New Glaucoma Surgical Procedures: Is Anything Better than Trabeculectomy?

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Evolution of glaucoma surgery

The changing popularity of filtering procedures:

- Elliot’s Trephination 1909 – 1940
- Iridencleisis 1940 – 1957
- Thermal Sclerostomy (Scheie) 1958 – 1968
- Posterior Lip Sclerectomy 1962 – 1968
- Trabeculectomy 1968 –

- Deep Sclerectomy 1998 –
  ...?... 2011 –

after: C. Davis Belcher III, 1992

Financial Disclosures

- Alcon, Inc
  – Glaucoma advisory board, speaker’s bureau

Glaucoma Filtering Surgery

- Trabeculectomy the “gold standard” to which other procedures are compared

- Surgical success rates typically 85-90% or higher, particularly if antifibrotic agents utilized

- Laser suture lysis and releasable sutures provide ability to titrate aqueous flow during postoperative period
Each new technique was first critically evaluated and compared with the currently popular technique...

Evolution of glaucoma surgery

After introducing the Trab in 1968:

Spaeth et al 1975:

“The relative indications for trabeculectomy include:

(1) malignant glaucoma in the other eye;
(2) chronic angle closure glaucoma;
(3) ‘high pressure glaucoma’ where pressure below 20 mm Hg is not essential;
(4) ‘low inflow glaucoma’ in which persistent flat anterior chambers may be expected following routine filtration surgery;

“Trabeculectomy gives such poor results in secondary glaucoma that the procedure is probably relatively contraindicated.”

After introducing the Trab in 1968:

1. Trabeculectomy: a re-evaluation after three years and a comparison with Scheie’s procedure.

“...The results suggest that the Scheie procedure [the old, known technique] lowers pressure to a lower level and for a longer duration than does the trabeculectomy [the new technique].“

“… the long-term visual result was apparently not different … [However] Trabeculectomy causes fewer flat anterior chambers than the Scheie procedure.“

Trab (w/o MMC) Success Rates in 1990:

- 75% - 85% - in phakic, naive eyes
- 60% - in re-operations
- 10% - after 3 or more Trabs
- 50% - in young patients
- 25% - 50% - in infantile glaucoma
- 25% - in neovascular glaucoma
- 25% - in uveitic glaucoma

C. Davis Belcher III, 1992
Trabeculectomy

Trabeculectomy is the most widely performed filtering procedure for glaucoma. Although it is a valuable operation, it is not the final solution to glaucoma surgery and should be chosen with recognition of its specific advantages and disadvantages.

**Summary**

Evolutionary improvements in trabeculectomy-like procedures
- Canaloplasty
- ExPRESS glaucoma filtration device

Increased use of long-tube shunts
- Ahmed, Baerveldt GDDs

New field: “Minimally invasive glaucoma surgery”
- Ultra-safe, quick procedures with modest IOP lowering

Surgical Trends: 1994-2004

Practice Patterns

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>1996</th>
<th>2002</th>
<th>2008</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Tube</td>
<td>Trab</td>
<td>Tube</td>
</tr>
<tr>
<td>Prior trab</td>
<td>7%</td>
<td>93%</td>
<td>20%</td>
</tr>
<tr>
<td>Prior EC/ICCE</td>
<td>8%</td>
<td>92%</td>
<td>22%</td>
</tr>
<tr>
<td>Prior phaco</td>
<td>5%</td>
<td>95%</td>
<td>4%</td>
</tr>
<tr>
<td>Prior PKP</td>
<td>24%</td>
<td>76%</td>
<td>38%</td>
</tr>
<tr>
<td>Prior SBP</td>
<td>22%</td>
<td>78%</td>
<td>39%</td>
</tr>
<tr>
<td>Prior PPV</td>
<td>22%</td>
<td>78%</td>
<td>31%</td>
</tr>
<tr>
<td>Uveitic glaucoma</td>
<td>15%</td>
<td>85%</td>
<td>31%</td>
</tr>
<tr>
<td>Neovascular glaucoma</td>
<td>37%</td>
<td>63%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>AVERAGE</strong></td>
<td>17%</td>
<td>83%</td>
<td>29%</td>
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Medicare data, courtesy of Dr. Bill Rich
Aqueous Shunt Surgery

- Indications
  - Generally reserved for difficult glaucoma where conventional filtering surgery is likely to fail
  - Patients who are poor candidates for trabeculectomy

Aqueous Shunt Surgery

- Present day drainage devices include:
  - Molteno (nonvalved)
  - Baerveldt (nonvalved)
  - Krupin (valved)
  - Ahmed (valved)
  - Schocket (nonvalved, tube attached to encircling element)
  - Express (nonvalved, trans-limbal, stainless steel tube)
- Reduction in IOP related to surface area of plate
  - Some have double plate model available to increase surface area (i.e., Molteno, Ahmed)

Aqueous shunt surgery

Commonly used aqueous shunts. (A) Single-plate (left) and double-plate (center and right) Molteno implants. (B) Baerveldt glaucoma implants: 250 mm² (left), 350 mm² (center), and 425 mm² (right). (C) Krupin eye valve with disk. (D) Ahmed glaucoma valve.

TREATMENT OUTCOMES IN THE TUBE VERSUS TRABECULECTOMY (TVT) STUDY AFTER FIVE YEARS OF FOLLOW-UP
Purpose

• To compare the safety and efficacy of tube shunt surgery to trabeculectomy with MMC in patients with previous ocular surgery

Inclusion Criteria

• Age 18-85 years
• IOP ≥ 18 mm Hg and ≤ 40 mm Hg on maximum tolerated medical therapy
• Previous cataract extraction with IOL implantation, trabeculectomy, or both

Treatment Groups

• Tube group
  – 350-mm² Baerveldt glaucoma implant
  – Superotemporal quadrant
  – Flow restriction
• Trabeculectomy group
  – Superior trabeculectomy
  – MMC 0.4 mg/ml for 4 minutes

Recruitment and Retention

Randomized (n = 212)

Tube Group (n = 107)

Trabeculectomy Group (n = 105)

Died (n = 14)
Missed follow-up visit
1-year (n = 7)
2-year (n = 15)
3-year (n = 13)
4-year (n = 21)
5-year (n = 24)

P = 0.22 for the difference in visit completion rate
Demographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Tube Group (n = 107)</th>
<th>Trabeculectomy Group (n = 105)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mean ± SD Range</td>
<td>70.9 ± 11.0</td>
<td>71.1 ± 9.9</td>
<td>0.89</td>
</tr>
<tr>
<td>Gender (n, %)</td>
<td></td>
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<tr>
<td>Male</td>
<td>43 (40%)</td>
<td>57 (54%)</td>
<td>0.055</td>
</tr>
<tr>
<td>Female</td>
<td>64 (60%)</td>
<td>48 (46%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>52 (49%)</td>
<td>43 (41%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Black</td>
<td>40 (37%)</td>
<td>42 (40%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>12 (11%)</td>
<td>18 (17%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3 (3%)</td>
<td>2 (2%)</td>
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Baseline Ocular Characteristics

<table>
<thead>
<tr>
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<th>Tube Group (n = 107)</th>
<th>Trabeculectomy Group (n = 105)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP (mean ± SD)</td>
<td>25.1 ± 5.3</td>
<td>25.6 ± 5.3</td>
<td>0.56</td>
</tr>
<tr>
<td>Glaucoma meds (mean ± SD)</td>
<td>3.2 ± 1.1</td>
<td>3.0 ± 1.3</td>
<td>0.17</td>
</tr>
<tr>
<td>Diagnosis (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POAG</td>
<td>88 (82%)</td>
<td>84 (80%)</td>
<td>0.057</td>
</tr>
<tr>
<td>CAGG</td>
<td>7 (7%)</td>
<td>11 (10%)</td>
<td></td>
</tr>
<tr>
<td>PXFG</td>
<td>7 (7%)</td>
<td>1 (1%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5 (5%)</td>
<td>9 (9%)</td>
<td></td>
</tr>
<tr>
<td>Humphrey VF MD (mean ± SD)</td>
<td>-16.0 ± 10.2</td>
<td>-15.8 ± 9.6</td>
<td>0.87</td>
</tr>
<tr>
<td>PSD (mean ± SD)</td>
<td>7.1 ± 3.5</td>
<td>6.9 ± 3.5</td>
<td>0.73</td>
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Intraocular Pressure

Treatment Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Tube Group (n = 73)</th>
<th>Trabeculectomy Group (n = 84)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Failure</td>
<td>24 (33%)</td>
<td>42 (50%)</td>
<td>0.034</td>
</tr>
<tr>
<td>Success</td>
<td>49 (67%)</td>
<td>42 (50%)</td>
<td>0.034</td>
</tr>
<tr>
<td>Qualified</td>
<td>31 (42%)</td>
<td>18 (21%)</td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>18 (25%)</td>
<td>24 (29%)</td>
<td>0.58</td>
</tr>
</tbody>
</table>
Reasons for Treatment Failure

<table>
<thead>
<tr>
<th></th>
<th>Tube Group (n = 24)</th>
<th>Trabeculectomy Group (n = 42)</th>
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</thead>
<tbody>
<tr>
<td>Inadequate IOP control</td>
<td>20 (83%)</td>
<td>28 (67%)</td>
</tr>
<tr>
<td>Persistent hypotony</td>
<td>3 (13%)</td>
<td>13 (31%)</td>
</tr>
<tr>
<td>Loss of LP vision</td>
<td>1 (4%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

P = 0.43 for the difference in distribution of reasons for treatment failure

Conclusions

• Tube shunt surgery had a higher success rate than trabeculectomy with MMC after 5 years of follow-up.

• A higher rate of reoperation for glaucoma was observed after trabeculectomy with MMC compared with tube shunt surgery.

• Both surgical procedures had similar IOP reduction and use of supplemental medical therapy at 5 years.

Review Article

• Ophthalmic Technology Assessment of Novel Glaucoma Procedures
• Provides an evidence-based summary of clinically relevant information about novel, or emerging surgical devices and procedures
• Devices that have FDA clearance or are currently in phase III clinical trials in the US were included

Minimally Invasive Glaucoma Surgery (MIGS)

• Alternative to current surgical options
• Very low risk
• A much earlier intervention
• Able to be performed by most surgeons
• Minimal additional equipment required
• Should not preclude success of future, more aggressive surgical intervention

Overview of Current MIGS Procedures
Commercialized and in Development

• Commercialized
  – Trabectome
    • Schlemm’s canal
  – Canaloplasty*
    • Schlemm’s canal

• Investigational
  – iStent
  – Hydrus
  – ELT
  – Cypass
  – SOLX
  – Aquesys

*not a true “MIGS” procedure

Patient Profiles: New Procedures

• MIGS-type procedures
  Ab-interno Schlemm’s/Suprachoroidal
• Mild-moderate disease
• Open-angle
• Modest IOP target (i.e., 15–16 mm Hg)
• Moderate IOP elevation (i.e., 20 – 28 mm Hg)
• Able to tolerate some meds

• Trab-type procedures
  Ex-PRESS
• Moderate-advanced disease
• Progressing normal pressure glaucoma
• Open, or narrow angle
• Low IOP target (i.e., <13 mm Hg)
• Very high IOP (i.e., >30 mm Hg)
• Intolerant to most meds

POAG : is TM the site of resistance?

yes: demonstrated by Grant in 1963

Trabeculotomy:
- normal eye: eliminates 50% of R
- GL eye: eliminates all abnl R

note: sclera has 50% of normal R:
- IOP will not drop to 0 mmHg

anterior chamber
GL 18LN

Schlemm’s Canal Procedures

• Ab-Externo Approach
  Trabectome
  iStent G1 & G2
  Hydrus
  Excimer Laser

• Ab-Interno Approach

Canaloplasty
Canaloplasty: Ab-Externo Schlemm’s Canal Tension Suture

- Elegant surgery, non-penetrating approach; bleb-less
- Open angle glaucoma, with or without phaco
- IOP-lowering less than trabeculectomy
- Improved safety
- Importance of suture tension
- Technically demanding

I-View: (post-op canaloplasty)

- I-View: high resolution ultrasound imaging system with center frequency of about 80 MHz

Schlemm’s Canal

- Insulated footplate acts as a guide within Schlemm’s Canal
Glaukos iStent Trabecular Micro-Bypass

- Self-trephinating tip
- Smallest implantable medical device
- 1 mm “half-pipe” base into canal
  - 3 retention arches
- 0.3 mm snorkel into AC
- Heparin coated surgical grade titanium
- Pre-loaded applicator

iStent® - Therapeutic Objectives

iStent® implanted during cataract surgery designed to:
- Reduce IOP while reducing or eliminating medication use
- Spare the conjunctiva
- Decrease risk of large IOP fluctuations associated with nonadherence to medication regimens
- Avoid serious complications associated with end-stage filtration and shunt procedures
- Eliminate risks of iatrogenic hypotony and bleb formation
- Safely preserve potential for future treatment options

AC to Suprachoroidal Space

- Ab-Externo Approach
- Ab-Interno Approach

Gold Micro-Shunt

Cypass

iStent G3

Caution: Investigational device limited by Federal (U.S.) law to investigational use only.
Gold Micro-Shunt

- GMS is a nonvalved flat-plate drainage device made of 24-karat medical-grade gold
- Designed to shunt aqueous from the anterior chamber to the suprachoroidal space

sGMS+ positioned into AC using bent 27g needle

Ab-Interno Suprachoroidal Procedures

- Clear corneal incision, gonioscopic approach
- Easy to use and quick
- Solo or combined with phaco
- Enhance aqueous outflow to uveoscleral outflow
- Iop-lowering target in mid-teens
- Bleeding rare
- Does not preclude future glaucoma surgery
Subconjunctival Outflow

- Ex-PRESS device
  - An evolutionary improvement in trabeculectomy
  - Indications are the same, although with improvement in safety and reproducibility

Evolution of the Guarded Filtration Procedure

- Anti-metabolite usage
- Laser suture lysis/releasable sutures
- Fornix-based flaps
- Non-penetrating approaches
- Ex-PRESS filtration device

- Enhanced safety
- Predictability
- Maintain efficacy
Purpose

- To compare the success and complications rates of glaucoma patients who had an Ex-PRESS Mini Glaucoma Shunt device implantation to those who had conventional trabeculectomy


Methods

- Retrospective comparison of patients who underwent either trabeculectomy or Ex-PRESS implantation.

- Trabeculectomy: 77 eyes of 65 subject
  Ex-PRESS: 76 eyes of 69 subjects

- Surgeries were performed by a single surgeon at Duke University Eye Center.
### Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>Ex-PRESS (N=76)</th>
<th>Trabeculectomy (N=77)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (Mean±SD)</strong></td>
<td>66.9±15.2</td>
<td>66.8±13.9</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>36 (47)</td>
<td>32 (41)</td>
</tr>
<tr>
<td>Female</td>
<td>40 (53)</td>
<td>45 (59)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Black</td>
<td>45 (59)</td>
<td>48 (62)</td>
</tr>
<tr>
<td>White</td>
<td>30 (39)</td>
<td>29 (38)</td>
</tr>
<tr>
<td><strong>Previous Surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>40 (53)</td>
<td>47 (61)</td>
</tr>
<tr>
<td><strong>Follow-up (Months)</strong></td>
<td>9.1 (3.5)</td>
<td>9.2 (4.9)</td>
</tr>
<tr>
<td><strong>Glaucoma Type</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary open angle</td>
<td>62</td>
<td>57</td>
</tr>
<tr>
<td>Other</td>
<td>14</td>
<td>20</td>
</tr>
</tbody>
</table>

### IOP Dynamics

![IOP Dynamics Graph](image)

### Success Rate

<table>
<thead>
<tr>
<th></th>
<th>Ex-PRESS</th>
<th>Trabeculectomy</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall Success</strong> *</td>
<td>62/76 (82%)</td>
<td>55/77 (71%)</td>
<td>0.182</td>
</tr>
</tbody>
</table>

P-value based on Fisher’s exact test of differences in proportions

*Success* =

- Most recent visit:
  - No need for further glaucoma surgery
  - IOP ≤ 21 at most recent visit
  - IOP ≥ 5 at the most recent visit

### Ex-PRESS vs. Trab: Prospective Randomized Study, De Jong 2009

- **Author:** Leo A. M. S. de Jong, MD, Academic Medical Centre, Ophthalmology Department, Amsterdam, The Netherlands.
- **Publication:** Advances in Therapy Journal, April 2009
- **Study Details:** Prospective randomized study to compare Ex-PRESS™ vs. Trabeculectomy

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Patients & Methods

- Prospective, randomized study of 80 eyes (40 eyes per group)
- Follow up: 12 months.
- Evaluation:
  - IOP, glaucoma medications, visual acuity
  - Success defined as IOP > 4 mmHg and < 18 mmHg or < 15 mmHg without glaucoma medications
  - Complications

The Ex-PRESS vs Trabeculectomy in Open-Angle Glaucoma: Prospective Randomized Study

- N = 80 eyes (Ex-PRESS 40, trab = 40)
- Follow up – 12 months
- The Ex-PRESS complete success (IOP ≤ 18 mmHg) was significantly higher

<table>
<thead>
<tr>
<th></th>
<th>Ex-PRESS</th>
<th>Trab</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
<td>84.6%</td>
<td>60.0%</td>
<td>0.023*</td>
</tr>
<tr>
<td>Qualified</td>
<td>97.4%</td>
<td>87.5%</td>
<td>0.2007</td>
</tr>
</tbody>
</table>

* significant difference

**Filtering procedures (bleb-surgery)**

Penetrating ↔ Minimally penetrating ↔ Non-penetrating

**Non-filtering proc. (blebless-surgery)**

Suprachoroidal ↔ Intra-Canalicular ↔ Trans-Trabecular

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**Glaucoma Surgery**

- Phacoemulsification alone
- Endocyclophotocoagulation
- iStent
- Trabectome
- Deep sclerectomy/Canaloplasty
- Tube shunt (Ahmed, Baerveldt)
- Express Device
- Trabeculectomy
- Trans-scleral cyclophotocoagulation

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**Summary**

- Although trabeculectomy remains the gold standard for incisional glaucoma surgery, the search for a procedure that can effectively and safely lower IOP and improve on these standards continues
- Majority of the novel procedures seek to avoid bleb formation entirely and rely on augmentation of the physiologic outflow pathways
- Randomized trials are needed