iTrack™

CLINICAL SPOTLIGHT

Glaucoma, MIGS and the Health of the Corneal Endothelium

Corneal endothelial cells line the posterior, innermost aspect of the cornea. This single layer of cells is referred to as the corneal endothelium. The role of the corneal endothelium is to maintain a healthy clear cornea and thus maintain clear vision.

Corneal endothelial cells cannot regenerate; preservation of endothelial cells is paramount.

Specular microscopy is a non-invasive photographic technique that allows visualization and analysis of the corneal endothelium, documenting cell count and cell shape in the scanned area.

In adult eyes, there are approximately 2400-3200 cells/mm^2. The number of cells decreases at about 0.6% per year and neighbouring cells enlarge to fill the space.

The minimum endothelial cell density (ECD) necessary for adequate function is in the range of 400-700 cells/mm^2. When ECD falls below this range and/or under conditions of physiologic stress, the corneal endothelium may be insufficient to maintain corneal hydration and corneal clarity.

Endothelial cell loss can result from intraocular surgery (cataract and glaucoma surgery), trauma, and/or glaucoma. Generally, **ECL after cataract surgery is acute and stabilizes after 3 months.**

There is an increased awareness of the impact of Minimally Invasive Glaucoma Surgery (MIGS) on corneal endothelial cell health following the 2018 market withdrawal of the **CyPass suprachoroidal stent (Alcon), which resulted in a consistent rise in ECL over a 60-month period.**

Based on the 12-month results of a prospective multi-center study evaluating ECD in eyes undergoing iTrack™ ab-interno canaloplasty in combination with cataract surgery, **iTrack™ results in minimal ECL at just -3.2% (SD ±9.0%) – with the majority of this ECL occurring within the first 6 months following surgery**. (D.M. Lubeck, MD, and R.J. Noecker, MD, unpublished data, 2021; presented at ASCRS 2021).

XCV

Table 1: Summary of Factors that Impact Corneal Endothelial Cell Health

INTRAOCULAR PRESSURE (IOP)

Elevations in IOP result in damage to the corneal endothelium, leading to reduced ECD in glaucomatous eyes and has been linked to three key factors (Gagnon et al., 1997):

1. Direct compression from higher IOP
2. Congenital alteration of the endothelium and trabecular meshwork
3. Glaucoma medication toxicity

High IOP can also damage the physical barrier function of corneal endothelial cells which can affect the function of the endothelial pump leading to changes in aqueous humor dynamics, which cause corneal stromal edema (Gagnon et al., 1997).

MEDICATIONS

Damage to the corneal endothelial cells can be caused by toxicity of anti-glaucoma medications (Yee, 2007; Schehlein, Novack & Robin, 2017).

The toxicity of benzalkonium chloride, commonly used in anti-glaucoma medications, contributes to ocular surface disease (OSD) and may result in damage to the corneal endothelium cells and central corneal thickness (Yu, Wu, & Qu, 2019).

SURGICALLY TREATED GLAUCOMA

MIGS is associated with a reduced rate of ECL, as compared to traditional glaucoma surgery. Traditional glaucoma surgery is associated with progressive ECL, leading to corneal decompensation

With trabeculectomy, ECL rates have been reported to be between 9.5% and 28.0% at 12 months (Arnavielle et al, 2007; Storr-Paulsen et al., 2008). The use of Mitomycin-C (MMC) in trabeculectomy surgery has also been suggested to contribute to ECL (Sihota et al., 2008).

Glaucoma drainage device surgery is associated with an average 8%-29% rate of corneal complications (Hua et al., 2009).

AQUEOUS ENVIRONMENT

Corneal endothelial cells are bathed in aqueous humor, and alterations in the aqueous environment can disrupt the endothelium i.e., lack of critical nutrients, introduction of proinflammatory and deleterious proteins.

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Table 2: Comparison of ECL Rates Between Different MIGS Procedures				
MIGS	**Author(s)**	**N**	**Follow-Up**	**Mean % ECL**
CONVENTIONAL OUTFLOW PATHWAY				
iTrack (with cataract surgery)	Lubeck et al (1)	77	12 months	3.2%
iStent inject (with cataract surgery)	Samuelson T. et al (2)	505	24 months	13.1% (12.3% control)
	Arriola-Villalobos et al (3)	20	12 months	13.2%
	Gillman et al (4)	54	12 months	14.6%
Hydrus (with cataract surgery)	Samuelson T. et al (5)	556	24 months	14.0% (10.0% control)
		556	36 months	15.0% (11.0% control)
OMNI	Not reported			
Kaook Dual Blade (KDB)	Not reported			
SUBCONJUNCTIVAL				
XEN Gel Implant (with cataract surgery)	Oddone et al (6)	40	6 months	11.3%
XEN Gel Implant (standalone procedure)	Oddone et al (6)	68	6 months	5.6%
PRESERFLO MicroShunt (standalone procedure)	Baker et al (7)	362	6 months	5.2%
SUPRACHOROIDAL				
CyPass Micro-Stent	Lass et al (8)	282	60 months	20.4% (10.1% control)

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AB-INTERNO CANALOPLASTY

Stent-free mechanism: No mechanical trauma to endothelium.

Natural aqueous flow (nourishes and maintains the health of the conventional outflow pathway): No chronic endothelial cell trauma caused by artificial flow (disrupts natural aqueous flow and increased risk of ECL) via one or more isolated points

Tissue-sparing: Does not tear or remove trabecular meshwork tissue and thus does not result in post-op inflammation leading to chronic endothelial cell trauma.

TRABECULAR MICRO-BYPASS STENT SURGERY (ISTENT, HYDRUS)

Artificial outflow: Alters aqueous currents by creating an artificial pathway via one or two points of exit for aqueous humor. This can result in this excessive damage to the corneal endothelium at these point(s) of exit, leading to ECL.

Note: Trabecular micro-bypass stents are located away from the corneal endothelium when correctly implanted in the angle and should not negatively impact on the health of the corneal endothelium. Further, migration of the iStent/Hydrus is uncommon.

SUBCONJUNCTIVAL IMPLANT (XEN, PRESERFLO)

Artificial outflow: Directs the flow of aqueous to the subconjunctival space via a filtration bleb. This creation of artificial flow can result in excessive damage to the corneal endothelium, leading to endothelial cell loss.

Inflammatory response: An increasing number of surgeons implant XEN via an ab-externo approach. The inflammatory response caused by the conjunctival incision may negatively impact corneal health, leading to endothelial cell loss.

GATT/GONIOTOMY (OMNI, KDB)

Inflammatory response: The removal/cutting of trabecular meshwork tissue triggers an inflammatory response, increasing the risk of damage to the corneal endothelium. Inflammatory response can also result in side effects such as peripheral anterior synechiae and scarring of the trabecular meshwork which can lead to post-operative inflammation.

SUPRACHOROIDAL (CYPASS)

Device malpositioning resulted in mechanical trauma, leading to damage to the corneal endothelium and subsequent ECL: ECL loss was correlated to the protrusion of the CyPass device into the anterior chamber.

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