

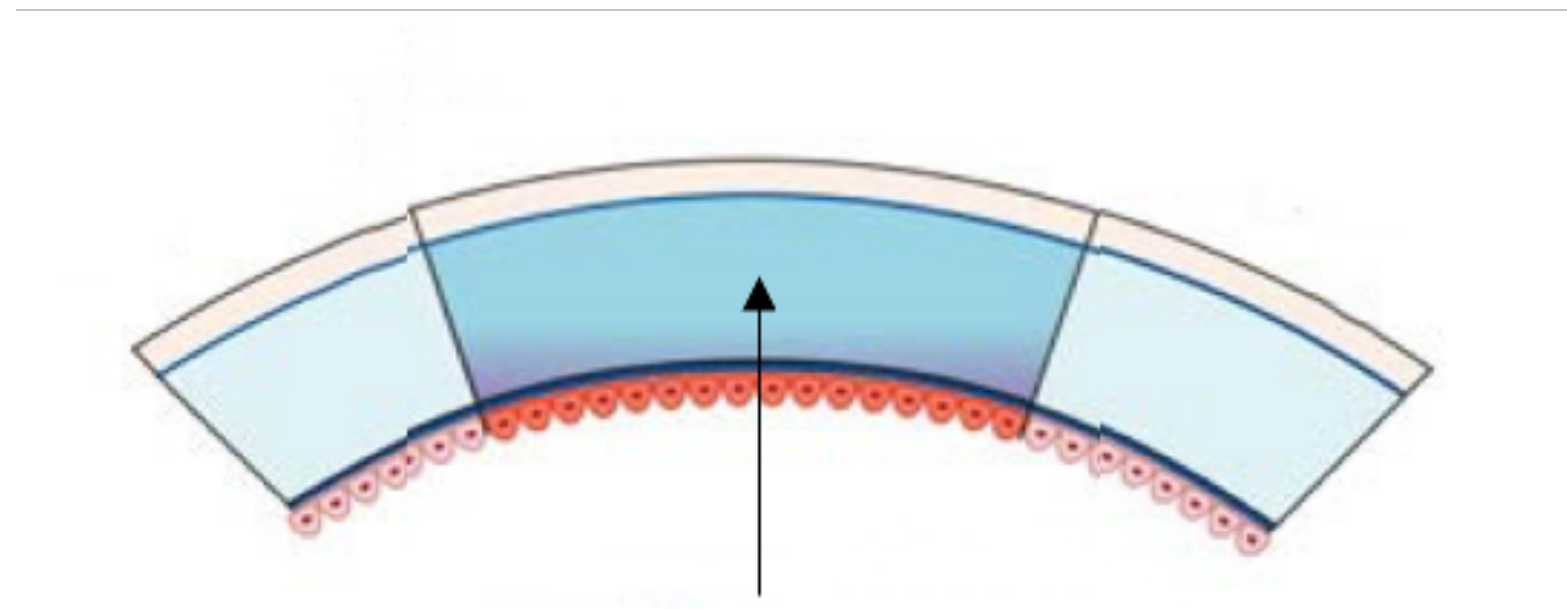
Beeran Meghpara, MD
Director of Refractive Surgery
Co-Chief of Cornea Service
Wills Eye Hospital

The Future Treatment of Endothelial Dysfunction

New Orleans Academy of Ophthalmology
75th Annual Symposium

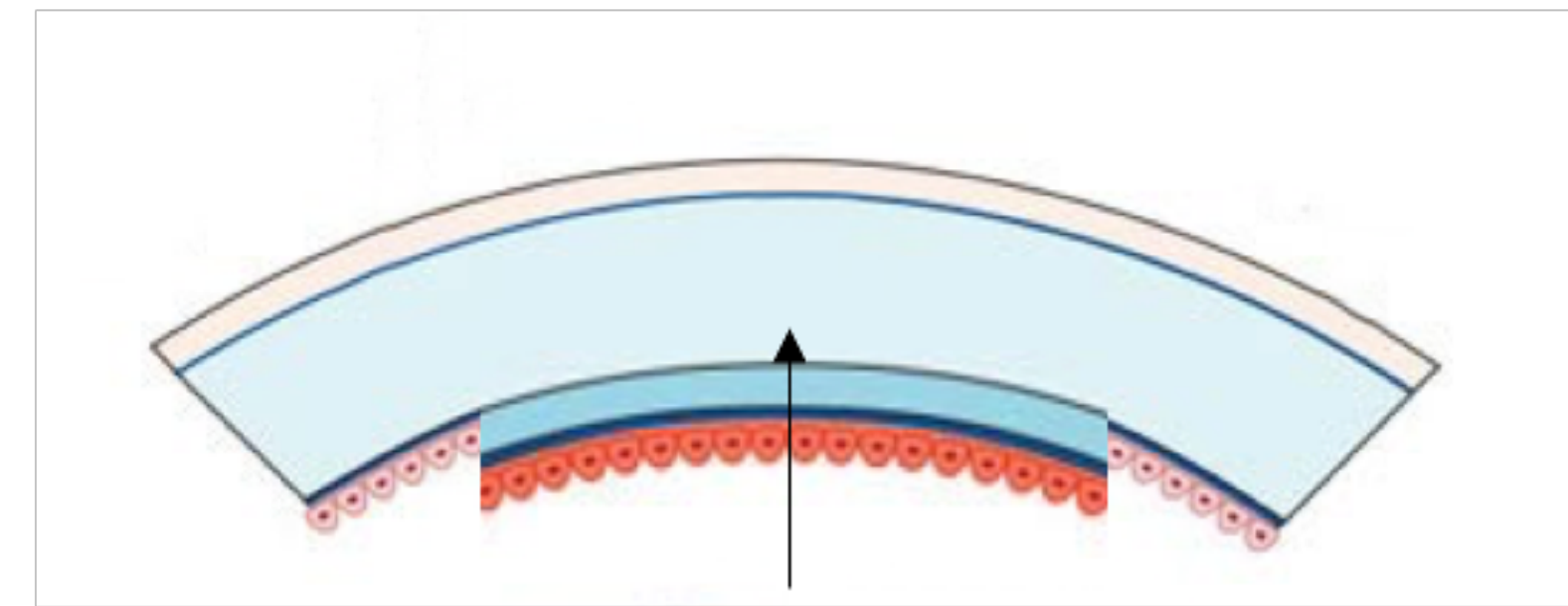
Current Treatments

Penetrating Keratoplasty



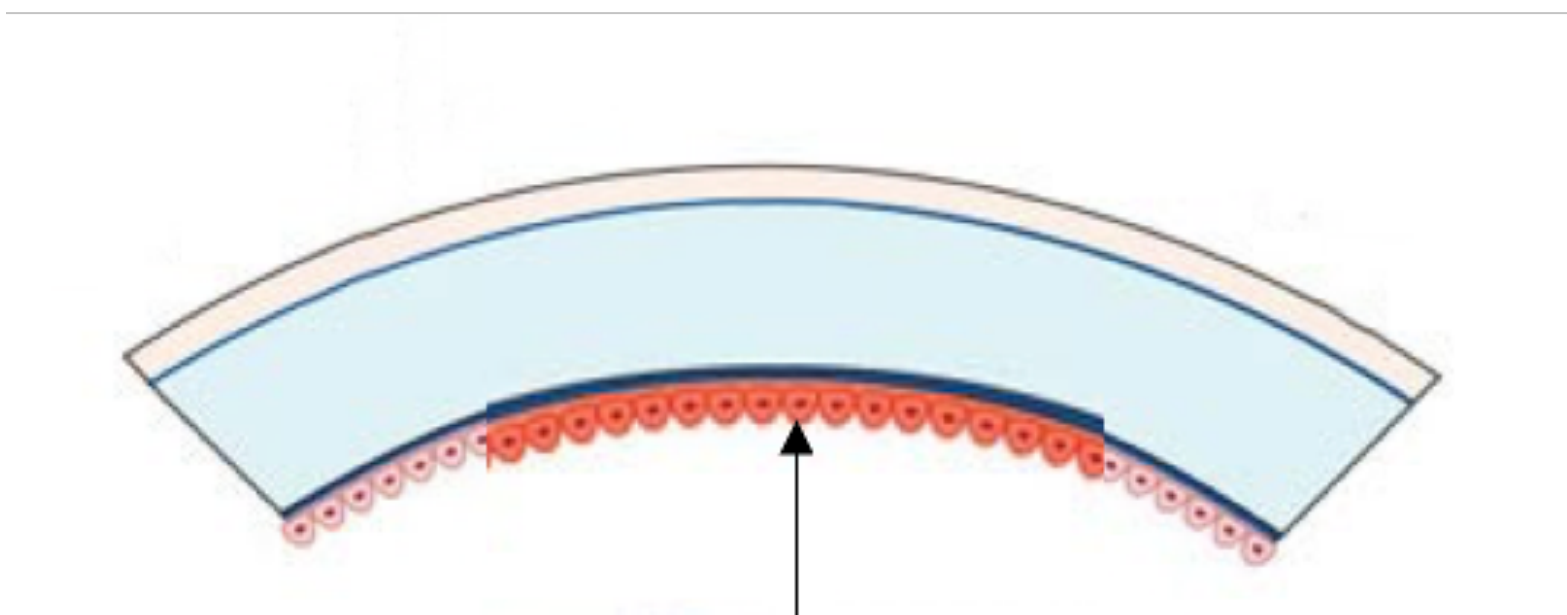
PK Graft

**Descemet's Stripping
Endothelial Keratoplasty [DSEK]**



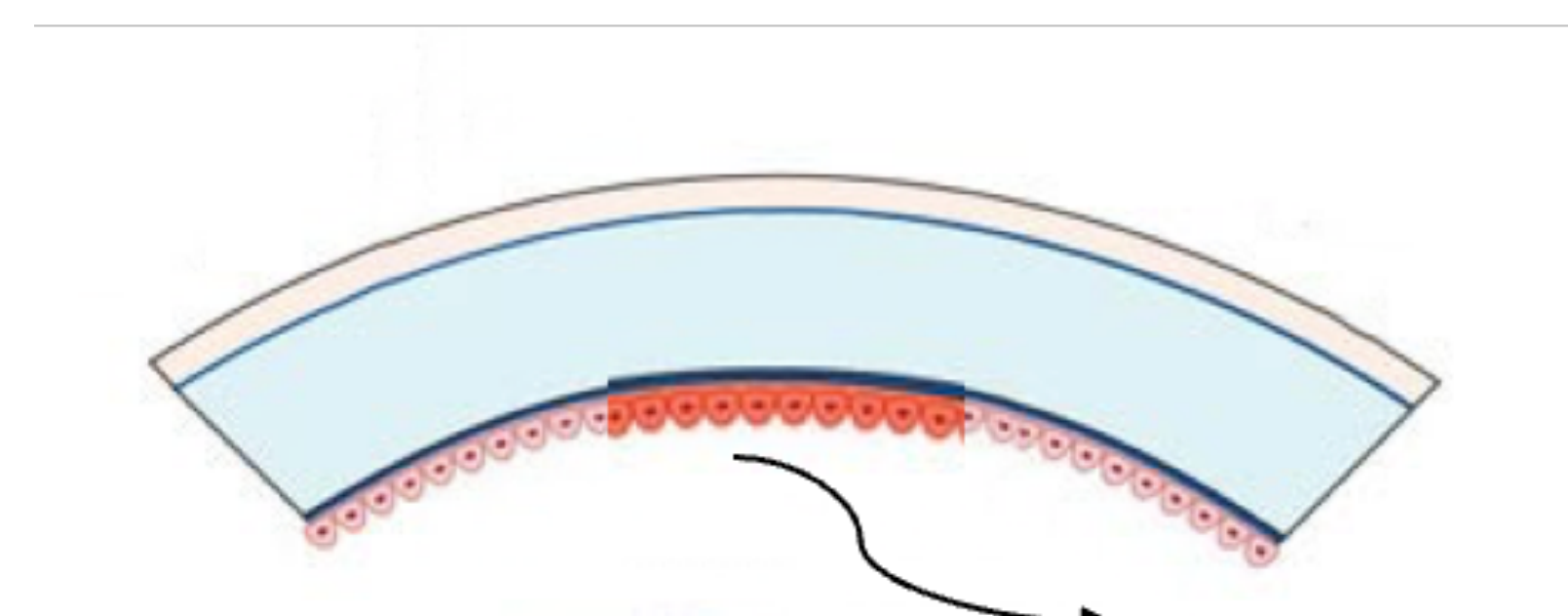
DSEK Graft

**Descemet's Membrane
Endothelial Keratoplasty [DMEK]**



DMEK Graft

**Descemet's Stripping Only
[DSO]**

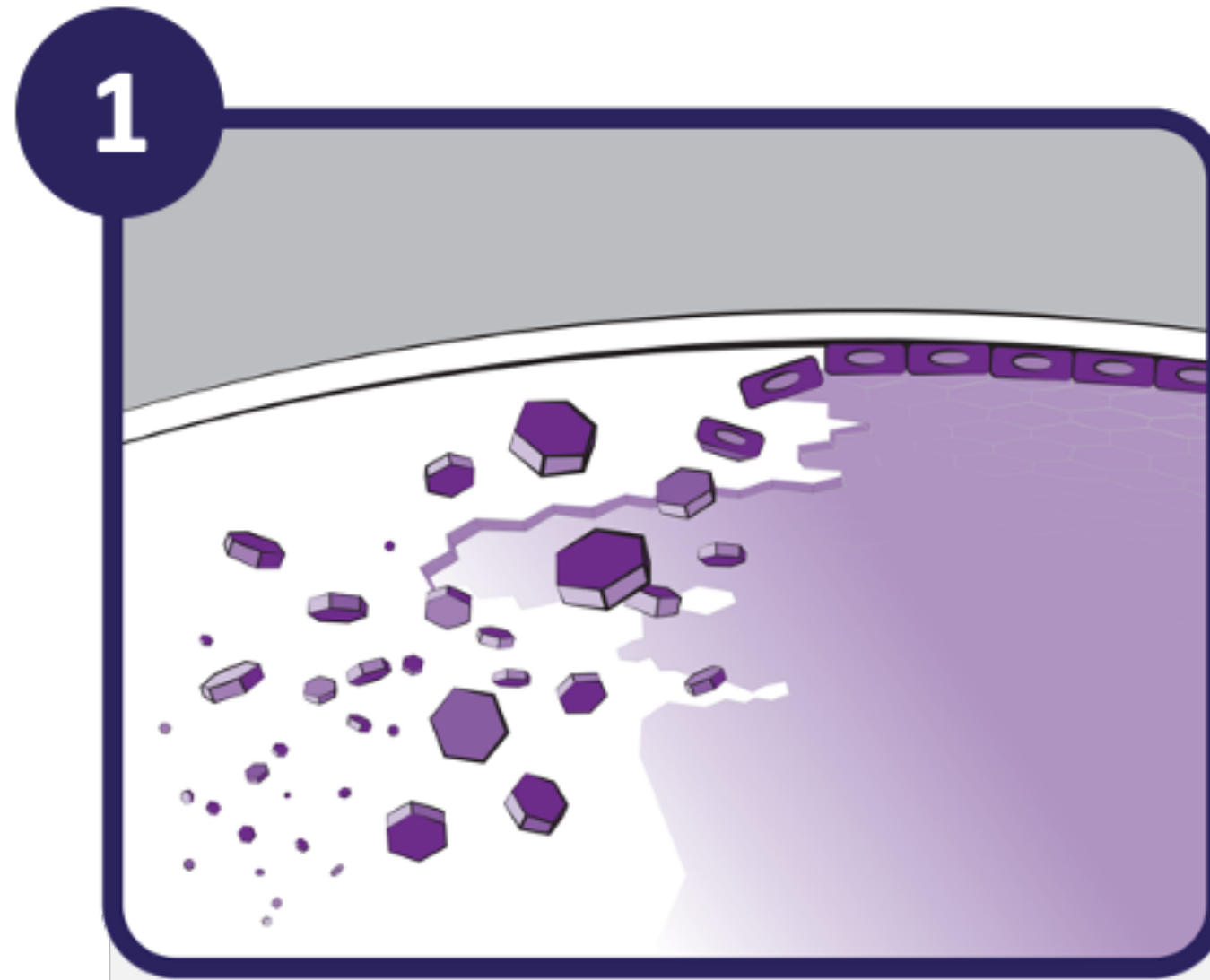


DM Stripped

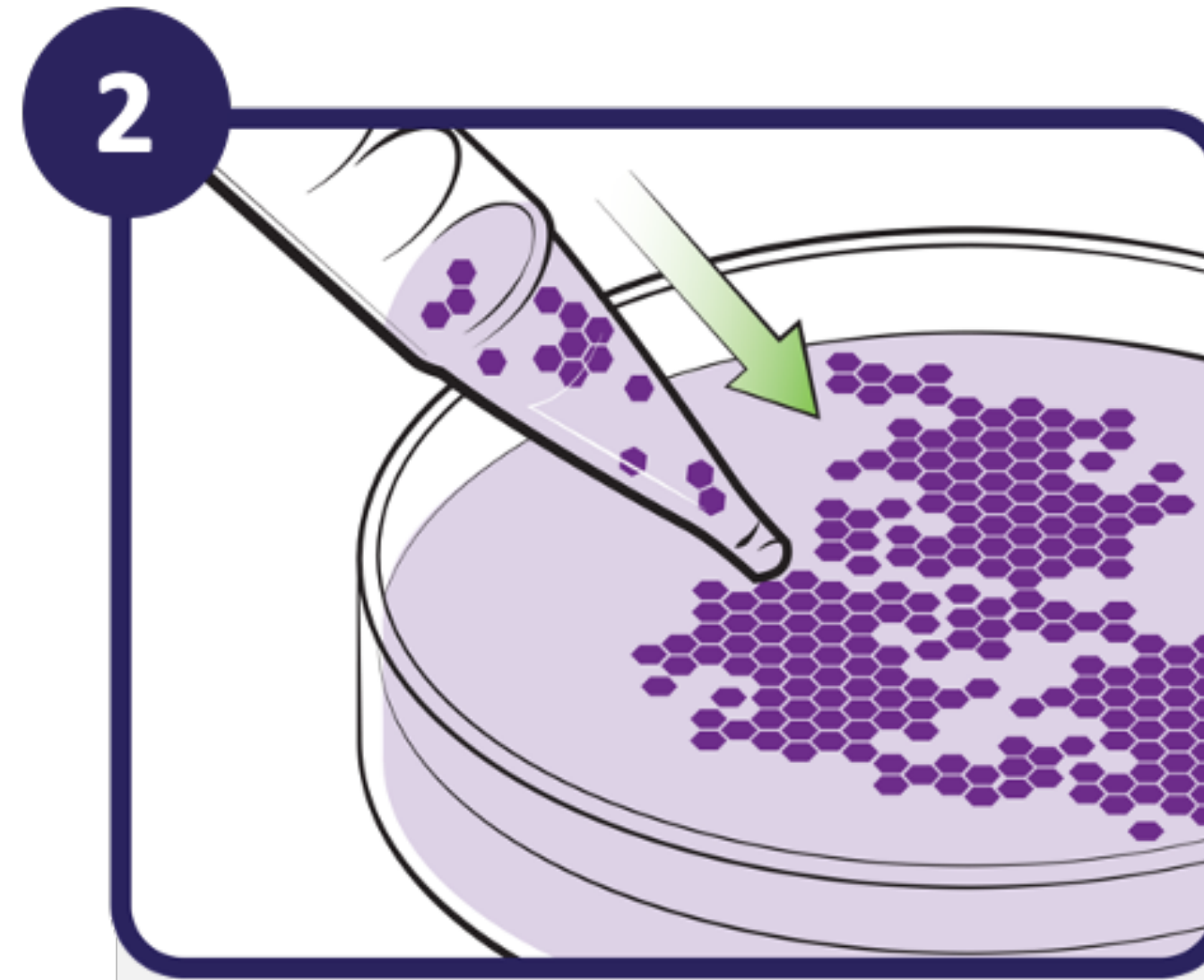
Challenges

- 1 Mastery of the procedure
- 2 Requires donor tissue
- 3 Onerous patient recovery

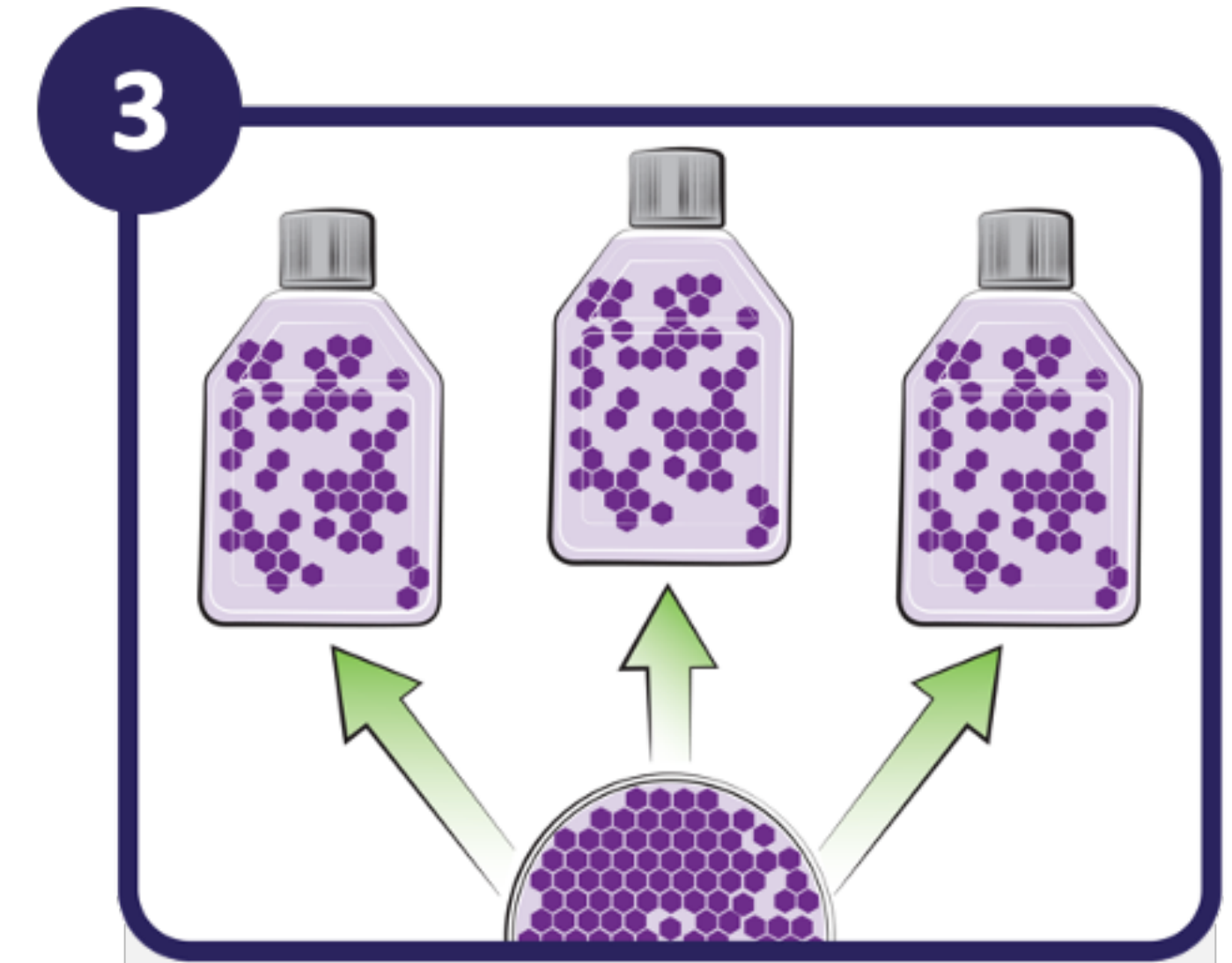
Endothelial Cell Therapy



- Donor cornea is harvested
- Corneal endothelial cells (CECs) are isolated *in vitro*



- Donor CECs are introduced to proprietary culture and propagation begins



- CECs are passaged into additional flasks for expansion
- Process repeats for multiple passages

Potentially Transformational

TRADITIONAL CORNEAL TRANSPLANTS

1  Donor



1  Patient Treated

AURION'S CORNEAL ENDOTHELIAL CELL THERAPY

1  Donor

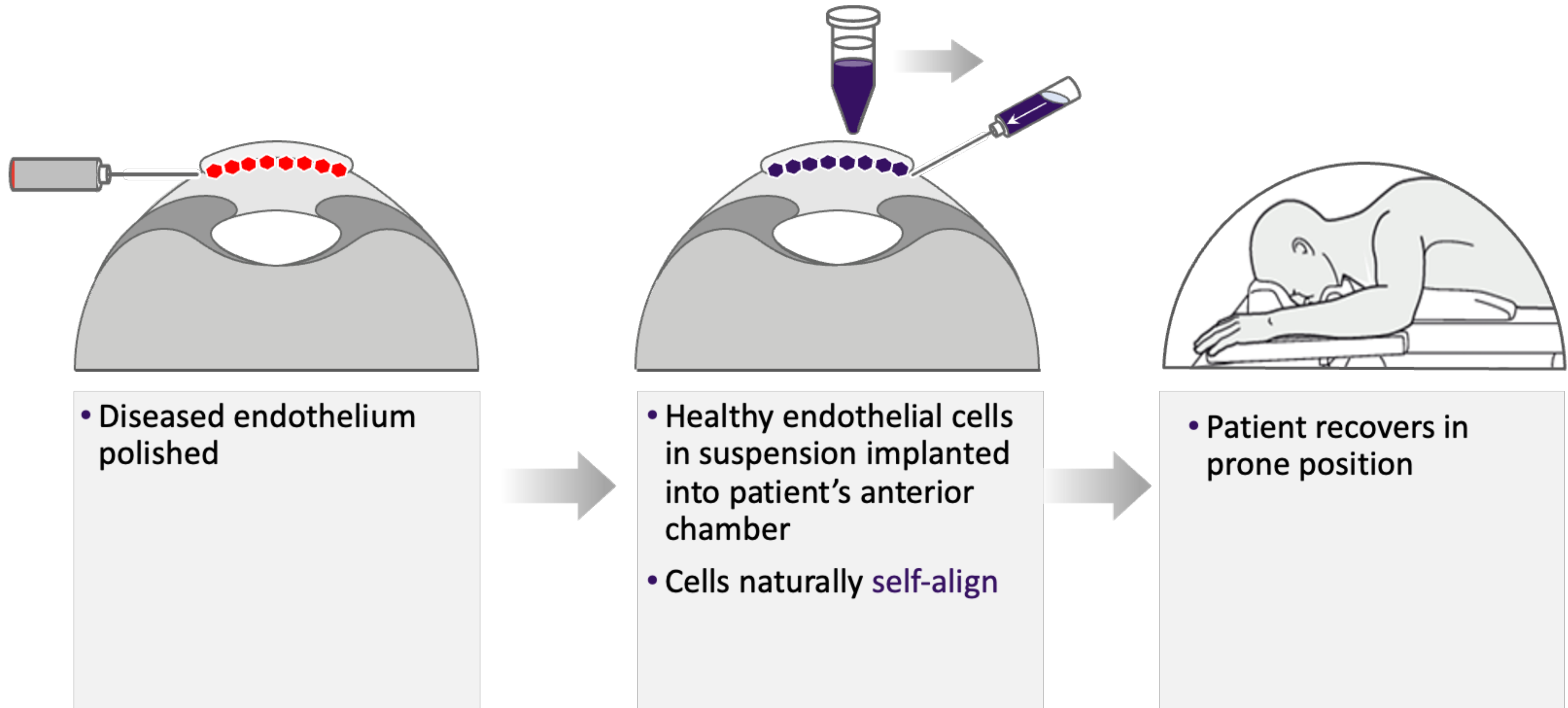


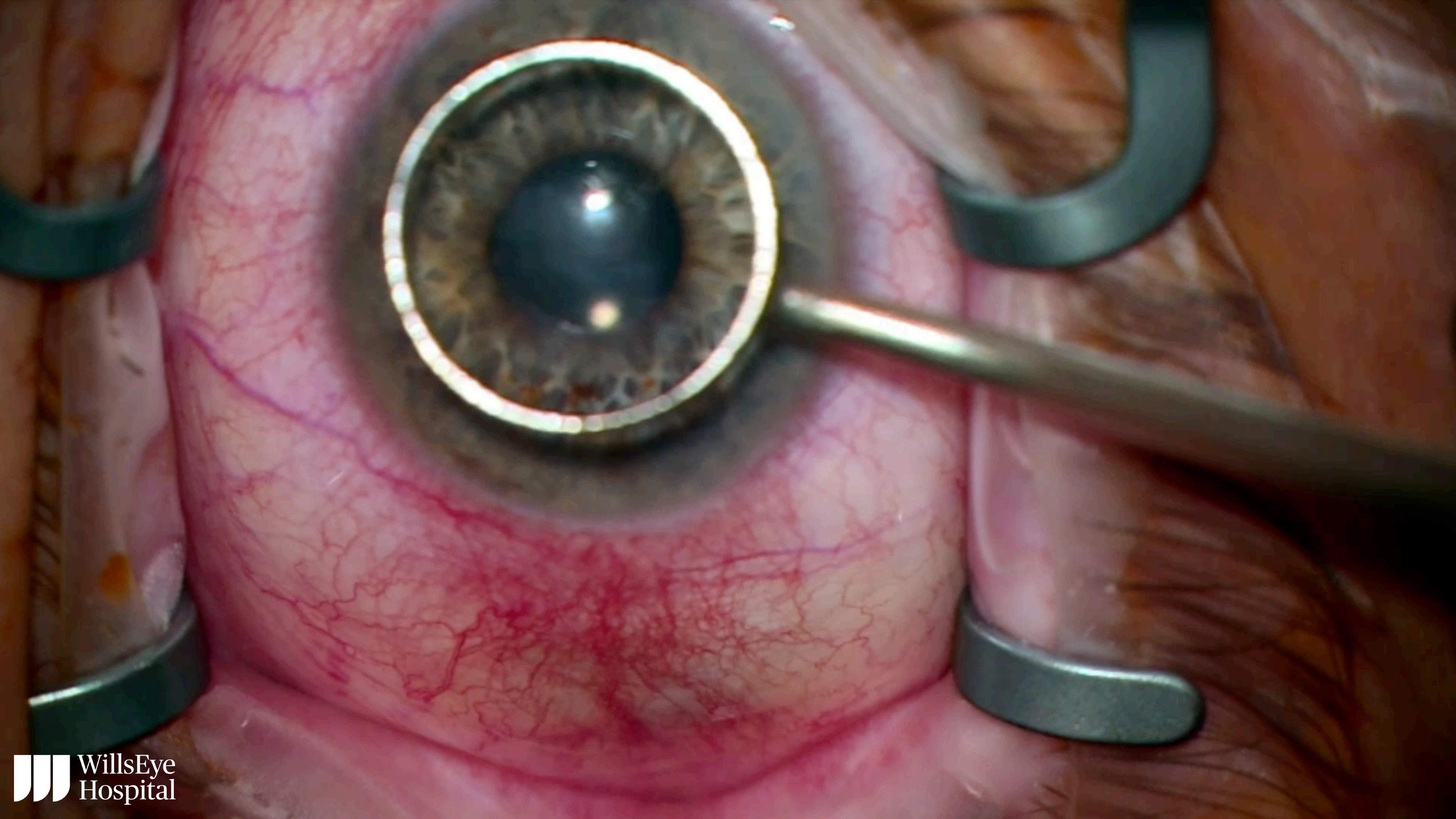
1000⁺     
    
    

Patients Treated

SCALING IS FUNDAMENTAL FOR OPTIMIZING DRUG COSTS

Endothelial Cell Therapy





Clinical Validation

275+ PROCEDURES | 7 CLINICAL TRIALS | 10+ YEARS OF FOLLOW-UP

Aurion’s Corneal Endothelial Cell Therapy Approved and Commercially Available in Japan Since 2024

Japan

2013 - 2019 (HCEC-1)

- I. First-in-human trial
- II. Dose-ranging trial
- III. Confirmatory trial
- Total of **65** procedures

Results published in *NEJM*¹ and *Ophthalmology Journal*^{2,3}

IOTA - El Salvador

November 2020 (HCEC-1)

- Proof-of-concept trial
- Humanitarian cases
- Total of **67** procedures

CLARA - US / Canada

October 2023 (AURN001)

- Phase I/II cell dose ranging vs. contributions of elements trial
- Total **97** procedures

Escalón - El Salvador

March 2022 (AURN001)

- Phase I ROCK inhibitor dose-ranging trial
- Total of **22** procedures

Results published in *Cornea*⁴

Apaneca - El Salvador

October 2024 (Cryo-AURN001)

- Phase II trial using cryopreserved AURN001
- Total **25** procedures

Clara Phase I/II Study

PROSPECTIVE, PARALLEL-ARM, DOSE RANGING, MULTI-CENTER, RANDOMIZED, DOUBLE-MASKED STUDY

POPULATION

Corneal edema secondary to corneal endothelial dysfunction

12 Month Safety + Efficacy

ENDPOINTS

Primary:

- Proportion of responders with a ≥ 15 -letter improvement from baseline in Best Corrected Visual Acuity (BCVA) at 6 months

Secondary:

- Change from baseline in BCVA & CCT at each timepoint

Safety:

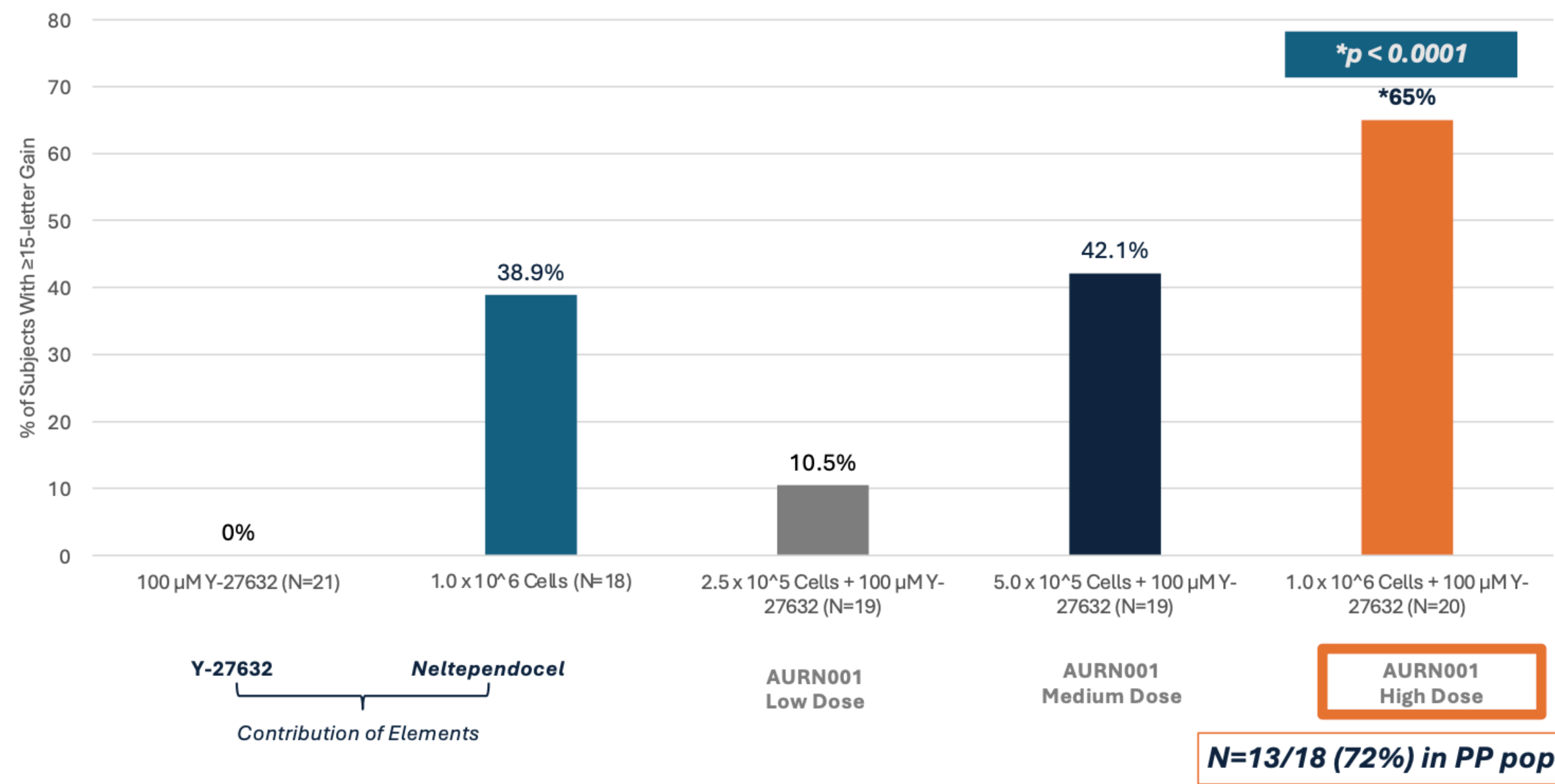
- Safety and tolerability measured by TEAEs, loss from baseline in BCVA > 15 letters, graft rejection and rescue rate

Screening	Arm 1	AURN001 High Dose: 1.0×10^6 <i>neltependocel</i> + 100 μ M Y-27632 with EP*	n=20
	Arm 2	AURN001 Medium Dose: 5.0×10^5 <i>neltependocel</i> + 100 μ M Y-27632 with EP*	n=19
	Arm 3	AURN001 Low Dose: 2.5×10^5 <i>neltependocel</i> + 100 μ M Y-27632 with EP*	n=19
	Arm 4	Y-27632 Solution : 100 μ M Y-27632 with EP*	n=21
	Arm 5	Neltependocel Suspension: 1.0×10^6 with EP*	n=18

*EP = Endothelial Polishing
V=Visit

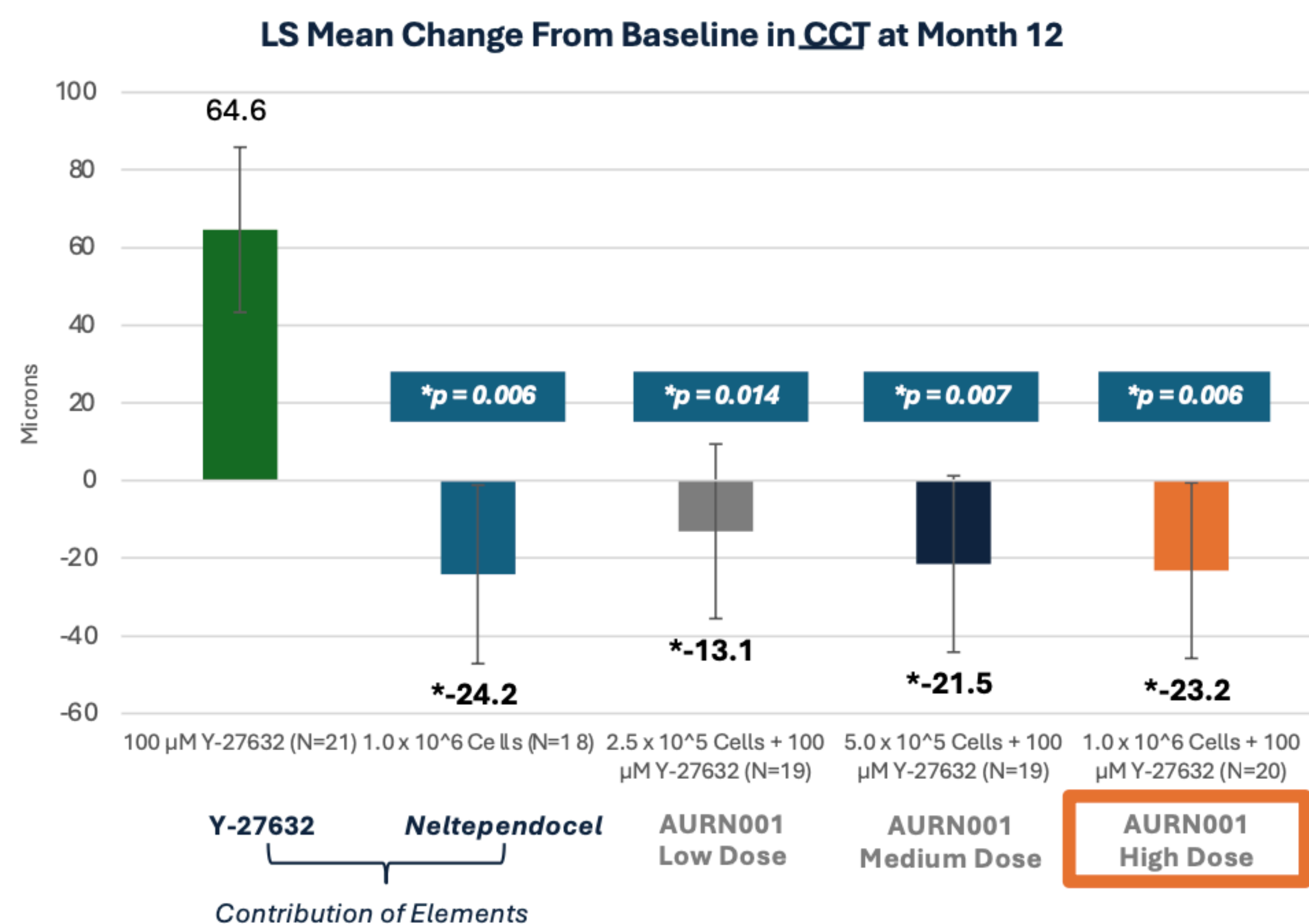
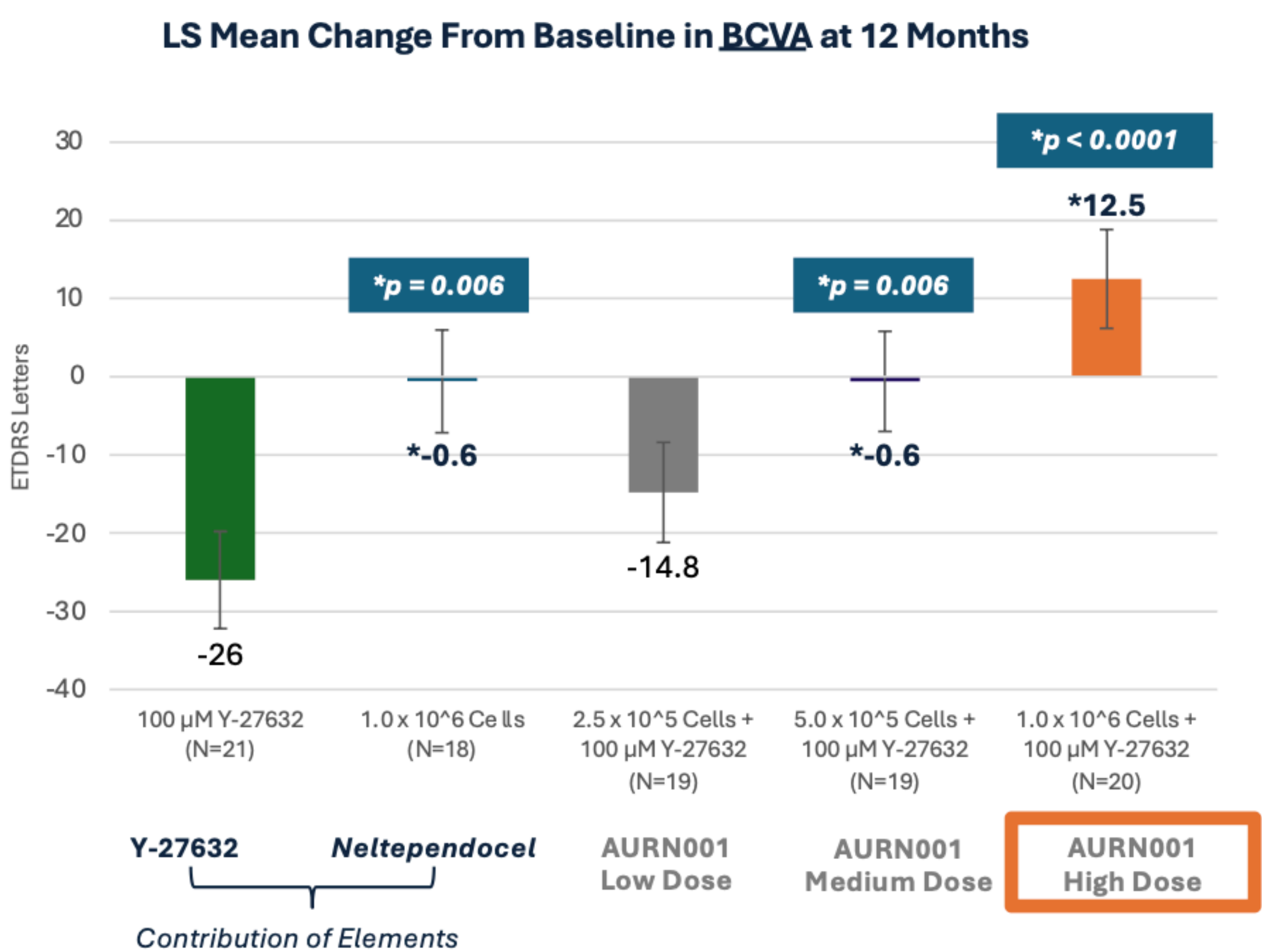
Clara Primary Efficacy Endpoint

Proportion of Responders with a ≥15-Letter Improvement From Baseline in BCVA At Month 12 (FAS)



1. CLARA trial not powered to show statistical significance. Statistical analyses are descriptive

Clara Secondary Efficacy Endpoints



Note: For CFB, LS mean, and Difference are calculated using the Analysis of Covariance (ANCOVA)

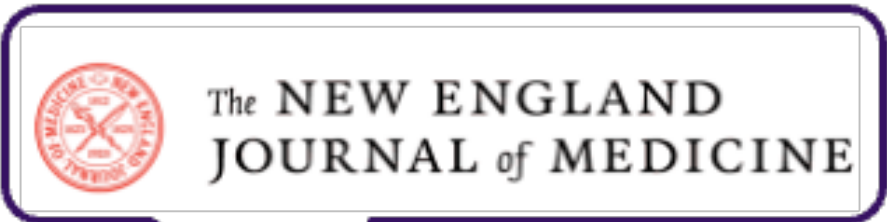
Note: For CFB, LS mean, and Difference are calculated using the Analysis of Covariance (ANCOVA)

Note: Error Bars represent Standard Error

1. CLARA trial not powered to show statistical significance. Statistical analyses are descriptive

First 11 Patients Treated in Japan

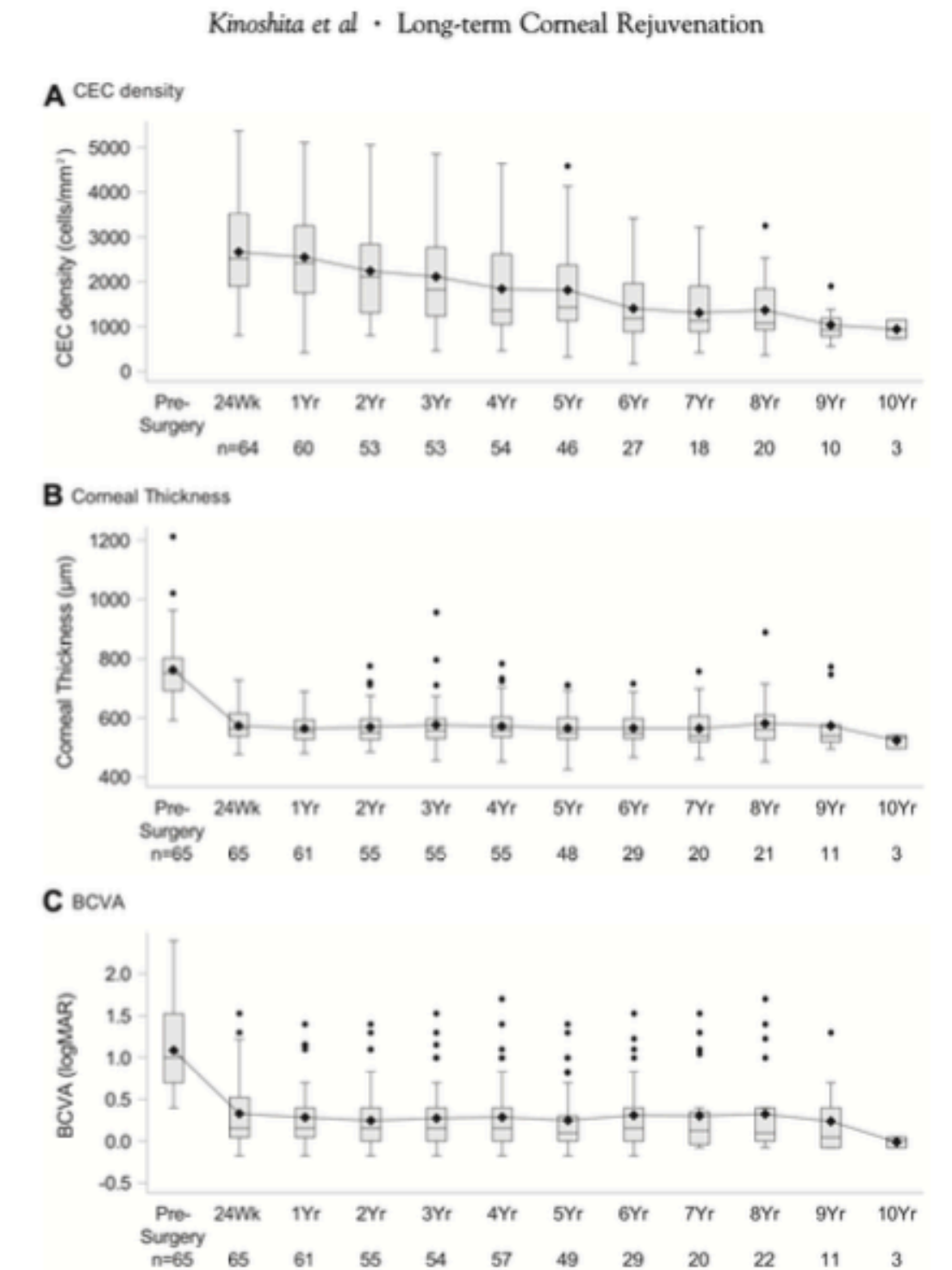
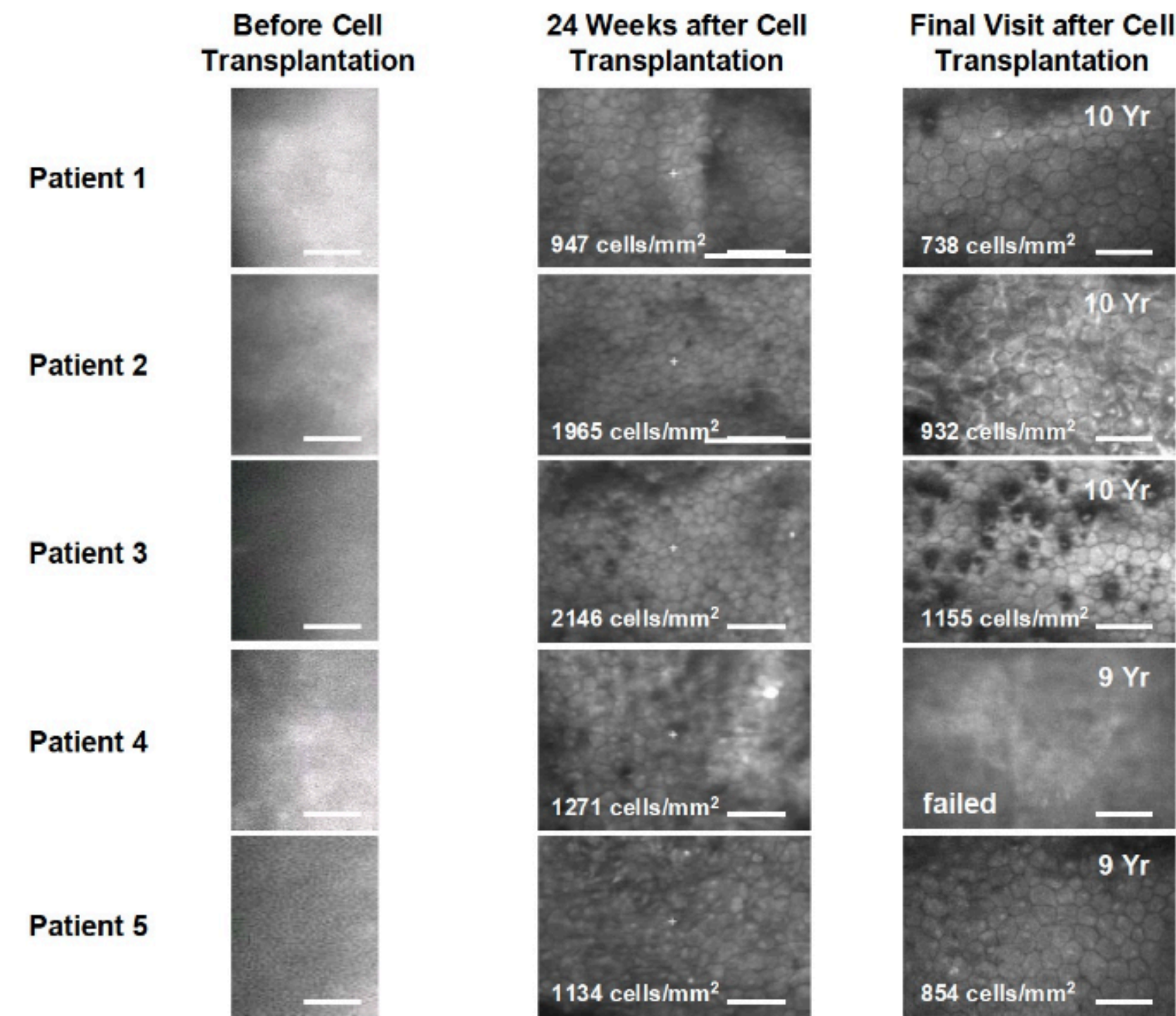
Long-Term Safety and Efficacy



Exploratory Endpoints	Pre-op	6 Months	2 Years	5 Years	Healthy Range ¹
Mean Corneal Thickness (µm)	743	549	552	555	540 - 555
Mean Visual Acuity (Snellen)	20/220	20/33	20/23	20/30	20/20 – 20/40
Safety / Tolerability	N/A	No SAE	No SAE	No SAE	N/A

¹<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3810328/>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3545036/#!po=8.33333>

10 YEAR SUSTAINED THERAPEUTIC EFFECT OF CORNEAL ENDOTHELIAL CELL THERAPY WITH NO REPORTED GRAFT REJECTIONS



Long-term Corneal Rejuvenation after Transplantation of Cultured Human Corneal Endothelial Cells

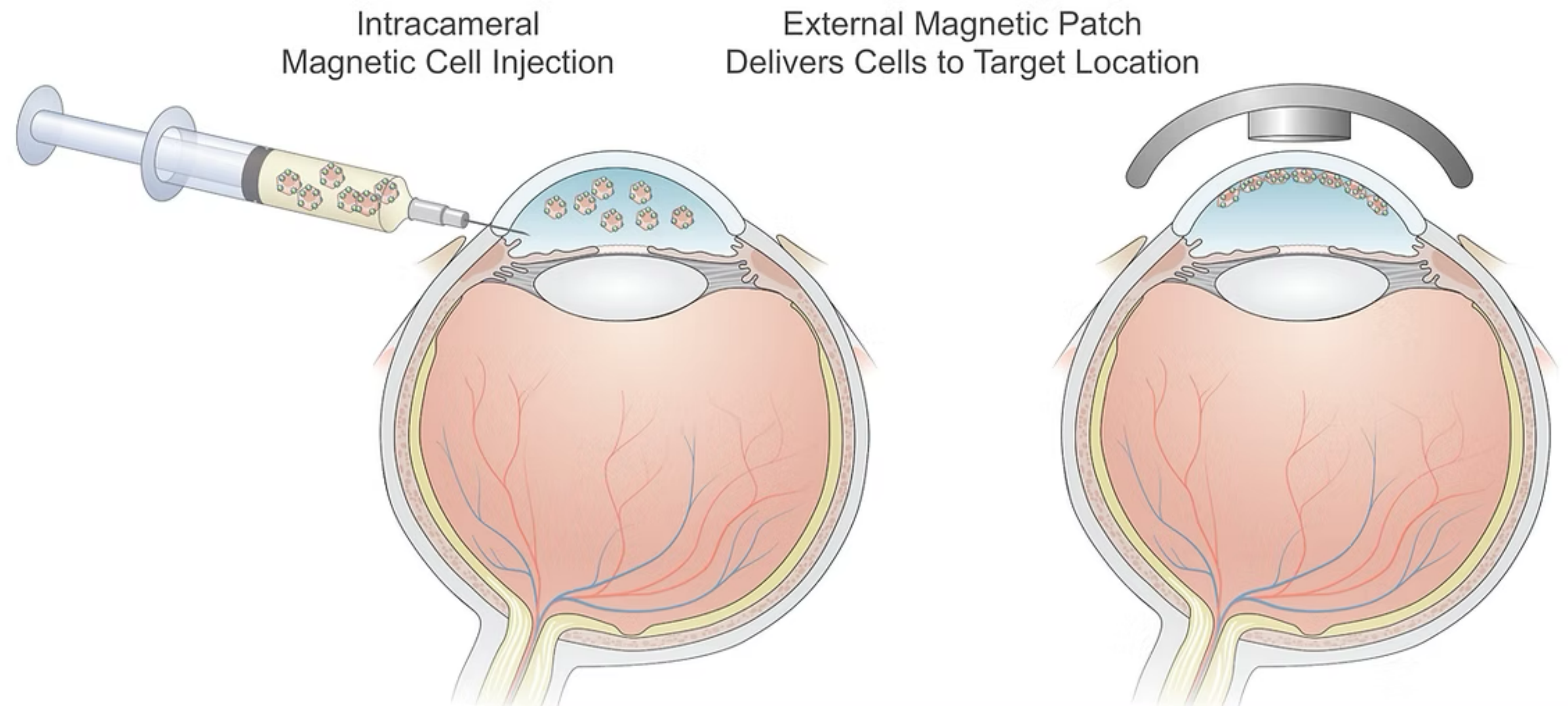
Shigeru Kinoshita, MD, PhD,^{1,*} Morio Ueno, MD, PhD,^{2,*} Munetoyo Toda, PhD,¹ Kojiro Imai, MD, PhD,³ Yasufumi Tomioka, MD, PhD,² Kohsaku Numa, MD, PhD,² Hiroshi Tanaka, MD, PhD,² Tsutomu Inatomi, MD, PhD,⁴ Takanori Kameda, MD, PhD,⁵ Akitaka Tsujikawa, MD, PhD,⁵ Michio Hagiya, PhD,² John Bush, BA,² Satomi Sakabayashi, BA,⁶ Satoshi Teramukai, PhD,⁶ Junji Hamuro, PhD,² Chie Sotozono, MD, PhD²

- Corneal clarity sustained through 10 years post-treatment
- Long-term stability in BCVA, CCT, and CECD
- **Excellent safety profile:** No increase in average IOP over time, no ocular serious adverse events (SAEs), and no graft rejection

Magnetic Endothelial Cell Delivery

Phase 1/2 Study Press Release

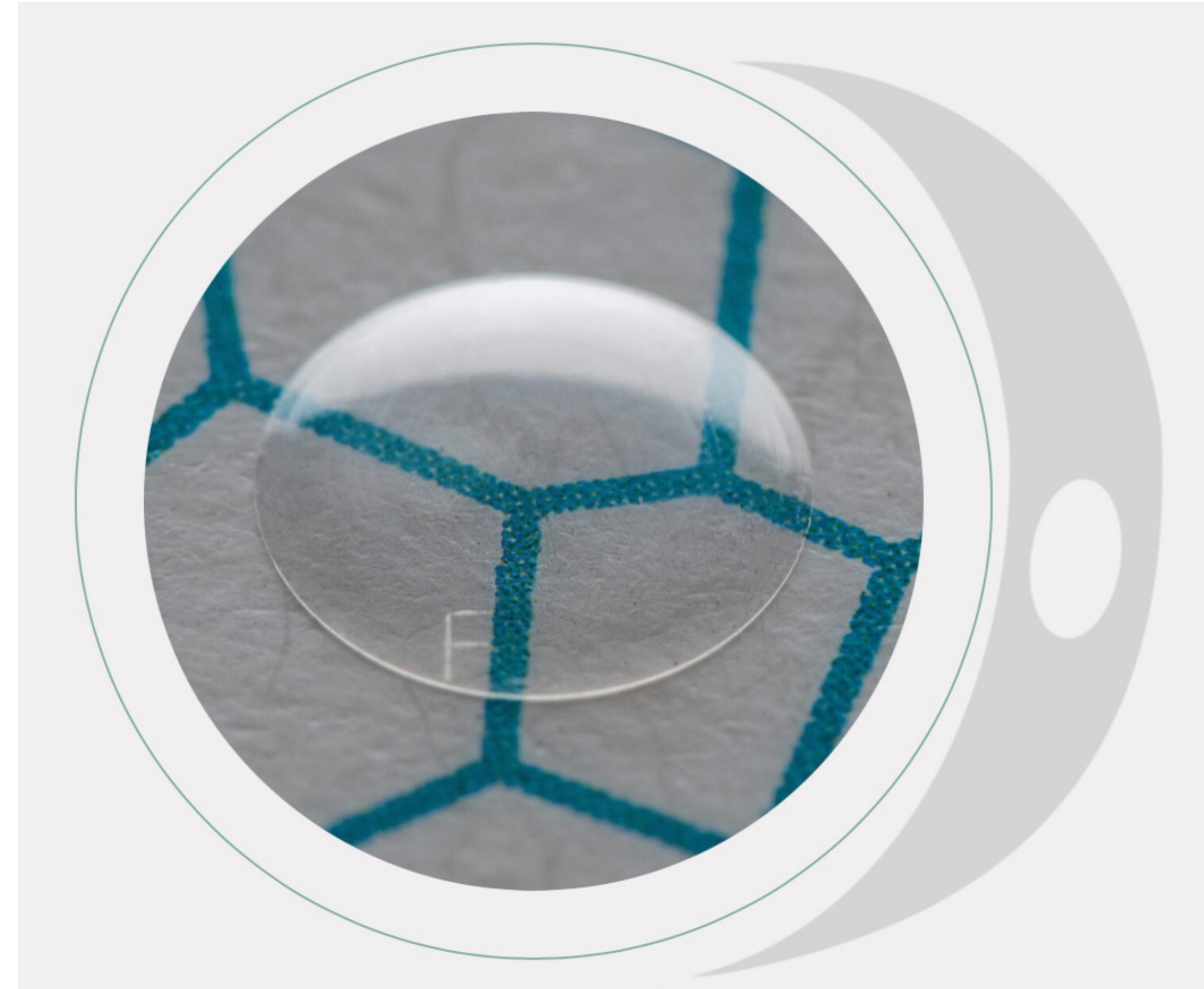
- Three different dose levels
 - 150,000, 500,000, and 1 million endothelial cells
- 150,000 cell cohort 6 months results
 - 11 letter mean change in BCVA
 - 38% subjects with at least 15 letter gain
- Subset of patients showed 50% reduction in central guttae



- Does not require removal of existing endothelial layer
- Can be done at the slit lamp

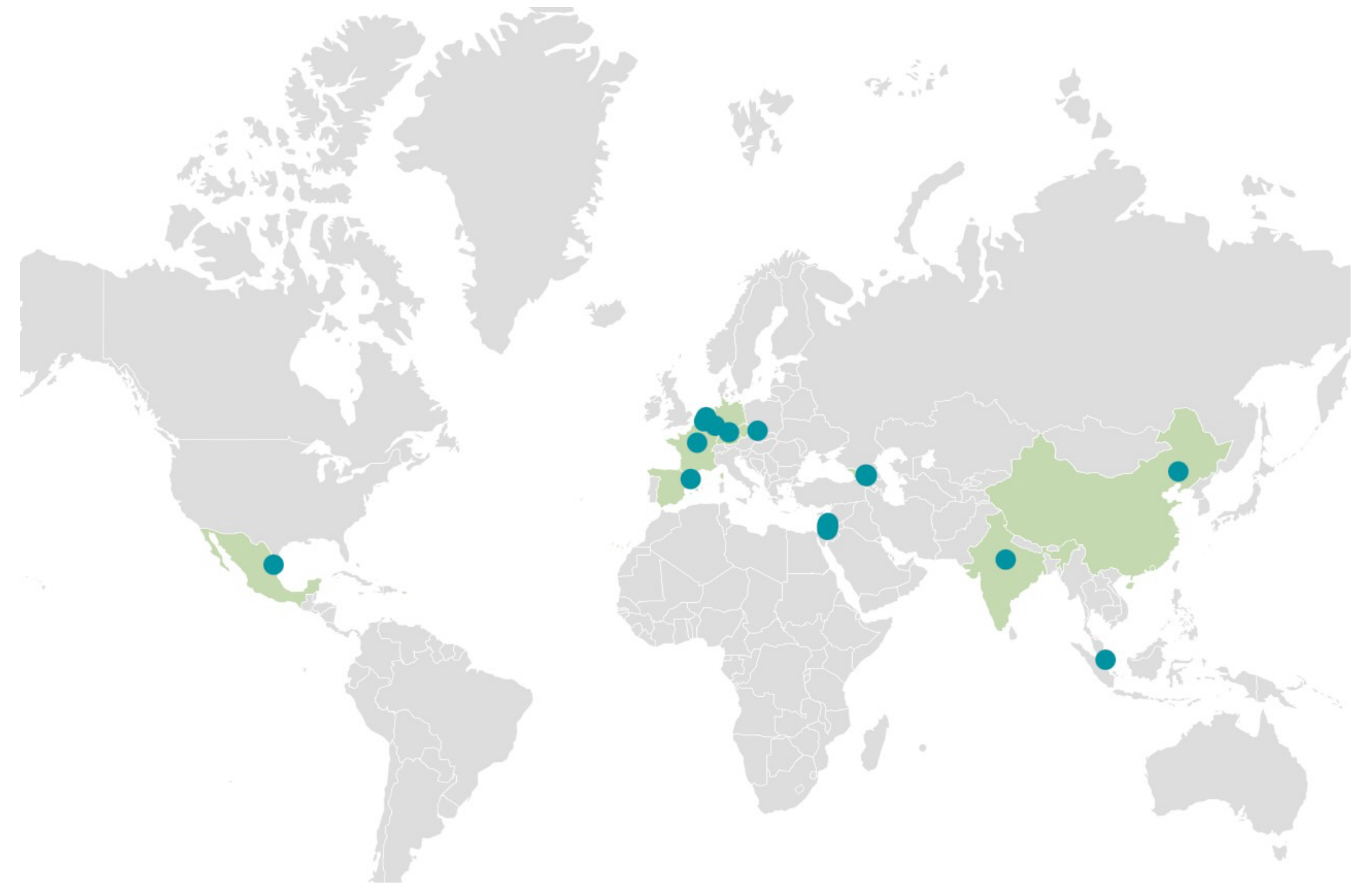
Artificial Endothelial Layer

- Synthetic hydrophilic flexible material
 - 6.5mm diameter
 - 50 micron thick
 - Dome shaped to match posterior cornea
- Artificial fluid barrier to replace disease endothelium
- Aqueous penetration into cornea is blocked leading to deturgescence

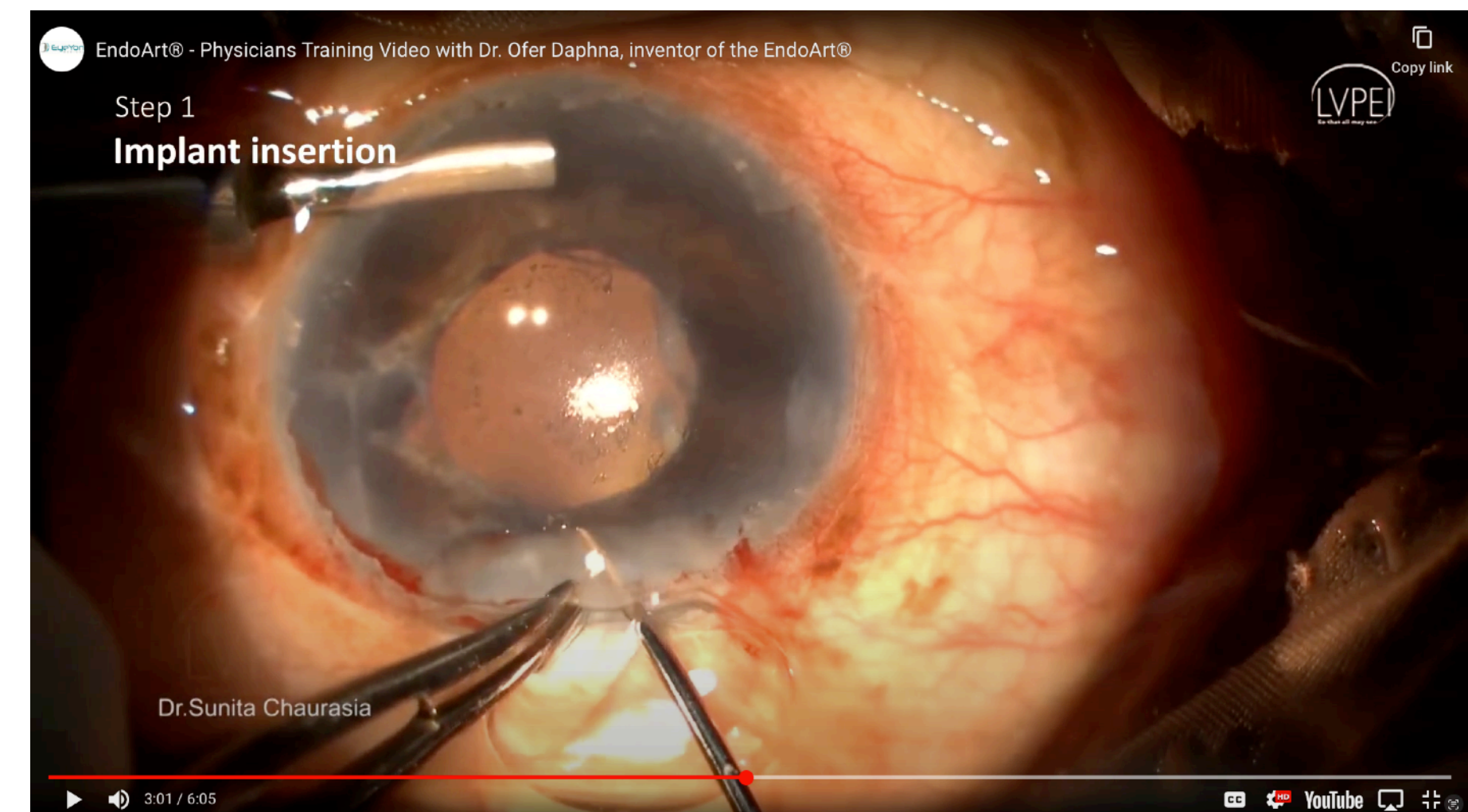
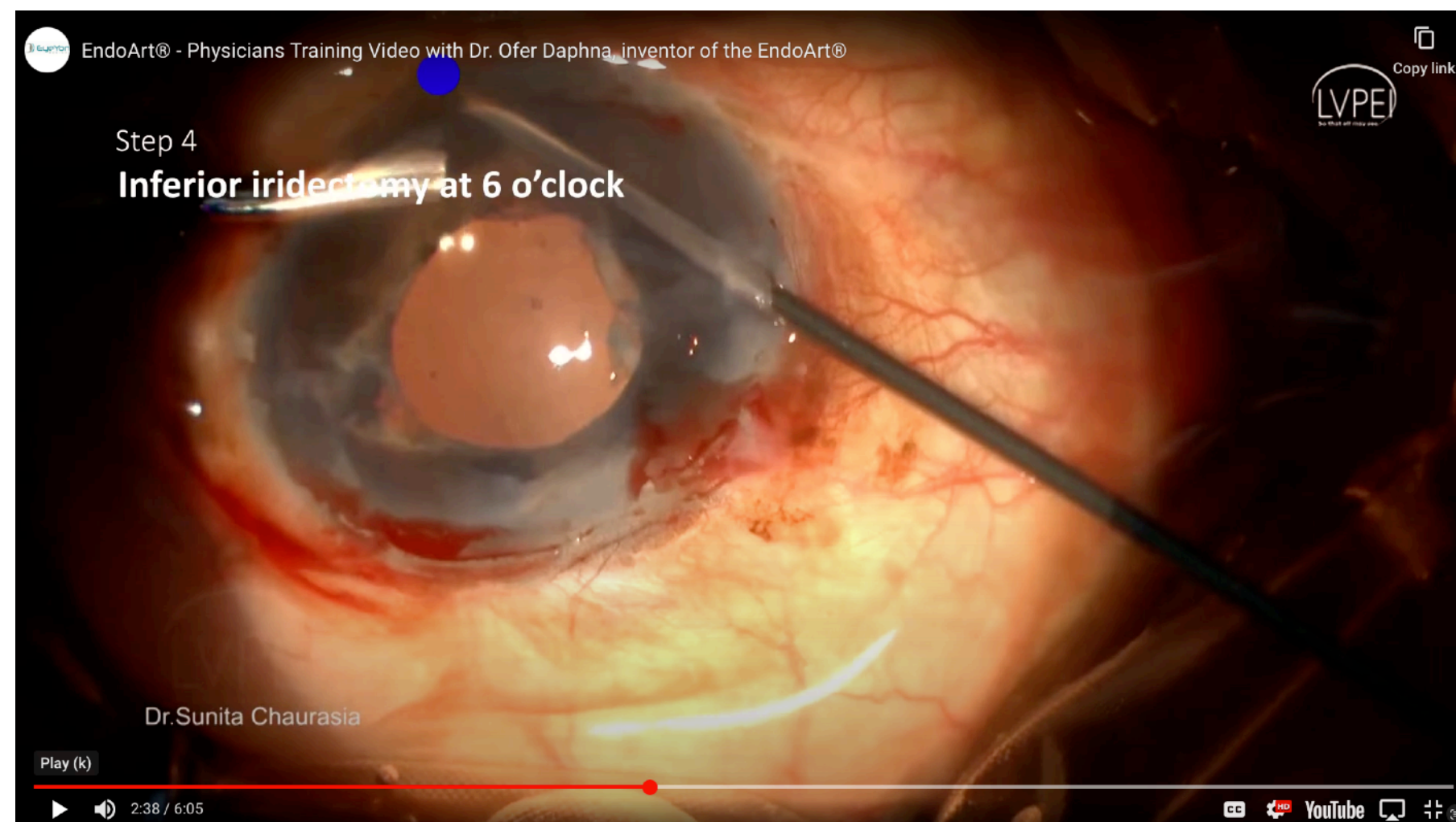
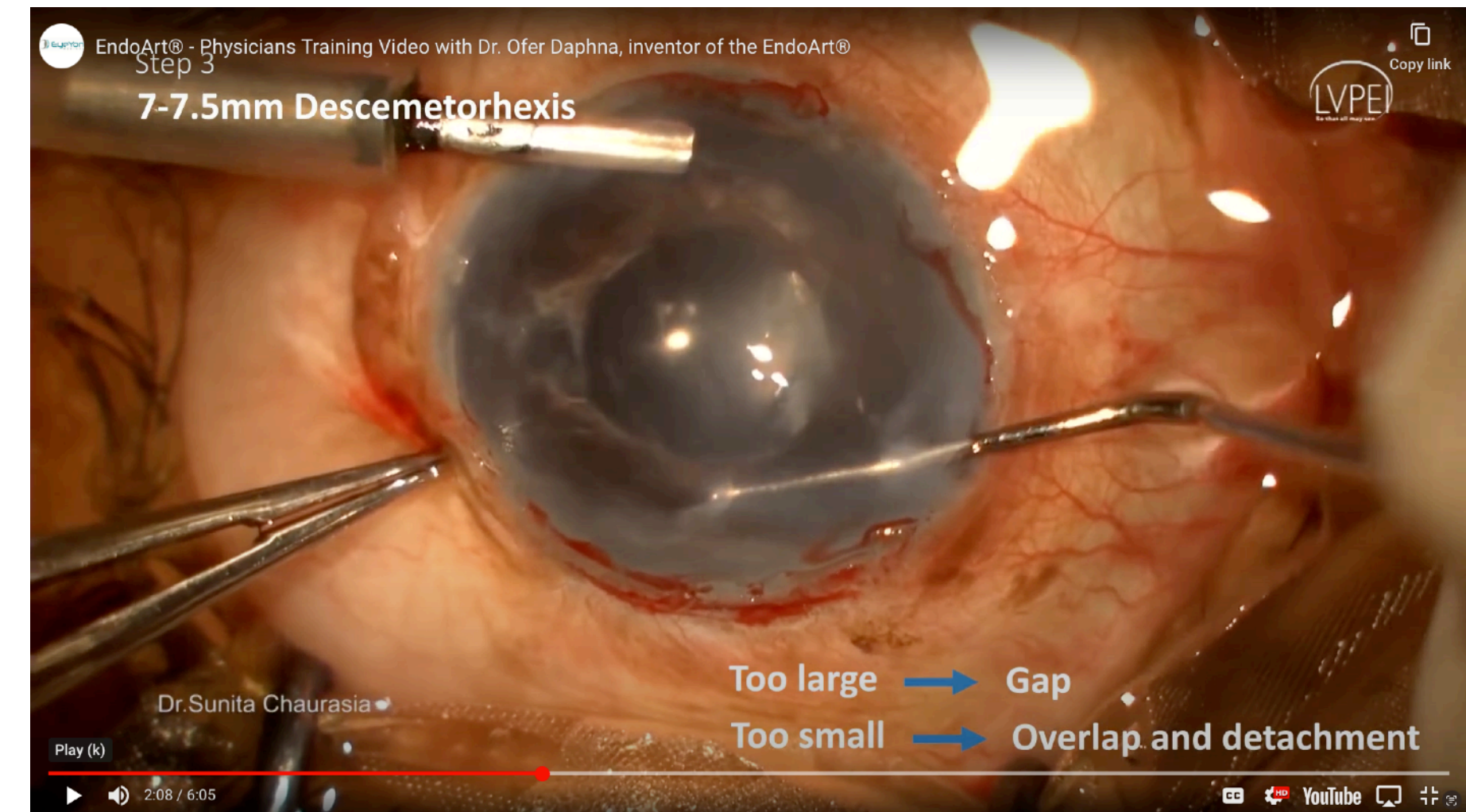
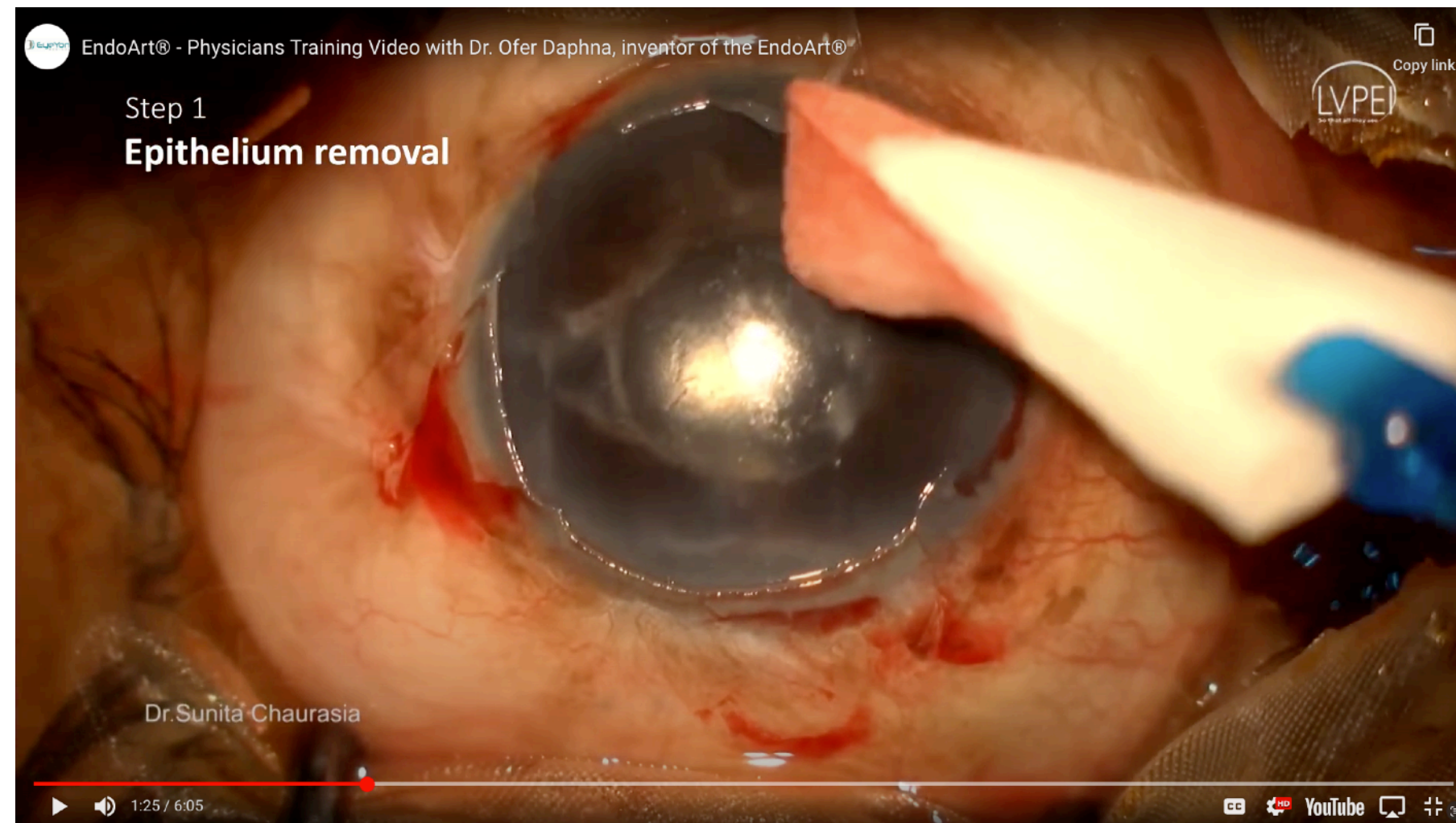


Artificial Endothelial Layer

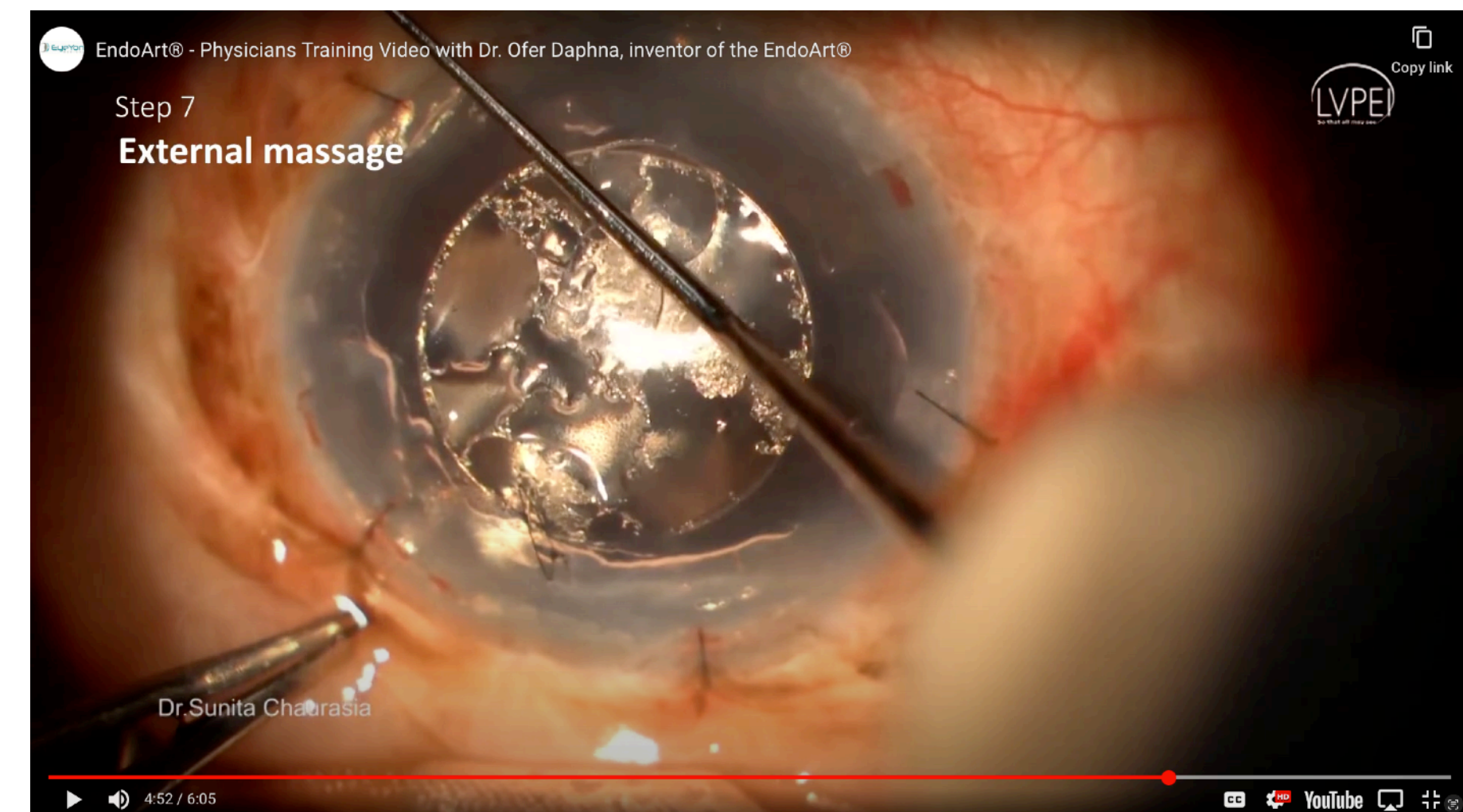
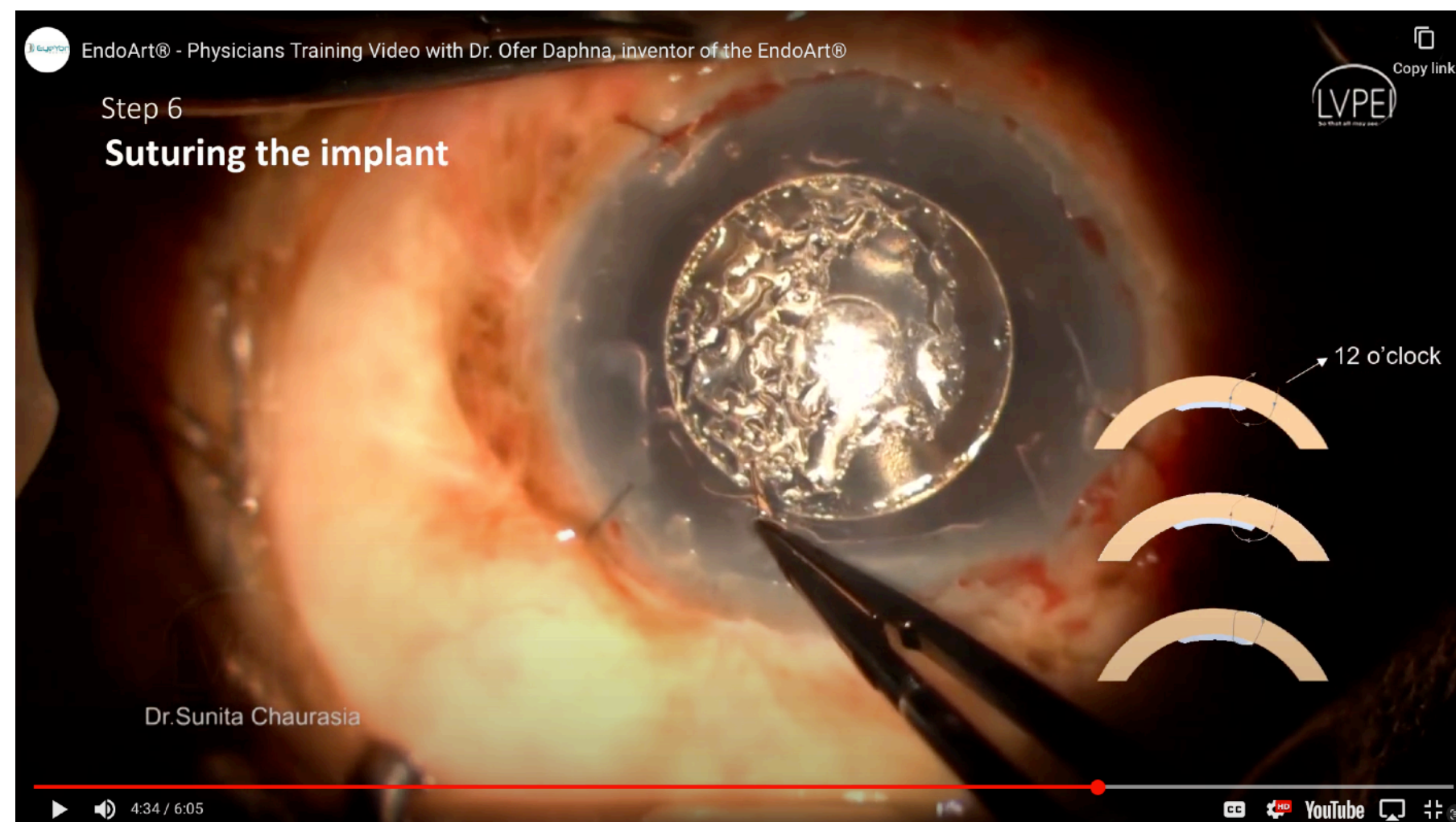
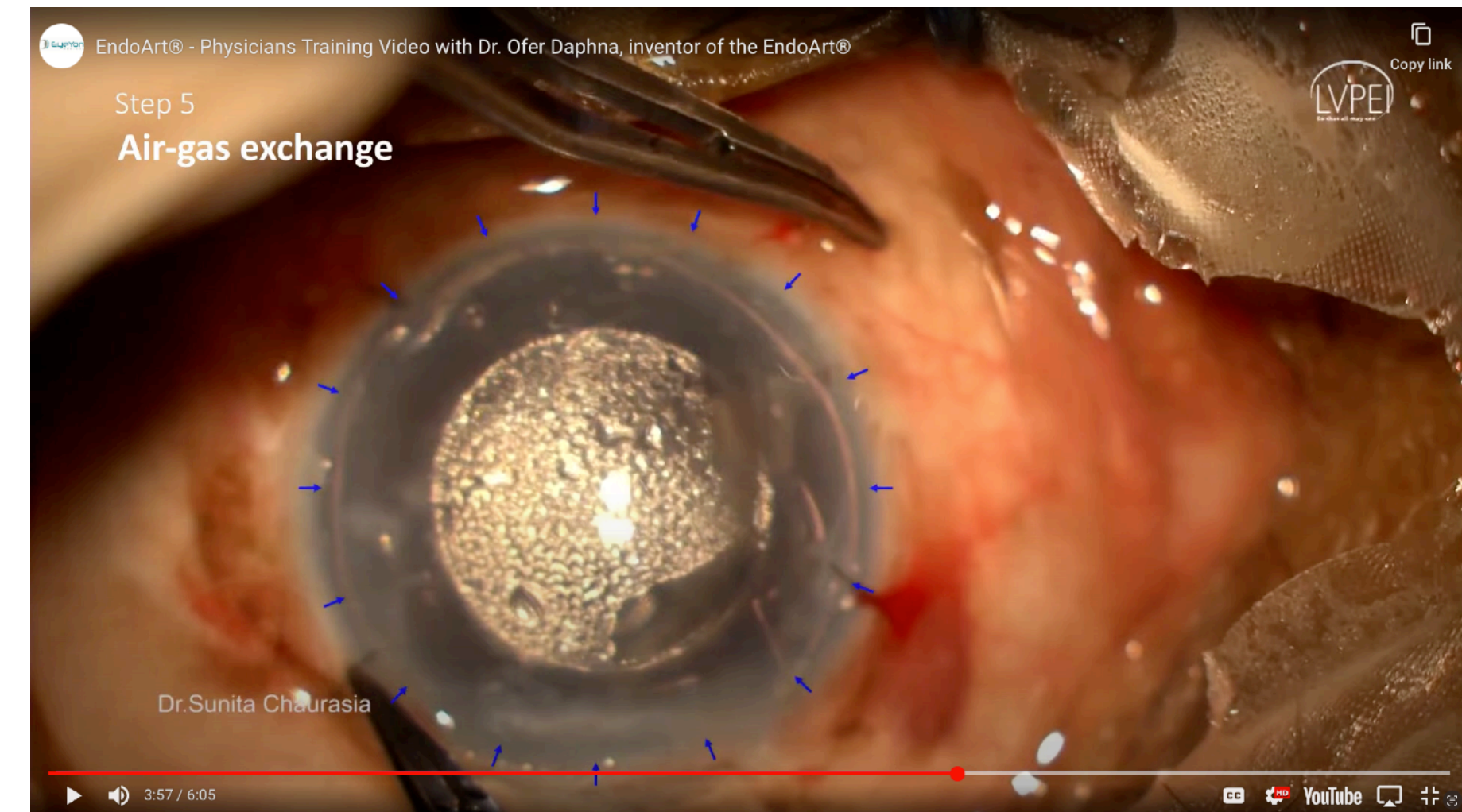
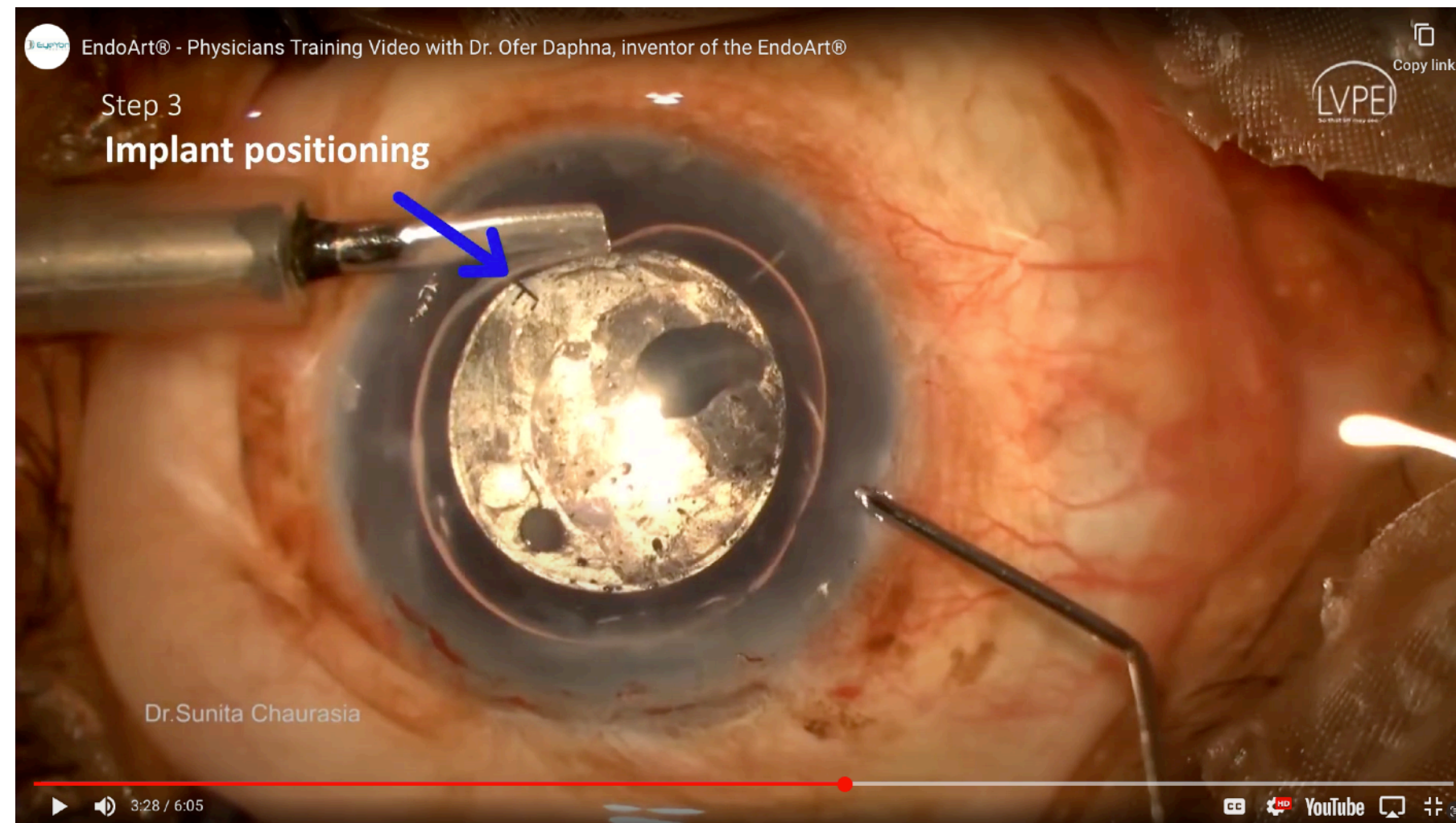
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Artificial Endothelial Layer



Artificial Endothelial Layer



Artificial Endothelial Layer

- First in human results
- 12 month followup
- 56% re-bubble rate with final technique

- 57% re-bubble rate

- 80% re-bubble rate

No device related serious adverse events that would question biocompatibility (i.e. corneal melt, neovascularization, anterior chamber inflammation)

OPEN

A Novel Artificial Endothelial Layer for the Treatment of Corneal Edema

Ofer Daphna, MD,†
Sunita Chaurasia, MD,‡

Purpose: The purpose of this study was to report the efficacy results of an artificial lamellar keratoplasty in patients with chronic corneal edema.

Methods: The EndoArt (EyeYon Medical, Ness Ziona, Israel) artificial endothelial replacement membrane was implanted in 24 eyes of patients with chronic corneal edema. We present the results of a prospective, open-label, single-arm study over a 12-month period.

Results: Twenty-four patients were included in the study. Sixty percent gained at least 3 early visual acuity lines. No serious adverse events were reported. Six months follow-up, showing a reduction in corneal thickness from $759 \pm 116 \mu\text{m}$ to $588 \pm 60 \mu\text{m}$ (excluding the EK graft) postoperatively ($P = 0.015$). No severe device-related complications developed after surgery, although most patients required more than 1 air-gas bubble injection to achieve complete implant adhesion. All patients experienced preoperative reduction in subjective ocular pain.

Conclusions: Synthetic endothelial replacement membrane implantation improves central corneal transparency and visual acuity in patients with failed EK and guarded prognosis for repeat keratoplasty. No significant implant-related adverse events occurred after surgery.

Key Words: artificial endothelial keratoplasty, bullous keratopathy, corneal graft failure, DSEK, late endothelial graft failure, endothelial transplantation, corneal edema

(*Cornea* 2024;43:1088–1094)

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OPEN

Corneal Endothelial Replacement Membrane Implantation After Failed Repeat Endothelial Keratoplasty

Luigi Fontana, MD, PhD,*† Natalie di Geronimo, MD,*† Michela Cennamo, MD,‡ Rita Mencucci, MD,‡
Piera Versura, BSD,*† and Antonio Moramarco, MD*†

Purpose: The purpose of this study was to report the outcomes of a novel artificial endothelial replacement membrane implant for treating corneal edema after failed repeat endothelial keratoplasty (EK).

Design: This was a retrospective interventional case series.

Methods: Patients with chronic corneal edema underwent removal of the EK graft and implantation of an artificial endothelial replacement membrane (EndoArt, EyeYon Medical, Israel) several months after 2 or more Descemet stripping endothelial keratoplasty procedures. The implant was secured to the posterior corneal surface using an air–gas bubble. Outcome measures included corrected distance visual acuity (logMAR), central corneal thickness, device-related complications, and ocular discomfort.

Results: Five eyes of 5 patients underwent EndoArt implantation. Six months after surgery, the synthetic endothelial replacement membrane was well-centered and adherent to the posterior corneal surface, with improvement in central corneal transparency in all patients. Corrected distance visual acuity increased from mean 1.26 ± 0.25 (logMAR) preoperatively to 0.74 ± 0.44 (logMAR) postoperatively ($P = 0.06$). Central corneal thickness significantly decreased from a mean of $805 \pm 135 \mu\text{m}$ (excluding the EK graft) preoperatively to $588 \pm 60 \mu\text{m}$ (excluding the EndoArt) postoperatively ($P = 0.015$). No severe device-related complications developed after surgery, although most patients required more than 1 air–gas bubble injection to achieve complete implant adhesion. All patients experienced preoperative reduction in subjective ocular pain.

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CLINICAL SCIENCE

OPEN

Early Outcomes of an Artificial Endothelial Replacement Membrane Implantation After Failed Repeat Endothelial Keratoplasty

Luigi Fontana, MD, PhD,*† Natalie di Geronimo, MD,*† Michela Cennamo, MD,‡ Rita Mencucci, MD,‡
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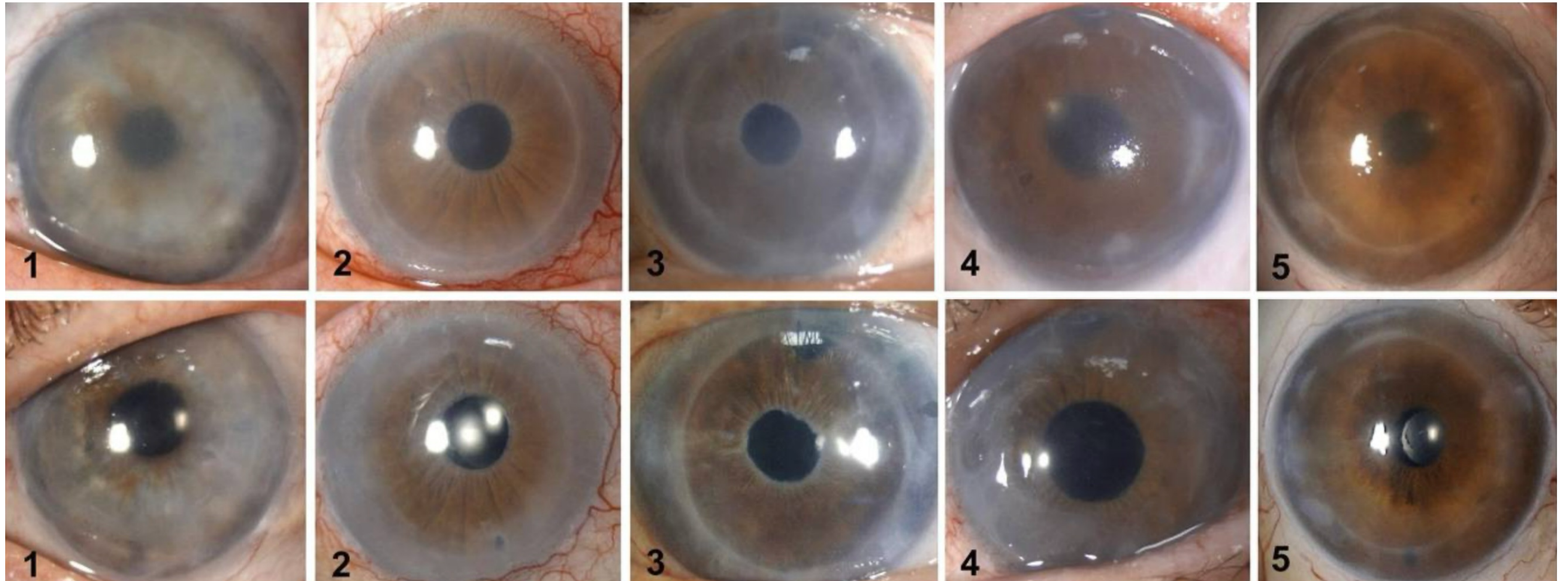
From the *Ophthalmology Unit, Dipartimento di Scienze Mediche e Chirurgiche, Alma Mater Studiorum University of Bologna, Bologna, Italy; †IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; ‡Ophthalmology Unit, Azienda Ospedaliero-Universitaria Careggi, UNIFARBA Department, University of Florence, Florence, Italy. The authors have no funding or conflicts of interest to disclose.

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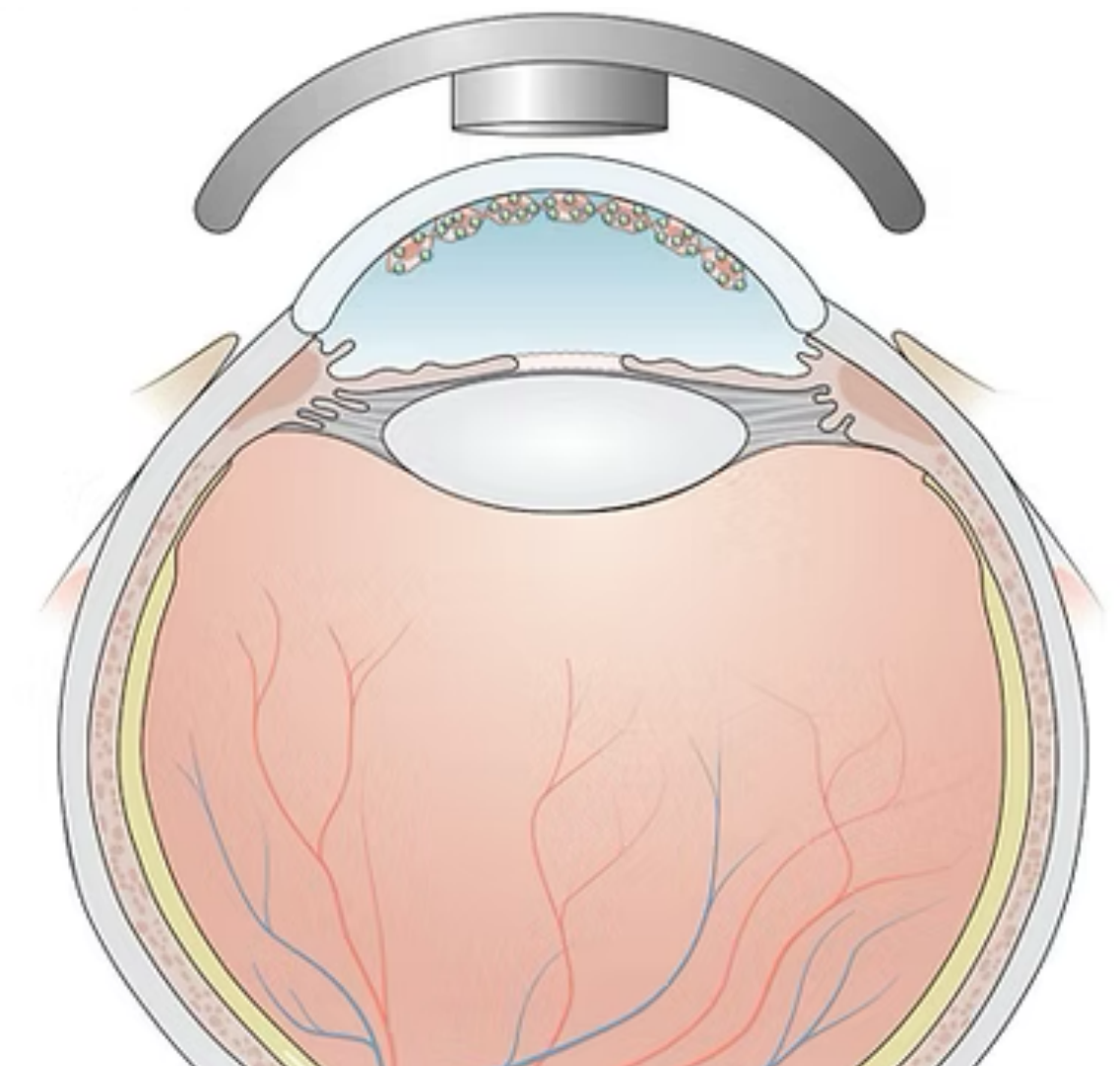
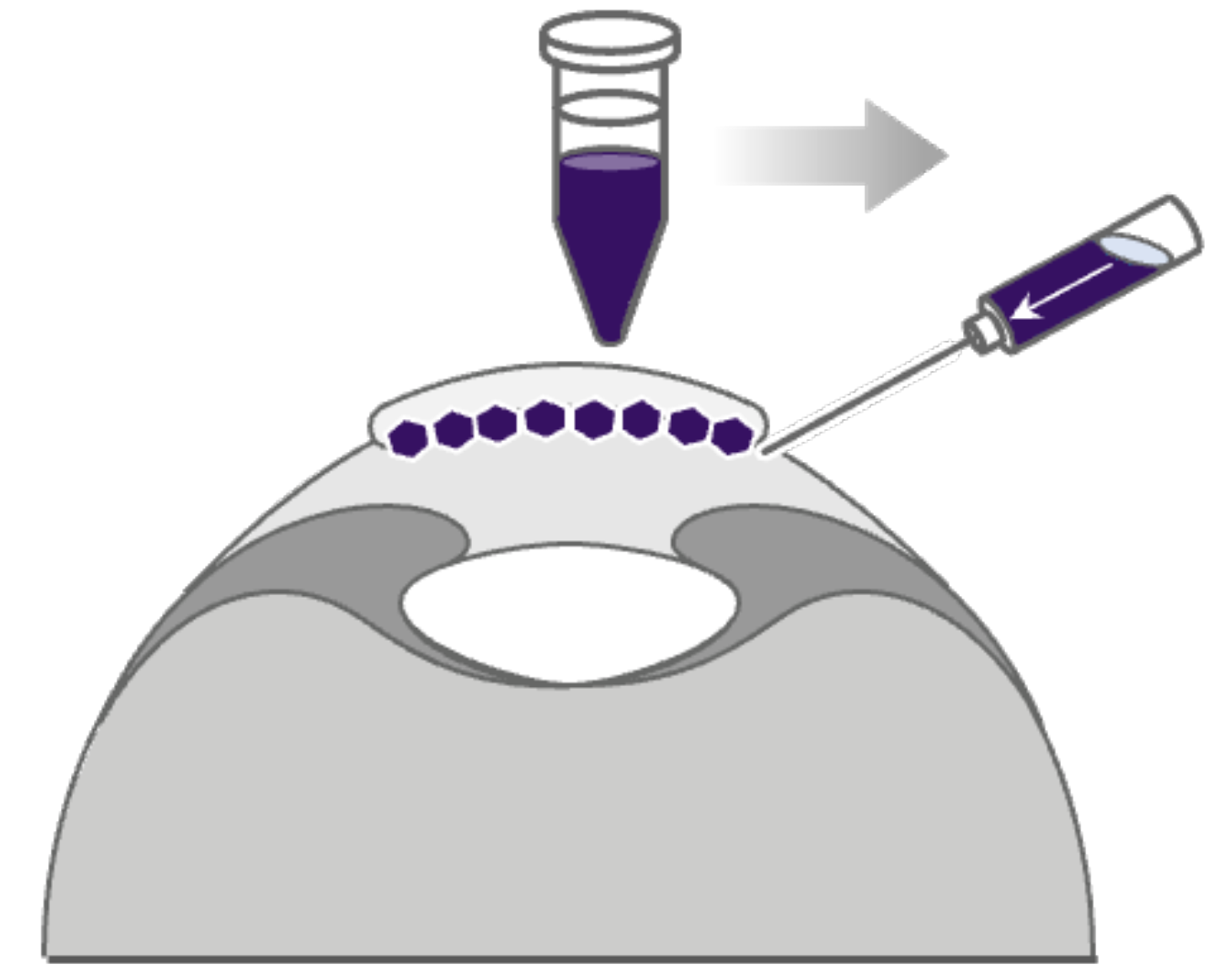
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Artificial Endothelial Layer



Program Updates

- Cell therapy phase III trial planned
1st half of 2026
- Magnetic cell delivery phase III trial
planned 2nd quarter 2026
- Artificial endothelial layer granted
IDE approval for US trial





Thank you
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