THE SURGICAL OUTCOMES OF DEEP SCLERECTOMIES PERFORMED AT A JOHANNESBURG ACADEMIC HOSPITAL

By

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DECLARATION

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DEDICATION

To my family,

Mams, Pops, Rob, Joshi and little Matt –

You are the finest of thread! You have weaved around me in comfort, under me in support, through me in understanding, over me in guidance – you have created an incredible tapestry that is me and it is your weave that allows for any accomplishment. Where I feel I am coming undone – your weave tightens; where tensions build, it relaxes; where I feel dull or drained, the vibrance of your tapestry overwhelms and invigorates me.

Thank you for giving of yourselves in such a substantial way – I cannot begin to express the depth of my gratitude.

Prof Susan Williams.

In my academic life, there is no greater hero.

You are a force that steered my academic life when I struggled to find my bearings. Your quiet, determined, and firm consistent presence was the empowering drive that kept me moving successfully through my specialist training.

Thank you, for the light that you so brightly shine, for the North Star that it is for so many, and for the gentleness with which it radiates and directs growth.

PRESENTATIONS AND PUBLICATIONS

No presentations or publications have been made at the time of submission.

ABSTRACT

Purpose: The primary aim of the study is to determine the overall outcomes of deep sclerectomy surgery at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and to compare it with that described in the available literature. Important outcomes considered are: (1) those denoting surgical success (acceptable IOP control and glaucoma non-progression – with or without drop therapy); (2) the need for secondary procedures (such as yag goniopuncture); (3) the occurrence of surgical complications (such as flat anterior chamber, hyphaema, hypotonous maculopathy and hypotonous choroidal detachment); and (4) those indicating surgical failure (the requirement for repeat surgery and loss of light perception vision).

Secondary aims are to describe the patient population undergoing deep sclerectomy surgery, as well as their underlying glaucoma disease profile.

Study Design: Retrospective record review

Methods: Patient records, including their intra-operative notes, were reviewed. The records reviewed, were those of patients attending the CMJAH glaucoma clinic and who underwent DS surgery between 01/06/2014 and 31/07/2015, with follow up extending up to 45 months post surgically. For the purpose of this study, important terms were defined as follows: *success* (mean IOP ≤ 18 without medical drop therapy); *qualified success* (mean IOP ≤ 18 with medical drop therapy OR mean IOP > 18 without medical drop therapy); *qualified failure* (mean IOP > 18 with medical drop therapy) and *failure* (Loss of light perception vision or requirement for repeat surgery)

Results: A total of 57 cases were reviewed. Within these, sex was comparably distributed (52.6% male; 47.4% female). In terms of race distribution, the majority of the cases reviewed were black (77.2%), 14% were white, 5.3% coloured and 3.5% Indian. In terms of the underlying glaucoma profile, most cases had POAG (61.4%) followed distantly by PXG (21.1%) and the greater majority had advanced disease with CDR of >0.8 in 82.4% of cases and >0.9 in more than half (59.6%) of the cases reviewed.

100% of all DS surgeries performed received adjunctive intra-operative MMC.

Surgical success rates and qualified success rates at CMJAH were 85% at 36 months and 62% at 45 months post-operatively. Overall, the mean surgical success rate was 89.8%. Success rates of the supervised junior surgeons were comparable to that of the senior surgeon.

Adjunctive laser goniopuncture was performed in 69.2% of cases – the majority being done between months 1 and month 3 post-operatively.

Complications were rare with no cases developing flat anterior chambers, only 1.9% presenting with hyphaema and choroidal detachment and 9.6% developing hypotonous maculopathy. Importantly, all these complications resolved spontaneously with medical therapy alone, except for 2 cases with hypotonous maculopathy – 1 of which had a bleb leak and required suturing, and another case was lost to follow up after month 6.

The mean overall surgical failure rate was small at only 10.2%.

Conclusion: Deep sclerectomy surgery at CMJAH is performed on a majority black population of equal sex distribution with advanced glaucoma, with a predominant underlying diagnosis of POAG. Deep sclerectomy surgery with adjunctive intra-operative MMC, on this group of patients, has a high success rate but may require adjunctive post-operative goniopuncture. It has a low overall complication rate, with specific reference to hypotony associated complications. It has predictable and reproducible overall results. As such DS surgery is a viable first line surgical option in our local glaucoma population as the surgical outcomes at CMJAH are comparable with those described in literature.

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LIST OF ABBREVIATIONS

1. **IOP**: intra-ocular pressure
2. **POAG**: Primary Open Angle Glaucoma
3. **DS**: Deep Sclerectomy
4. **OAG**: Open Angle Glaucoma
5. **MMC**: Mitomycin-C
6. **5-FU**: 5-Flourauracil
7. **CMJAH**: Charlotte Maxeke Johannesburg Academic Hospital
8. **NPS**: Nonpenetrating Glaucoma Surgery
9. **DSCI**: Deep Sclerectomy surgery with Collagen Implant
10. **VC**: Viscocanalostomy
11. **RCT**: Randomised Controlled Trial
12. **VA**: Visual Acuity
13. **PXG**: Pseudoexfoliative Glaucoma
14. **JOAG**: Juvenile Onset Open Angle Glaucoma
15. **PDS**: Pigment Dispersion Syndrome
16. **SOAG**: Secondary Open Angle Glaucoma
17. **ARG**: Angle Recession Glaucoma
18. **CACG**: Chronic Angle Closure Glaucoma
19. **LGP**: Laser Goniopuncture

CHAPTER 1: INTRODUCTION TO THE STUDY

1.1.BACKGROUND AND LITERATURE REVIEW

1.1.1. GLAUCOMA

Glaucoma is the second leading cause of blindness worldwide and in South Africa[1] with over half of patients affected being unaware of their disease. Unfortunately, at present there is no cost-effective population-based screening programme for glaucoma. Reduction of the intra-ocular pressure (IOP) remains the single most important modifiable risk factor in preventing blindness in these patients.[2] Glaucoma becomes increasingly more common with advancing age and if left untreated is predicted to progress from mild early disease to at least unilateral blindness in 23 years. [2]

Glaucoma is more prevalent in Africans and occurs at an earlier age in this population.[1] Primary open angle glaucoma (POAG) is the predominant subtype in Africans and is defined as a chronic and progressive disease, characterised by acquired loss of optic fibres, glaucomatous disc progression, visual field changes, and open angles in the absence of a known underlying cause. [2]

1.1.2. MANAGEMENT OF GLAUCOMA

Management of glaucoma consists of medical, laser and surgical options.[3]

Medical treatment is divided into topical and systemic preparations. Within the topical preparations there are five main classes of drugs: beta-blockers, cholinergics, carbonic anhydrase inhibitors, alpha-2 agonists, and prostaglandin analogues.

Laser options in the management of glaucoma include primary laser therapies aimed at lowering intra-ocular pressures as a stand-alone procedure, or they may be used in combination as part of an over-all management plan to further improve aqueous outflow facility or augment surgical treatments. Laser glaucoma treatments which primarily increase outflow facility, and may be used as a stand-alone procedure, include non-selective and selective laser trabeculoplasty. Other laser options usually used as an adjunct to medical or other surgical managements, depending on the subtype of glaucoma, include: laser iridotomy in angle closure glaucoma; iridoplasty in glaucoma secondary to plateaux iris; or as in the case after deep sclerectomy, facilitative yag goniopuncture.

Within the surgical options available there are penetrating and non-penetrating surgeries that can be performed with the aim of reducing the intra-ocular pressure (IOP). The non-penetrating surgeries have the advantage of having a superior safety profile. Deep sclerectomy (DS) is one such non-penetrating surgery used to treat open-angle glaucoma (OAG). Trabeculectomy, a penetrating glaucoma surgery, is still however the commonest glaucoma surgery performed to date. [3]

Traditionally the treatment of glaucoma has been primarily medical, followed by laser and finally surgery for medically refractive cases. The reason that surgery has been reserved as the last resort for treatment is due to the relatively high complication rates involved in penetrating trabeculectomy. In developing countries surgery has often been chosen as a first line therapy (when available) due to the high cost of glaucoma medications. [2] This said, however, there is a paucity of studies in the literature evaluating the cost-effectiveness of medical versus surgical management of glaucoma. One study done in Brazil in 2012 showed that DS was less costly and more effective than maximally tolerated medical therapy. [4] The caveat of this study is that it assumes that the glaucoma surgery performed will be completely successful. If only partially successful, the cost of the medical drug therapy post-operatively would make surgery the more expensive option.[4]

Another reason why surgical management of glaucoma in a developing world setting, such as South Africa, may be preferable to medical therapy is that patients often have to travel long distances to attend clinics and follow ups which is often not possible and will affect compliance with chronic medications. [4]

According to the current South African Department of Health guideline: ‘National guideline: Prevention of blindness in South Africa’, [1] surgical management is first line for glaucoma, specifically trabeculectomy with Mitomycin-C (MMC) or 5-Flourauracil (5-FU). The suggested trabeculectomy surgery rate – the number of trabeculectomies performed per million members of the population per year is 500.

Medical management is not first line mainly due to cost and compliance issues. If trabeculectomy fails, medical management is suggested with first line therapy being topical beta-blockers, second line topical parasympathomimetics and third line oral carbonic anhydrase inhibitors.[1]

At Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), we tend to follow developed country guidelines, treating patients with medical therapy first, opting for prostaglandin analogues as first line medical therapy and only moving on to surgical intervention once the patient has failed medical therapy. The surgical intervention most widely used in our academic hospitals is that of the trabeculectomy. Deep sclerectomy (DS) surgery has recently gained popularity at CMJAH.

1.1.3. DEEP SCLERECTOMY SURGERY

DS is performed by removing the inner wall of Schlemm's canal and the juxta-canalicular trabecular meshwork. This reduces the IOP by increasing aqueous outflow. A trabeculo-descemet's membrane is left intact that provides controlled aqueous outflow. [3] This is in contrast to traditional trabeculectomy which removes Schlemm's canal and the trabecular meshwork to penetrate directly into the anterior chamber allowing free egress of aqueous which is controlled only by re-securing the overlying surgically created scleral flap as well as conjunctival pocket with sutures. The mechanical tension created by the sutures is inversely related to the aqueous outflow and remains unpredictable despite a multitude of surgical variations and modifications.

DS can be used to treat both primary and secondary OAG.[3] It also is of benefit in uveitic glaucoma as it causes less post-operative inflammation.[3] The more controlled drop in IOP with DS is also safer in highly myopic patients who are at risk of choroidal detachment if the IOP falls too rapidly.[3]

1.1.3.1. Contra-indications for DS

In certain patients DS is contra-indicated. These are patients with neovascular glaucoma and iridocorneal endothelial syndrome due to the formation of a fibrovascular membrane over the irido-corneal angle. DS is also not the procedure of choice in narrow-angle glaucoma as the proximity of the iris can lead to complications such as anterior synechiae and iris entrapment.[3]

DS has found limited use in the setting of paediatric glaucoma. It has been proposed as an alternative method in high risk glaucoma cases such as Sturge-Weber syndrome where the risk of choroidal detachment following post-operative hypotony is high. This procedure however has not been widely used or studied in this arena. [5]

1.1.3.2. Complications of DS

Complications relating to DS are relatively rare. The reason for this is that it is essentially an extraocular procedure and that the IOP decrease through the intact trabeculo-descemet's membrane is more controlled. Hence complications associated with trabeculectomy such as a flat anterior chamber, choroidal detachment, hypotonic maculopathy and post-operative infections are uncommon.[3]

Complications of nonpenetrating glaucoma surgery (NPS) can be intraoperative, early postoperative, or late postoperative. Probably the most common intraoperative complication of NPS is perforation of the trabeculo-descemet's membrane. It is acceptable to have a perforation rate of about 30% in the first 10-20 cases. After the initial learning phase, the surgeon should expect a perforation in about 2-3% of cases.[6]

Early post-operative complications include inflammation, hypotony and associated complications, descemet's membrane detachment, hyphaema, wound and bleb leaks, blebitis, infectious keratitis, implant migration, retinal detachment and post-operative increases in IOP secondary to haemorrhage or insufficient surgical dissection.[6]

Late complications include late rupture of the trabeculo-descemet's membrane, peripheral anterior synechiae and iris prolapse, bleeding during gonioscopy, bleb fibrosis, scleral ectasia and corneal refractive and endothelial cell layer changes.[6]

1.1.4. LONG-TERM EFFICACY

The main concerns regarding DS have been long-term efficacy with studies showing conflicting results. DS achieves excellent early IOP control, but this effect is not maintained over long-term follow up. There are a number of adjunct procedures that can be performed to increase the long-term success: the intraoperative use of antimetabolites which reduce scarring post-operatively; the use of space-maintaining implants to keep the scleral lake open and performing Nd:Yag laser goniopuncture early when filtration through the trabeculo-descemet's membrane is considered to be insufficient because of elevated IOP.[3] It has been argued that because goniopuncture is performed commonly after DS, the surgery is in fact a perforating procedure done in two stages. Nevertheless, the combined complication rates of deep sclerectomy and goniopuncture are significantly lower than the complication rates associated with trabeculectomy.[6]

1.1.5. SUCCESSFUL DS

In a prospective series of 43 patients undergoing DS without implant or antimetabolites, (where successful surgery was defined as a post-operative IOP of 21mmHg or less without the use of any glaucoma medications), a success rate at 12, 24 and 30 months of 61.4%, 36.6%, and 18.9% respectively was achieved.[7] When implants are used to maintain the intrascleral space the long-term results appear to improve. For example, a study comparing DS in one eye and DS with collagen implant (DSCI) in the other found complete success at 48 months in 38.5% of DS eyes and 69.2% of eyes after DCSI. [8] Furthermore, a study done in Korea with surgeons experienced in DS showed excellent results when DS was combined with collagen implants and MMC. At 5 years the complete success rate was 36.7% and the qualified success rate almost 80%. [9] Implants are an expensive addition to the surgical procedure and are therefore not used at CMJAH.

Other studies have shown improved success rates with the use of the antimetabolite MMC. A study comparing DS and DS augmented with MMC (0.2 mg/ml for 2.5 min) with a 36 month follow-up showed a larger IOP reduction and improved success rate, with 72.5% of DS without MMC achieving qualified success (IOP less than 21mmHg with or without the use of medications) versus 95% of DS augmented with MMC.[10] Interestingly, a study performed in Nigeria, in a predominantly black African population, evaluated DS with or without low dose MMC (0.25 mg/ml for 2 min) and failed to show a significant benefit from the MMC with low success rates in both the DS and MMC augmented DS groups. [11] This was attributed to aggressive scarring in this population group. This raised concerns over whether this treatment approach is the correct one in our predominantly black African patients serviced at CMJAH.

In the black African population, the failure rate following trabeculectomy is also higher due to a higher scar formation rate at the surgical site. A study done in South Africa however showed that the addition of beta radiation to trabeculectomy showed a decrease in post-operative scarring.[12] This might be a consideration for future studies on DS.

1.1.6. DS IN COMPARISON TO ALTERNATIVE SURGERY

When comparing DS to other forms of glaucoma surgery, multiple studies have been performed and are available in the literature.

There have been several studies comparing the effectivity of DS versus trabeculectomy. A study randomly assigning 39 patients to have DS or trabeculectomy in one eye and the opposite procedure in the other eye found IOP reductions of 15.6 +/- 4.2mmHg in DS and 14.1 +/- 6.4mmHg in trabeculectomy, with a complete success rate of 79% and 85% respectively. [13] Another study showed no significant difference in outcomes between DS and trabeculectomy.[14]

A recent Cochrane review done in 2014 including 5 studies comparing NPS with trabeculectomy showed no difference in complete success rate between DS and trabeculectomy but did show that viscocanalostomy (VCO), another non-penetrating glaucoma surgery, had a lower complete success rate.[15] The authors did however note that the study methodologies were poor and that large prospective randomized studies would be needed to definitively answer this question.

A systematic review published in 2011 compared DS alone to VCO, and to trabeculectomy. A total of 29 randomised controlled trials (RCT) were reviewed. The results showed that for the primary endpoint of total success rate in IOP reduction, both DS and VCO were inferior to trabeculectomy at 4 years. However, where adjunctive MMC or implants were used the results at 4 years were comparable and had the advantage of fewer complications than that seen in the trabeculectomy group. [16]

In a large meta-analysis of 18 studies comparing trabeculectomy to NPS (including DS, VCO and canaloplasty), the 6-month follow-up showed that the trabeculectomy patients had an average 2mmHg lower IOP. The addition of MMC to both surgeries reduced this difference to 0.8mmHg in favour of trabeculectomy. The addition of implants did not further reduce this difference. In this meta-analysis, the absolute risk of all complications was higher in the trabeculectomy group. [17] Of the three NPS, DS had the least difference in efficacy versus trabeculectomy. The conclusion of this review stated that DS seemed to be a reasonable clinical compromise between safety and efficacy and that MMC should be used when performing DS to improve IOP reduction. [17]

1.1.7. CONCLUSION

In conclusion, there is consensus showing that DS has fewer complications than trabeculectomy. The outcomes are also comparable provided the surgeon has sufficient experience in DS. Given that DS is a more technically challenging procedure than trabeculectomy, the learning curve is flatter and prolonged, with an average of 20 cases needed before proficiency is obtained. This is a drawback with DS as compared to trabeculectomy. [3] In the setting of a specialised glaucoma service such as that offered at CMJAH, it is not beyond expectation that surgical proficiency in DS technique can be attained with outcomes comparable to that seen elsewhere and that seen in trabeculectomy cases.

It is now yet known where DS will fit into the sequential management of OAG. Since it has a lower complication rate it has been proposed that it may play a role earlier on in disease management. [3]

1.2. STUDY AIM

The primary aim of the study was to determine the overall outcome of deep sclerectomy surgery at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and to compare it with that described in the available literature.

Secondary aims were to describe the patient population undergoing deep sclerectomy surgery, as well as their underlying disease profile and to determine whether any of these factors could be used as predictors of surgical outcome.

1.3. HYPOTHESIS

DS surgery is a viable first line surgical option in our local glaucoma population as the surgical outcomes at CMJAH are comparable with those described in literature:

1. It has a high success rate: successfully reduces intra-ocular pressure but may require adjunctive post-operative gonio-puncture.
2. It has a low overall complication rate, with specific reference to hypotony associated complications.
3. It has predictable and reproducible overall results.

1.4. OBJECTIVES

1.4.1. PRIMARY OBJECTIVES

The primary objectives were to determine overall surgical outcomes ([1]IOP control as well as [2]surgical success and failure rates), [3]associated complications and [4]adjunctive laser goniopuncture requirement in cases undergoing DS surgery performed at CMJAH.

1. Post-operative pressure control was determined by assessing:
    a. Mean intra-ocular pressure (IOP)
    b. Percentage IOP drop
    c. Number of additional medical glaucoma drops.

    As CMJAH is a training hospital, the post-operative pressure control achieved by DS surgery was compared between surgeries performed by senior vs supervised junior surgeons. This was done in order to assess whether the outcomes of the DS were significantly affected by supervised junior surgeons performing the surgery.
2. Surgical success and failure rates were determined and compared to that described in available literature. Rates were determined according to the following definitions:
    a. success (mean IOP ≤ 18 without medical drop therapy)[20]
    b. qualified success (mean IOP ≤ 18 with medical drop therapy OR mean IOP > 18 without medical drop therapy)
    c. qualified failure (mean IOP > 18 with medical drop therapy)
    d. failure (requirement for repeat surgery or loss of light perception vision)

       Explanatory Note: Loss of light perception vision is a contra-indication for repeat surgery – for all patients with vision, repeat surgery will be performed should IOP be unacceptable or glaucomatous damage be noted to be progressive. Progressive glaucomatous damage is picked up via loss of VF and / or VA, an increase in CDR or a rise in IOP.
3. Peri-operative complication rates at CMJAH were determined and compared to that described in literature. Specific complications include:
    a. Intra-operative micro-perforation
    b. Post-operative development of:
        i. Flat anterior chamber
        ii. Hyphaema
        iii. Hypotonous maculopathy

iv. Choroidal haemorrhage or detachment
v. Cataract formation

4. Adjunctive laser goniopuncture rates were determined and compared to that noted in literature. The time period between surgery and the performance of the laser was assessed and associated laser complication rates (iris plugging) was determined.
5. Using the above data, it was determined whether Deep Sclerectomy surgery at CMJAH is an acceptable surgical option for local glaucoma patients, with comparable outcomes to that seen in literature.

1.4.2. SECONDARY OBJECTIVES

Secondary objectives of this study were to attempt to identify factors predictive of a positive (success or qualified success) or negative (qualified failure or failure) surgical outcome, only where statistically significant numbers were reached.

Whether any of the following are predictors for positive or negative surgical outcomes was detemined:

1. Patient demographics:
    a. Age
    b. Race
    c. Sex
2. Underlying glaucoma disease profile:
    a. Diagnosis
    b. Visual acuity (VA)
    c. IOP
3. Other Pre-existing ocular disorders:
    a. Inflammatory
    b. Scarring
4. Previous ocular surgery:
    a. Cataract surgery
    b. Glaucoma surgery

CHAPTER 2: MATERIALS AND METHODS

2.1. STUDY DESIGN

Retrospective record review located at the CMJAH glaucoma clinic.

CHJAH is a 1200 bed, tertiary academic hospital which is associated with the University of the Witwatersrand. It is located in Parktown, Johannesburg and serves both the East Rand and central Johannesburg district. The Ophthalmology division of the department of Neurosurgery runs the glaucoma clinic once weekly, treating approximately 150 patients per month.

2.2. ETHICS

Ethical clearance was received from the WITS University's Ethical Standard Committee for research involving human participants (Appendix 1).

2.3. SAMPLE

All patients who had undergone deep sclerectomy surgery at CMJAH between 01/06/2014 (when deep sclerectomy surgery was first started at CMAJH) and 31/07/2015. The study period chosen enabled enough cases to be included to allow for a statistically sufficiently powered study as well as allowing for a prolonged follow-up period. All cases who underwent deep sclerectomy surgery, also received intra-operative MMC.

2.4. INCLUSION CRITERIA

All patients at the study site who fell into the study population during the study period. Patients must have completed follow-up for at least six months post-operatively and had sufficiently detailed clinical records. Unilateral and bilateral surgical cases were included. All ages and races were included. All glaucoma subtypes were included if no exclusion criteria were met.

2.5. EXCLUSION CRITERIA

Those patients who fell outside of the study period, who did not complete follow-up for at least six months post-operatively, or for whom the clinical records were not sufficiently detailed, were excluded. Eyes with previous drainage surgery were excluded. Any cases with additional stents or assistive devices used intra-operatively were excluded (other than intra-operative use of MMC or Avastin). Eyes with significant comorbid ocular pathology (like severe, advance diabetic retinopathy or retinal detachment) were excluded.

2.6. DATA CAPTURE

The study site clinic records of the study population were reviewed.

Those patients determined to be part of the study were given a study number to ensure anonymity. All patient information included in the study was taken from the patient clinic files from the glaucoma clinic at CMJAH and entered onto data collection sheets. (Appendix 2).

Patient demographics and details regarding underlying disease profile were collected directly from patient files. Demographics included race, age, sex and systemic co-morbidities. Disease profiling focused on glaucoma diagnosis, medical therapy being received, visual acuity, intra-ocular pressure, cup-to-disc ratio (CDR) visual field (according to mean deviation) and optic nerve fibre layer analysis (GDX – according to nerve fibre index). The data entry into patient records for visual field and nerve fibre layer analysis was extremely scant and inconsistent which precluded analysis of these parameters later on in the study.

Surgical notes for patients receiving deep sclerectomy surgery between 01/06/2014 and 31/07/2015 were analysed, noting the use of adjunctive MMC. Post-operative notes extending beyond this time period were included as these included follow-up notes as taken on day one, week 1 and at months 1, 3, and 6. Where post-operative notes were available for months 9, 12, 18, 24, 30, 36, 42 and 45 post-operatively, this data was recorded and analysed. Post-operative notes were specifically analysed for visual acuity, IOP readings and the additional eye drop therapy required to maintain this IOP.

IOP of less than 18mmHg in a patient that is drop free was considered successful surgery, a pressure under 18mmHg in a patient that is receiving drop therapy or a pressure over 18mmHg but drop free was considered qualified success, a pressure over 18mmHg on drop therapy a qualified failure whereas repeat surgery or the loss of light perception was considered a failure.

The presence or absence of complications was also noted on these dates as well as whether or not laser goniopuncture was performed. The specific complications which were noted included the presence of flat anterior chamber, hypotonous maculopathy, hyphaema, choroidal haemorrhage or detachment and cataract formation. For notes surrounding adjunctive laser goniopuncture, it was recorded whether or not iris plugging at the site complicated the procedure.

2.7. STATISTICAL ANALYSIS

Descriptive statistics, including frequency tables, means, medians, modes, and standard deviations were run to describe the data. VA was compared between pre-surgery and each of the follow-up time-points post-surgery through Wilcoxon Signed Rank Tests. IOP was compared between pre-surgery and each of the follow-up time points post-surgery through making use of Paired Samples T-tests. A Kaplan-Meier Survival Analysis was run and a survival curve obtained in which failure of surgery was plotted against time. Finally, a Cox regression analysis was run to determine whether there were any significant predictors of the risk of surgery failing.

2.8. LIMITATIONS OF THE STUDY

The limitations of this study include, but may not be limited to:

1) Retrospective study design:
   a) does not allow for control of variables that could confound the results.
   b) Imposes data gaps, which results in an inconsistency in the sample size which could be analysed for each variable at each time period. This inconsistency affects the statistical strength and interpretation accordingly. Factors which resulted in data gaps:
      i) missing notes
      ii) variable follow-up time periods for cases results in data gaps at certain time intervals.
      iii) poor record keeping with inconsistent checking / recording of data – resulted in data gaps even when the patient was present at the follow up at the specified time period.
   c) Accuracy or reliability of data captured may be compromised
      i) patients are often followed up by registrars with various levels of training, tendency to accuracy and examination techniques.
      ii) Incomplete or illegible record keeping
   d) Affects the ability to include a specified end-point to the study – this is due to the fact that available records followed unpredictable review patterns and time periods. Should an earlier end point be specified, much of the data and analysis would be lost as many of the patients returned at unpredictable later dates which still offered extremely valuable outcome data such as ongoing IOP and the status of drop therapy etc. From this data it is possible to determine whether surgical success or failure is present at earlier time periods.
2) CMJAH is a referral centre and therefore the study population may not represent the general population.
3) Other variables contributing to glaucoma and its progression are not taken into consideration for example the severity or duration of the confounding factors as well as patient compliance to treatment.
4) The effect of alternate concurrent medical drugs was not considered.

5) The study was performed over a limited time period – a study of greater duration and therefore greater sample size, would increase reliability.
6) No records are available for previous glaucoma procedures performed at CMJAH with which to compare the DS surgical outcomes

CHAPTER 3: RESULTS

3.1. SAMPLE ANALYSIS

Sample analysis was performed by analysing data available at every time point. As records were inconsistent, data gaps were present at various stages of the review period, including a certain number of cases lacking pre-operative and directly post-operative IOP measurements. As such, the number of cases with relevant records available, were interpreted accordingly for each time period or specific analysis.

3.1.1 DEMOGRAPHIC DATA

Patient records were obtained for 57 cases. Individuals who had undergone Deep Sclerectomy Surgery (DSS) were 61.33±12.78 years of age, with an age range of 58 years (22 years of age minimum and 80 years of age maximum). There is an even balance of representation of sex with 52.6% of the sample male patients and 47.4% females. The sample ethnicity (defining categories as proposed by SA census) comprised 77.2% Black Africans (n=44), 22.8% Caucasian (n=13) *(Caucasian population = 14.0% White (n=8) + 3.5% Indians (n=2))* and 5.3% Coloureds (n=3). Diagnosis pre-operation was POAG in 61.4% of cases (n=35), a further 21.1% (n=12) were diagnosed as PXG (Table 1).

Table 1: Baseline Demographic Data

Error! Reference source not found. Demographic Data	**ABSOLUTE**	**% OF COHORT**
Number of Patients	57	n/a
Age (years)	61.3±12.78	
Sex: Males/Females	30 / 27	52.6% **/** 47.4%
Laterality: RE/LE	27 / 30	47.4% / 52.6%
Race		
Black African	44	77.2%
White	8	14.0%
Coloured	3	5.3%
Indian	2	3.5%
***Diagnoses**		
POAG	35	61.4%
PXG	12	21.1%
JOAG	3	5.3%
PDS	2	3.5%
ACG	2	3.5%
SOAG	1	1.8%
ARG	1	1.8%
CACG	1	1.8%
Pre-operative IOP (mm Hg)	24.92±8.47	n/a
Pre-operative Cup-to-Disc Ratio	0.93±0.11	
<0.8	6	10.5%
0.8 – 0.9	13	22.8%
>0.9	34	59.6%
Pre-operative Medications		
0 Drops	2	3.5%
1 Drop	0	0
2 Drops	1	1.8%
3 Drops	27	47.4%
3 + Drops	25	43.9%
MMC Use (“yes”)	57	100%

Primary Open Angle Glaucoma (POAG). Pseudoexfoliative Glaucoma (PXG). Juvenile Onset Open Angle Glaucoma (JOAG). Pigment Dispersion Syndrome (PDS). Angle Closure Glaucoma (ACG). Secondary Open Angle Glaucoma (SOAG). Angle Recession Glaucoma (ARG). Chronic Angle Closure Glaucoma (CACG).

3.1.2 SAMPLE SIZE WITH AVAILABLE, DOCUMENTED DATA FOR ANALYSIS, AT EACH FOLLOW UP PERIOD, FOR SPECIFIED VARIABLES.

NOTE: due to poor record keeping, missing data and variable protocols being followed (being a retrospective record review), the sample number analysed varies according to available data for every time period and parameter. For example: Although 57 cases are included in the study, only 52 had IOPs recorded pre-operatively, 30 on day 1, 47 in month 6 etc. This table provides a summary of the number of files with relevant data available for every variable at each time period. This overview provides the reader with transparency regarding the sample size which is analysed for the important variables and outcomes below.

Table 2: Sample size analysed, per variable, per time period.

Follow-up time interval	Sample size per specified variable							
	IOP		No. of drops		Yag LGP performed		*Success / Failure rates	
	Number of records with data which could be analyzed	Number of records with Missing data	Number of records with data which could be analyzed	Number of records with Missing data	Number of records with data which could be analyzed	Number of records with Missing data	Number of records with data which could be analyzed	Number of records with Missing data
Pre-op	52	5	49	8	N/A	N/A	N/A	N/A
Day 1	30	27	40	17	39	18	51	6
Week 1	52	5	55	2	52	5	52	5
Month 1	52	5	51	6	49	8	51	6
Month 3	51	5	51	6	51	6	51	6
Month 6	47	10	47	10	47	10	51	6
Month 9	27	30	27	30	27	30	42	15
Month 12	20	37	20	37	20	37	38	19
Month 18	20	37	19	38	20	37	38	19
Month 24	25	32	24	33	25	32	38	19
Month 30	37	20	35	22	36	21	40	17
Month 36	34	23	32	25	31	26	33	24
Month 42	16	41	16	41	16	41	20	37
Month 45	9	48	9	48	9	48	13	44

*Sample size numbers analysed are larger in this group for the following reason: Failure was defined as an IOP maintained above 18mmHg – as such where IOPs are not available at a preceding visit but were noted to be maintained below 18 at follow-up visits, the preceding visit was labelled as success/qualified success. Where IOP was noted to be maintained at greater than 18 at follow-up visits, the time period with missing data was marked as ‘missing data’. Where surgery was noted as a failure or re-operation occurred at an earlier date – all follow-up visits were marked as ‘failure’.

3.2 INTRA-OCULAR PRESSURE (IOP)

3.2.1 MEAN ABSOLUTE IOP

The mean pre-operative IOP was 24.92±8.57mmHg with a mode of 22, minimum of 10 and maximum of 45mmHg. In comparison, the mean postoperative IOP (across all time periods up until and including 45 months post-operatively) is 13.46±3.39mmHg with a mode of 13, a minimum of 7.4 and a maximum of 22.73mmHg.

A paired samples t-test was used to determine if the differences seen in the mean pre- and post-operative IOP is statistically significant. The difference between the mean IOP between the two pairs is 11.69±6.8mmHg. The paired sample t-test shows that there is a statistically significant difference in the mean pre-operative and post-operative IOP scores, $t(47) = 9.405$; $p < 0.05$.

Table 2 below shows detailed IOP analysis for each time period over 45 months of post-surgical follow-up. At Day 1 post-surgery, IOP drops significantly to 11.93±6.56 mm Hg. IOP at Week 1 post-DS surgery is lowest (11.06±5.81 mm Hg) after which it rises again reaching a post-DS surgery high of 16.11±9.94 mm Hg at 45 months post-surgery. At all post-operative time points the IOP is significantly lower.

Table 3: Mean IOP prior to DS surgery and at each check-up post-surgery up to 45 months

	Sample size	No. of Records Missing data	Mean	Mode	Standard Deviation	Minimum	Maximum
Pre-op	52	5	24.92	22	8.572	10	45
Day 1	30	27	11.93	10	6.566	2	30
Week 1	52	5	11.06	10	5.581	0	24
Month 1	52	5	13.67	10	5.843	6	34
Month 3	51	5	15.48	10	9.401	2	60
Month 6	47	10	14.45	14	8.169	2	60
Month 9	27	30	12.74	12	4.880	0	22
Month 12	20	37	14.55	12	5.726	8	28
Month 18	20	37	15.55	12	5.934	4	28
Month 24	25	32	14.16	12	3.262	7	23
Month 30	37	20	15.11	15	5.339	2	34
Month 36	34	23	13.58	12	4.537	0	26
Month 42	16	41	15.56	10	7.155	8	39
Month 45	9	48	16.11	14	9.943	6	40

A visual depiction of the fluctuation in IOP scores (commencing prior to DS surgery and up to 45 months post-surgery) is presented in figure 1. It can be seen that IOP both drops significantly and remains significantly lower post-operatively when compared to pre-operative values.

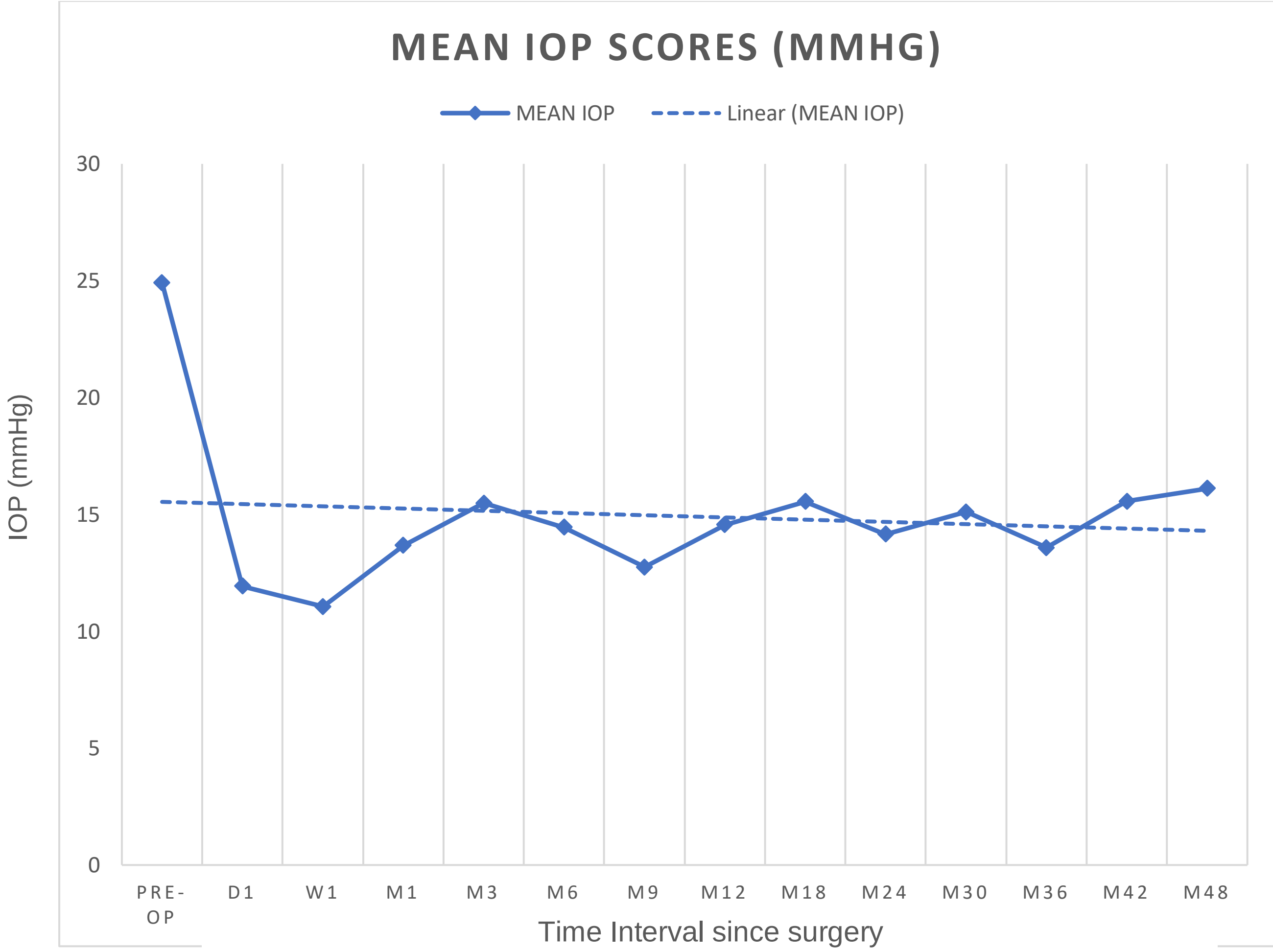

Figure 1: IOP change over time

*Pre-op – Pre-Operative, D - Day, W - Week, M - Month

3.2.2 IOP DROP POST-OPERATIVELY

The mean absolute IOP drop (pre-operative IOP – post-operative IOP) is 13.14mmHg (46.1% decrease) day 1 post-operatively. The greatest mean IOP drop is found at week 1 post-operatively with a mean drop of 14.2mmhg (52.6% decrease). The mean IOP drop is 11.91mmHg (38.9%) at 1 year and 13.33mmHg (46.8%) at 45 months after surgery.

A visual depiction of the fluctuation in absolute drop in IOP scores (commencing prior to DS surgery and up to 42 months post-surgery) is presented in Figure 2.

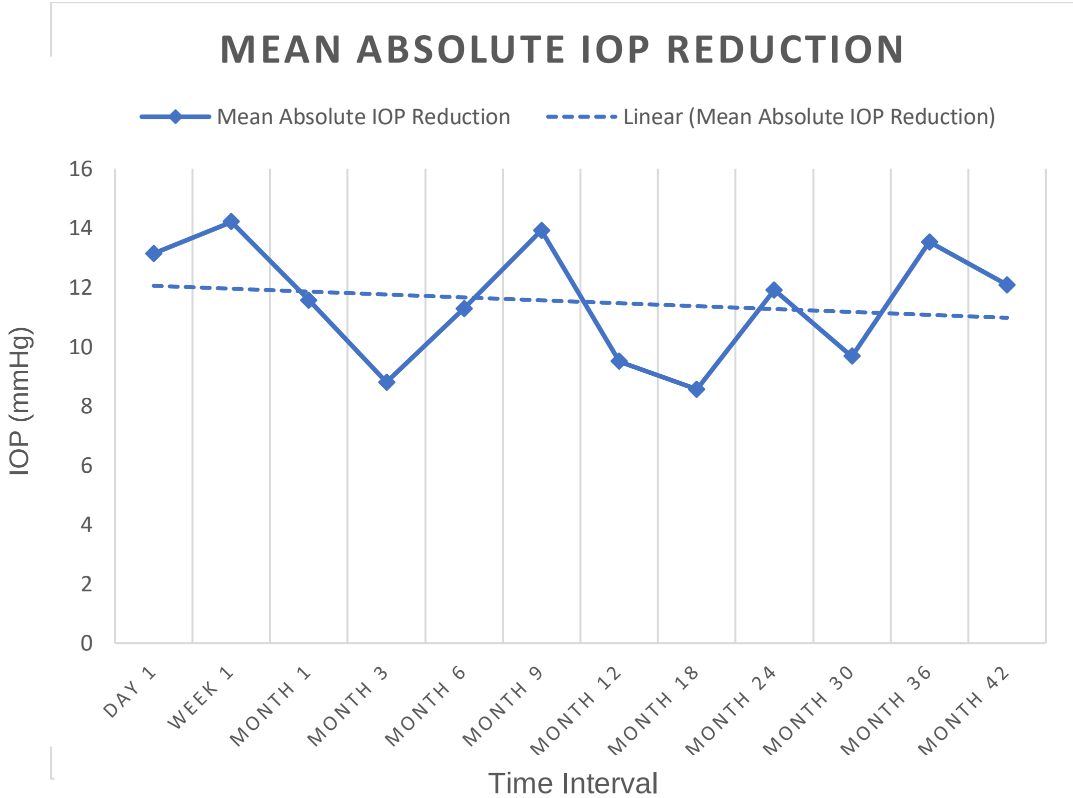

Figure 2: Mean absolute IOP reduction over time

*Pre-op – Pre-Operative, D - Day, W - Week, M - Month

3.2.4 SUB-GROUP IOP ANALYSES OF JUNIOR VS SENIOR SURGEONS

3.2.4.1. Comparative absolute mean IOP over time

Of all eyes included in this analysis (n=51), 9 cases (17.6%) were operated on by junior surgeons (supervised by senior surgeon, Dr Susan Williams) while 42 (82.4%) were operated on by the senior surgeon herself, Dr Susan Williams. Table 4 below contrasts the mean IOP per time interval for each junior vs senior surgeon. Table 4 also, importantly, reflects the number of cases analysed at each time period – the sample size for junior surgeons is exceedingly small and so results must be interpreted with caution.

Table 4:Junior vs Senior mean absolute IOP

TIME INTERVAL	**JUNIOR MEAN ABSOLUTE IOP (mmHg) (n=9 cases)**	**SENIOR MEAN ABSOLUTE IOP (mmHg) (n=42 cases)**
PRE	21.2 (n=9)	25.3 (n=39)
D1	18 (n=2)	11.5 (n=26)
W1	10.0 (n=9)	9.1 (n=40)
M1	11.0 (n=9)	14.1 (n=40)
M3	14.3 (n=8)	17.0 (n=40)
M6	11.7 (n=9)	15.1 (n=38)
M9	10.4 (n=5)	13.3 (n=22)
M12	12.0 (n=2)	14.9 (n=17)
M18	12.0 (n=3)	16.2 (n=17)
M24	12.0 (n=4)	14.6 (n=21)
M30	14.2 (n=6)	15.3 (n=30)
M36	13.8 (n=5)	13.6 (n=26)
M42	15.0 (n=2)	15.6 (n=14)
M45	14 (n=2)	16.7 (n=7)

*D - Day, W - Week, M - Month

A visual depiction of the comparative fluctuation in mean post-operative IOP scores between junior and senior surgeons (commencing prior to DS surgery and up to 42 months post-surgery) is presented in Figure 3. Trend lines are superimposed to better understand the presented data.

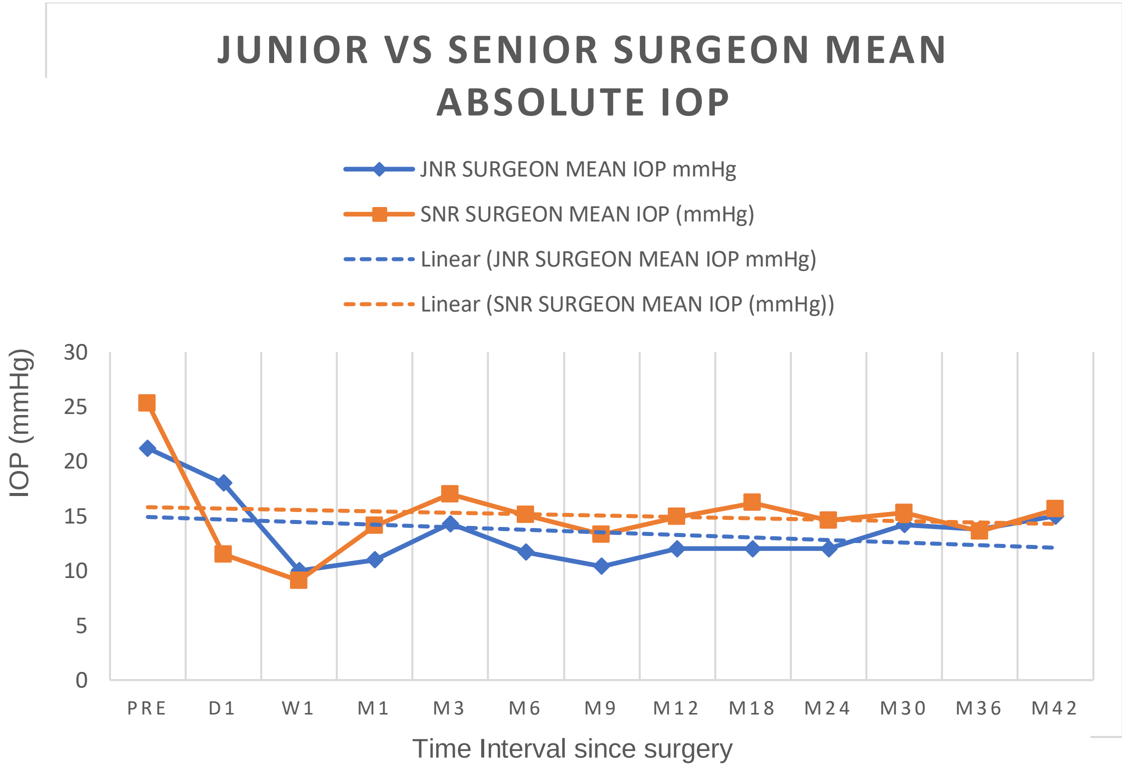

Figure 3: Junior vs senior comparative, mean absolute IOP over time.

*Pre – Pre-Operative, D - Day, W - Week, M - Month

The trend lines above demonstrate similar outcomes between the 2 groups. Senior surgical cases start with higher IOPs pre-operatively which carry over to higher post-operative IOPs. Day 1 data for the junior groups reflects the mean of only 2 cases (one case had a day 1 post-operative IOP of 12mmHg and the other an IOP of 24mmHg) and thus skews the gradient of the trend line to a slightly sharper decline. When day 1 post-operative IOP is removed and the graph is started with week 1 IOP scores – the trend lines for senior and junior cases run relatively parallel, with senior surgical results demonstrating a slightly superior gradient, as can be noted in figure 4 below.

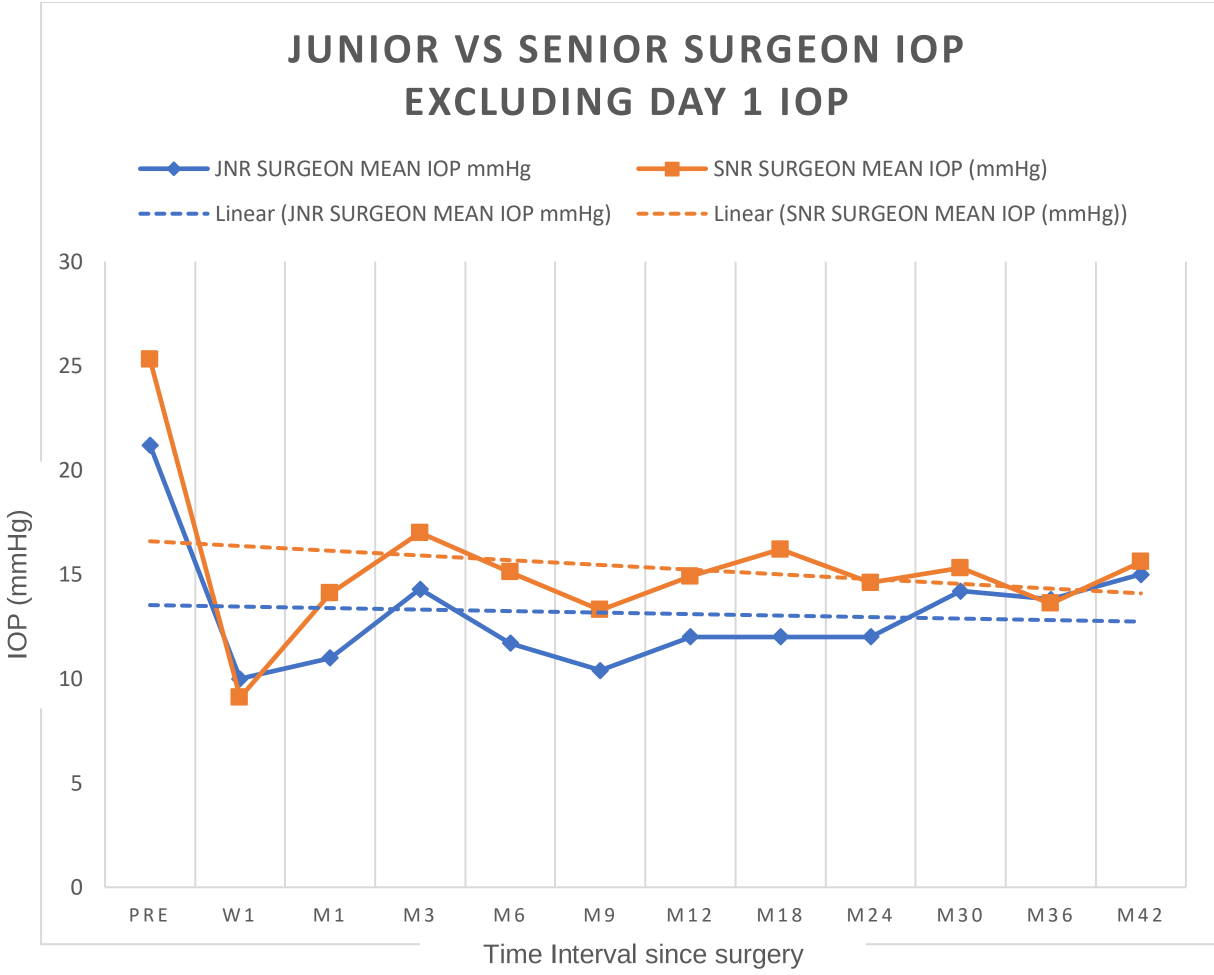

Figure 4: Junior vs Senior mean absolute IOP excluding day 1 post-operative IOP

*Pre – Pre-Operative, D - Day, W - Week, M - Month

3.2.4.2. Comparative mean IOP reduction over time.

Excluding day 1 post-operative data, the senior surgeon has superior results when it comes to absolute IOP reduction, having a greater mean IOP reduction average of 2.1mmHg (1.3% greater percentage IOP reduction than junior surgeons)

A visual depiction of the comparative fluctuation in mean post-operative IOP reduction scores between junior and senior surgeons (commencing prior to DS surgery with post-operative results demonstrated from week 1 up to 42 months post-surgery) is presented in Figure 5 below.

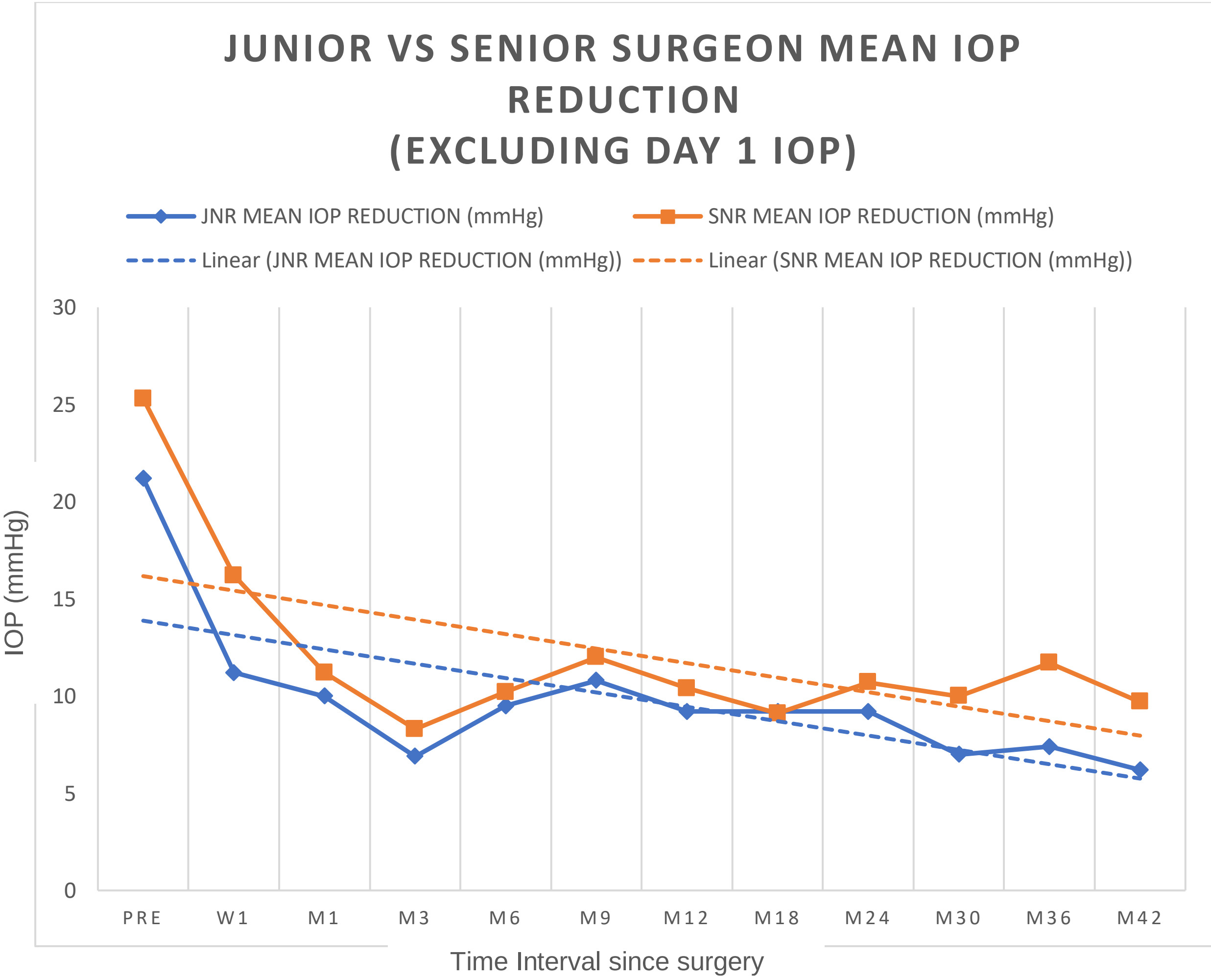

Figure 5: Junior vs senior mean IOP reduction over time

*Pre – Pre-Operative, D - Day, W - Week, M - Month

In figure 5, it can be seen that mean IOP reduction is comparable between junior and senior surgeons, with trend lines running more or less parallel between the 2 groups but slightly higher in the senior group.

3.3 THE AVERAGE NUMBER OF DROPS USED AT EACH TIME POINT

No drops are used immediately post-operatively with a trend to an increasing number of drops being used over time. By 45 months the greatest number of patients require maximal drop therapy to maintain IOP. This trend toward increasing drops being required over time is an indication of decreasing surgical success over time.

Table 5: Number of drops used over time.

	Mean	Mode	Standard Deviation	Minimum	Maximum
D 1	0.0000	0.00	0.00000	0.00	0.00
W 1	0.0800	0.00	0.56569	0.00	4.00
M 1	0.0612	0.00	0.42857	0.00	3.00
M 3	0.1429	0.00	0.45644	0.00	2.00
M 6	0.2708	0.00	0.70679	0.00	3.00
M 9	0.2222	0.00	0.69798	0.00	3.00
M 12	0.4500	0.00	0.99868	0.00	3.00
M 18	1.2632	0.00	1.24017	0.00	3.00
M 24	1.1200	0.00	1.20139	0.00	3.00
M 30	1.3514	0.00	1.37873	0.00	4.00
M 36	1.2424	0.00	1.29977	0.00	3.00
M 42	1.2500	0.00	1.48235	0.00	4.00
M 48	1.2308	0.00	1.53590	0.00	4.00

*D - Day, W - Week, M - Month

Figure 6 below presents a trend line, superimposed on data from the above table (commencing day 1 after DS surgery and up to 45 months post-surgery), and demonstrates a clear increase in the number of drops used over time.

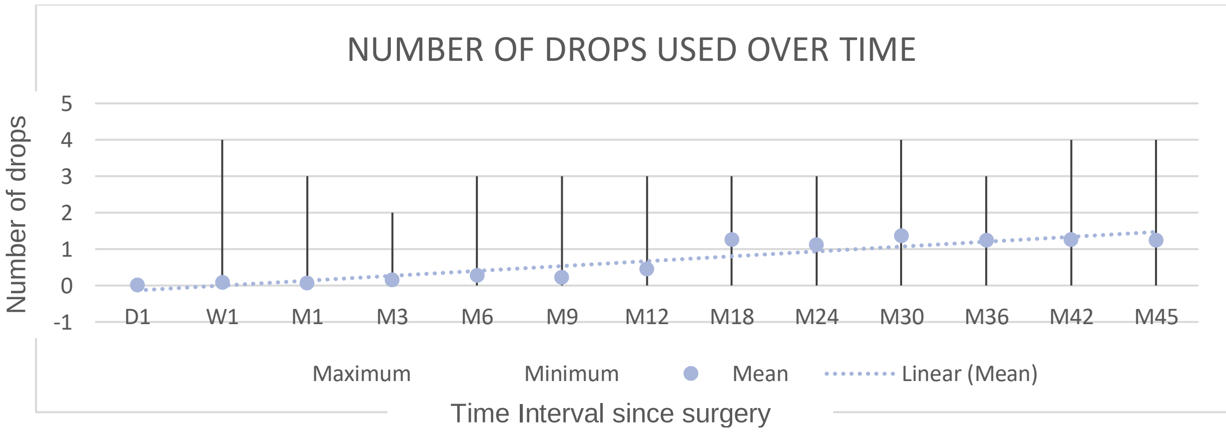

Figure 6: Number of drops used over time.

*D - Day, W - Week, M - Month

3.4 SURGICAL SUCCESS, QUALIFIED SUCCESS, QUALIFIED FAILURE AND FAILURE

Figure 7 below represents a visual representation of surgical success and qualified success versus qualified surgical failure and surgical failure over time.

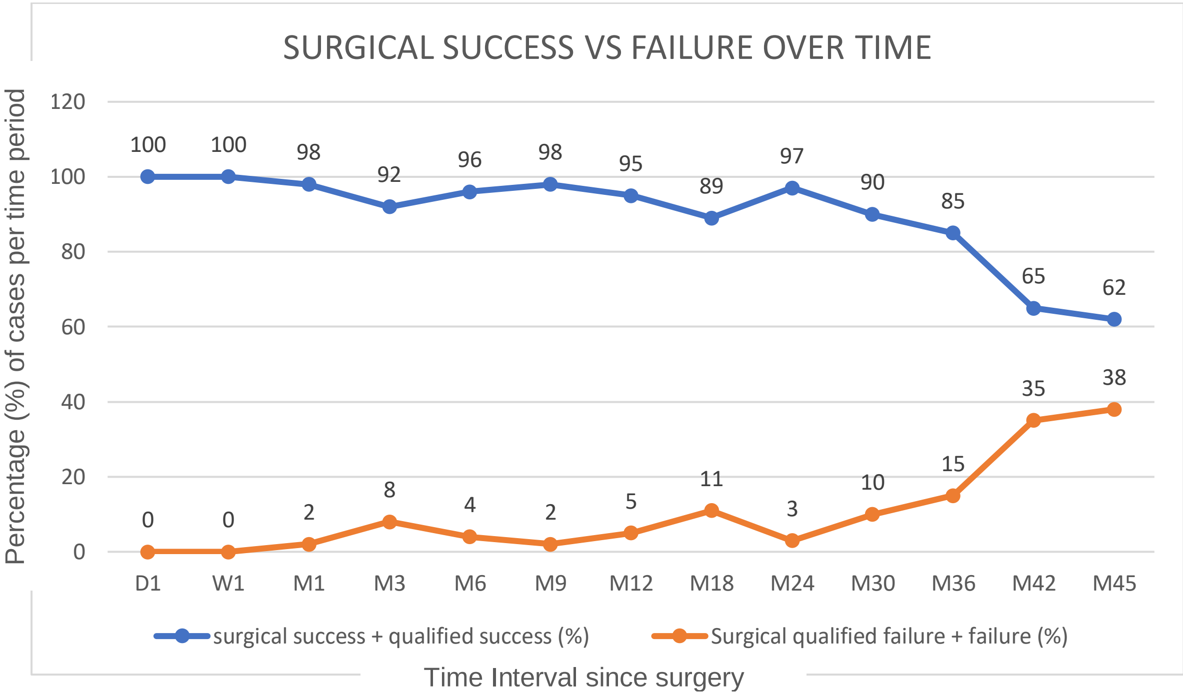

Figure 7: Surgical success vs surgical failure over time

* D - Day, W - Week, M - Month

As noted above, surgical success is high, staying within in the 90th percentiles until 30 months post-operatively and decreasing slightly at 36 months post-operatively to 85%. Overall, there is a gradual decrease in success rate over time. The steep drop-off at 42 and 45 months post-operatively may be confounded by:

1. a high patient loss to follow-up with problematic patients demonstrating a higher tendency to follow-up.
2. a large number of patients who have not yet reached the required post-operative time period to have data entered to be analysed.

Overall, the mean surgical success rate is 89.8% and the overall failure rate is 10.2%.

3.5 KAPLAN-MEIER SURVIVAL ANALYSIS

In this analysis, failure is specified as the event and was defined as the first time point where IOP > 18 with medical drop therapy and where the IOP stayed above 18 for all other time points or loss of light perception/need for repeat surgery occurred. All cases who never met these criteria over the time period, or who dropped out before meeting this criterion, were categorised as "censored". Due to missing data, Month 1 was used as the starting point for all participants (Day 1 and Week 1 was excluded). The Time variable is measured in months. Table 6 below represents the Kaplan-Meier case processing summary.

Table 6: Kaplan-Meier case processing summary

Case Processing Summary

Total N	N of Events	Censored	
		N	Percent
52	9	43	82.7%

From the table above it can be seen that there are 9 participants for whom surgery failed sometime in the specified time period, whilst 43 participants (82.7%) either did not meet the criteria for failure within the specified time period or dropped out before they met the criteria for failure.

With regards to patients who met the criteria for failure over time:

- 1 patient met the criteria for failure at month 12
- 1 patient met the criteria for failure at month 18
- 4 patients met the criteria for failure at month 30
- 2 patients met the criteria for failure at month 42 and
- 1 patient met the criteria for failure at month 45.

When the last failure occurred at month 45, surgery was still seen to be successful (complete + qualified success) for 64.8% of patients. These results are illustrated in the Kaplan-Meier survival graph below (Figure 8: Kaplan-Meier survival function graph).

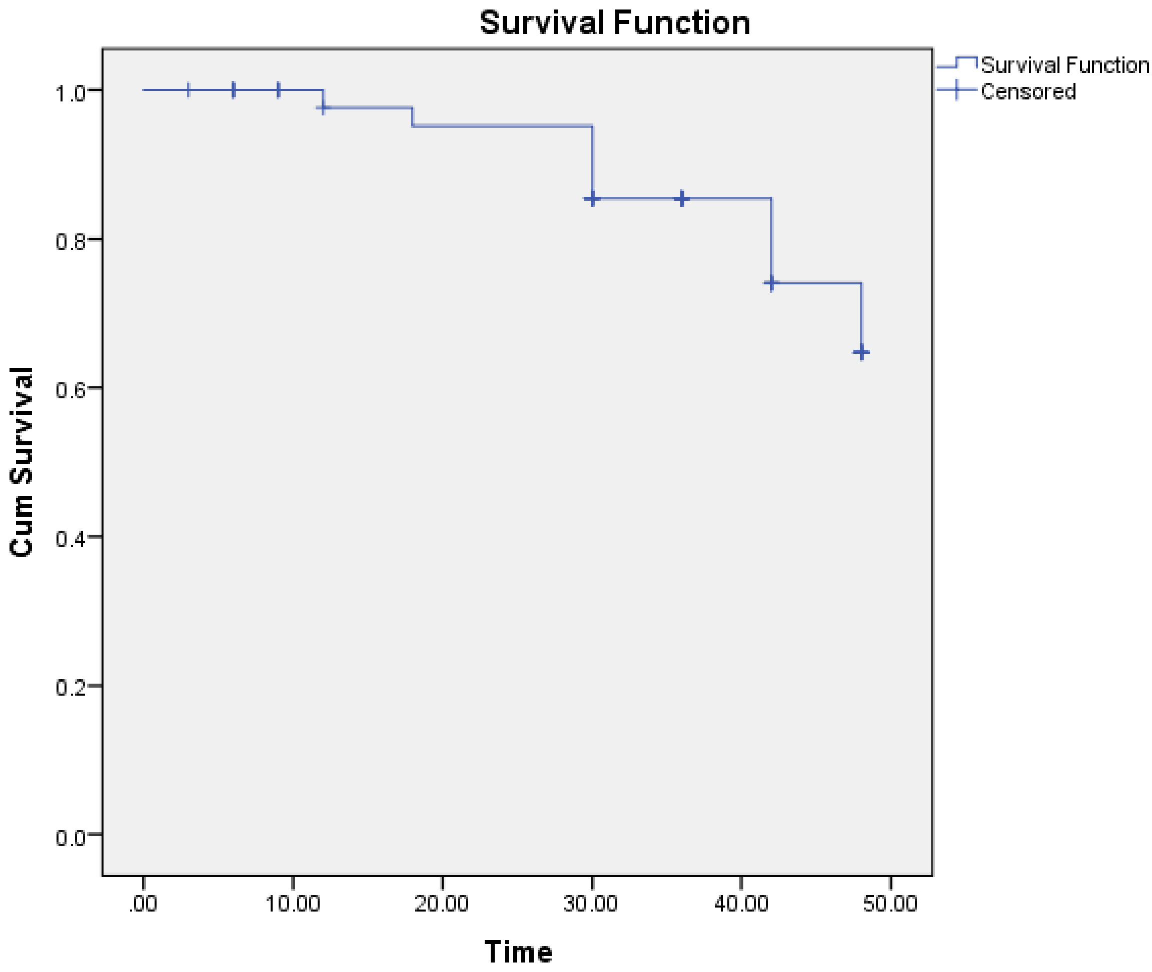

Figure 8: Kaplan-Meier survival function graph

The dramatic drop off in survival at 42 and 45 months may be skewed due to:

1. Patient drop off – with only 20 cases following up at month 40 and 13 cases at month 45 versus 33 cases at month 36 and higher at earlier time points.
2. A large number of patients not yet reaching the required post-operative time period to have data entered to be analysed.

3.6 POST-OPERATIVE LASER GONIOPUNCTURE

Of the Deep Sclerectomy Procedures comprising the entire sample, 69.2% of cases required laser goniopuncture (LGP) (36 out of 52 cases) at some point during the 45 month follow-up period. 8 of these cases (22% of all cases receiving LGP) required multiple LGPs.

Table 7 below gives the absolute number of LGPs performed at every time interval studied and presents the number as a percentage of the sample size analysed at said time interval. It can be seen that the greatest absolute number of LGPs performed per post-operative time period occurred between months 1 and month 6.

Table 7: Breakdown of Laser Goniopuncture procedures performed per time interval

Time interval	Number of procedures performed at each time interval	Sample Size (No. of records with data available to analyze.)	% of sample per time interval receiving goniopuncture
D1	1	39	2.6
W1	2	52	3.8
M1	10	49	20.4
M3	14	51	27.5
M6	9	47	19.1
M9	3	27	11.1
M12	4	20	20
M18	1	20	5
M24	2	25	8
M30	1	36	2.8
M36	1	31	3.2
M42	0	16	0.0
M45	1	9	11.1
TOTAL	49		

Figure 9 below represents the percentage of overall LGP procedures performed per time interval and presents a similar pattern to Table 7 above.

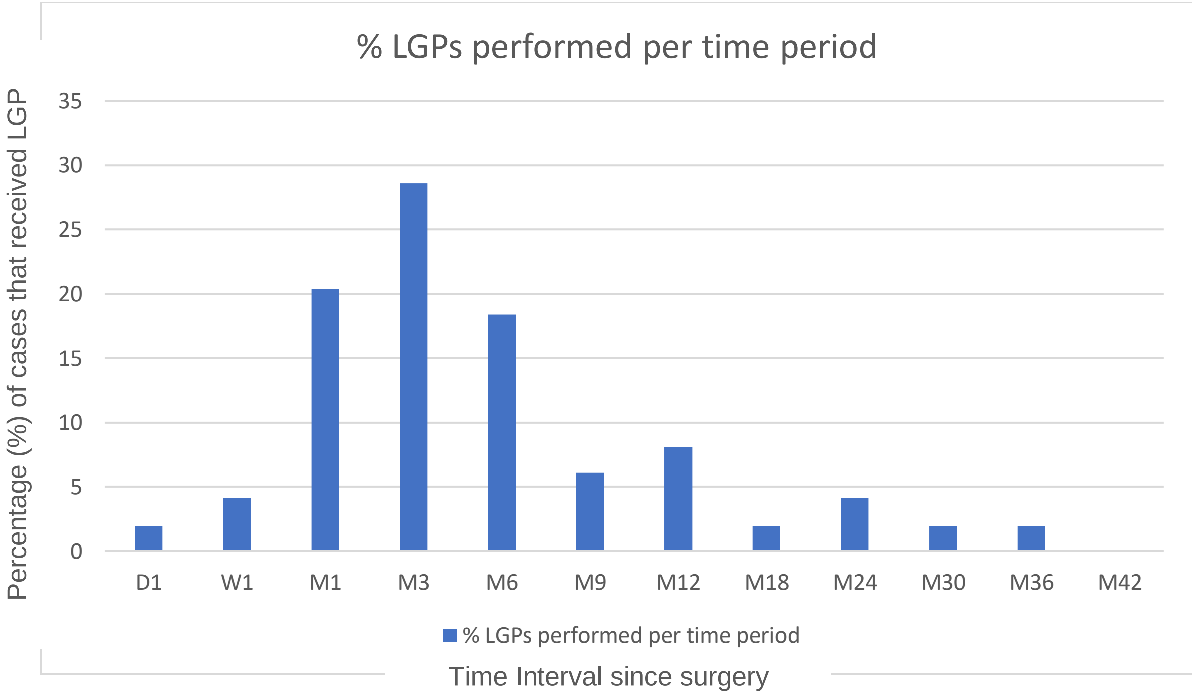

Figure 9: Percentage of overall laser goniopunctures performed per follow-up visit

Of all LGP performed, the greatest number were performed in month 1 (20.4%) and month 3 (28.6%) post deep sclerectomy surgery. Overall, 26.5% of all LGPs were performed within the first month post-DS, 55.1% in the first 3 months post-DS and 73.5% within the first 6 months post-surgery. 87.7% of all LGPs were performed within the first year post DS surgery. Only 6% of all LGPs performed were done after 1 year post DS surgery.

LGP was complicated by iris plugging in 3 cases, 5.8%.

3.7 ADDITIONAL PROCEDURES OTHER THAN LGP

In addition to LGP, the following procedures were performed to manage post-operative IOP and improve operative success rates:

1. Bleb needling – bleb needling was performed in 2 cases (3.9%), 1 was performed in month 18 and the other in month 30.
2. Intra-bleb MMC – MMC was administered to 1 case (1.9%) post-operatively on month 9.
3. Suture release - this was performed on 1 case (1.9%) post-operatively at month 30
4. SLT – SLT was performed on 2 cases (3.9%) post-operatively, 1 in month 12 and another in month 30 post DS surgery.

3.8 PERI-OPERATIVE COMPLICATION RATES

1) Intra-operative perforation rates

Intra-operative perforation of the trabeculo-descemet's membrane occurred in 1 case (0.2% of cases) and required the creation of a surgical peripheral iridotomy. This case did not develop hypotonous complications.

Intra-operative micro-perforation (indicative of good aqueous outflow and not considered a complication) was documented in 23.5% of cases (n=12). Of these, 16.7% (n=2) presented with hypotonous maculopathy. Intra-operative micro-perforation was not statistically significantly associated with hypotonous maculopathy as this was equally likely to occur whether or not intra-operative micro-perforation was documented in the surgical notes.

2) Post-operative complication rates

I. *Flat Anterior Chamber*

No cases were recorded with flat anterior chambers.

II. *Hyphaema*

One case (n=1, 1.9% of sample) was recorded at Day 1 and Week 1 post-operatively, the hyphaema was completely resolved by the 1 month check-up.

III. *Hypotonous Maculopathy*

At Day 1 post-operatively, two cases (n=2, 3.8%) of hypotonous maculopathy were noted. At Week 1 this rose to four cases (n=4, 7.7%) of the sample. At the first month post-operatively, five cases had hypotonous maculopathy (n=5, 9.6%). At months 3, 6 and 9 only one case of hypotonous maculopathy was noted. This individual did not attend further follow-up.

Thus, the highest rate of hypotonous maculopathy was noted at 1 month post operatively. One of these cases was due to a bleb leak which was repaired and resulted in resolution. All other cases, except for one, resolved on conservative management – receiving topical steroids. The final case of hypotonous maculopathy defaulted follow up and whether or not resolution occurred is unknown.

IV. Choroidal Haemorrhage or Detachment

At Day 1 there were no cases of choroidal haemorrhage or detachment. At week 1 post-operatively there was one instance (n=1, 1.9%). This individual did not attend a check-up at Month 1 but was present for a follow up at month 3, at which point the choroidal detachment was still noted. The individual presented at months 6, 9 and 12 but no further mention of choroidal detachment was made in the medical notes, indicating resolution of the choroidal detachment by month 6 post-operatively.

V. Cataract Formation

Clinic records regarding the status of the lens were poor and data was insufficient to determine the rate of cataract formation.

3.9 RISK ANALYSIS

Cox Regression analysis is used to check whether any statistically significant factors can be identified which may act as either risk factors for or factors protective against surgical failure.

From the significance row in Table 8 below, it can be seen that none of the predictors statistically significantly predict the risk that the surgery will fail. For example, a one unit increase in age does not significantly increase or decrease the probability of surgical failure on any given month. Similarly, increases in IOP pre-surgery or Visual acuity pre-surgery also has no significant effect on the probability of surgical failure. There is no difference between the races or genders in the probability of surgical failure at any given month. There is also no difference between patients who had a pre-existing inflammatory disorder and those who did not on the probability of surgical failure on any given day. Finally, there is no significant difference in the probability of surgical failure between patients who had previous cataract surgery and those who did not, or between patients who had pre-existing scarring and those who did not ($p>0.05$ for all predictors).

Table 8: Cox Regression Analysis

Factor	Age	Race	Sex	VA (pre-op)	IOP (pre-op)	Pre-existing inflammatory disorder	Previous cataract surgery	Previous scarring.
Significance	0.100	0.798	0.748	0.069	0.250	0.995	0.471	0.986

3.10. VISUAL ACUITY (PRE AND POST) DS SURGERY

Visual Acuity (VA) was assessed pre-DS surgery, post-surgery at week 1, and at months 1, 3, 6, 9 and 12. Wilcoxon Signed Rank tests were utilised as the data was found to be symmetrical.

3.10.1. VA one week post DS surgery

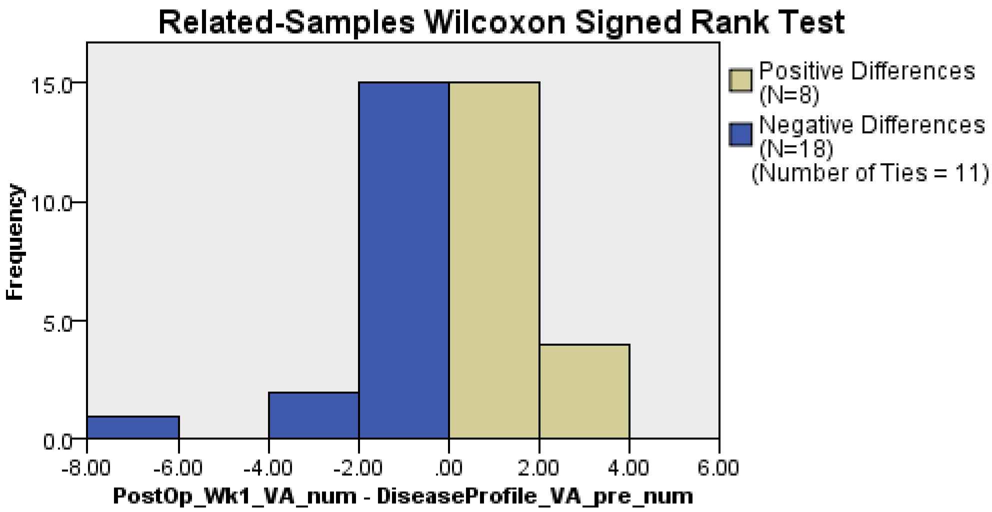

Figure 10: VA one week post DS surgery

There is no statistical difference between the pre-operative VA findings and post-operative VA findings (week 1, $p<0.05$). Of 37 patients for whom there were data, eight candidates (21.6%) showed a positive VA improvement, eighteen patients (48.6%) showed a decline in VA and 11 individuals (29.7%) showed no change on VA at this time check (Figure 10).

3.10.2. VA one month post DS surgery

There is no statistical difference in VA scores pre- and post-operation at 30 days ($p<0.05$, Figure 11). Patient data were obtained for 41 individuals at this check-up. Of these, 16 cases (39.0%) demonstrated a positive shift in VA compared to pre-operative measures (improved sight). In contrast 31.7% (n=13) demonstrated VA scores that were worse than pre-operative levels, and 29.3% (n=12) showed no change

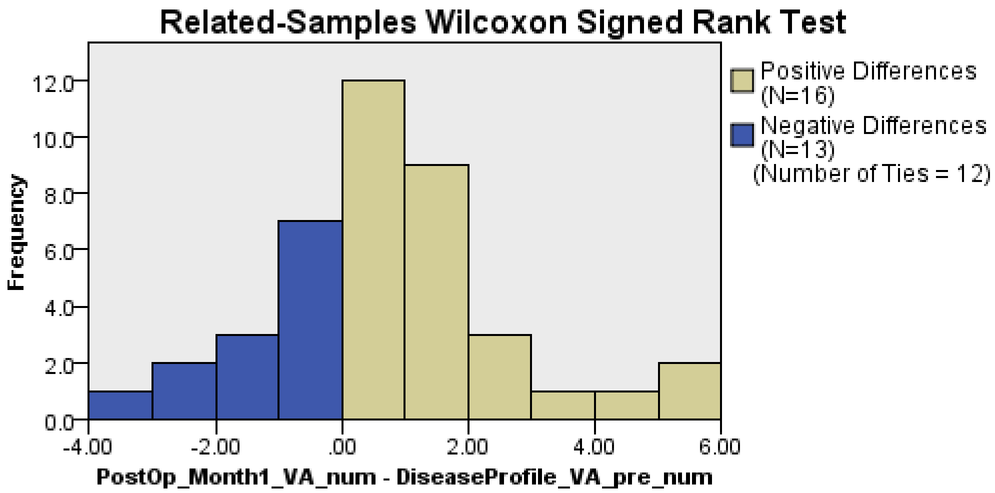

Figure 11: VA one month post DS surgery

3.10.3. VA three months post DS Surgery

There is no statistical difference in VA scores at 90 days ($p<0.05$). However, of the 42 cases for whom there were data at this check-up, 40.5% demonstrated an improved VA score and 23.8% had VA that stayed constant. A further 35.7% (n=15) demonstrated worse VA than prior to undergoing DS surgery (Figure 12).

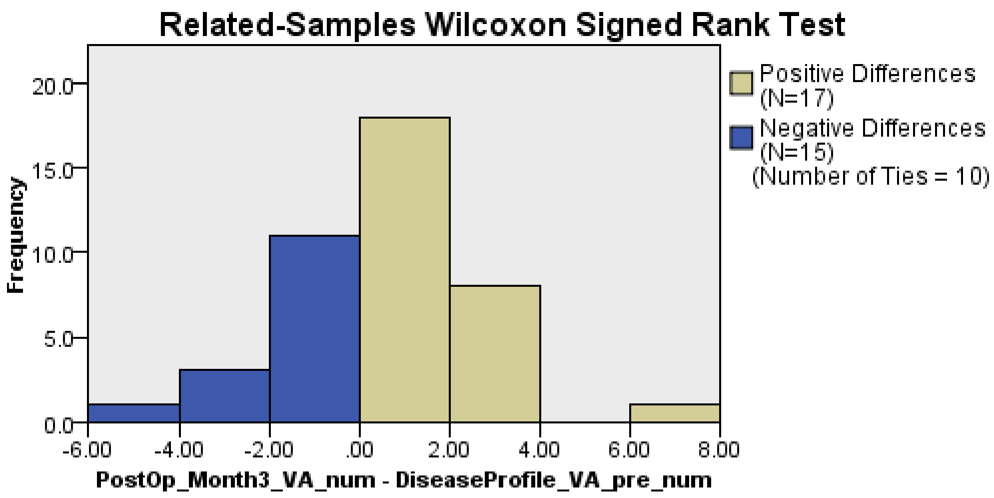

Figure 12: VA three months post DS surgery

3.10.4. VA six months post DS surgery

At six months there is no statistical difference between the pre-operation and post-operation visual acuity scores ($p<0.05$). Positive VA changes were identified in 29.7% of the sample (n=11 of 37 cases), while 40.5% (n=15) demonstrated lower VA scores than prior to the DS surgery (Figure 13). No change in VA was noted in 29.7% of instances.

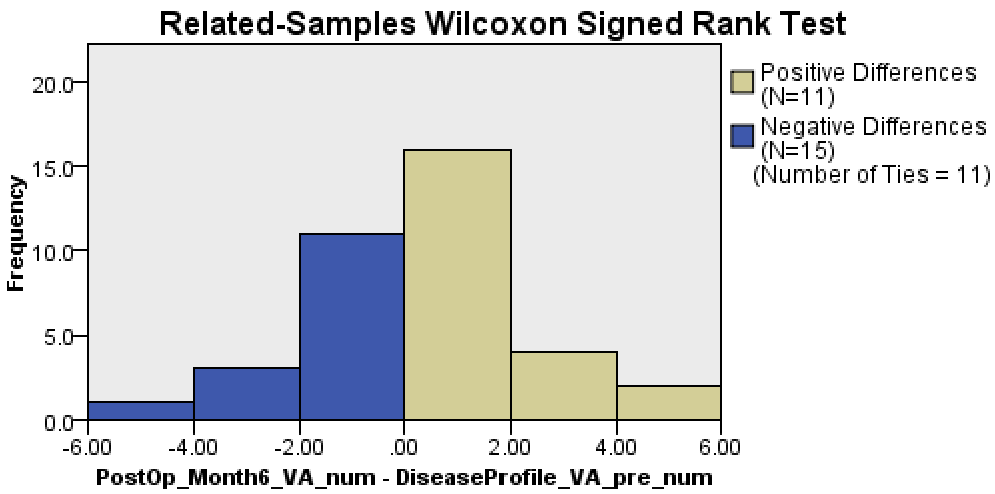

Figure 13: VA six months post DS surgery

3.10.5. VA nine months post DS surgery

Follow-up records were only available for 21 individuals at the nine-month post-DS surgery check-up (Figure 14). There is no statistical difference between pre- and post-DS surgery VA scores at nine months ($p<0.05$). At this check-up 23.8% of candidates (n=5) were judged to have improved VA scores, 42.9% (n=9) to have poorer scores than prior to undergoing surgery and a further 33.3% (n=7) had no pre to post VA score change.

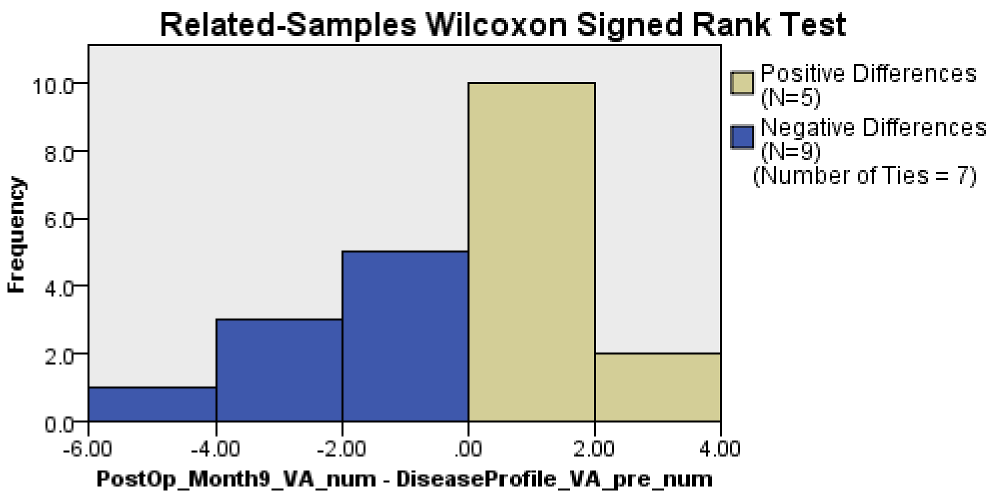

Figure 14: VA nine months post DS surgery

3.10.6. VA twelve months post DS surgery

Visual Acuity at one-year (12 months) post-DS surgery is statistically significantly (p=0.016) worse than prior to undergoing the procedure. Of consideration, however, is the small sample size available at 12 months post-operation (n=16) indicative of a combination of drop-off rates for follow-up over time as well as poor record keeping in terms of documenting post-operative visual acuity. At 12 months after the DS procedure, 18.8% (n=3) of patients' VA scores were better than pre-DS scores, 6.3% remained unchanged (n=1) and 75.0% (n=12) had demonstrably poorer VA at this check-up (Figure 15).

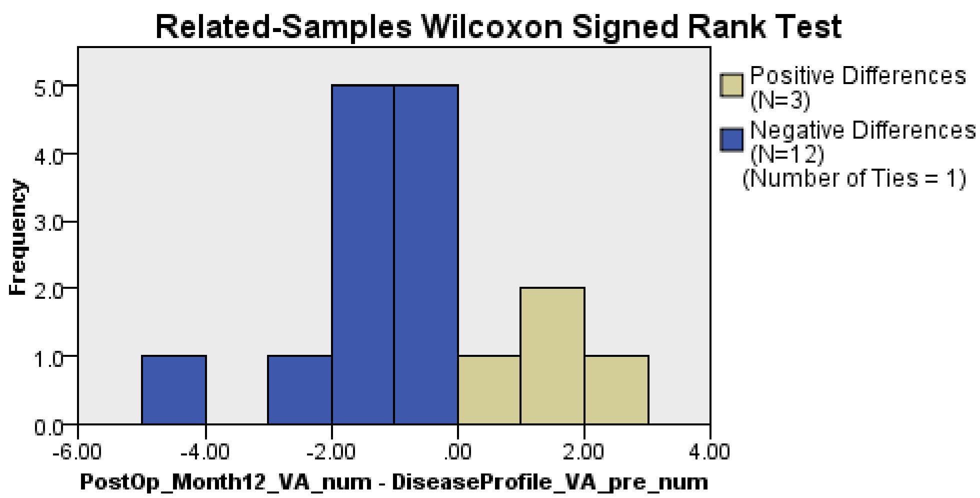

Figure 15: VA twelve months post DS surgery

3.10.7. Summary of Visual Acuity Findings[1]

A summary of the VA scores at each time point is presented in Table 9 below.

Table 9: VA score summary per time interval

	PRE-OP	POST 1 week	POST 1 month	POST 3 months	POST 6 months	POST 9 months	POST 12 months
N (number of patient records)	51	37	41	42	37	21	16
Mean	6.62	6.02	6.82	6.61	6.60	6.25	6.10
Mean VA Score (actual VA ratio)	0.17	0.17	0.17	0.17	0.17	0.17	0.17
Median	6.00	6.00	6.50	6.00	7.00	6.00	6.00
VA Score Mode (actual VA ratio)	0.17	0.17	0.17	0.17	0.25	0.17	0.17
Mode	4	4.00	4.00	4.00	4.00	5	6.00
VA Score Mode (actual VA ratio)	CF	CF	CF	CF	CF	0.1	0.17
Std. Deviation	2.42	2.26	2.43	2.45	2.61	2.83	1.71
Minimum	3.00	4.00	3.00	4.00	1.00	1.00	3.00
Minimum VA recorded (actual VA ratio)	HM	CF	HM	CF	NLP	NLP	NLP
Maximum	13.00	13.00	11.00	13.00	12.00	12.00	9.00
Maximum VA recorded (actual VA ratio)	1.2	1.2	0.8	1.2	1.0	1.0	0.5

Table note: shaded rows reflect numeric code applied to VA ratios to facilitate statistical analyses. Non-shaded rows present the actual VA ratios.

[1] In order to analyse the VA scores statistically, the following numeric codes were applied: 1 = NLP; 2 = LP; 3 = HM; 4 = CF; 5 = 0.1; 6 = 0.17; 7 = 0.25; 8 = 0.33; 9 = 0.5; 10 = 0.67; 11 = 0.8; 12 = 1; 13 = 1.2.

3.11. SUMMARY OF RESULTS

The primary aim of this retrospective analysis was to determine the outcome of the Deep Sclerectomy Surgeries performed at Charlotte Maxeke Academic Hospital in Johannesburg South Africa. Secondary aims were to describe the patient population, describe the underlying disease profile and determine any predictors of surgical outcomes.

The results presented indicate that the patients undergoing Deep Sclerectomy surgery at this hospital are primarily Black African (77.2%), with an average age of 61.33±12.78 years (noting the wide age range of 58 years amongst this sample) and may be either sex. Most patients are diagnosed with POAG (60.8%) or PXG (23.5%).

Intra-Ocular Pressure (IOP) showed a statistically significant drop from a pre-operative IOP of 23.73±9.14 mm Hg (p=0.000). Compared to pre-operative scores, IOP remained significantly lower from day 1 post-operatively, across all time points up to and including the 45month check-up (16.11±9.96mmHg). At day 1, the absolute and percentage drop in IOP was 13.14mmHg and 46.0%, at 12 months postoperatively they were 9.5mmHg and 35.9%, at 36 months, 13.52mmHg and 41.6%, and at 45 months post-operatively they were 13.33mmHg and 46.8%. IOP reduction is similar when comparing senior to supervised junior surgical cases.

Surgical success and qualified success were 100% on day 1 post-operatively then dropped off to 95 % at 12 months, 85% at 36 months and 62% at 45 months. According to Kaplan-Meier survival curves – surgical survival was 64% at 45 months. The drop in surgical success and surgical survival at 45 months was certainly influenced by a high patient number that had not yet reached the required post-surgical follow-up time and due to high patient loss to follow-up at this time point.

LGP was required by the majority of patients (69.2%) by the end of the 45 month follow-up period and the majority were performed in month 1 and month 3 after deep sclerectomy surgery. Iris plugging occurred in 5.8% of cases.

Complications were rare with hyphaema occurring in 1.9% of cases, hypotonous maculopathy in 9.6% (but only persisted in 1 case (1.9%) at month 6 post-operatively which was lost to follow up there after) and choroidal detachment in 1.9%. All complications were transient, resolving on medical therapy alone, except for a single case of hypotonous maculopathy secondary to a bleb leak which required suturing, and another case lost to follow up.

No factors, including age, sex, pre-operative VA or IOP were predictive of surgical success or failure in this retrospective review.

Visual Acuity did not show deterioration statistically over time and visual acuity was maintained in this sample until 12 months post-operation. The statistical drop in VA at this time point is most likely due to extraneous factors, such as cataract formation (records of which were too poor to analyse).

CHAPTER 4: DISCUSSION

First off, it is important to recognise that this study has severe limitations due to the design being that of a retrospective record review. Inconsistent and incomplete records, missing data, inconsistent follow up periods and lack of measurement and follow up protocols leaves reliability and interpretation of data wanting. Sample size which is analysed is erratic and constantly adapted throughout the study to allow for interpretation of data despite the large data gaps – this results in a negative impact on statistical reliability. This said, however, the results seem to be consistent with what one would expect and echoes those found elsewhere in South Africa, Africa and internationally.

The primary objective of this study was to determine overall surgical outcomes and associated complications of DS surgery at CMJAH. The aim of this being to determine whether surgical outcomes are comparable to international standards and whether DS is an acceptable surgical alternative for the control of glaucoma in select patients at CMJAH.

Patient demographics at CMJAH represent the South African population with a majority black (77%) patient profile. The epidemiology of glaucoma in this study population is also in keeping with that found in literature where our study patients presented with predominantly POAG and a distant but definite second being glaucoma secondary to PXG. According to a study by Rotchford that looked at the prevalence and subtypes of glaucoma in Temba, South Africa, this population presented with POAG as their most common underlying diagnosis having an adjusted prevalence of 2.9% (95% CI, 1.9% - 4.3%).[18] The prevalence of secondary forms of glaucoma was approximately 2/3 of that number with a prevalence of 2%. Of the secondary glaucoma's, PXG was the most common cause being responsible for 16% of all cases in Temba.[18] PXG was also noted to be responsible for 21.6% of all glaucoma in Hlabisa, South Africa.[19]

In this study of a majority black south African population, the age range for the diagnosis of POAG is wide – occurring early with aggressive disease. This same observation was underscored in a study by Kyari et al which looked at the epidemiology of glaucoma in Sub-Saharan Africa. Kyari et al found that POAG is the most common cause of glaucoma in Sub-Saharan Africa.[19] Moreover, they found that it has an early onset in this predominantly black population and that it progresses faster in comparison to the same disease in caucasians. They specifically noted that African derived groups tended to have higher base line IOP and thinner central corneal thickness which are both specifically determined to be risk factors lending towards both the development of glaucoma as well as more aggressive disease.[19]

Regarding post-operative pressure control outcomes:

Surgical outcomes in this retrospective review are far superior to a previous randomised controlled trial done on a majority black population in west Africa. In the randomised controlled trial, 39 patients were enrolled into the study and randomised to either receiving or not receiving MMC intra-operatively[11]. In the group receiving intra-operative MMC, the success rates of achieving an IOP of less than 18 were 79% at 12 months and only 38% at 18 months versus 95% and 89% respectively in this review of the surgical outcomes of deep sclerectomies performed at a Johannesburg academic hospital. This retrospective review proves that surgical success can be achieved in a majority black population.

In a systematic review, by Cheng et al, looking at the efficacy of nonpenetrating glaucoma surgery in the treatment of POAG, it was found that the mean percentage drop in IOP at 24 months was 41.7%, at 36months it was 39.8% and at 48months, 36.2%.[16] In this retrospective review, the surgeons at CMJAH achieved similar percentages with a mean drop in IOP at 24 months of 38.9%, at 36 months of 41.6% and at 45 months, 46.8%.

When looking at the qualified success rates (IOP ≤ 21mmHg ± medical drop therapy), Cheng et al found this to be 78% at 48 months compared to the surgeons at CMJAH achieving a qualified success rate (IOP≤18mmHg± medical drop therapy) of 85% at 36 months and 62% at 45 months.[16] The difference in the success rates here may be explained by:

1. the disparity in definition of qualified success, where Cheng et al used an IOP of 3 points higher than is used in this retrospective review.

2. the high drop-off rate for patient follow-up after the 36 months follow up visit in this retrospective review (where follow-up of problematic cases is favoured)
3. the high number of patients in this retrospective review that have not yet achieved a 45 month follow-up post operatively to enable inclusion of their data.

From the above numbers it can be seen that the surgical outcomes of deep sclerectomy surgery at CMAJH is comparable to international standards. As surgical success in deep sclerectomies is a factor of time, further studies of greater power than a retrospective review are recommended to assess the true surgical success rates where longer term follow-up is required.

Laser goniopuncture rates vary greatly in literature, a study by Ambersin et al finds a goniopuncture rate of 45% and another study by Bissig et al finds a goniopuncture rate of 59.8%.[3] This retrospective review finds that laser goniopuncture was an extremely commonly used adjunct to deep sclerectomy surgery and was used in 69.2% of cases. Other less frequently used post-surgical interventions were suture lysis, bleb needling, intra-bleb MMC and SLT.

When comparing the surgical complication rates found in this retrospective review with those found internationally – CMJAH is again comparable, if not superior, with that found in literature. When looking at intra-operative complications, the surgical perforation rate was 1.9% at CMJAH - in keeping with international standards where a rate around 2-3% is expected.

Post-operative complication rates, as per the systematic review by Cheng et al, are hyphaema in 13.7% of all DS cases, flat anterior chambers in 11.0%, hypotony in 8.2% and choroidal detachment in 11.6% of cases.[16] In direct comparison, the complication rates at CMJAH for the same conditions in that order were: 1.9%; 0.0%; 9.6%; and 1.9%. The excellent rates noted at CMJAH in this review will need to be further studied as reporting bias can occur with retrospective reviews.

Overall, success rates achieved at this Johannesburg academic hospital supersede those reported in other studies on a majority black population and are comparable to the results reported in systematic reviews and meta-analyses regarding deep sclerectomy surgeries performed internationally. Complications are rare in Deep sclerectomies performed in this setting and results are predictable and reproducible.

This retrospective review confirms the safety and efficacy of deep sclerectomy surgery when performed in select patients with open angle glaucoma and done either by or under the supervision of a senior glaucoma surgeon in a specialised glaucoma unit.

A future, prospective, randomised controlled trial is advised to verify the above findings. This trial should have a defined end point of no shorter than 2 years with consistent and strict protocols covering and including standardised surgical techniques as well as clinical review protocols and techniques. A study with greater statistical power and reliability which confirms the findings above could positively influence general patient management protocols at such a specialised unit. This in turn will have far reaching effects in terms of the improvement in the transference of scarce skills and overall glaucoma management.

CHAPTER 5: CONCLUSION

In the setting of a specialised glaucoma service such as that offered at CMJAH, surgical proficiency in DS technique is attained, as demonstrated in this retrospective review, with outcomes comparable to that seen internationally.

Since DS has a lower complication rate than trabeculectomy surgery – the surgery currently commonly performed at Johannesburg academic hospitals, it may play a role earlier on in disease management than does trabeculectomy surgery.

REFERENCES

1. Department of Health. National guideline: Prevention of blindness in South Africa. December 2012.
2. Ting N, Li Yim J, Ng J. Different strategies and cost-effectiveness in the treatment of primary open angle glaucoma. *Clinicoeconomics and outcomes research*. 2014 Dec 6:523-530
3. Varga Z, Sharawy T. Deep Sclerectomy: Safety and efficacy. *Middle East Afr J Ophthalmol*. 2009 Jul-Sep; 16(3): 123–126
4. Guedes RA, Guedes VM, Chaoubah A. Cost-effectiveness comparison between non-penetrating deep sclerectomy and maximum-tolerated medical therapy for glaucoma within the Brazilian National Health System (SUS). *Arq Bras Oftalmol*. 2012;75(1):11–15
5. Morales J, Al Shawan S, Al Odyhab S. Al Jadaan I, Edward DP. Current Surgical Options for the Management of Pediatric Glaucoma. *J Ophthalmol*. 2013;76:1-16
6. Mendrinos E, Mermoud A, Sharawy T. Non-penetrating glaucoma surgery. *J Surv Ophthalmol*. 2008; 53;6
7. Khairy HA, Green FD, Nassar MK, Azuara-Blanco A. Control of intraocular pressure after deep sclerectomy. *Eye*. 2006 ;20:336–40
8. Shaarawy T, Mermoud A. Deep sclerectomy in one eye vs deep sclerectomy with collagen implant in the contralateral eye of the same patient: long-term follow-up. *Eye*. 2005;19:298–302
9. Seungsoo R, Sung YK, Samin H, Gong JS, Jong JJ, et al. Long-term Results of Deep Sclerectomy with Small Collagen Implant in Korean. *Korean J Ophthalmol.* 2013;27(1):34-38
10. Kozobolis VP, Christodoulakis EV, Tzanakis N, Zacharopoulos I, Pallikaris IG. Primary deep sclerectomy versus primary deep sclerectomy with the use of mitomycin C in primary open-angle glaucoma. *J Glaucoma*. 2002;11:287–93
11. Mielke C, Dawda VK, Anand N. Deep sclerectomy and low dose mitomycin C: a randomised prospective trial in West Africa. *Br J Ophthalmol*. 2006;90:310–3
12. Kirwan JF, Cousens S, Venter L, Cook C, Stulting A, et al. Effect of beta radiation on success of glaucoma drainage surgery in South Africa: randomised controlled trial. *BMJ*. 2006;333(7575):942
13. El Sayyad F, Helal M, El-Kholify H, Khalil M, El-Maghraby A. Nonpenetrating deep sclerectomy versus trabeculectomy in bilateral primary open-angle glaucoma. *Ophthalmology*. 2000;107:1671–4
14. Cillino S, Di Pace F, Casuccio A, Calvaruso L, Morreale D, et al. Deep sclerectomy versus punch trabeculectomy with and without phacoemulsification: a randomised clinical trial. *J Glaucoma*. 2004;13:500–6
15. Eldaly M, Bunce C, Elsheika O. Wormald R. Non-penetrating filtration surgery versus trabeculectomy for open angle glaucoma. *Cochrane Database of Systematic Reviews* 2014, Issue 2.
16. Cheng JW, Cheng SW, Cai JP, Li Y, Rui-Li W. Systematic overview of the efficacy of nonpenetrating glaucoma surgery in the treatment of open angle glaucoma. *Med Sci Monit*. 2011; 17(7): RA155-163
17. Rulli E, Biagioli E, Riva I, Gambirasio G, De Simone I, et al. Efficacy and Safety of Trabeculectomy vs Nonpenetrating Surgical Procedures: A

Systematic Review and Meta-analysis. *JAMA Ophthalmol*. 2013;131(12):1573-1582
18. Rotchford AP, Kirwan JF, Muller MA, Johnson GJ, Roux P. Temba Glaucoma study: a population-based cross-sectional survey in urban South Africa. *Ophthalmol.* 2003 Feb;110(2):376-382
19. Kyari F, Mohammed M.A, Bastawrous A, Gilbert CE, Faal H. Epidemiology of Glaucoma in Sub-Saharan Africa: Prevalence, Incidence and Risk Factors. *Middle East Afr J Ophthalmol.* 2013 Apr-Jun;20(2):111-125
20. Coleman AL. Advances in Glaucoma Treatment and Management: Surgery. *IOVS.* 2012;53(5):2491-2494

APPENDICES

APPENDIX 1: ETHICS CLEARANCE CERTIFICATE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr IM Freed

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M160217

NAME: (Principal Investigator)	Dr IM Freed
DEPARTMENT:	School of Clinical Medicine Department of Neurosciences Division of Ophthalmology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	The surgical outcomes of deep sclerectomies performed at a Johannesburg academic hospital
DATE CONSIDERED:	26/02/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr S Williams
APPROVED BY:	Professor CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	10/05/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Philip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. I agree to submit a yearly progress report. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in February and will therefore be due in the month of February each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

15/5/2018
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX 2: DATA COLLECTION SHEET

1. Patient study number:
2. Patient demographics:
   2.1. Age:
   2.2. Race: Black / White / Asian / Other
   2.3. Sex: M / F
3. Underlying disease profile (pre-operative recordings):
   3.1. Diagnosis :
   3.2. VA (see Table 1, below)
   3.3. IOP (see Table 1, below)
   3.4. VF (MD):
   3.5. GDX (NFI):
   3.6. Medical therapy (see Table 2, below)
   3.7. Previous laser treatment: YES/NO
4. Pre-existing ocular conditions:
   4.1. Medical: LEFT/RIGHT/BILATERAL/NIL
      4.1.1. Inflammatory / Scarring
      4.1.2. Other
   4.2. Surgical History:
      4.2.1. Previous cataract surgery: LEFT/RIGHT/BILATERAL/NIL
         4.2.1.1. E+I / P+I
         4.2.1.2. Other
      4.2.2. Previous glaucoma surgery: LEFT/RIGHT/BILATERAL/NIL
         4.2.2.1. Trabeculectomy / Deep sclerectomy
         4.2.2.2. Other
5. Surgical Notes:
   5.1. Laterality: LEFT / RIGHT / BILATERAL
   5.2. Adjunctive treatment: YES/NO
      5.2.1. Mitomycin-C
      5.2.2. Avastin
   5.3. Intra-operative complications: YES / NO
      5.3.1. Microperforation
      5.3.2. Other

5.4. Combined procedure: YES / NO

5.4.1. Phacoemulsification and cataract extraction

5.4.2. Phacoemulsification, cataract extraction and lens implantation

5.4.3. Other

6. Post-operative analysis:

6.1. VA (see table 1)

6.2. IOP (see table 1)

6.3. Complications: (see Table 1, below)

7. Laser gonio-puncture received: YES / NO

7.1. When was the gonio-puncture performed? (see Table 1, below)

7.2. Was it complicated by iris plugging? YES / NO

Data Collection Table 1:

	Pre-Operative	Post-operative Analysis						
		Day 1	Week 1	Month 1	Month 3	Month 6	Month 9	Month 12
VA								
IOP								
Flat Anterior Chamber								
Hyphaema								
Hypotonous Maculopathy								
Choroidal haemorrhage / detachment								
Cataract								
Medical therapy increased?								
Adjunctive Gonio-puncture?								

Data Collection Table 2:

Medical Therapy	Pre-Operative	Post-operative Analysis						
		Day 1	Week 1	Month 1	Mont h 3	Mont h 6	Mont h 9	Month 12
1 Drug class:								
alpha-agonists								
beta-agonists								
prostaglandin (PG) analogues								
acetazolamide								
2 Drug classes								
Alpha + Beta Agonists								
Alpha-agonist + PG analogues								
PG analogues + beta agonists								
3 drug classes								
PG Analogue + Beta agonist + Alpha agonist								
PG Analogue + Beta agonist + Acetazolamide								
>3 drug classes								