


# Supraciliary versus intrascleral implantation with hema implant (Esnoper V-2000) in deep sclerectomy: a multicenter randomized controlled trial

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## ABSTRACT.

**Purpose:** To compare the supraciliary versus intrascleral implantation of the hema implant (Esnoper V-2000) in terms of the efficacy and safety in nonpenetrating deep sclerectomy (NPDS).

**Patients and methods:** Prospective, randomized, unmasked, competitive and multicenter clinical trial. Eighty-three eyes from 83 patients suffering from open-angle glaucoma (40 males, 43 females) were enrolled and followed up for 12 months. Main outcome measures were best-corrected visual acuity (BCVA), intraocular pressure (IOP), perimetry (mean defect, MD and Visual Field Index, VFI), pachymetry, number of antiglaucoma medications and analysis of blebs according Moorfields Bleb Grading.

**Results:** The IOP was significantly reduced in both groups from  $23.74 \pm 6.9$  mmHg (implant sutured to the sclera, group 1) and  $23.46 \pm 6.47$  mmHg (implant placed in the suprachoroidal space, group 2) to  $15.43 \pm 4.27$  mmHg ( $p < 0.001$ ) and  $14.62 \pm 3.64$  mmHg ( $p < 0.001$ ), respectively. There were no statistically significant differences in mean IOP values between the groups a year after the surgery ( $p = 0.581$ ). BCVA did not show statistical differences in comparison with baseline ( $p = 0.09$ , group 1;  $p = 0.42$ , group 2). The mean number of antiglaucoma medications was reduced in both groups from  $2.58 \pm 0.04$  and  $2.68 \pm 0.02$  before the surgery to  $0.32 \pm 0.76$  and  $0.24 \pm 0.66$  after surgery.

**Conclusion:** Nonpenetrating deep sclerectomy using hema implant (Esnoper V-2000) is safe and effective regardless of the positioning of the implant. We achieved IOP decrease and reduction in antiglaucoma medications during the first year after surgery without significant differences between both techniques.

**Key words:** Esnoper V-2000 – glaucoma – nonpenetrating deep sclerectomy – supraciliary surgery

## Introduction

Glaucoma is an optic neuropathy associated with characteristic structural damage of the optic nerve (ON) due to progressive loss of the retinal nerve fibre layer (RNFL) with subsequent appearance of characteristic visual field defects. In most cases, glaucomatous damage is associated with an increase in intraocular pressure (IOP) caused by an inadequate drainage of the aqueous humour (AH). For this reason, the target of both medical and surgical antiglaucoma treatment is the control of the IOP as it is the key modifiable factor (Prum et al. 2015). Glaucoma filtration surgery is an effective method for the treatment of the disease in patients with uncontrolled disease. The aim of the surgery is to increase the aqueous outflow therefore constantly maintaining a low IOP. Nonpenetrating deep sclerectomy (NPDS) is one of the surgical procedures used for lowering IOP in patients with uncontrolled open-angle glaucoma (OAG). Although NPDS has reduced the number of complications, when compared to conventional surgery, trabeculectomy still seems to be the most effective surgical procedure for reducing IOP in patients with OAG (Rulli et al. 2013). The surgery creates an

intrascleral space separated from the anterior chamber (AC) by a thin membrane formed by the trabecular meshwork and Descemet's membrane (TDM) (Fiodorow et al. 1989). From this location, the AH is drained via three routs: subconjunctival (as after trabeculectomy), intrascleral and suprachoroidal. Unfortunately, postoperative fibrotic reaction of the filtration bleb remains a problem which may lead to failure of the surgery. The long-term results of NPDS can be enhanced using specific implants designed to maintain a permanent intrascleral space by preventing the adhesion between the scleral flap and the trabecular meshwork. Both reabsorbable (collagen, cross-linked hyaluronic acid) and nonresorbable materials such as hydroxyethyl methacrylate (HEMA) have been used in the implant manufacture. Hema is a nonionic polymer with a very low tendency to cause protein deposits. The hema implant (Esnoper V-2000; AJL, Ophthalmic, Miñano, Alava, Spain) is a second-generation device developed to prevent the collapse of the intrascleral lake. Compared to the first generation, the new device presents internal channels to facilitate AH flow through the implant. Secondly, lateral notches were created for nonstitching supraciliary placement, further facilitating the drainage via this route. However, the safety and effectiveness of these two new pathways have not been thoroughly examined. The aim of this study was to analyse the efficacy and incidence of complications in two groups of patients undergoing NPDS with the Esnoper V-2000, with the first group having the implant sutured to the scleral bed, and the second positioned in the suprachoroidal space.

## Materials and Methods

### Patients

The Esnoper V-2000 study was a prospective, randomized, open-label, competitive study performed in six Spanish centres and a Swiss centre. The ethical committees at each of the study sites approved the study protocol. Adult participants (>18 years of age) with OAG were included if target IOP was not achieved using at least two antiglaucoma medication for at least 3 months, or that did not tolerate well the antiglaucoma medication and presented visual field defects or nerve

abnormalities characteristic of glaucoma confirmed by OCT. Patients were excluded if they had undergone previous filtration surgery or cataract surgery in the preceding 3 months or selective laser trabeculoplasty or argon laser trabeculoplasty or any type of surgery that might have affected the conjunctiva at the site of the intervention. Other exclusion criteria included moderate or severe diabetic retinopathy and other causes of ocular neovascularization, glaucomas with a high risk of failure, such as neovascular, aphakic, inflammatory, juvenile, post-traumatic and postoperative glaucoma. After obtaining the informed consent from all participants, a comprehensive screening examination was performed. The preoperative data evaluated were age, sex, IOP, number of IOP-lowering medications, pachymetry, BCVA (Snellen visual acuity converted to the logMAR scale for comparisons) and perimetry (Humphrey 740i, Humphrey Systems, Dublin, CA, USA) mean Defect (MD) and Visual Field Index (VFI). This was a single-blind study where IOP measurements were taken by an ophthalmologist other than the surgeon involved in the operation who did not know to which group the patient belonged to. Goniopuncture using an Nd:YAG laser was performed when percolation of AH was considered insufficient, in the anterior portion of the TDM.

### Randomized assignment

Patients were randomly assigned to one of the two study groups: the first group had the implant placed in the scleral bed and the second in the suprachoroidal space. Randomization was carried out using an online software specifically designed for the study based on a single sequence of random assignments.

### Surgical technique

Sub-Tenon or peribulbar anaesthesia was applied using a standard technique. An intracorneal traction suture was created using 8-0 silk suture. A fornix-based conjunctival flap was made after minimal diathermy, and a superior scleral flap of 5 × 5 mm was dissected to 1/3 of the scleral thickness extended 1–2 mm into clear cornea. Mitomycin C (MMC, 0.02%) was

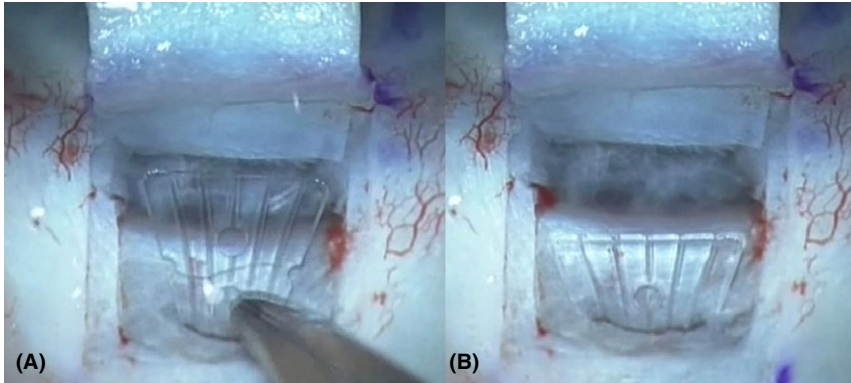
applied for 2 min between the sclera and conjunctiva. Then, the area was irrigated thoroughly with a balanced salt solution. Subsequently, a deeper 4 × 4 mm<sup>2</sup> scleral flap was dissected and removed, and Schlemm's canal was deroofed using Capsulorhexis or Merz forceps. Implant placement depended on the study group to which the patients were randomly assigned. The patients were enrolled in two groups. In group 1, the implant was sutured with Nylon 10/0 onto the scleral bed, so it did not overlap the trabeculodescemet membrane (TDM), with the channels up (Fig. 1). In group 2, a full-thickness suprachoroidal bag was made 2 mm behind the scleral spur, following the technique first described by Muñoz (2009). The implant was then placed with the channels up until it was embedded in the side-notches (Fig. 2A,B). The scleral flap was secured with one or two loose sutures. In all the eyes, the conjunctiva was closed with 3–4 single Nylon 10/0 sutures or continuous absorbable vicryl sutures (8/0). Postoperative treatment consisted of topical ofloxacin (Exocin<sup>®</sup>, Alcon Cusí SA, El Masnou, Barcelona, Spain) four times a day during 1 week and prednisolone acetate (10 mg/ml; Predforte<sup>®</sup>, Allergan Pharmaceuticals Ireland, Westport, Ireland) six times a day, the latter in a descending dosage over 6 weeks.

### Primary and secondary outcome measures

Postoperative follow-up visits were scheduled at 1, 7, 30, 90, 180 and 360 days after surgery. Outcome measures evaluated postoperatively included IOP values, BCVA, number of IOP-lowering medications and complications related to the surgery. More specifically, bleb leakage was examined under cobalt blue slit-lamp



**Fig. 1.** Group 1: Esnoper V-2000 sutured onto the scleral bed without overlapping of the trabeculodescemet membrane. The channels are upwards.



**Fig. 2.** Group 2: a full-thickness suprachoroidal bag was made 2 mm behind the scleral spur. The implant was placed with the channels up (A) and fixed with the two lateral notches (B).

had the Esnooper V-2000 implant sutured to the scleral bed. The second group (Group 2) consisted of 41 patients (22 right and 19 left eyes) and had the implant placed in the suprachoroidal space (Fig. 3). The average age of the subjects was  $68.17 \pm 13.27$  years in group 1 and  $65.65 \pm 14.77$  years in group 2 ( $p = 0.52$ ). The mean number of IOP-lowering medications was similar in the two groups,  $2.58 \pm 0.04$  and  $2.68 \pm 0.02$  before the surgery.

**Baseline characteristics**

The baseline characteristics of the patients are summarized in Table 1. There were no statistically significant differences between the two groups. All patients included in the study completed the follow-up of 360 days after the surgery. Two eyes of group 1 were considered failure during the follow-up. None of the patients presented with any adverse effects during the postoperative period (Table 1).

Baseline mean BCVA for all patients was  $0.19 \pm 0.25$  logMAR and  $0.2 \pm 0.27$  logMAR 360 days after surgery

illumination, with a moistened sterile fluorescein strip gently applied to the bleb surface. A Seidel was diagnosed if there was any apparent AH leakage. At all follow-up visits, a single observer blinded to retrospective treatment, evaluated the filtration blebs using the standardized Moorfields Bleb Appearance Grading Scale (MBGS; Wells et al. 2006). The scale permitted evaluation of the area, height and vascularization of the blebs.

The primary end-point for complete success was defined as a decrease in IOP  $\leq 21$  mmHg at 12 months after surgery without the use of IOP medications. The secondary efficacy end-point was defined as the proportion of subjects with IOP  $\leq 21$  mmHg regardless of IOP-lowering medications at month 12 (relative success). Failure was defined if IOP  $> 21$  mmHg.

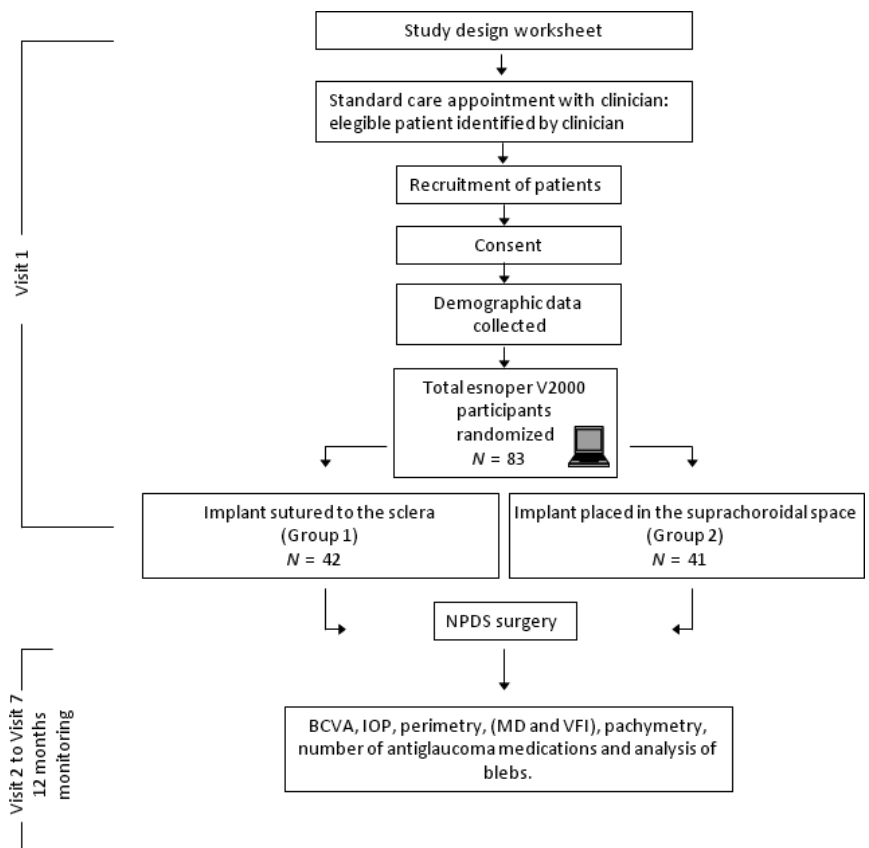
**Statistical analysis**

Data are presented as mean  $\pm$  standard deviation. All statistical analyses were performed using spss statistical software (ver. 19.0; SPSS, Inc., Chicago, IL, USA). The sample size was estimated using Altman’s nomogram with a significance level of 0.05, the power of 0.098 and case loss of 0.02. Independent student *t*-tests were used to evaluate between and within-group differences. Categorical variables and proportions were analysed using Pearson’s chi-squared tests. Success rates in both groups were compared using Kaplan–Meier life table analysis and the log-rank test. A *p* value of 0.05 or less was considered statistically significant.

**Results**

**Recruitment**

A total of 83 OAG patients (40 males and 43 females) were enrolled between June 2013 and December 2013. Only one eye per patient was included in the study. Patients were subsequently randomly divided into two groups. The first group (Group 1), composed of 42 patients (19 right eyes and 23 left eyes),



**Fig. 3.** Participant study pathway.

( $p = 0.5$ ). BCVA did not show any significant difference when comparing baseline to 360 days after surgery values in either group ( $p = 0.09$  group 1 and  $p = 0.42$  group 2; Table 2).

**IOP Reduction**

The IOP was significantly reduced in both groups, from  $23.74 \pm 6.9$  mmHg to  $15.43 \pm 4.27$  mmHg ( $p < 0.001$ ) in

group 1 and from  $23.46 \pm 6.47$  mmHg to  $14.62 \pm 3.64$  mmHg ( $p < 0.001$ ) in group 2. Furthermore, both groups showed a statistically significant ( $p < 0.05$ ) decrease in IOP at each time-point (1, 7, 30, 90, 180 and 360 days) in comparison with basal IOP (Fig. 4 and Table 3). However, there were no statistically significant differences in mean IOP values between the groups a year after the surgery. Goniopuncture was performed in 22 eyes from group 1 (52.38%) and 15 eyes (36.58%) in group 2 (Table 4) A similar IOP reduction in the two groups was reported: 6.36 mmHg in group 1 and 6.88 mmHg in group 2. In both groups, two injections of MMC were performed postoperatively (0.05 ml at 0.02%) to reduce fibrotic reaction and obtain a successful outcome.

**Table 1.** Demographic and preoperative characteristics.

Variable statistics	Groups		p Value
	Group 1: Sutured	Group 2: Suprachoroidal	
Subjects analysed (N) 82	42	41	
Mean age (years) $\pm$ SD	$68.17 \pm 13.27$	$65.65 \pm 14.77$	0.5277
Range 36–94	41–94	36–90	
Gender			
Male 40 (48.19%)	40%	57.15%	0.151*
Female 43 (51.81%)	60%	42.85%	
Additional glaucoma diagnosis			
POAG (77.11%)	33	31	0.32*
PEXG (22.89%)	9	10	0.212*
Lens status			
Phakic (49%)	18	23	0.81
Pseudophakic (51%)	24	18	
Mean medications $2.63 \pm 0.07$	$2.58 \pm 0.04$	$2.68 \pm 0.02$	0.796*
Mean medicated IOP (mmHg) $\pm$ SD	$23.74 \pm 6.90$	$23.46 \pm 6.47$	0.74
Mean pachymetry ( $\mu$ m) $543.30 \pm 39.47$	$546.30 \pm 39.28$	$540.48 \pm 40.01$	0.54
MD	$-11.98 \pm 7.92$	$-9.66 \pm 9.18$	0.4
VFI	$64.87 \pm 29.78$	$78.06 \pm 26.62$	0.2

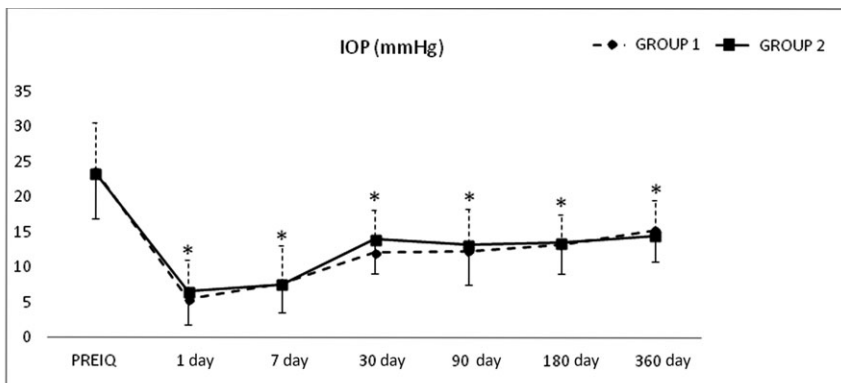
Statistics test: *t*-test.

\* Chi square test.

**Table 2.** Best-corrected visual acuity logMAR values before and 360 days after surgery.

Groups	logMAR presurgery	logMAR 360 days	p Value
Group 1	$0.20 \pm 0.24$	$0.25 \pm 0.31$	0.09
Group 2	$0.17 \pm 0.24$	$0.15 \pm 0.23$	0.42

Group 1: Scleral; Group 2: Suprachoroidal.



Group	IOP 0	IOP 1	IOP 7	IOP 30	IOP 90	IOP 180	IOP 360
Group 1	$23.74 \pm 6.9$	$5.51 \pm 5.6$	$7.8 \pm 5.3$	$12.17 \pm 6.02$	$12.44 \pm 5.95$	$13.35 \pm 4.26$	$15.43 \pm 4.27$
Group 2	$23.46 \pm 6.47$	$6.6 \pm 4.76$	$7.6 \pm 4.05$	$14.09 \pm 4.87$	$13.29 \pm 5.7$	$13.58 \pm 4.44$	$14.62 \pm 3.64$

\*  $p < 0.001$

IOP intraocular pressure mmHg

**Fig. 4.** Mean intraocular pressures. Both groups showed a statistically significant decrease in intraocular pressure (IOP) at each time-point (1, 7, 30, 90, 180 and 360 days) in comparison with the basal IOP.

**Bleb analysis**

Regarding the Moorfields bleb grading system, no statistically significant difference between the two groups was present at the end of the study neither in bleb maximal area ( $p = 0.956$ ) nor in bleb height ( $p = 0.695$ ; Table 5). Group 1 showed a negative correlation between the height of the bleb and IOP value at 30 days ( $p = 0.007$ ;  $r^2 = -0.4$ ) and 180 days ( $p = 0.10$ ;  $r^2 = -0.4$ ) after the surgery. In contrast, in group 2, we only found a positive correlation between the area of the bleb and IOP at day 7 after the surgery ( $p = 0.05$ ;  $r^2 = 0.3$ ). When comparing the two groups, no differences were seen in maximum area and height at any of the studied time-points (Fig. 5).

**Medical therapy**

When taking into consideration both primary and secondary outcome measures (i.e. IOP  $< 21$  mmHg with and without topical treatment), the success rate was of 97%. More specifically in 14 cases of both groups (20.8%), the result can be defined as a relative success as the patient needed topical treatment [eight (17.2%) cases in group 1 and six (14, 6%) cases in group 2]. In this respect, both groups behaved in a very similar manner, as shown in the survival curve in Fig. 6. The mean number of antiglaucoma medications was reduced in both groups from  $2.58 \pm 0.04$  and  $2.68 \pm 0.02$  before

**Table 3.** Values of the intraocular pressure (IOP) at different times of the study.

Variable statistics	Group 1: Sutured	Group 2: Suprachoroidal	p Value
IOP pre	23.74 ± 6.9	23.46 ± 6.47	0.922
IOP 1 day	5.51 ± 5.6	6.6 ± 4.76	0.352
IOP 7 days	7.8 ± 5.3	7.6 ± 4.05	0.072
IOP 30 days	12.17 ± 6.02	14.09 ± 4.87	0.257
IOP 90 days	12.44 ± 5.95	13.29 ± 5.7	0.289
IOP 180 days	13.35 ± 4.26	13.58 ± 4.44	0.57
IOP 360 days	15.43 ± 4.27	14.62 ± 3.64	0.581

IOP intraocular pressure mmHg; Student *t*-test *p* < 0.05.

**Table 4.** Decreased intraocular pressure (IOP) related with goniotomies performed.

Groups	Pre-IOP (mmHg)	Post-IOP (mmHg)	Diff. mmHg	Time (days)	p Value
Group 1	21.54 ± 5.69	15.18 ± 5.17	6.36	210	0.0083
Group 2	19.44 ± 8.18	12.55 ± 3.6	6.88	165	0.016

*p* Value group 1 versus group 2 = 0.8615.

**Table 5.** Bleb parameters in both groups.

Group	Bleb maximal area (mm <sup>2</sup> )	Bleb height (mm)
Group 1	3.01 ± 1.39	1.74 ± 0.786
Group 2	2.98 ± 1.39	1.78 ± 0.737
<i>p</i> -Value	0.956	0.695

the surgery to 0.32 ± 0.76 and 0.24 ± 0.66 after surgery.

**Visual field changes**

Regarding the visual field, in group 1, the values of MD were -11.98 ± 7.92 dB before surgery and -13.06 ± 8.54 dB 360 days after surgery (*p* = 0.22). In group 2, the MD values were -9.66 ± 9.18 dB and -9.93 ±

8.36 dB (*p* = 0.77) before and after surgery, respectively. The values of VFI did not show statistical differences, either. In group 1, VFI values before surgery were 64.87 ± 29.78% and 65.5 ± 30.26% (*p* = 0.76) 360 days after surgery. In group 2, VFI values were 78.06 ± 26.62% and 80.93 ± 22.18% (*p* = 0.52) before the surgery and a year after surgery, respectively.

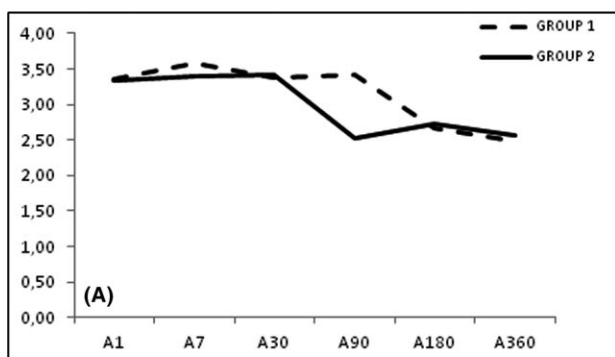
**Discussion**

Our study was designed to compare the outcomes and complications of two different implantation techniques of the hema implant (Esnoper V-2000) in NPDS. Both supraciliary and intrascleral implantation lowered IOP and medication use significantly in comparison with the baseline.

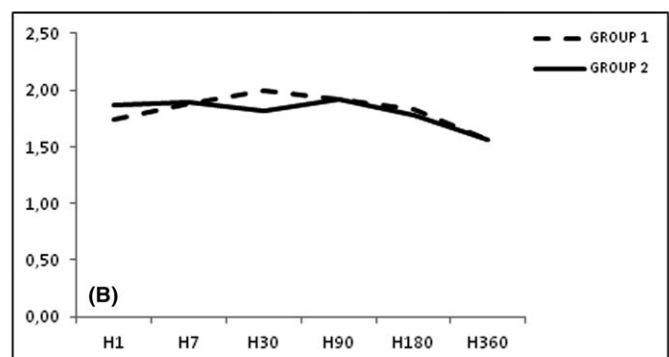
Few publications on the subject have appeared with supraciliary implantation in NPDS (Muñoz 2009; Bonilla et al. 2012; Loscos Arenas et al. 2015a) The reported incidence of complications has been similar to the incidence associated with intrascleral implantation. In addition, other studies have reported the use of uveoscleral implants (Loscos Arenas et al. 2015b), located in both of these potentially advantageous spaces. However, this is the first prospective study comparing the intrascleral and supraciliary implementations in terms of efficacy and safety.

In our study, the IOP reduction obtained in the two groups was statistically significant. However, we could not differentiate between the two groups 1 year after surgery, although a slightly greater hypotensive effect (0.81 mmHg) was observed in the suprachoroidal group 1 year after surgery (14.62 ± 3.64 mmHg) when compared to the first group where the implant was sutured to the scleral bed (15.43 ± 4.27 mmHg).

Even though the observed differences were not statistically significant,



AREA MAX	A1	A7	A30	A90	A180	A360
GROUP 1	3,36	3,58	3,38	3,42	2,67	2,47
GROUP 2	3,33	3,39	3,42	2,51	2,73	2,57
SD GROUP 1	0,87	0,91	0,75	1,18	1,09	1,26
SD GROUP 2	1,08	0,80	1,08	1,35	1,62	1,56
<i>P</i>	0,95	0,68	0,94	0,21	0,94	0,90



HIGH	H1	H7	H30	H90	H180	H360
GROUP 1	1,74	1,88	1,99	1,92	1,83	1,56
GROUP 2	1,86	1,90	1,81	1,92	1,78	1,56
SD GROUP 1	0,52	0,36	0,47	0,32	0,37	0,78
SD GROUP 2	0,51	0,39	0,35	0,36	0,45	0,81
<i>P</i>	0,67	0,92	0,44	0,99	0,83	1,00

**Fig. 5.** (A) Maximal area of the bleb in the groups of the study. (B) Mean height of the bleb in the groups of the study. There were no differences in any of the studied time-points (*p* < 0.05).

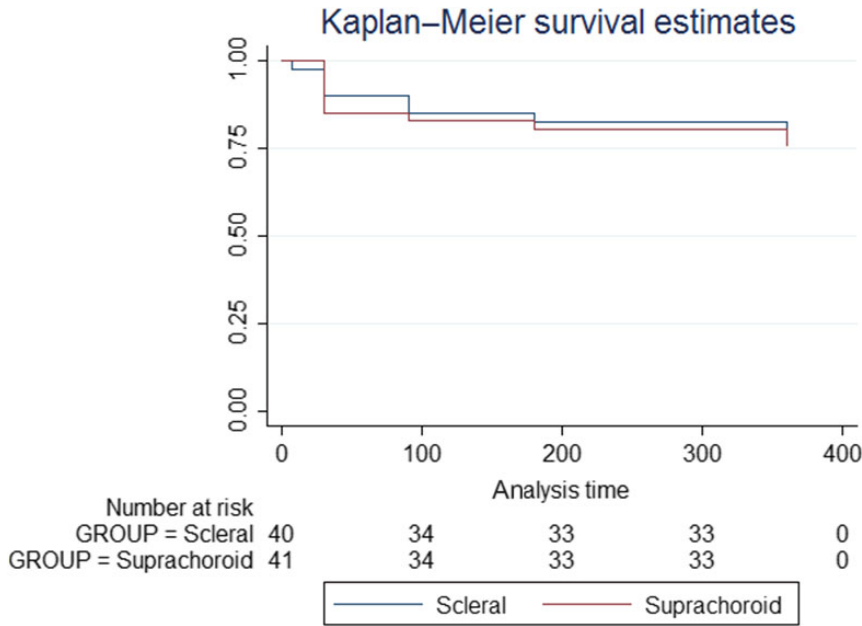


Fig. 6. Kaplan-Meier cumulative probability curve of relative success.

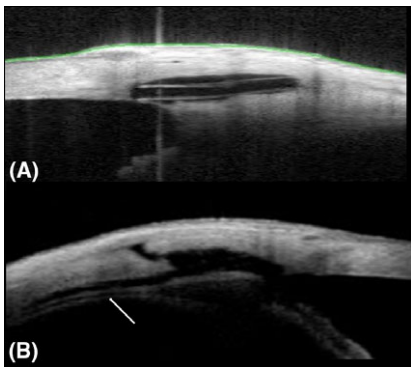


Fig. 7. Anterior segment optical coherence tomography (AS-OCT) scan A: group 1 (Intrascleral): eye with an anterior displacement of the implant over the trabeculodescemet membrane (TDM). No suprachoroidal space is seen. B Group 2 (Supraciliary): eye with no conjunctival bleb with a patent uveoscleral route (suprachoroidal space. arrow).

the supraciliary location might promote a reduction in IOP by an increased uveoscleral flow or by a minimal detachment of the ciliary body with a secondary decrease in the production of AH (Fig. 7). Only two cases of failure amongst the total of 83 patients (4.8%) included in the study were reported both in group 1. The reduction in IOP observed after the surgery was statistically significant during the follow-up period in each group. Similarly, the number of drugs administered before and after the procedure and after 12 months of follow-up

decreased from  $2.58 \pm 0.04$  to  $0.32 \pm 0.76$  in group 1 and from  $2.68 \pm 0.02$  to  $0.24 \pm 0.66$  in group 2. We also included in our study patients unable to correctly instil eye drops or that did not tolerated well the antiglaucoma medication so we analyse our results with a cut-off less than 18 mmHg in both groups. Twenty-five eyes (65%) achieved an IOP <18 mmHg without treatment in group 1 and 26 eyes (62.5%) in group 2 without significant differences in both groups. In agreement with other reports (Muñoz 2009; Bonilla et al. 2012; Loscos Arenas et al. 2015a,b), our study showed that the NPDS using a supraciliary implant was a safe procedure that avoids the need for suturing. There were no intraoperative and the postoperative complications limited to the presence of conjunctival leakage (seidel) in two cases (2.38%, one in each group) and two cases (4.76%) of hyphema both in group 1. Seidel phenomenon is not specific to any technique and hyphema appears in a variable percentage in the different studies published (Muñoz 2009; Loscos Arenas et al. 2015a). The hyphema may appear in any surgery that produces postoperative ocular hypotension, and the incidence could be similar in both techniques favoured by subtle movements of the implant when it is not completely fixed. All complications resolved spontaneously within a week.

Although the characteristics of intrascleral bleb associated with successful pressure treatment have been described (Mavranakas et al. 2010; Cabrejas et al. 2011; Loscos Arenas et al. 2014), the role of the suprachoroidal or uveoscleral path is not well defined and still is considered controversial. The NPDS facilitates pressure reduction by enhancing the drainage of AH via the subconjunctival, intrascleral and suprachoroidal routes (Galassi et al. 2002). There are several physiological differences between the conventional and unconventional paths. In the suprachoroidal pathway, analysed in this study, the AH flows easily through the ciliary body and the iris, due to the lack of an epithelial barrier. From there, the gap in the ciliary muscle directs the AH to an area between the choroid and sclera known as the suprachoroidal space. This space acts as a molecular sieve for the AH entering the scleral vessels or pores to access the episcleral tissue (Pederson et al. 1977; Goel et al. 2010). AH is carried into the orbit by the choroidal and scleral vessels and enters the systemic circulation through the lymph vessels (Nilsson 1997). This uveoscleral route is largely driven by differences between the hydrostatic pressure in the AC and the suprachoroidal space and is independent of the IOP (Alm & Nilsson 2009). A suprachoroidal or an empty supraciliary space, the sign of a clear uveoscleral path, has been described in between 7% and 60% of cases (Mansouri et al. 2010). However, these reports are not comparable because they use different implant series with different time tracking. It is discussed if after surgery, the uveoscleral outflow is more related to a pressure control in the short-to-medium term than to long-term control (Contreras et al. 2006; Sarodia et al. 2007; Mavranakas et al. 2010).

The goniopuncture is critical to the success of the nonpenetrating surgery and gives the results similar to those achieved by trabeculectomy. Trials with a low frequency of goniopuncture have been less successful than those with a high frequency. Mendrinos et al. (2008) suggests that the fibrotic phenomena at the TDM level determine the outcome of surgery from the ninth month onward. Although, goniopuncture is increasingly performed earlier on than in the past, there is no

consensus on when it should be performed. The decision is driven by different criteria including the target IOP, the definition of success, or pre-operative IOP (Vuori 2003; Anand & Pilling 2010). The reported rate of goniopuncture varies, ranging from 4.7% to 63% (Mermoud et al. 1999; Anand & Pilling 2010; Rulli et al. 2013). It is not clear whether the goniopuncture is more effective in the supraciliary procedures than in the intrascleral techniques. In our study (Table 4), we achieved a similar pressure drop in the two groups (6.36 and 6.88 mmHg); the difference between the groups was not statistically significant. While we cannot answer the question whether goniopuncture is as necessary and effective in supraciliary techniques as in the intrascleral implementations, our analysis opens up new avenues for discussion. In group 2, where we had a lower baseline IOP, we obtained a greater pressure reduction. However, in this group, goniopuncture was performed earlier, after 165 days (on average) in comparison with 210 days in group 1. There were 22 goniopunctures performed in group 1 (52.38%) and 15 (36.58%) in group 2. The difference could be explained by the hypothetical tendency in the intrascleral group to an anterior displacement of the implant despite the suture. This anterior movement of the implant could restrict the flow through the TDM, stimulate fibrotic events and limit the effect of goniopuncture (Fig. 7). This is unlikely in the supraciliary implantations because the attachment of ESNOPER V-2000 in these cases is more secure due to its two side-notches, specifically designed for this use (Fig. 2).

We cannot find statistically significant conjunctival bleb differences between the two groups and we cannot answer the question whether the presence of uveoscleral outflow 1 year after NPDS is an alternative when subconjunctival outflow is limited or offers just a plus of IOP decrease. The real benefit of supraciliary surgery is still unknown, so a study with a cut-off <14 mmHg or a morphological analysis of surgical area with anterior segment optical coherence tomography (AS-OCT) should be carried out to clarify this issue.

A limitation of our study was represented by the lack of a control group. By having a third group of patients

undergoing classic DS without the use of the implant, we would have been able to better discriminate between the two types of implantation techniques.

## Conclusions

Nonpenetrating deep sclerectomy using hema implant (Esnoper V-2000) is safe and effective, regardless of the positioning of the implant. Both techniques, achieved statistically significant reductions in IOP and in number of drugs taken during the first year after the surgery but without significant differences. However, a longer follow-up period is needed to study the long-term outcomes in terms of efficacy and safety of the supraciliary versus intrascleral implantation.

## References

- Alm A & Nilsson SF (2009): Uveoscleral outflow: a review. *Exp Eye Res* **88**: 760–768.
- Anand N & Pilling R (2010): NdYAG laser goniopuncture after deep sclerectomy: outcomes. *Acta Ophthalmol* **88**: 110–115.
- Bonilla R, Loscos-Arenas J, Valldeperas X, Parera MA & Sabala A (2012): Supraciliary hema implant in combined deep sclerectomy and phacoemulsification: one year results. *Open Ophthalmol J* **6**: 59–62.
- Cabrejas L, Rebolleda G, Muñoz-Negrete FJ & Losada D (2011): An ultrasound biomicroscopy study of filtering blebs after deep sclerectomy with a new acrylic implant. *Eur J Ophthalmol* **21**: 391–399.
- Contreras I, Noval S, Muñoz-Negrete FJ, Rebolleda G & Garcias-Feijóo J (2006): Ultrasound biomicroscopy in deep sclerectomy with a new acrylic implant. *Arch Soc Esp Oftalmol* **81**: 445–450.
- Fiodorow SN, Kozlow WI & Timoszkina NT (1989): Nonpenetrating deep sclerectomy in open angle glaucoma. *Ophthalmosurgery* **3–4**: 52–55.
- Galassi F, Sodi A, Ucci F, Pieri B & Renieri G (2002): Deep sclerectomy in primary open-angle glaucoma: comparison among different implants. *Acta Ophthalmol Scand Suppl* **236**: 63–64.
- Goel M, Picciani RG, Lee RK & Bhattacharya SK (2010): Aqueous humor dynamics: a review. *Open Ophthalmol J* **4**: 52–59.
- Loscos Arenas J, Valldeperas X, Parera A, Langhor K, De la Cámara J, Domingo M, Castellvi J & Sabala A (2014): An ultrasound biomicroscopy study after deep sclerectomy with supraciliary implant. *Arch Soc Esp Oftalmol* **89**: 439–446.
- Loscos Arenas J, Valldeperas X, Langhor K, Parera A, Romera P, Sabala A & De la Cámara J (2015a): Deep sclerectomy with supraciliary hema implant (Esnoper V-2000): results and complications. *Int Ophthalmol* **35**: 693–699.
- Loscos Arenas J, Parera-Arranz A, Romera-Romera P, Castellvi-Manent J, Sabala-Llopart A & de la Cámara-Hermoso J (2015b): Deep sclerectomy with a new nonabsorbable uveoscleral implant (Esnoper-Clip): 1-year outcomes. *J Glaucoma* **24**: 421–425.
- Mansouri K, Tran HV, Ravinet E & Mermoud A (2010): Comparing deep sclerectomy with collagen implant to the new method of very deep sclerectomy with collagen implant: a single-masked randomized controlled trial. *J Glaucoma* **19**: 24–30.
- Mavrakanas N, Mendrinos E & Shaarawy T (2010): Postoperative IOP is related to intrascleral bleb height in eyes with clinically flat blebs following deep sclerectomy with collagen implant and mitomycin. *Br J Ophthalmol* **94**: 410–413.
- Mendrinos E, Mermoud A & Shaarawy T (2008): Nonpenetrating glaucoma surgery. *Surv Ophthalmol* **53**: 592–630.
- Mermoud A, Karlen ME, Schnyder CC, Sickenberg M, Chiou AG & Hédiguer SE (1999): Nd:Yag goniopuncture after deep sclerectomy with collagen implant. *Ophthalmic Surg Lasers* **30**: 120–125.
- Muñoz G (2009): Nonstitch suprachoroidal technique for T-flux<sup>®</sup> implantation in deep sclerectomy. *J Glaucoma* **18**: 262–264.
- Nilsson SF (1997): The uveoscleral outflow routes. *Eye (Lond)* **11**: 149–154.
- Pederson JE, Gaasterland DE & MacLellan HM (1977): Uveoscleral aqueous outflow in the rhesus monkey: importance of uveal reabsorption. *Invest Ophthalmol Vis Sci* **16**: 1008–1017.
- Prum BE, Herndon LW, Moroi SE et al. (2015): Primary angle closure preferred practice pattern guidelines. *Ophthalmology* **123**: 1–40.
- Rulli E, Biagioli E, Riva I, Gambirasio G, De Simone I, Florian I & Quaranta L (2013): Efficacy and safety of trabeculectomy vs non penetrating surgical procedures: a systematic review and meta-analysis. *JAMA Ophthalmol* **131**: 1573–1582.
- Sarodia U, Shaarawy T & Barton K (2007): Non penetrating glaucoma surgery: a critical evaluation. *Curr Opin Ophthalmol* **18**: 152–158.
- Vuori ML (2003): Complications of neodymium: YAG laser goniopuncture after deep sclerectomy. *Acta Ophthalmol Scand* **81**: 573–576.
- Wells AP, Ashraff NN, Hall RC & Purdie G (2006): Comparison of two clinical Bleb grading systems. *Ophthalmology* **113**: 77–83.

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