Glaucoma: Less is More? MIGS & SLT

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About the IGA
- Based in Kent, but working across the UK and beyond
  - Founded in 1974
  - c. 5,000 members
  - 4,000 people with glaucoma
  - 1,000 professionals
  - 15 staff
  - 25 Volunteers
  - Turnover £1.25m
  - Funded entirely through charitable income - donations, legacies & membership income
  - Services are free to all

IGA quarterly membership magazine

IGA - what we do
1. Support research into detection and treatment - via an annual grant making programme and through our support for the IGA Professor of Glaucoma at UCL.
2. Prevention of needless sight loss - by running national campaigns to raise awareness and understanding of glaucoma, and reduce needless sight loss by encouraging people to take care of their eyes - especially those most at risk.
3. Helping people live well with glaucoma - by providing advice and information on managing the condition, via our telephone helpline, online forum and local patient support groups around the UK. Publishing and distributing a wide range of booklets and leaflets aimed at patients, carers and professionals. This information is regularly updated and approved by specialists, and is also available via our website.

Our vision is that everyone living with glaucoma, and all those at risk, should have the knowledge and access to the care they need to avoid preventable sight loss.

To make this a reality we do three things:

About the IGA
IGA advice & information

IGA campaigns

IGA campaigns

IGA Helpline (sightline)

IGA telephone helpline

Why do people contact us?

What is Glaucoma?

- A group of diseases
  - Open / closed angle
  - Primary / secondary
  - Childhood / adult
- Common feature is change in optic nerve
  - Thinning of nerve tissue
  - ‘Cupping’
- Usually associated with visual field changes
  - Visual fields may be normal in early glaucoma
- Often associated with raised eye pressure (IOP)
  - Not always
Burden of monitoring glaucoma

- UK: One million hospital visits per year

...enormous variability in progression rates...
...most treated patients in clinics are not at high risk of progressing to blindness...

Saunders et al. IOVS 2014

Rate of glaucoma progression 1

- Slow

- Ordinary linear regression of MD(dB) on time
- Estimate speed of loss (dB/year)
Rate of glaucoma progression 2

-0.15 dB/yr

Medium
Rate of glaucoma progression 3

-0.74 dB/yr

Fast

Big data, visual fields and glaucoma

David Crabb
• Median speed of loss: ~ 0.1 dB/year but huge variability
• Only ~ 25% 'progressing' at a 'significant' rate

• -0.5 to -1.0 dB/year ~ 16%

• -1.0 to -1.5 dB/year ~ 5%

• Worse than -1.5 dB/year ~ 3%
Finding them in the haystack is difficult.

- How does speed of loss affect the patient?
- Life expectancy and both eyes

Results

- Patients 'at risk' of visual impairment in their lifetime
  - Approximately 5%

Results

- Patients at risk of visual impairment in their lifetime
  - All had at least one eye worse than -6 dB at diagnosis
Glaucoma - Eye Pressure
- IOP = Intra-Ocular Pressure
- IOP is often raised in glaucoma
  - But not always
- Not everyone with glaucoma has raised eye pressure
  - Low pressure glaucoma (aka NTG, Normal Tension Glaucoma)
- Not everyone with raised IOP has glaucoma
  - Ocular Hypertension
- Lowering IOP effectively treats glaucoma
  - Even if the IOP was not raised in the first place
- ‘Normal’ range of IOP around 10-24 mmHg
  - Usually 10-21 mmHg is quoted
  - New population studies suggest higher normal upper limit

Glaucoma - Treatment
- Medications
  - Drops
  - Tablets
- Laser
  - Iridotomy (PI)
  - Trabeculoplasty (ALT / SLT)
  - Cyclo-photocoagulation (Cyclodiode / ECP)
- Surgery
  - Trabeculectomy (‘Trab’)
  - Glaucoma drainage devices (‘Tubes’)
  - Cataract surgery (‘Phaco’)
  - MIGS (with or without phaco cataract surgery)

Outflow & Inflow: ‘Plumbing’
Anatomy Based Treatment Approaches

Examinations & Investigations: Gonioscopy
Normal Eye Structures

Laser Treatments
- Reduce aqueous production
  - TCP/ECP
- Relieve obstruction to flow
  - PI/ALPI
- Increase outflow
  - ALT/ SLT

Laser Treatment
Cyclophotocoagulation
- Laser diode cyclophotocoagulation preferable to other forms of ciliary body treatment
- Reduces aqueous production by destruction of ciliary epithelium
- Options:
  - Trans scleral
    - (Neodymium: YAG laser cyclo-photocoagulation [1064 nm])
    - Diode (810 nm) - Cyclodiode
  - (Transpupillary)
  - Endoprobe (ECP, a MIGS procedure)
SLT v ALT: Technique

- In ALT endpoint - blanching or production of a tiny bubble
- In SLT there is no endpoint - use microbubbles as guide. The aiming beam is centered over the trabecular meshwork and straddles the entire Trabecular Meshwork

LT Mechanism (ALT / SLT)

- Potential mechanisms for lowering IOP:
  1. Mechanical effect with focal shrinkage of the anterior meshwork puts the posterior filtering meshwork on stretch
  2. Cellular effect, a diffuse loss of meshwork cells (even in untreated areas between burns)
  3. Biochemical effect causing an alteration in both the rate and composition of the trabecular meshwork’s extracellular matrix

SLT - LIGHT study

- Laser in Glaucoma & Ocular Hypertension
- Primary treatment - Laser vs Drops
- Did not show better quality of life
  - They used a very basic questionnaire
- 75% of SLT patients still off drops at 3 years
- May change the landscape for initial treatment

Cyclodiode

New Glaucoma Dedicated Laser System: CYCLO G6™
MicroPulse® P3 – Innovative Cyclophotocoagulation with MicroPulse Technology

- Efficient & straightforward for doctor and patient
- Excellent safety profile
- Non-incisional, so can be performed in outpatients or operating theatre
- Predictable
- Minimal inflammation post-op
- Repeatable

ECP Technology
The 3 in 1 Micro-Endoscope

ECP (Laser MIGS)
- Localised shrinkage of ciliary processes
- Direct vision - relative tissue sparing
- Observed end point
- Titratble - 90/180/270/360°
- Reduced ciliary body aqueous production
- Reduction in blood flow
- Partial reperfusion - may retreat
- Hypotony (IOP too low) rare
- MIGS
  - Quick
  - Sutureless
  - Ocular surface friendly

Trabeculectomy

New Surgical Techniques in Glaucoma
What are We Looking For?
- Trab replacement?
- Wound healing modulation?
- Medication alternative?
- Adjunct to cataract procedure?
- Blebless?

Stages of surgical innovation

Surgical Innovation, New Techniques & Technologies
www.rcseng.ac.uk/standardsandguidance
What shall we try next?

Untrabitional glaucoma surgery

What is MIGS?
(Minimally Invasive Glaucoma Surgery)

- Ever-expanding plethora of procedures
- Minimally traumatic / invasive
- Minimal tissue interaction (less effect of wound healing)
- High safety profile
- Rapid recovery
- Frequently combined with cataract extraction
- Provides more modest IOP lowering than trabeculectomy
- Usually via an ab-interno approach
  - Conjunctiva-sparing vs conjunctiva-involving
  - Physiological outflow (Schlemm’s canal) vs. non-physiological
    routes (via the supra-choroidal or sub-conjunctival spaces)
- Inflow procedures: reduction of aqueous production

Untrabitional glaucoma surgery:
MIGS

- Outflow
  - Conventional sub-conjunctival drainage
  - Trabeculotomy / tube
  - Deep cut
  - MIGS sub-conj drainage
    - Xen (multifocal tube revision, incising conjunctiva)
    - MIGS Schlemm’s canal surgery
    - iStent, Hydrus
    - MIGS angle surgery
    - Pillar tube, ExKh tube
    - MIGS non-conventional outflow
    - Cypass / iStent Supra

- Inflow
  - Conventional (trans-conjunctival)
    - Cyphablast
    - Lasertube (Wandro / HFU)
  - MIGS
    - GCP

Rigorous Assessment by NICE:
Guidelines for all New Procedures

Minimally Invasive Glaucoma Surgery: MIGS

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- MIGS
  - GCP
Familiarity with Surgical Anatomy

**Mechanism: Aqueous Outflow**

- **Conventional outflow pathway**
  - 90% total flow
  - Trabecular meshwork
  - Juxtacanalicular connective tissue
  - Endothelial lining of Schlemm’s canal
  - Schlemm’s canal
  - Collecting channels and aqueous veins
  - Episcleral veins
  - Blood stream

- **Non-conventional pathway**
  - 10% total flow
  - Uveo-scleral flow

**Technique - Microscope & Head Positions**

**Glaucoma Drainage Angle Surgery:**
Placement

iStent®
- Inserter held like a pen
- Index finger activates release button in the eye

iStent Video (G1)

iStent Position (G1)

iStent Inject Surgery

iStent Inject Video (G2)
CyPass Inject Position

No Statistical Difference in Percent of Subjects with ECL > 30% Between CyPass and Control Through Month 24

All available data from safety population. Error bars represent 95% confidence intervals.

Statistically Significant Difference in ECD between CyPass and Control at Months 48 and 60

Statistically Significant Difference in ECD between CyPass and Control at Months 48 and 60

Increase in Percent of CyPass Subjects with > 30% ECL at 48 and 60 Months

Example of CyPass MicroStent Position

3 rings

1 ring
New treatment paradigms: Wither (sic) MIGS? (after Assaadini)

- Reduced dependence on topical medication
- Stepwise approach for mild to moderate disease
  - Early/primary selective laser trabeculoplasty
  - Preservative-free topical or injectable therapies
  - Ab interno MIGS/procedures, with or without lens surgery
  - More invasive conjunctiva-involving filters for more severe disease and/or those who fail initial treatments
- Moderate to advanced disease / low target IOP
  - Traditional MMC or anti-VEGF augmented trab (follow 10/10/10)
  - Tube surgery - complex, secondary glaucomas and/or failed previous surgery

MIGS: the Good ….. SAFETY

- Complications uncommon
  - Mild
  - Self-limiting
- Haemorrhage
  - Blood in Schlemm's Canal
  - Iris / CB trauma
- IOP spike
  - Manage as normal
- Device occlusion

Risk & Benefit

- Risk of doing something (trab)
  - Complications
- Risk of doing nothing (MIGS)
  - Disease progression
  - More sight loss

MIGS the bad: …. EFFICACY

- Schlemm's canal routes seem to have a physiological 'floor' of around 16mmHg due to downstream resistance to flow *
- How much of the effect is due to concurrent cataract surgery?

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*Basic science behind trabecular meshwork surgeries. D. Overby Acta Ophthalmologica Vol 91, s252; 2013
MIGS: the Ugly

- Evidence base
  - (spoiler alert) - not huge
- Cost
  - Complex
- Unexpected consequences
  - The CyPass story
- Regulatory issues

MIGS guru opines ... (Ike Ahmed)

- "A common misperception of MIGS is that it needs to be compared with the gold standard of MMC trabeculectomy to show its effectiveness"
- This inappropriate interpretation is based on the idea that MIGS procedures are designed to replace conventional filtering surgery
- In fact, MIGS devices are designed to address the treatment gap that exists between medical therapy and more aggressive traditional surgical options"

Summary

- MIGS is a useful option
  - To replace drops
  - Before significant functional damage
  - Poor patient compliance
  - Phaco plus
  - No free lunches
- MIGS is not a natural comparator for trabeculectomy
  - (But 500s probably are)
- Trabeculectomy is currently our best option for patients with proper glaucoma
- Do not delay surgery ...
- MIGS procedures clearly hold great promise (Hazard)
  - We have a duty to use them responsibly
  - Objectively investigate risks & benefits
- Less is indeed more ...

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  - Leon Au / Ike Ahmed

Cost issues are complex

- Theatre time
  - Surgical time
  - Turnaround time
- Equipment / disposable costs
- Device costs
  - Multiple implants
- Follow up costs
- Costs of more surgery
- Economic & human costs of visual loss
- Costs of implementation of new technologies
  - Industry sponsorship and commercial pressures
- New studies should include economic assessment

What is the answer?

- 42?
  - HHGTTG
- 12
  - AGIS

42!
THE ANSWER TO LIFE, THE UNIVERSE AND EVERYTHING