 mm Hg) in most of those studies. In this study, the modified DS technique resulted in 27 eyes (51.9%) requiring YAG LGP within the first postoperative year with a further one eye by the end of the second year. This percentage is slightly higher than previously reported but the success rates of LGP, the reduction in mean IOP, as well as the time interval between surgery and laser intervention were similar to those reported in other trials [7,8,20–21]. Comparing eyes with and without LGP, there was a higher mean IOP in patients who required LGP or needling. In these eyes, incomplete juxtacanalicular tissue dissection or increased fibrotic potential could not be ruled out. In our case and considering that it is a third-level hospital, we usually treat patients with moderate-advanced advanced VF damage. The mean pre-operative MD value in this study was -13.71 dB. For that reason, it is important for us to keep the IOP as low as possible.

The common perception and published evidence is that non-penetrating glaucoma surgery in general, and augmented NPDS more specifically, result in fewer postoperative complications with a nearly comparable IOP outcome compared to trabeculectomy [5,21]. Our results confirm this. In addition, we did not observe any reported complication related to the loosely sutured superficial scleral flap, to the presence of the collagen matrix overcoming the lips of the flap, or to the use of a supraciliary implant. Secondary to a high bleb obtained after the modified DS technique during the first postoperative days bubble dysesthesia with or without dellen could be seen. In our experience, this responds well to topical lubricant therapy. It was not reported as a complication as was transient and had not any severe consequence for the patient. The height of the intrascleral lake is a controversial issue in NPDS almost a matter of faith. Some authors have found no relation whatever between intrascleral bleb height and IOP control, neither with intrascleral nor supraciliary spacer implantation [22–23]. On the other hand, Mavrakanas et al [24] reported that postoperative IOP is related to intrascleral bleb height in eyes with clinically flat blebs following NPDS with an intrascleral collagen spacer and MMC augmentation. Romera-Romero et al [7] observed that a higher intrascleral lake height was related to less IOP control following uveoscleral implantation. Intrascleral lake height is of course also influenced by the amount of subconjunctival drainage, which is in turn determined by outflow via the scleral flap lips. This in turn is not only influenced by how tight the flap is tied but also depends on the amount of fibrosis which may result in a larger scleral lake height but not lower IOP due to reduced subconjunctival drainage. The idea of augmenting our previously established NPDS technique (including supraciliary implant) with collagen matrix spanning the scleral flap edges (modified DS technique) evolved from this concept: to preserve aqueous drainage into the subconjunctival space by maintaining long-term transcleral outflow through the scleral lips. In our experience, the conjunctival bleb is still an important success factor after NDPS, not as decisive as in trabeculectomy.

Long term NPDS success is not related to the high of the scleral bleb. The modified DS technique results in a relatively shallow but diffuse subconjunctival bleb. However, traditional bleb classification methods, such as the Indiana and Moorfields systems, cannot be directly applied. This is also partly due to the presence of the absorbable collagen matrix which changes the characteristics of the conjunctival bleb. Both microcysts and vascularization can indeed be discerned in the early postoperative period but in our experience they are not present in the long term [25–30].

This study seems to suggest that NPDS using a supraciliary implant with a modified DS technique may decrease the need for postoperative bleb needling procedures. We observed five cases in the first year and one in the second, representing rates of 9.6% and 11.4% respectively. These results were overall lower than other NDPS reports. Byszewska et al [31] reported needling in 24% of the operated eyes with NPDS at 2y follow up. Romera-Romero et al [7] observed a needle revision rate of 22.5% and 27.7% in operated eyes with NPDS using a nonabsorbable uveoscleral implant without collagen matrix implant at 12 and 24mo, respectively.

There still is no general consensus on the use of absorbable versus non-absorbable spacer implants in NPDS. In our experience with previously published results [6–7], implants make a difference in the long term outcomes of NPDS, particularly as they avoid complete intrascleral collapse by acting as space maintainers as intrascleral lake height tends to decrease over time. A study by one of our co-authors seemed to show that there is no significant difference comparing intrascleral versus supraciliary implantation of an HEMA implant [21]. Supraciliary implantation acts as an alternative aqueous humor route when subconjunctival drainage and the intrascleral bleb dynamics are blocked, so the effect of supraciliary implantation is not a quantitative benefit in terms of IOP reduction. In our long-term follow-up using (VISANTE OCT-SA. Carl Zeiss Meditec, Inc, Dublin, CA, USA) [7], we did not observe high uveoscleral outflow in combination with high functional conjunctival blebs, with the latter do not being present when high uveoscleral outflow is evident. Some degree of uveoscleral outflow can exist in both situations which means that in some eyes with very high fibrotic potential the supraciliary pathway could be a good alternative option for IOP control specially when transscleral flow is blocked.

Manufacture and sterilize a mixed implant (absorbable plus non absorbable) seem to be an interesting option but to the best
of our knowledge it is a very expensive procedure. Cost-effectiveness is also important when considering any modification in glaucoma surgery technique. We have therefore set up a prospective clinical trial to determine if the uveoscleral implant plus matrix collagen is as effective as matrix collagen alone to reduce IOP at 24mo (https://clinicaltrials.gov/ct2/show/NCT04586738?term=J%C3%A9ssica+Botella&draw=2 &rank=1). 

**Limitations** First, it is a retrospective single-center study with a limited number of patients and without control group. We also recognize that the study may be underpowered and there was a 15% patient attrition rate between the one and two-year marks. We consider another limitation of the study to include patients who underwent simultaneous cataract surgery because the evaluation of the hypotensive effect may be distorted.

In conclusion, the modified DS technique is a safe and effective therapeutic option for the management of POAG. It combines the advantages of an absorbable plus a non-absorbable implant, trying to keep open all the spaces involved in the aqueous humor drainage open: an intrascleral bleb, a supraciliary space, and an open communication between the intrascleral and the subconjunctival space. This new perspective, keeping a free communication between the scleral flap and conjunctiva at the same time we offered an alternative route of filtration in high fibrotic patients is what modified DS technique offered in glaucoma surgery. Our results show how after gonipuncture there is huge IOP significant drop, which means filtration route is still functional with implants help. More studies with anterior segment OCT trying to locate filtration route (suprachoroidal or subconjunctival) should be done.

Other prospective studies with a larger number of patients comparing the use of absorbable implants vs non-absorbable implants are necessary to give more information about the efficacy and safety in glaucoma surgery.

**ACKNOWLEDGEMENTS**

**Conflicts of Interest:** Botella-García J, None; Balboa M, None; Romera-Romero P, None; Stijnen T, None; Sánchez-Fortún A, None; Mercieca K, None; Loscos-Arenas J, None.

**REFERENCES**


