EXPERT REVIEWS

Nonpenetrating deep sclerectomy

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With the introduction of nonpenetrating deep sclerectomy (NPDS), the safety profile of filtering surgery has dramatically improved owing to the extraocular nature of the procedure that addresses abnormally increased aqueous outflow resistance in Schlemm's canal and the juxtacanalicular trabecular meshwork without entering the anterior chamber. The use of space-maintaining devices, antimetabolites and neodymium:YAG laser goniopuncture as adjuvant tools in NPDS has improved the long-term results, so that they are comparable with those of trabeculectomy. Therefore, NPDS has become the procedure of choice in the last few years for primary open-angle glaucoma, as well as some other forms of secondary open-angle glaucoma with surgeons who have mastered the procedure. NPDS involves removal of 4 × 4-mm deep scleral flap to deroof Schlemm's canal and expose Descemet's membrane, forming a decompression space or scleral lake. Aqueous humor reaches the scleral lake via the newly created trabeculo-Descemet's membrane to be drained through different routes. The relatively long surgical learning curve remains the main disadvantage of NPDS. In this article, surgical technique, mechanism and routes of filtration, indications, contraindications, complications and results of NPDS will be discussed.

Keywords: goniopuncture • implant • nonpenetrating deep sclerectomy • nonpenetrating glaucoma surgery • trabeculo-Descemet's membrane

The goal of glaucoma filtration surgery is to reduce elevated intraocular pressure (IOP) in order to preserve residual viable elements of the optic nerve head. Trabeculectomy has been the 'gold-standard' filtration procedure for the last 40 years. In trabeculectomy, a full-thickness sclerostomy is created under a partial scleral flap. The aim of the scleral flap is to overcome the vast majority of complications associated with full-thickness filtration procedures by controlling the passage of aqueous from the anterior chamber (AC). This control mainly depends on the tightness of the scleral flap closure. However, frequent and serious intraoperative, and early and late postoperative complications continue to occur, such as hyphema, cataract, vitreous loss, corneal endothelial cell loss, intraocular inflammation, suprachoroidal hemorrhage and bleb-related infections and overfiltration with its complications, including shallow or flat AC, hypotony, choroidal detachment and hypotony maculopathy [1–15].

Nonpenetrating glaucoma surgery aims to overcome most of the complications that are usually associated with full-thickness filtration surgery. It was first described by Epstein [16] and Krasnov [17] in the late 1950s and 1960s, respectively. They suggested deroofing Schlemm's canal (SC) as a means to lower IOP. The popularity of this procedure was limited since its effect is only short term, owing to conjunctival scarring over the bare trabeculum. In addition, the trabeculectomy technique, introduced by Sugar in 1959 [18] and Cairns in 1968 [19], was easier to perform and had much longer longevity. Modifications of nonpenetrating glaucoma surgery in the early 1980s by Fyodorov *et al.* (deep sclerectomy [DS]) [20] and Zimmerman *et al.* (nonpenetrating trabeculectomy [NPT], in which a portion of the SC is excised under a superficial scleral flap) [21] has brought nonpenetrating glaucoma surgery back to the picture.

Today, most of the performed nonpenetrating DS (NPDS) procedures combine the original DS and NPT, in which the floor of the SC and the juxtacanalicular meshwork are removed at the surgical site.

Kozlov *et al.* in 1990 were the first to introduce a space-maintaining device in DS, using a highly purified collagen implant, and this was then followed by different, absorbable and non-absorbable, expensive and low-cost implants [22]. Multiple studies have demonstrated the long-term beneficial effect of these devices on IOP reduction [23–33]; however, other studies failed to reveal such a benefit [34–36].

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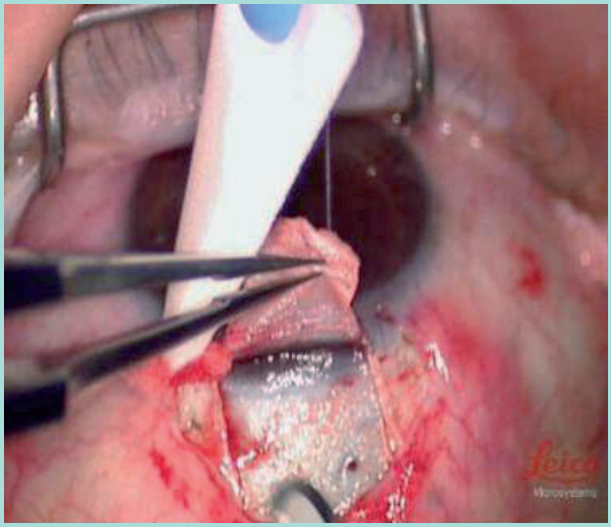

Figure 1. The superficial flap is dissected and advanced 1–1.5 mm into clear cornea.

Nonpenetrating deep sclerectomy

Techniques

Fixation suture (traction suture)

A 4-0 silk suture to the superior rectus muscle or a 6-0 vicryl suture to the superior cornea may be preferable to avoid hemorrhage from the superior rectus and possible postoperative ptosis.

Conjunctival & superficial scleral flaps

Either a limbus- or fornix-based conjunctival flap is created in the superonasal or superotemporal quadrant, with relaxing incisions to expose enough sclera. A 5 × 5-mm (a third-to-half scleral-thickness), superficial scleral flap is outlined with a sharp knife (e.g., super-sharp blade number 75 or equivalent). Dissection of the flap is carried out as in trabeculectomy, extending 1–1.5 mm anterior to the limbus in order to be able to reach the Descemet's membrane, later in the dissection of the deep scleral flap (Figure 1).

A sponge soaked in 0.2 mg/ml mitomycin C (MMC) solution may be placed for 1–3 min under the superficial scleral flap and the Tenon's capsule. A thorough irrigation with 20 cm^3 of balanced salt solution is performed to wash the surgical site.

Deep scleral flap & exposure of the trabeculo–Descemet's membrane

A 4 × 4-mm deep scleral flap is outlined with a small diamond knife (Figure 2), leaving a step of sclera on the lateral and posterior border of the floor of the superficial flap to ensure tight superficial scleral flap closure in case of perforation and conversion to trabeculectomy. Dissection of the deep flap should only leave a very thin layer (50–70 µm) of the scleral tissue over the uvea using a ruby knife or an equivalent. Dissection is carried out from the posterior part of the flap. The scleral spur is a very important anatomical landmark, in which the scleral fibers take a circumferential orientation. SC, which is just anterior to the scleral spur, is then unroofed and percolation of aqueous humor starts in most cases. Exposure of the trabeculum and Descemet's membrane (trabeculo–Descemet's membrane [TDM]) is the most difficult part of the procedure and carries the risk of perforation. Therefore, the exposure is carefully performed by cutting two radial corneal incisions with a fine diamond knife or equivalent, bevel up. The trabeculum and Descemet's membrane will detach from the corneal stroma spontaneously (Figure 3), and fine attachments can be broken with wet sponge. The floor of SC and the juxtacanalicular trabecular meshwork (TM) is then peeled off in one layer with a fine-toothed forceps (Figure 4). More percolation of aqueous is obvious at this point.

A deep scleral flap is excised with a fine diamond knife and vannas scissors with caution, since this step carries a high risk for perforation (Figure 5). An implant may be used at this point (Figure 6). A superficial flap is then secured with 10-0 nylon sutures at the posterior corners (Figure 7) and the conjunctival flap is closed in a watertight fashion.

Adjuvant tools in NPDS

Implants

Animal-, synthetic- and chemical-based devices have been used to reduce scar formation and to keep the decompression space (floor of the deep flap or scleral lake) open in order to enhance filtration from the scleral lake. Koslov *et al.* were the first to use a collagen implant, a highly purified porcine collagen dehydrated into a cylinder measuring 2.5 × 1.0 × 0.5 mm, which was secured to the anterior part of the bed of the decompression space with a single 10-0 nylon suture [22]. The superficial scleral flap was then secured in place with 10-0 nylon sutures at the posterior corners. The device swells by absorbing aqueous humor to fill most of the decompression space and is absorbed within 6–9 months after surgery [37].

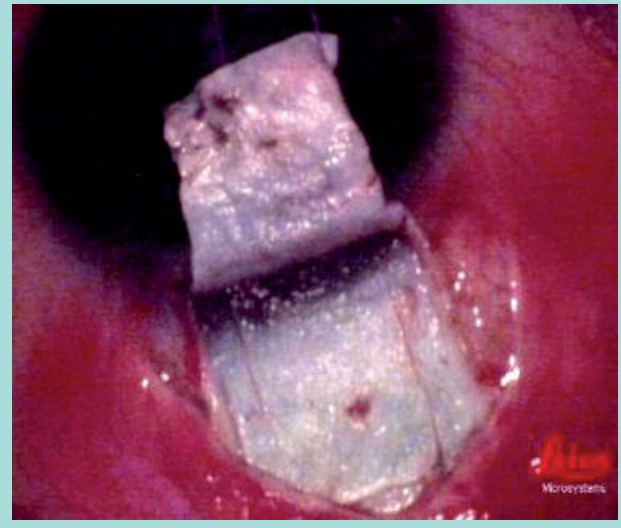

Figure 2. The deep scleral flap is outlined, leaving a step of sclera on the two lateral and posterior borders of the floor of the superficial flap.

The reticulated hyaluronic acid implant (SKGEL™, Corneal, Paris, France), an equilateral triangle of two sizes (3.5 mm long, 0.55 mm thickness and 4.5 × 3 mm with thickness of 0.5 mm) made from a biocompatible material composed of crosslinked sodium hyaluronate derived from a biosynthetic process (bacterial fermentation of a natural wild strain of *Streptococcus equi*) and hydrated in phosphate buffer solution, is another space-maintaining device that is placed in the bed of the excised deep scleral flap and secured by repositioning the superficial flap over it with 10-0 nylon sutures. In rabbit eyes, the device undergoes slow bioabsorption, and the intrascleral space was still visible after 2 months [38]. In a clinical study of NPDS with the SK-GEL implant, the intrascleral space remained visible for 3 months but completely disappeared after 1 year in 7% of 30 cases [39].

More recently, a nonabsorbable hydrophilic acrylic implant (T-flux® implant, IOL Tech Laboratories, La Rochelle, France) has been developed [40,41]. It is a T-shaped implant with a body height of 2.75 mm and a thickness of 0.1–0.3 mm. The arms should occupy the cut ends of SC, and the body of the implant is fixed with a single 10-0 nylon through the foot hole of the implant, which is anchored to the bed of the decompression space. It is designed to provide active drainage by means of capillarity and osmosis.

Absorbable and nonabsorbable space-maintaining devices continue to be developed, such as a new low-cost, nonabsorbable acrylic implant made of 2-hydroxyethylmethacrylate that has been demonstrated to be safe and efficient and may replace collagen implants [42]. Another cross-shaped, rigid, nonabsorbable polymethylmethacrylate implant has also been developed recently [43]. Other low-cost implants, such as autologous sclera [44,45], catgut suture material [46,47] and amniotic membrane, have been tried as implants [48].

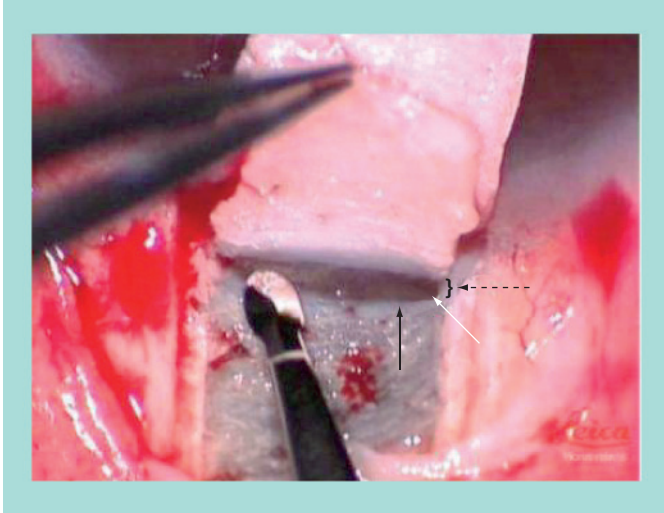

Figure 3. Dissection of the deep sclera flap, leaving a very thin scleral layer on the uveal tissue. Creation of the trabeculo–Descemet's membrane (dotted arrow); solid arrow indicates scleral spur; white arrow indicates Schlemm's canal just anterior to the scleral spur.

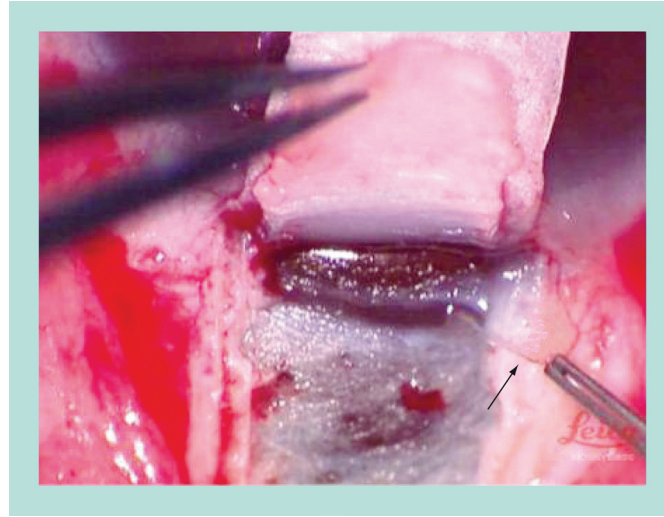

Figure 4. Peeling of the floor of the Schlemm's canal with fine-toothed forceps.

Antimetabolites: mitomycin C & 5-fluorouracil as antifibrotic agents

Although NPDS was first described without the use of antifibrotic agents to moderate wound healing, their beneficial effect has improved penetrating glaucoma surgery outcome [49–52]. Their use in NPDS surgery continues to be controversial. A prospective, randomized study performed by Kozobolis *et al.* included 90 eyes with primary open-angle glaucoma or pseudoexfoliative open-angle glaucoma [53]. Eyes were randomly assigned to undergo DS alone or DS with 0.2 mg/ml MMC for 2.5 min prior to superficial scleral flap dissection. Complete success rate (defined as IOP ≤ 21 mmHg without medications) was 42.5% in the DS group and 50% in the DS plus MMC group. Total success rate (defined as IOP ≤ 21 mmHg with or without medication) was 72.5% in DS and 95% in DS plus MMC. The complication rate was similar in both groups and the authors concluded that the use of MMC during DS significantly reduced the postoperative IOP and increased the success rate of the procedure. Anand *et al.* retrospectively studied 71 eyes that were at high risk for postoperative scarring in 71 patients who underwent DS using SK-GEL without MMC (52 eyes) or with 0.2 mg/ml MMC for 2 min (19 eyes) [54]. Eyes that received MMC had significantly lower IOP and were less likely to require goniopuncture but also had a higher incidence of avascularized bleb and transconjunctival oozing. Other prospective and retrospective studies have also reported the beneficial effect of antifibrotic agents on the final outcome of surgery [55–57].

Other studies did not show a statistically significant difference in the final outcome of NPDS with and without antifibrotic agents. Detry-Morel retrospectively analyzed the safety and efficacy of DS with SK-GEL implant (DS plus SK-GEL group) versus DS plus SK-GEL and 5-fluorouracil versus DS plus 5-fluorouracil only [58]. Their results did not show a beneficial effect of 5-fluorouracil on the final outcome. Guedes and Guedes retrospectively studied 104 patients, of whom

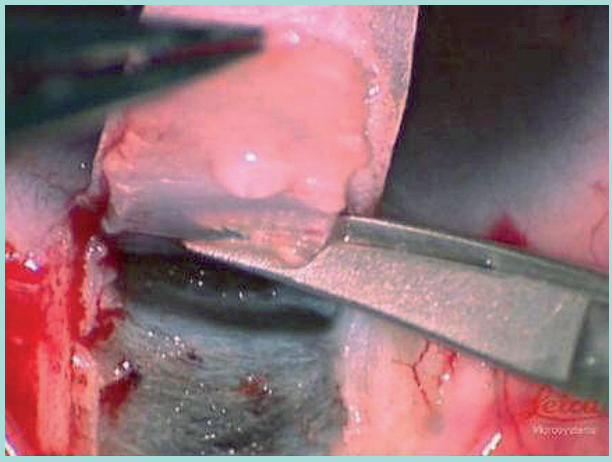

Figure 5. Excision of the deep scleral flap using a fine diamond knife and fine vannas scissor.

80 received MMC [59]. Complete success (IOP < 18 mmHg without medications) and qualified success (IOP < 18 mmHg with and without medications) rates at 19 months were 82.5 and 93.8%, respectively, in the MMC group, and 83.3 and 91.7%, respectively, in the group without MMC. Mielke *et al.* reported a randomized prospective trial in which 18 patients underwent DS with MMC and 21 patients were a control group without MMC [60]. IOP levels of lower than 18 mmHg without medications was achieved in 24 and 13% at 18 months for the control and DS MMC groups, respectively. Use of MMC was not associated with better IOP control.

Neodymium:YAG laser goniopuncture

The most common cause of IOP elevation in the midterm course of NPDS is insufficient passage of aqueous humor through the TDM, either due to fibrosis, as part of the healing process at the TDM [61,62], or due to excessive deposition of debris and/or pigment (Figure 8). Goniopuncture is effective when underfiltration is due to poor function of the TDM and not due to other causes, such as poor dissection plane, excessive bleb fibrosis or other more serious causes. Using the gonioscopy contact lens, the aiming beam is precisely focused just anterior to the slightly pigmented part of the TDM. Using the free-running Q-switched mode with energy adjusted to 3–4 mJ, a few shots are usually enough to induce microperforation in the TDM. A thin TDM is essential for a successful goniopuncture [61] and efficient IOP reduction. The procedure is quite simple and noninvasive, similar to neodymium:YAG laser posterior capsulotomy. Topical 1% prednisolone acetate eye drops for few days is sufficient to quiet the eye in most cases. However, more frequent and longer duration of treatment with prednisolone acetate eye drops is recommended in uveitic glaucoma (from personal experience). Goniopuncture converts the procedure from being nonpenetrating to penetrating, but with far fewer and less serious complications compared with classic penetrating glaucoma surgery.

Hamel *et al.* performed neodymium:YAG laser goniopuncture in 71.4% of their total number of patients [61]. The mean time between surgery and goniopuncture was 24.8 ± 21.4 months. The mean IOP was 20.3 ± 3.5 mmHg prior to goniopuncture and 11.8 ± 7.0 mmHg after ($p < 0.001$). Mermoud *et al.* performed goniopuncture in 23% of of their total number of studied eyes, after a mean time between surgery and goniopuncture of 9.1 ± 6.0 months [62]. IOP was 21.0 ± 2.1 and 12.0 ±4.2 mmHg prior to and after goniopuncture, respectively. Their success rate of goniopuncture was 80%. Bissing *et al.* performed goniopuncture in a total of 61 patients, with the time between surgery and goniopuncture ranging from 1 to 119 months (median: 20 months) [63]. The mean reduction of IOP was 39.45%; others reported similar results [35,64].

In his study, Al Obeidan performed goniopuncture in 48% of the eyes with uveitic glaucoma that were included in the investigation [65]. Mean pre- and post-goniopuncture IOPs were 26 and 15.45 mmHg, respectively. The mean time between surgery and goniopuncture was 8.95 months, with a success rate of 55%. In another study [Al Obeidan S *et al.*, Unpublished Data] of 102 eyes with open-angle glaucoma that underwent DS and implant plus MMC, goniopuncture was performed in 21 (20.5%) eyes. Mean pre- and post-goniopuncture IOP was 35.28 and 15.09 mmHg, respectively, and the success rate was 61.9% (13 eyes). The mean time between surgery and goniopuncture was 6 months.

Goniopuncture is a simple, noninvasive and safe, but not totally complication-free, procedure. Iris prolapse [66,67], iris incarceration [66,68] and synechiae formation [67] are the most common complications following goniopuncture. Transient elevation of IOP is frequently associated with these complications. Pilocarpine and laser (argon and/or YAG) manipulation of the iris may help to reduce the incarcerated iris and release synechiae. However, exploration of the filtration site may be necessary in some cases.

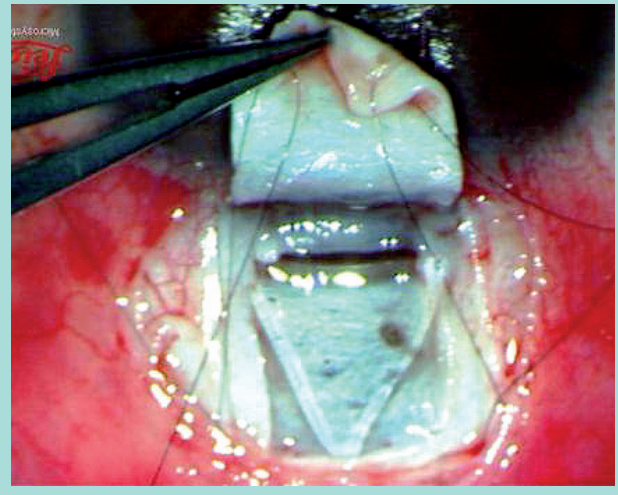

Figure 6. SK-GEL™ placed in the floor of the deep flap.

Choroidal detachment is another possible complication of goniopuncture. Mermoud *et al.* reported a 5% incidence rate of choroidal detachment in 41 patients who underwent goniopuncture [68]. Furthermore, severe hypotony and hypotonous maculopathy are possible complications after goniopuncture, especially when it is performed in the early postoperative course in the setting of highly elevated IOP. Our experience consists of two patients. In the first patient, goniopuncture was performed a few days after DS with T-flux for uveitic glaucoma at an IOP of 42 mmHg. With one shot of neodymium:YAG laser, at an energy level of 3 mJ, to the TDM, the whole membrane opened, a very large bleb formed with choroidal effusion, and IOP dropped to a low, single-digit reading. The choroidal detachment resolved within 2 weeks, and IOP stabilized in the low teens without medications. In the second patient, goniopuncture was performed 2 weeks after DS with SK-GEL implant for angle recession glaucoma at an IOP of 35 mmHg. Severe hypotony with maculopathy and poor visual acuity persisted for several months. The patient underwent intrableb autologous blood injection twice, after which the IOP increased to 12 mmHg without medications and visual acuity improved to pregoniopuncture levels. From these two cases, we have learned that goniopuncture can be a serious procedure, and precautions should be taken regarding timing (i.e., avoiding early goniopuncture) and IOP (i.e., lowering highly elevated IOP with medications prior to goniopuncture).

NPDS: how does it work?

Nearly 70–80% of aqueous humor drainage takes place through conventional outflow pathways, passing from the TM to SC and then, from collector channels, to the episcleral venous plexus. Most of the remaining outflow occurs via the uveoscleral pathway [69]. Aqueous outflow resistance is mainly located in the TM, with approximately 75% of this resistance in normal eyes and all abnormal glaucomatous resistance residing in the juxtacanalicular TM and inner wall of SC, as demonstrated by Grant [69]. Hamard *et al.* [70] and others [71,72] showed, by confocal microscopic examination of TM that was removed during *ab externo* trabeculectomy, that corneoscleral trabecular layers of TM also share the aqueous outflow resistance in glaucomatous eyes. NPDS surgery is designed to address this area of aqueous outflow resistance by deroofing SC and peeling its floor with juxtacanalicular TM and part of corneoscleral layers of TM [72]. Therefore, aqueous humor drainage may occur at the level of the posterior trabeculum through the remaining corneoscleral and intact uveal part of the TM (TDM) to reach the bed of the excised deep scleral flap, forming a scleral lake [21,62,73,74].

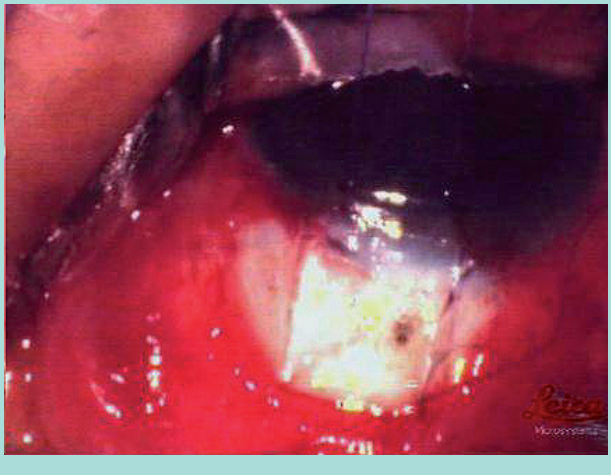

Figure 7. Superficial scleral flap is repositioned with 10-0 nylon sutures at the posterior corners.

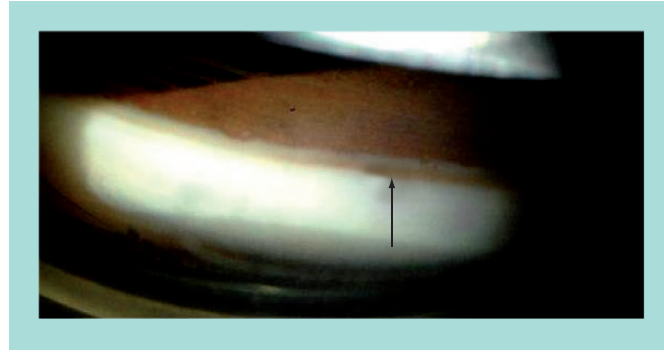

Figure 8. Gonioscopic view of the trabeculo–Descemet's membrane with clear deposition of pigments and debris indicating the area of filtration (arrow).

Drainage routes from the scleral lake

The aqueous reaches the subconjunctival space as demonstrated by the presence of a filtering bleb in almost all successful cases. The filtering bleb in most cases of NPDS is more diffuse and less ischemic compared with blebs after trabeculectomy with antifibrotic agents, which may explain the lower incidence rate of bleb-related problems [53,75,76].

A second possible route is that the aqueous humor may reach the suprachoroidal space through the thin scleral wall in the decompression space [37,39,77–79].

A third possible route is a transcleral pathway, as demonstrated by ultrasound biomicroscopy. Hyporeflectivity of scleral tissues around the scleral lake is present in 50% of cases [39,80,81], indicating possible trans-scleral drainage.

Finally, aqueous humor enters SC from the scleral lake through the cut ends, to be drained by collector channels to the episcleral venous plexus [82,83].

Indications & results of NPDS

Traditional teaching in glaucoma considers surgical intervention to be appropriate when medical and laser therapies fail to control disease progression [84]. Unfortunately, glaucoma may progress to an advanced stage before a standard filtration surgery is undertaken. This concept was propagated because of the relatively high complication rate and relatively unpredictable results associated with filtration surgery [1–7]. Two long-term studies by Migdal *et al.* [85], and Jay and Murray [86], showing

Table 1. Results of nonpenetrating deep sclerectomy versus trabeculectomy in primary and secondary open-angle glaucoma.

Study (year)	Design	Eyes (n)	Procedure	Mean follow-up (months)	Mean IOP (mmHg)		Definition of success (IOP in mmHg)	Success (%)		Mean medications (n)		Ref.
					Preop.	*Postop.*		*Complete*	*Qualified*	*Preop.*	*Postop.*	
Mermoud *et al.* (1999)	PS	44	DS and CI	14.4 ± 6.3	26.7 ± 7.3	13.8 ± 3.7	≤21	69	95	2.2 ± 0.8		[62]
	RS	44	Trab	16.3 ± 8.8	25.4 ± 7.3	11.9 ± 4.4		57	95	2.4 ± 0.8		
El Sayyad *et al.* (2000)	PS	39	DS	12	27.9 ± 5.9	15.6 ± 4.2	≤21	79	92.3	2.4 ± 0.7	0.30 ± 0.4	[64]
		39	Trab	12	28.2 ± 4.7	14.1 ± 4.6		85	94.7	2.6 ± 0.6	0.27 ± 0.5	
Chiselita (2001)	PS	17	DS	18	27.70 ± 22.22	NA	≤21	44.57	NA	NA	NA	[94]
		17	Trab	18	27.29 ± 2.08	NA		42.59	NA	NA	NA	
Ambresin *et al.* (2002)	PS	20	DS and CI	24.3 ± 19.1	22.9	13.9	≤21	40	90	2.5 ± 0.8	1.0 ± 1.0	[96]
	RS	20	Trab	24.3 ± 10.9	29.3	12.9		45	90	1.8 ± 1.1	1.2 ± 1.1	

CI: Collagen implant; DS: Deep sclerectomy; IOP: Intraocular pressure; NA: Not available; Preop.: Preoperative; Postop.: Postoperative; PS: Prospective; RS: Retrospective; Trab: Trabeculectomy.

the benefit of early surgical intervention in the preservation of visual functions and have changed this concept dramatically. In my opinion, NPDS, with its low complication rate [21,23,27,28,62,77,83,87], can be offered as a first-line treatment for a variety of reasons:

- If medical and/or laser therapy treatment may be insufficient to control the disease or when long-term compliance with medical therapy is expected to be poor, such as in young patients;
- The success rate of surgical intervention may be better in eyes not subjected to long periods of topical antiglaucoma treatment, which can change the conjunctival cell profile, thereby increasing scarring and intraoperative bleeding [88,89];
- Successful surgery has been shown to blunt IOP fluctuations, which are a risk factor for glaucoma progression [90–92];
- With early surgical intervention, the target IOP may not necessarily be as low as the level needed in advanced cases.

In NPDS, SC and the adjacent part of the TM (juxtacanalicular TM) are removed. For this reason, NPDS surgery may be indicated in all types of glaucoma with an open angle, in which the resistance to aqueous outflow is presumed to be located at or distal to the juxtacanalicular TM and the SC.

Primary open-angle glaucoma

The site of pathology in primary open-angle glaucoma is believed to be largely in the juxtacanalicular TM and inner wall of SC [69–72]. Removing these structures during NPDS without entering the AC has two main advantages: first, decreasing the aqueous outflow resistance by reshaping the outflow channels; and second, avoidance of a sudden drop of IOP with its potentially serious intraoperative and postoperative complications. Furthermore, the gradual reduction of aqueous outflow resistance is not governed by the surgical technique of scleral flap closure but by a natural barrier at Descemet's membrane and the TDM. With NPDS being an extraocular procedure, the aqueous humor dynamics are insignificantly altered, yielding the advantages of significantly reduced inflammation, which is an extremely important factor in the final outcome, especially in uveitic and pseudoexfoliative glaucoma [93,94], and decreased chance of developing aqueous misdirection, as well as conditions simulating aqueous misdirection (e.g., ciliochoroidal and choroidal detachment), in which changes in AC depth during full-thickness trabeculectomy are believed to be a risk factor. The efficacy and excellent safety profile of NPDS in open-angle glaucoma are well documented by several studies [62,63,65,95,96]. Table 1 shows the outcome of NPDS compared with standard trabeculectomy. Table 2 details the additional beneficial effect of adjuvant tools (i.e., implant, antimetabolites and goniopuncture) on the final outcome.

Pseudoexfoliation & pigmentary glaucoma

The mechanism of increased aqueous outflow resistance in these conditions is due to deposition of abnormal exfoliative material and pigment, leading to decompensation of the TM and

Table 2. Results of nonpenetrating deep sclerectomy in primary and secondary open-angle glaucoma with and without adjuvants.

Study (year)	Design	Eyes (n)	Procedure	Mean follow-up (months)	Mean IOP (mmHg)		Definition of success (IOP in mmHg)	Success (%)		Mean medications (n)		Ref.
					Preop.	*Postop.*		*Complete*	*Qualified*	*Preop.*	*Postop.*	
Kozobolis *et al.* (2002)	PS	40 40	DS DS and MMC	36	25.84 ± 3.60 27.64 ± 4.53	18.71 ± 2.90 15.96 ± 1.7	≤21	42.5 50	72.5 95	3.18 ± 0.81 3.02 ± 0.62	0.96 ± 0.96 0.64 ± 0.73	[53]
Shaarawy *et al.* (2004)	RS	52 52	DS DS and implant	44.5 ± 21 43.9 ± 14	23.3 ± 72 25.6 ± 49	14 12.7	≤21	34.6 63.4	78.8 94	2.1 ± 0.8 2.2 ± 0.7	1.00 ± 1.00 0.4 ± 0.6	[24]
Shaarawy *et al.* (2004)	PS	105	DS and implant	43.2 ± 14.3	26.8 ± 7.7	12.24 ± 4.6	<21	57	91	2.3 ± 0.7	0.5 ± 0.7	[29]
Ravinet *et al.* (2004)	PS	11 11	DS and Healon GV® DS and implant	24	23.5 ± 8.3 28.1 ± 14.4	12.2 ± 8.3 13.2 ± 3.0	≤21	95.4 100	100 100	2.2 ± 1.0 2.5 ± 0.9	0.2 ± 0.4 0.4 ± 0.7	[41]
Neudorfer *et al.* (2004)	PS	13 13	DS and CI DS and CI plus MMC	24	26.5 ± 2.5 31.5 ± 5.7	17.8 ± 2.8 15.8 ± 5.6	NA	NA NA	NA NA	2.9 ± 0.6 3.7 ± 0.6	1.8 ± 0.9 2.00 ± 1.5	[55]
Wevill *et al.* (2005)	PS	16	DS and CI	37.1 ± 9	25.9 ± 4.1	16.6 ± 2.1	<21	77	100	NA	NA	[47]
Devloo *et al.* (2005)	RS	69 24	DS DS and SC	16 15	23.8 ± 5.82 25.6 ± 7.31	16.1 ± 5.05 15.8 ± 6.21	21	41 54	83 75	1.78 ± 0.62 1.85 ± 0.87	0.75 ± 0.81 0.50 ± 0.66	[44]
Shaarawy *et al.* (2005)	PS	13 13	DS DS and implant	49 ± 20 56.5 ± 14	24.1 ± 7 25.3 ± 6	16 ± 3 10 ± 4	≤21	38 69	69 100	2.4 ± 0.8 2.2 ± 0.7	1.1 ± 1.00 2.4 ± 0.6	[25]
Mielke *et al.* (2006)	PS	21 18	DS DS and MMC	18.3 14.3	29.5 ± 8.0 26.4 ± 5.88	NA NA	18	24 13	35 38	1.47 ± 1.12 2.05 ± 0.64	NA NA	[60]
Jungkim *et al.* (2006)		32	DS and implant	12	32.88 ± 5.7	15.44 ± 1.6	<21	75	93.75	2.75 ± 0.61	0.11 ± 0.32	[33]
Mansouri *et al.* (2006)	PS	27 26	DS and CI DS and PMMA	15.1 ± 7.7 20.4 ± 12.4	21.0 ± 5.4 21.4 ± 7.1	13.9 ± 3.3 13.00 ± 3.5	<21	44 42	96.3 100	2.4 ± 1.1 2.4 ± 1.00	0.7 ± 0.8 0.6 ± 0.6	[43]
Khairy *et al.* (2006)	PS	43	DS	28.1 ± 8.2	24.6 ± 5.5	18.5 ± 4.6	<22	18.9	NA	NA	NA	[76]
Mousa (2007)	PS	20	DS and SC	12	33.1 ± 6.2	14.6 ± 3.8	<18	50	85	NA	NA	[45]
Bissig *et al.* (2008)	PS	105	DS and CI	101.5 ± 43.1	26.8 ± 7.7	12.2 ± 4.7	≤21	47.7	89	2.3 ± 0.7	1.3 ± 1.1	[63]
Al Obeidan *et al.* (2009)‡	PS	102	DS and implant (TF53, SK-GEL 45 no implant 4)	35.5 ± 23.9	27.3 ± 9.8	13.2 ± 4.3	≤21	85.2	96.1	2.87 ± 0.88	0.24 ± 0.65	

*Intraocular pressure in mmHg.
‡Unpublished data.
CI: Collagen implant; DS: Deep sclerectomy; IOP: Intraocular pressure; MMC: Mitomycin C; NA: Not available; PMMA: Polymethylmethacrylate; Preop.: Preoperative; Postop.: Postoperative; PS: Prospective; RS: Retrospective; SC: Autologous sclera.

Table 3. Efficacy of nonpenetrating deep sclerectomy in uveitic glaucoma.

Study (year)	Design	Eyes (n)	Procedure	Mean follow-up (months)	Mean IOP (mmHg)		Definition of success (IOP in mmHg)	Success (%)		Mean medications (n)		Ref.
					Preop.	*Postop.*		*Complete*	*Qualified*	*Preop.*	*Postop.*	
Auer *et al.* (2004)	RS	14	DS and implant* plus MMC*	12	42.8 ± 13.6	12.1 ± 4.0	<21	45	90.8	3.7 ± 0.5	1.2 ± 0.8	[109]
Souisi *et al.* (2006)	RS	8	DS	42.2	32.3	15.2	NA	50	87.5	2.9	0.6	[108]
Arruabarrena (2007)	RS	6	DS and implant	12	39.67 ± 14.06	16.67 ± 3.26	<21	66.67	100	2.67 ± 0.52	0.50 ± 0.84	[110]
Al Obeidan *et al.* (2008)	PS	13	DSand implant plus MMC	21	28.7	13.85	<21	84.6	92.3	3.07	0.2	[111]
Al Obeidan (2008)	PS	23	DS and implant plus MMC	24	35.04 ± 7.5	13.65 ± 4.15	<21	78.2	95.6	3.22 ± 52	0.30 ± 64	[65]

*Not in all cases.
DS: Deep sclerectomy; IOP: Intraocular pressure; MMC: Mitomycin C; Preop.: Preoperative; Postop.: Postoperative; PS: Prospective; RS: Retrospective.

elevation of IOP [69,72]. Early surgical intervention is encouraged in pseudoexfoliative glaucoma, because it is an aggressive disease with a reduced response to medical therapy and a higher degree of IOP fluctuation [93,94] and visual field loss [94,97].

Aphakic/pseudophakic glaucoma

Trabeculectomy outcome in patients with medically uncontrolled aphakic or pseudophakic glaucoma is guarded compared with phakic open-angle glaucoma [98,99] because of conjunctival scarring by previous surgery, since vitreous may occlude the internal ostium in aphakic and pseudophakic eyes that had posterior capsulotomy, and because of a higher incidence of hypotony and choroidal detachment postoperatively. NPDS is an extraocular procedure that addresses the pathological site in open-angle glaucoma and, therefore, has a better chance of success with fewer serious operative and postoperative complications. The author's experience consists of two eyes with pseudophakic uveitic open-angle glaucoma and two with aphakic open-angle glaucoma that underwent NPDS with implant, either T-flux or SK-GEL. After a mean follow-up of 24 months, all patients achieved an IOP of lower than 18 mmHg, three without medical treatment and the fourth with three topical medications. The most impactful complication was persistent hypotonous maculopathy in two eyes, which resolved after autologous blood injection 3 and 4 months after surgery, with improvement of visual acuity and control of IOP in the lower teens without medication. Severe hypotony with a severe bullous choroidal detachment occurred in the third eye following YAG goniopuncture, which was performed within the first few days after surgery. This condition resolved spontaneously within 10 days.

Zimmerman *et al.* reported their experience with 28 aphakic eyes that underwent NPT, of which 18 eyes had chronic open-angle glaucoma (first group) and ten eyes had secondary glaucoma (second group) [21]. Two eyes in the second group had chronic angle closure and one eye had neovascular glaucoma. After 1 year of follow-up, 89 and 37.5% of the first and second groups achieved an IOP of 24 mmHg or lower (with or without medication), respectively, with no major intraoperative or postoperative complications. However, these authors did not remove the inner wall of SC, and they included three cases with closed angle in the second group and did not report on gonioscopy in the other seven cases of the second group. They concluded that NPDS is superior to trabeculectomy in aphakic and pseudophakic glaucoma.

Uveitic glaucoma

Glaucoma associated with uveitis is one of the most therapeutically challenging forms of secondary glaucoma [100]. Trabeculectomy has been the standard surgical procedure, until now, for both open- and closed-angle uveitic glaucoma. Outcomes have been reasonable [101–103], but the high frequency of potentially serious complications, such as increased inflammation, cataract formation and persistent hypotony, is a major concern. Bleb-related infections are another major issue, since most patients with uveitis are immune suppressed [104–107]. Recently,

retrospective and prospective studies of NPDS [64,108–111] have proved it to be superior to standard trabeculectomy in terms of safety and efficacy in uveitic glaucoma (Table 3).

Tube surgery is another valuable approach in the surgical management of uveitic glaucoma, especially in patients with extra risk factors for trabeculectomy failure, such as aphakia and previously failed filtration surgery. It has a good short-term success rate, ranging between 57 and 94%, which declines significantly with longer follow-up [104,105]. Unique complications to tube surgery, such as corneal decompensation (27%) [106] and tube occlusion (26.3%) [107], are quite significant.

Congenital & childhood glaucoma

Glaucoma in a young child who is in the amblyogenic age group is a very frustrating problem, not only from the technical point of view but also from the fear of amblyopia, which adds urgency to the restoration of media clarity in order to ensure proper visual development. Goniotomy and trabeculotomy are the conventional surgical approaches and their success rate varies depending on the severity of disease and the experience of the surgeon [112–119]. Combined trabeculotomy and trabeculectomy did not show a statistically significant improvement of success rate [120]. Serious complications, such as lens injury, stripping of Descemet's membrane and vitreous loss, have been reported, in addition to bleb-related problems in combined procedures [120,121].

Nonpenetrating DS has been employed recently in primary congenital and juvenile glaucoma, as well as in secondary glaucoma, in children with similar success rates to the aforementioned traditional procedures but with much lower rates of intraoperative and postoperative complications (Table 4) [122–126].

Recently, Feusier *et al.* advocated a newly developed procedure for pediatric glaucoma, in which trabeculectomy was combined with DS (penetrating DS) and reported their results on 35 eyes of 25 patients [124]. The overall success rate (IOP < 18 mmHg) was 84% 3.5 years after surgery. Three eyes (8.6%) suffered severe complications that led to enucleation. Although the overall outcome was encouraging, we suspect that the conversion of NPDS to a penetrating procedure is likely to be associated with loss of the safety profile, as evidenced by the high rate of severe complications reported in this study.

In summary, the results of NPDS in pediatric glaucoma reported in the literature are quite encouraging, apart from the poor outcome reported by Luke *et al.* on DS in ten eyes with refractory congenital glaucoma and previous glaucoma surgery [126]. The procedure is safe and effective and, therefore, deserves to be an important alternative to conventional surgery in primary congenital glaucoma.

Narrow-angle glaucoma

Although narrow-angle and appositionally closed-angle glaucoma are considered relative contraindications for NPDS, we believe that NPDS can be performed in these settings, keeping in mind the likelihood of laser goniopuncture at a later stage. Recently, Yuen *et al.* reported encouraging results in a retrospective study of 29 eyes in 26 patients with chronic angle-closure glaucoma and cataract who underwent combined NPDS and phacoemulsification [127].

Table 4. Efficacy of nonpenetrating deep sclerectomy in childhood glaucoma.

Study (year)	Design	Eyes (n)	Procedure	Mean follow-up (months)	Mean IOP (mmHg)		Definition of success (IOP in mmHg)	Success (%)		Mean medications (n)		Ref.
					Preop.	*Postop.*		*Complete*	*Qualified*	*Preop.*	*Postop.*	
Trixier *et al.* (1994)	RS	12	DS	10	NA	NA	<16	75	90	NA	NA	[122]
Luke *et al.* (2002)	RS	4	DS	12.7 ± 6.3	31.9 ± 5.6	NA	≤18	0.00	0.00	NA	NA	[126]
Roche *et al.* (2007)	RS	30	DS	22.8	18.8	NA	<12.5	83	NA	NA	NA	[123]
Denis *et al.* (2008)	RS	37	DS and 5-FU	38.2	NA	NA	≤16			NA	NA	[125]
Feusier *et al.* (2009)	RS	35	DS and Trab	42 ± 34.8	31.9 ± 11.5	13.3 ± 5.6	<18	52.3	70.6	1.1 ± 1.7	0.4 ± 0.7	[124]
Al Obeidan *et al.* (2009)*	PS	22	DS and implant plus MMC	51.09 ± 23.2	33.36 ± 10.42	14.09 ± 4.09	≤21	68.1				

*Unpublished data.
5-FU: 5-fluorouracil; DS: Deep sclerectomy; IOP: Intraocular pressure; MMC: Mitomycin C; NA: Not available; Preop.: Preoperative; Postop.: Postoperative; PS: Prospective; RS: Retrospective; Trab: Trabeculectomy.

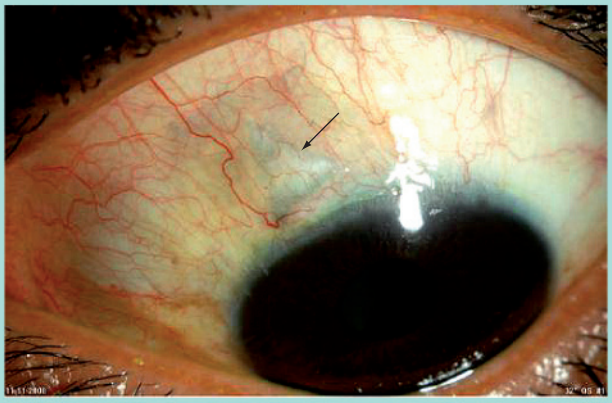

Figure 9. SK-GEL™ implant migrated under the conjunctiva (arrow).

The complete success rate (IOP ≤ 21 mmHg without medication) was 52% and the qualified success rate (IOP ≤ 21 mmHg with medication) was 86% after a mean follow-up of 33.8 months. Choroidal effusion in one eye and three wound leaks were the only early and late postoperative complications encountered.

Contraindications of NPDS

Nonpenetrating DS is indicated in glaucomas with functioning inner layers of TM (uveal and corneoscleral TM), where no pathological elements can prevent the aqueous humor from reaching the deeper layers of TM (juxtacanalicular TM) and SC. Therefore, NPDS is absolutely contraindicated in neovascular glaucoma (all stages), where the angle may appear open but is covered by a translucent fibrovascular membrane or that membrane may grow into the angle later during the course of the disease. The procedure is also contraindicated in closed-angle glaucoma owing to synechiae. Relative contraindications include occludable and appositionally closed angles [61], even after laser peripheral iridotomy, because the iris will still be in close relation to the TM. Angle-recession glaucoma may be considered a relative contraindication, as transtrabecular outflow may be compromised.

Complications associated with NPDS & their management

Published reports of NPDS have documented its excellent safety profile compared with conventional filtration surgery [62,65,128–133]. However, certain complications are unique to the procedure. These complications can be intraoperative, early postoperative or late postoperative.

Intraoperative complications

Perforation or tear in the TDM is the most common intraoperative complication, especially in the early period of conversion from traditional trabeculectomy to NPDS. This reflects the relatively long learning curve of the procedure. The management of inadvertent perforation depends on its size. If it is small and without iris prolapse, it can be ignored and the procedure can be completed as usual. Alternatively, a small amount of viscoelastic material can be injected through a paracentesis in the superior part of the AC. One drop of 1–2% pilocarpine should be instilled at the end of the procedure in order to hold the iris away from the TDM. If the perforation is large with iris prolapse, iridectectomy is mandatory and conversion to trabeculectomy is required. The reported incidence of perforation varies between 30 and 40% during the learning curve of the procedure and decreases to 2–3% after mastering the procedure [28,62].

Early postoperative complications

Hypotony

Hypotony is the most common problem following NPDS in the initial postoperative days [30,62,134]. An IOP of between 0 and 6 mmHg is common and considered a good prognostic factor for

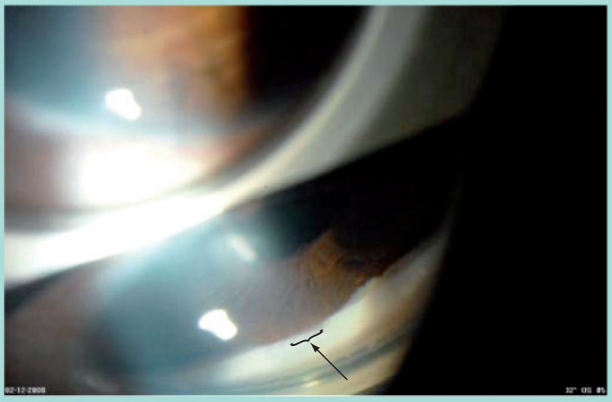

Figure 10. Iris adherent to most of trabeculo–Descemet's membrane (arrow,) discovered on routine gonioscopic examination. No previous goniopuncture had been performed, and intraocular pressure was well controlled without medications.

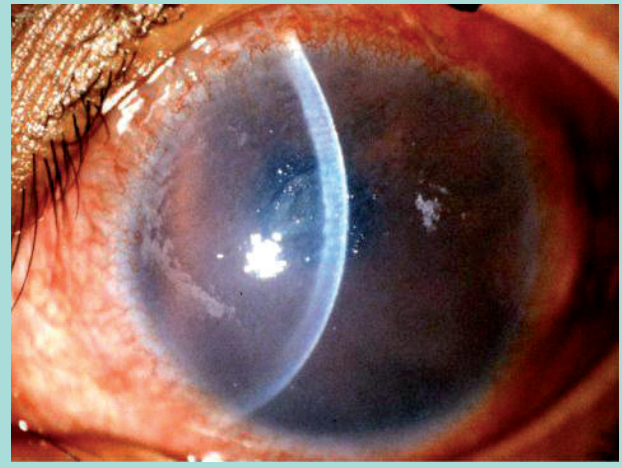

Figure 11. Descemet's membrane detachment, noted on the third postoperative day showing hazy cornea.

long-term IOP control [29,135]. Usually, the IOP builds up within a few days to the level of 8–10 mmHg and, in most cases, the AC remains deep. The complications that are usually associated with postoperative ocular hypotony, such as choroidal detachment, shallow AC and hypotonous maculopathy, are extremely rare and, if present, usually resolve spontaneously within few days. Sanchez *et al.* reported the incidence rate of hypotonous maculopathy after NPDS to be 1.2% [23]. Such a low incidence is probably due to the gradual reduction of IOP by the natural barrier of the TDM. By contrast, hypotony has been reported in up to 20% of eyes after trabeculectomy [1].

Choroidal detachment

Choroidal detachment following NPDS is an uncommon complication that is reported in less than 5% of eyes [136], despite the high frequency of early postoperative hypotony. An incidence rate of choroidal detachment of 17% has been reported following NPDS in uveitic glaucoma [65]. This relatively high incidence rate may be explained by the high preoperative IOP usually found in these eyes and by the nature of the disease. Choroidal detachment is usually self-limited and tends to resolve within a few days. The reported incidence rate of choroidal detachment following trabeculectomy is approximately 20% [1]. Hypotony, leaking bleb and overfiltration are the main risk factors for choroidal detachment.

Hyphema

Hyphemas following NPDS are rare. They are usually small and resolve spontaneously within few days without intervention. The most common cause is the presence of perforation.

Inflammation

Postoperative inflammation associated with NPDS is much less common than with trabeculectomy. This is one of the main advantages of the procedure because iridectomy, replacement of aqueous humor, and intraocular manipulation are avoided [111].

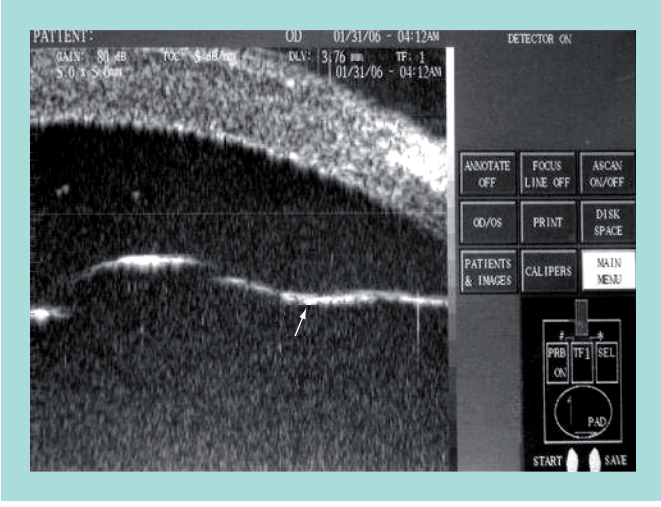

Figure 12. Ultrasound biomicroscopy showing the total Descemet's membrane detachment (arrow).

Figure 13. Clearing of the cornea flowing injection of sulfur hexafluoride in the anterior chamber.

These are extremely important factors, especially in eyes at high risk for severe postoperative inflammation, such as uveitic glaucoma. Chiou *et al.*, in a study comparing postoperative inflammation after NPDS with collagen implant versus trabeculectomy, reported significantly lower postoperative flare in the deep DS and the time needed to reach the preoperative level of inflammation was 1 week in the DS group versus 4 weeks in trabeculectomy patients [137].

Implant migration

Implant migration and exposure is a possible, unique complication with NPDS that can occur early or late in the postoperative course. Management depends on the new site of the implant and the associated complications. The problem has been described in two previous reports. Dahan *et al.* described migration of an unsutured T-Flux implant (nonabsorbable) to the AC in a patient with obstructive pulmonary disease and chronic cough 1 week postoperatively [35]. The implant was removed without sequelae. Wevill *et al.* reported migration of chromic suture material that had been used as an implant in NPDS to the AC after blunt trauma to the eye 3 weeks postoperatively [47]. The presence of the implant in AC led to intraocular inflammation with corneal edema that necessitated its removal. Our experience with implant migration occurred in a patient who underwent NPDS with SK-GEL implant. The implant was noted under the conjunctiva 10 weeks postoperatively (Figure 9). The eye was quiet and IOP was controlled; thus, no intervention was required.

Elevated IOP

Postoperative elevation of IOP usually occurs weeks to months after NPDS. Early postoperative elevation of IOP can occur owing to adhesion of the iris to the TDM, especially in the presence of narrow angles and microperforation (Figure 10). These adhesions can be confirmed by gonioscopy and managed with argon and/or YAG laser. Another possible cause of elevated IOP in the early postoperative period is the tight closure of the

superficial scleral flap, which can be managed by suture lysis. Other rare, but more serious, causes of postoperative high IOP should be ruled out, such as aqueous misdirection [30,32,37], conditions simulating malignant glaucoma [138,139] and suprachoroidal hemorrhage [140].

Descemet's membrane detachment

Descemet's membrane detachment after pure DS is very rare; most cases occur with viscocanalostomy. In DS, it probably develops secondary to the passage of aqueous humor from elevated pressure in the subconjunctival and decompression space reservoir of aqueous humor. Trauma and vigorous rubbing of the eye is another possible cause [30,53,141]. Our experience consisted of a single case with total Descemet's detachment that developed on day 3 after successful NPDS with total corneal edema precluding view of the AC (Figure 11). Diagnosis of total detachment was made with ultrasound biomicroscopy (Figure 12). The case was managed successfully with sulphur hexafluoride injection into the AC, and nearly total resolution occurred within few weeks with controlled IOP (Figure 13).

Late postoperative complications

All late postoperative complications associated with trabeculectomy can occur with NPDS but with a much lower incidence rate. These include late bleb leak, cataract formation and progression, retinal detachment, scleral ectasia, corneal endothelial cell loss and bleb-related infections. However, bleb-related endophthalmitis following NPDS has not yet been reported, which is probably explained by the presence of a natural barrier (TDM), as well as by the type of bleb that is commonly seen after NPDS compared with that of trabeculectomy with MMC (Figures 14 & 15) [136]. Elevated IOP in the midterm course (6–12 weeks) is a unique complication in almost 40–50% of the cases due to insufficient passage of aqueous humor through the TDM. Such an event can be successfully managed in a large number of cases by neodymium:YAG laser goniopuncture, with a success rate ranging between 68 and 93% of cases [22,26,61–66,142].

Figure 14. Appearance of the bleb as usually seen with nonpenetrating deep sclerectomy.

Figure 15. Appearance of the bleb as usually seen with trabeculectomy (early blebitis).

Expert commentary

The major advantage of NPDS is derived from its excellent safety profile. The vast majority of serious complications inherited to trabeculectomy are precluded with NPDS because it is an extraocular procedure. Most eyes remain quiet with good visual function in the immediate postoperative period, which has a positive impact on the patient's psychology and productivity. The use of implants, antimetabolites and neodymium:YAG laser goniopuncture as adjuvant tools has significantly improved the long-term efficacy of NPDS so that it is comparable to that of trabeculectomy.

Five-year view

The remaining unsolved obstacle to the widespread acceptance of NPDS is the long learning curve and the high rate of perforation in the early period of conversion from trabeculectomy to NPDS. The near future will probably witness the use of more precise tools, such as laser energy, to overcome this difficulty. NPDS may also be applied in the future to cases that are currently considered as relatively contraindicated; for example, narrow-angle or appositional angle-closure glaucoma. This may be accomplished by staging of the procedure: first, widening the angle by laser peripheral iridotomy and/or iridoplasty; and second, at a later stage after inflammation subsides, performing DS followed by neodymium:YAG laser goniopuncture.

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Key issues

- Glaucoma is an irreversibly blinding disease.
- Serious complications associated with standard filtration surgery are a major consideration at the time of surgical decision.
- Nonpenetrating deep sclerectomy (NDPS) has a superior safety profile compared with traditional filtration surgery (trabeculectomy).
- The use of adjuvant tools with NPDS has improved its long-term results, which are comparable with those of trabeculectomy.
- NPDS is becoming the procedure of choice in primary and secondary open-angle glaucomas, such as uveitic glaucoma.
- Preliminary data suggest that NPDS may be the procedure of choice in primary congenital glaucoma.
- Owing to the low complication rate of NPDS, surgeons are able to consider earlier surgical intervention.
- Endophthalmitis, the most devastating complication following glaucoma-filtering procedures has not yet been reported after NPDS.

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