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CLINICAL STUDY

Deep sclerectomy in one eye *vs* deep sclerectomy with collagen implant in the contralateral eye of the same patient: long-term follow-up

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Abstract

Purpose **To compare prospectively the results of deep sclerectomy (DS) *vs* deep sclerectomy with collagen implant (DSCI)**
Methods **Randomized prospective trial involving 26 eyes (13 patients) with medically uncontrolled primary and secondary open angle glaucoma. Collagen implant was randomly assigned to one eye of each patient.**
Results: **The mean follow-up period was 49.5 (SD 20) months for the DS-treated eyes, and 56.5 (SD 14) months for the DSCI-treated eyes ($P=0.4$). The mean preoperative intraocular pressure (IOP) was 24.1 (SD 7) mmHg for the DS-treated eyes, and 25.3 (SD 6) mmHg for the DSCI-treated eyes ($P=0.5$). The mean IOP at the first postoperative day was 6.4 (SD 3) mmHg for the DS-treated eyes, and 3.7 (SD 2) mmHg for the DSCI-treated eyes ($P=0.05$). The mean IOP at 12 months postoperative day was 15.4 (SD 3) mmHg for the DS group, and 10.4 (SD 4) mmHg for the DSCI-treated eyes ($P=0.04$), while at 48 months it was 16 (SD 3) mmHg for the DS group, and 10 (SD 4) mmHg for the DSCI-treated eyes ($P=0.005$). Complete success rate, defined as an IOP lower than 21 mmHg without medication, was 38% (5/13 patients) at 48 months for the DS-treated eyes, and 69% (9/13 patients) for the DSCI-treated eyes. Qualified success rate: patients who achieved IOP below 21 mmHg with or without medication, was 69% (9/13 patients) at 48 months and 100% (13/13 patients) for the DSCI group. The mean number of medications was reduced from 2.4 (SD 0.8) to 1.1 (SD 1) after DS, and was reduced from 2.2 (SD 0.7) to 0.4 (SD 0.6) in the DSCI group ($P=0.001$). For those eyes treated with DSCI, IOP was 3.21 mmHg lower than for those treated with DS ($P<0.0001$).**
Conclusion **The use of a collagen implant in DS seems to enhance the success rates, provides significantly lower IOP levels, and lowers the need for postoperative medications.**
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Introduction

Deep sclerectomy (DS) is a nonpenetrating filtration procedure for the surgical treatment of medically uncontrolled open angle glaucoma. The more classical trabeculectomy, with or without antimetabolites, has a well-documented complication rate.[1,2] DS was designed in an attempt to lower the risk of incidence of such complications, thus offering both the surgeon and patient a safer and more convenient option.[3]Implants have been used in DS in the hope of increasing the success rates of this surgery, and although several of studies have been published reporting on the success rates of the use of these implants,[4–8] unfortunately very few studies compared the success rates of DS with an implant, to DS without an implant.

Patients and methods

Setting

The Glaucoma Unit, Ophthalmology Department, University of Lausanne, Switzerland.

Case selection

A total of 26 eyes of 13 patients with medically uncontrolled bilateral primary open angle and

Table 1 Demographics

	DS	*DSCI*
Number of eyes	13	13
Female Patients	10	10
Age	79.3 (SD 11.7)	79.2 (SD 11.9)
Preoperative IOP	24.1	25.3
Preoperative visual acuity	0.68	0.66
Number of glaucoma medications	2.4	2.2
Diagnosis		
Primary open angle glaucoma	10	10
Pseudoexfoliative glaucoma	3	3

exfoliative glaucoma were selected consecutively and randomly assigned (random number tables were used) (Table 1). The study patients were enrolled after the approval of the Ethical Committee of the University of Lausanne. Informed consent was obtained from all participants. The patients selected were all medically uncontrolled with maximal medical therapy. Uncontrolled glaucoma was defined as uncontrolled intraocular pressure (IOP) (>21 mmHg), measured with a Goldmann applanation tonometer under maximal tolerable medical treatment and with well-documented progression of visual field defects and optic nerve morphology.

Exclusion criteria were unwillingness to participate, known allergy to collagen, advanced lens opacities, previous laser trabeculoplasty, and previous eye surgery less than 6 months prior to enrolment in this study.

Data recorded preoperatively

On the day before surgery, patients underwent best-corrected visual acuity assessment (Snellen chart at 5 m). IOP was measured using a Haag–Streit (Bern, Switzerland) Goldmann applanation tonometer mounted on a slit lamp. Patients also underwent biomicroscopy, gonioscopy, visual field testing using the G1 programme of the octopus 101 (Interzeag AG, Schlieren, Switzerland), and fundus biomicroscopy.

Postoperative follow-up

After surgery, all the previously mentioned examinations, except for visual field assessment, were conducted on the first and the seventh day as well as in 1, 3, 6, 9, 12, 18, 24, 30, 36, 48, 54, 60, and 66 months. Visual field examination was repeated every 6 months.

Complications have been defined as follows: hyphaema was considered to be present when erythrocytes were seen in the anterior chamber. Hypotony was defined as a postoperative IOP $\leqslant 4$ mmHg for more than 2 weeks. Anterior chamber depth was clinically assessed in comparison with the fellow eye. Anterior chamber was considered shallow when there was an iridocorneal touch in the periphery, and flat when there was a lens–corneal touch, as seen on biomicroscopy. Anterior chamber inflammation was considered to be present when flare could be seen by biomicroscopy. Choroidal detachment was considered to be present when seen in the peripheral retina, using an indirect ophthalmoscope. In the postoperative follow-up, cataract was either observed as a direct consequence of filtration surgery, and termed 'surgery-related cataract', or appeared progressively and has therefore been called 'cataract progression'. Surgery-related cataract has been defined by a rapid decrease (over a period of 1 month) of visual acuity and mainly the development of cortical opacity, whereas cataract progression has been defined as a slow progressive decrease in visual acuity of more than two lines (Snellen chart) due to lens opacification, mainly nuclear sclerosis.

Statistical analysis

The results were analysed using the Student's *t*-test and repeated measures analysis of variance for comparison of means, χ^2 analysis for 2×2 tables, a doubly repeated measures analysis of variance design was used to investigate the effect of procedure type on postoperative IOP. For comparison between groups, the Wilcoxon test was used. Statistical software PC SAS version 8.1 (SAS institute Inc.) as well as Excel 2000 (Microsoft) were used for statistical analyses.

Surgical procedure

The surgical procedures have been previously described[4] (Figure 1).

Success criteria

Surgery was considered a complete success when IOP was $\leqslant 21$ mmHg without glaucoma medication and a

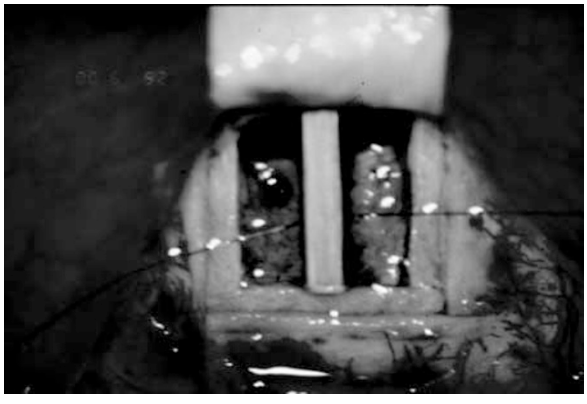

Figure 1 The collagen implant is placed in the scleral bed and sutured.

qualified success when IOP was $\leqslant$21 mmHg with or without glaucoma medication. It was considered a failure when IOP was >21 mmHg with or without glaucoma medication, or when an eye required further glaucoma drainage surgery, developed *phthisis bulbi*, or lost light perception. Three measures of the IOP were performed to determine the mean IOP; when this mean was >21 mmHg, the operation was considered a failure.

When the filtering bleb at any postoperative visit was encysted or showed signs of fibrosis, subconjunctival injections of 5 mg of 5-fluorouracil (5-FU) were administered in the lower quadrant, opposite the DS site. The subconjunctival injections consisted of 0.1 ml of a 50-mg/ml solution of 5-FU (250 mg/5 ml FU, Roche®, Basel, Switzerland). Subconjunctival 5-FU injections were repeated up to seven times, when necessary.

Goniopuncture with the Nd:YAG laser (Microruptor II, Lasag AG, Thun, Switzerland) was performed when the filtration through the TDM was suspected to be insufficient, because of a shallow filtration bleb and elevated IOP. The goniopuncture procedure was previously described.

Results

The mean follow-up period was 49. 5 (SD 20) months for the DS-treated eyes, and 56.5 (SD 14) months for the DSCI-treated eyes ($P=0.4$). The mean preoperative IOP was 24.1 (SD 7(maximum 48, minimum 21, median 23)) mmHg for the DS-treated eyes, and 25.3 (SD 6(maximum 34, minimum 21, median 26)) mmHg for the DSCI-treated eyes ($P=0.5$). The mean IOP at the first postoperative day was 6.4 (SD 3(maximum12, minimum 1, median5)) mmHg for the DS-treated eyes, and 3.7 (SD 2(maximum 7, minimum 1, median 4)) mmHg for the DSCI-treated eyes ($P=0.05$). The mean IOP at 12 months postoperative day was 15.4 (SD 3(maximum 19, minimum 10, median 15)) mmHg for the DS-treated eyes, and 10.4 (SD 4(maximum 16, minumum 6, median 10)) mmHg for the DSCI-treated eyes ($P=0.04$), while at 48 months it was 16 (SD 3(maximum 19, minumum 11, median 16)) mmHg for the DS-treated eyes, and 10 (SD 4(maximum 16, minumum 6, median 11)) mmHg for the DSCI-treated eyes ($P=0.005$) (Figure 2 and Table 2).

The complete success rate, defined as IOP lower than 21 mmHg without medication, was 38% (5/13 patients) at 48 months for the DS-treated eyes, and 69% (9/13 patients) for the DSCI-treated eyes. Qualified success rate: patients who achieved IOP below 21 mmHg with or without medication was 69% (9/13 patients) at 48 months and 100% (13/13 patients) for the DSCI-treated eyes. The mean number of medications was reduced from 2.4 (SD 0.8) to 1.1 (SD 1) after DS, and was reduced from 2.2 (SD 0.7) to 0.4 (SD 0.6) in the DSCI-treated eyes ($P=0.001$)

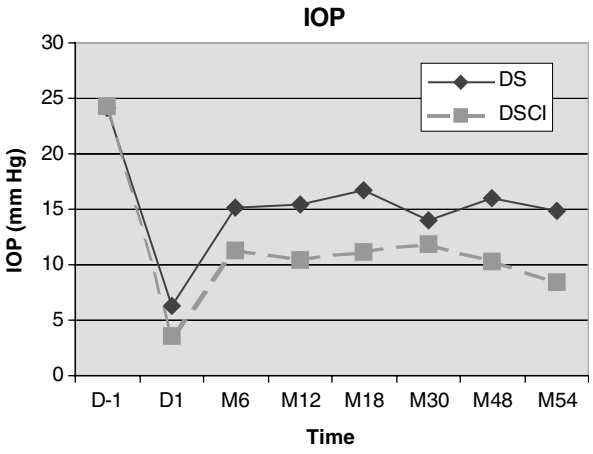

Figure 2 Mean intraocular pressure.

Table 2 IOP

IOP	*DS*	*DSCI*	P
Preoperative	24.1	25.3	0.5
Day 1	6.3	3.6	0.05
Month 6	15.1	11.3	0.2
Month 12	15.4	10.4	0.04
Month 18	16.7	11.1	0.02
Month 30	14	11.8	0.007
Month 48	16	10.25	0.005
Month 54	14.8	8.5	0.0005

A doubly repeated measures analysis of variance design was used to investigate the effect of procedure type on postoperative IOP. Two variables were repeated for each subject: time and eye. That is, each subject presented data from both eyes and over repeated times. The covariance structure used to model these repeated observations unstructured between eyes and autoregressive (AR1) over time. This covariance structure was implemented in SAS PROC MIXED using a direct product.

In addition to procedure type, preoperative IOP was included in the model as a baseline covariate. Time was also included to determine if IOP increased or decreased over time. Finally, an indicator was used to flag the start time for medications.

Baseline IOP was not predictive of subsequent IOP ($P=0.1788$). Measures of IOP taken from onset of medications were significantly higher by 3.79 mmHg ($P=0.0153$). One might expect that medication use would be associated with a decrease in IOP rather than the obtained increase. However, one must remember that these are the eyes not responding to surgical treatment, having higher IOP when medication is initiated. Time showed an increasing trend for IOP ($P=0.0872$). The coefficient of 0.046 indicates that IOP was increasing

about 0.5 mmHg per year. A strong and significant effect was found for procedure. For those eyes treated with DSCI, IOP was 3.21 mmHg lower ($P<0.0001$). The possibility of a differential trend over time for DS and DSCI was explored. However, the interaction was not significant.

As data were more complete in the first several years postsurgery, the above model was repeated using only the first 3 years of data. The results obtained were quite similar. DSCI was still strongly associated with the outcome, showing close to a 3 mmHg lowering in IOP ($P=0.0011$). In restricting the analysis to the first 3 years, a significant trend over time appeared. IOP significantly increased at an approximate rate of 1.5 mmHg per year ($P=0.0014$). Medication use was positively associated with IOP ($P<0.0001$). An analysis of differential trends over time by procedure was investigated, but no significant difference was found.

Qualified success, maintenance of IOP <21 mmHg, regardless of medication use, was achieved by 22 of 26 eyes. The four failures were eyes treated with DS. However, extensive censoring of the data (22 of 26) does not permit a meaningful statistical comparison of the time to failure. Furthermore, eyes were paired and therefore not independent observations, an assumption required by the model.

Complete success, maintenance of IOP <21 mmHg without the use of medications, was achieved by 14 eyes: nine DSCI, and five DS. The median time to failure could not be calculated in the DS treated eyes, due to the small number of events. However, a weak trend to favouring the DSCI procedure was evident.

The preferred method of analysis to compare the effects on IOP of procedure type in this small study is an analysis of variance. This model is able to account properly for dependence among the data, which is not addressed in the survival analysis. Furthermore, this method is more powerful, as it is able to capture graded differences in IOP that are missed when a binary criterion is used. The two analyses of variance models presented show that DSCI will result in IOP that is 3 mmHg lower than if a DS procedure is performed.

Best-corrected visual acuity (BCVA) dropped on the first postoperative day from a mean of 0.67 (SD 0.18) preoperatively, to a mean of 0.39 (SD 0.2) for the DS-treated eyes, and from 0.66 (SD 0.3) to 0.50 (SD 0.2). Visual acuity returned to preoperative levels 1 week after surgery and remained stable over the next 4 years achieving a mean BCVA of 0.56 (SD 0.2) and 0.58 (SD 0.3) at 24 months for the DS- and the DSC-treated eyes, respectively. At 48 months, there was a mean BCVA of 0.58 (SD 0.2) and 0.57(SD 0.3) for the DS- and the DSCI-treated eyes, respectively.

There were no significant operative complications recorded in this series. Postoperative complications that occurred are listed (Table 3). No shallow or flat anterior chamber, no bleb-related endophthalmitis, and no surgery-induced cataract was observed in either treatment. The mean number of preoperative medications dropped from 2.2 to 1.1 in the DS-treated eyes, while in the DSCI-treated eyes it dropped from 2.2 to 0.4.

Goniopuncture with ND:YAG laser was performed on six patients (46%) of the DS-treated eyes and six (46%) of the DSCI-treated eyes (Table 4). The mean time between DS and goniopuncture was 13.2 months *vs* 14.5 months in the DSCI-treated eyes, the mean IOP before goniopuncture was 19.5 (SD 5.8) and 14.5 (SD 4.2) mmHg for the DS- and the DSCI-treated eyes, respectively. The mean IOP after goniopuncture was 14.7 (SD 10) and 7.3 (SD 6) mmHg for the DS- and the DSCI-treated eyes, respectively ($P=0.01$).

Discussion

The major advantage of nonpenetrating surgery is that it precludes the sudden hypotony that occurs following trabeculectomy by creating progressive filtration of the aqueous humour from the anterior chamber to the surgically created intrascleral space, through the trabeculo-Descemet's membrane.[9,10]

Hamard *et al*[11] in a recent study have shown that the membrane peeled in DS consists of the inner wall of Schlemm's canal, and the juxta-canalicular tissue, which are considered to be the site of highest outflow

Table 3 complications

Complications	*DS*	*DSCI*
Early		
Hyphaema	0	1
Hypotony	0	0
Choroidal detachment	0	0
Shallow anterior chamber	0	0
Late needling	0	1
Cataract progression	5	4
Others 5-FU	5	4
Mean # of inject.	2.5	1.5
Mean time of inject. (months)	1.5	2

Table 4 Nd:YAG goniopuncture

	DS	*DSCI*
Number	6	6
YAG time (months)	13.2	14.5
IOP before	19.5	22
IOP after	14.7	7.3

resistance.[12–14] Multiple studies[10,15] have demonstrated that DS exposes a physiological membrane consisting of the rest of trabecular tissue (after peeling) and Descemet's membrane. These studies have demonstrated that aqueous percolates at the level the trabeculum and to a much lesser extent at the level of Descemet's membrane. This is in line with a study[16] reporting on the relative low permeability of Descemet's membrane in rabbits isolated eyes. The creation of the trabeculo-Descemet's membrane dramatically increases facility of outflow, but at the same time offers enough resistance to prevent sudden globe decompression that commonly occurs after trabeculectomy.[10]

The concept of occupying the intrascleral space with a space-occupying device has been proven to improve significantly success rates in DS in the short[17] and long term.[18]

Sanchez *et al*[17] examined the results of DSCI compared to DS in a prospective nonrandomized group of 168 patients (168 eyes) with various types of medically uncontrolled open angle glaucoma; 86 (86 eyes) underwent DSCI, and 82 (82 eyes) underwent DS. The mean follow-up period was about 9 months in both procedures. Complete and qualified success rates were better when the collagen implant was used (Log-Rank test: $P = 0.0002$ and 0.033 for complete and qualified success, respectively). The need for postoperative glaucoma medications was significantly lower when the collagen implant was used (0.2 ± 0.5 *vs* 0.5 ± 0.7 medication per patient in the DSCI and DS, respectively, $P = 0.0038$). There was significantly less bleb fibrosis when the collagen implant was used (2 and 11% in DSCI and DS, respectively, $P = 0.029$). They concluded that the use of collagen implant is safe, increases the success rate of DS, and lowers the need for postoperative glaucoma medications.

The idea[8] behind the collagen implant is that it can occupy the surgically created intrascleral space for 6–9 months,[19,20] before dissolving. During the period of its existence in the intrascleral space, the implant bridges the maximum period of scarring postoperatively, and by the time the implant disappears, the healing process would have already quieted.

In our study, the use of collagen implant in DS enhanced the success rates and lowered the need for postoperative medications. Issues concerning the mechanisms of function of the implant, and the effect of size, material, and shape of the implant on the success rates still deserve further attention.

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