Implantable Miniature Telescope (IMT™ by Dr. Isaac Lipshitz) for End-Stage Age-Related Macular Degeneration

P050034

Presentation to the Ophthalmic Devices Advisory Panel

July 14, 2006

Implantable Miniature Telescope™ (IMT by Dr. Isaac Lipshitz) for End-Stage AMD

- **Introduction**
  - Judy F Gordon, DVM – Clinical and Regulatory Consultant
- **Background and Device Description**
  - Jeffrey S Heier, MD – Medical Monitor Retina, Clinical Investigator
- **Surgical Procedure and Study Design**
  - Stephen S Lane, MD – Medical Monitor Anterior Segment, Clinical Investigator
- **Effectiveness Outcomes**
  - Jeffrey S Heier, MD - Clinical Investigator
- **Safety Outcomes**
  - Doyle Stulting, MD, PhD - Clinical Investigator
- **Discussion and Questions from Panel**
  - Drs. Gordon, Lane, Heier, Stulting
  - Mark Bullimore, MCOptom, PhD – Low Vision, Vision Science Consultant
  - Yi-Jing Duh, PhD - Statistician
  - Henry Edelhauser, PhD – Specular Microscopy Reading Center

P050034
Implantable Miniature Telescope™ (by Dr. Isaac Lipshitz)

The IMT is indicated for use in adult patients with bilateral, stable moderate to profound central vision impairment (20/80 to 20/800) due to macular degeneration

Patients selected for implantation should meet the following criteria:

- 55 years of age or older with bilateral, stable central vision deficit resulting from AMD as determined by fluorescein angiography, and evidence of cataract
- Distance BCVA between 20/80 and 20/800, and adequate peripheral vision in one eye (the non-implanted eye) to allow for orientation and mobility
- Achieve at least a five-letter improvement on the ETDRS chart in the eye scheduled for surgery using an external telescope
- Show interest in participating in a postoperative visual rehabilitation program

Background and Device Description

Jeffrey Heier, MD

Medical Monitor, Retina
Clinical Investigator

End-Stage Age Related Macular Degeneration

- Approximately 60,000 to 80,0000 cases per year in the U.S.[1,2]
- Majority of patients are legally blind as a result of central vision loss in both eyes due to:
  - Dry AMD (geographic atrophy)
    - No treatment available
  - Stable wet AMD (disciform scar)
    - Completed all laser and drug treatments for exudation in and around the macula

[1]AREDs Report No. 11. Arch Ophthalmol 2003;121:1621-1624
[2]Wang JJ et al. Bilateral involvementby age-relatedmaculopathy lesions in a population. Br J Ophthalmol 1998;82:743-747

Vision with and without Scotoma

Normal Central Vision

End-Stage AMD

Effect on Functional Status

- End-stage AMD has a profound effect on Activities of Daily Living (ADL)
- Patients have extreme difficulty with:

Household Activities/Self-Care	*Preparing tea, shaving, make-up*
Social Interaction	*Recognizing friends, facial expressions*
Reading or TV/Computer	*News, leisure reading*
Consumer Interaction	*Identifying products and paying*

Current Options for Patient Management in End-Stage AMD

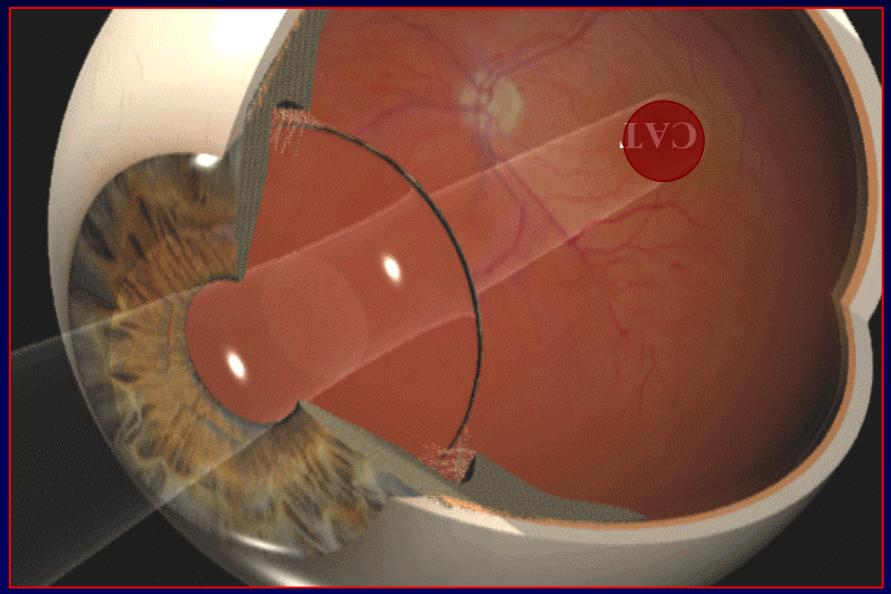
- Visual rehabilitation and training in the use of low vision aids, including external telescopes, loupes, hand-held magnifiers for reading, illumination
- Limitations of current treatment
  - Only 30% of visually impaired adults use optical devices per Lighthouse National Survey on Vision Loss (1995)
  - Low utilization of rehabilitation services
  - Limited psychosocial benefits
  - Difficulty using low vision aids in both static and dynamic activities

The Implantable Miniature Telescope (IMT™ by Dr. Isaac Lipshitz)

- Optical prosthesis
- Two models - WA2.2X, WA3.0X
- Improves central vision
- Distance/near vision refined with with spectacles
- Quartz tube housing with two wide angle microlenses
- Diameter 3.6 mm
  Length 4.4 mm
- Carrier haptic 13.5 mm diameter

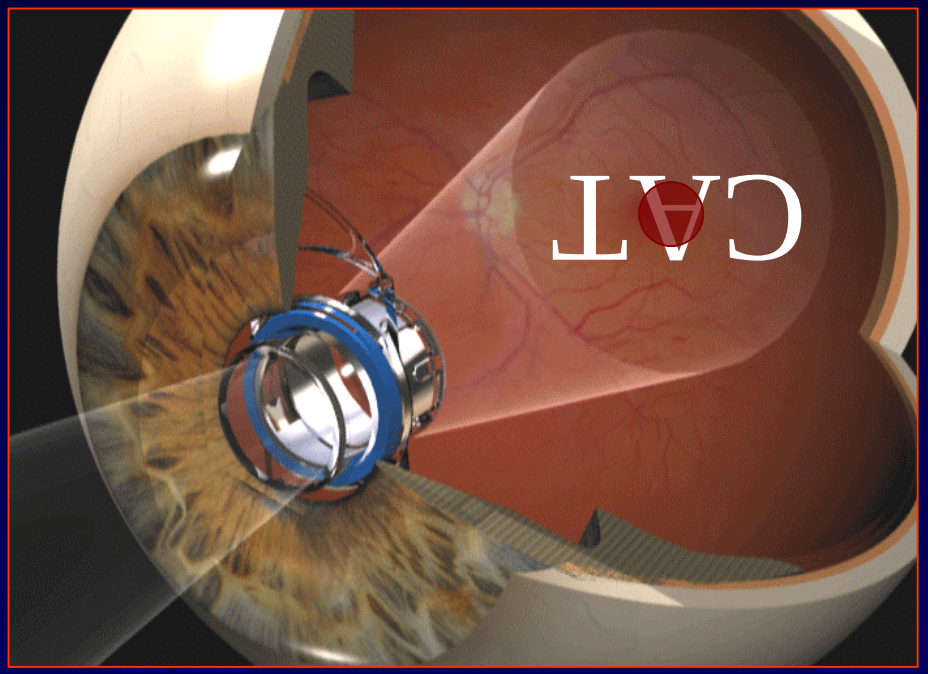
Projection on Retina

- Designed to improve vision by magnifying the retinal image
- Key differences from external telescopes
  - Wide visual field
  - Natural eye movements
  - Normal cosmetic appearance



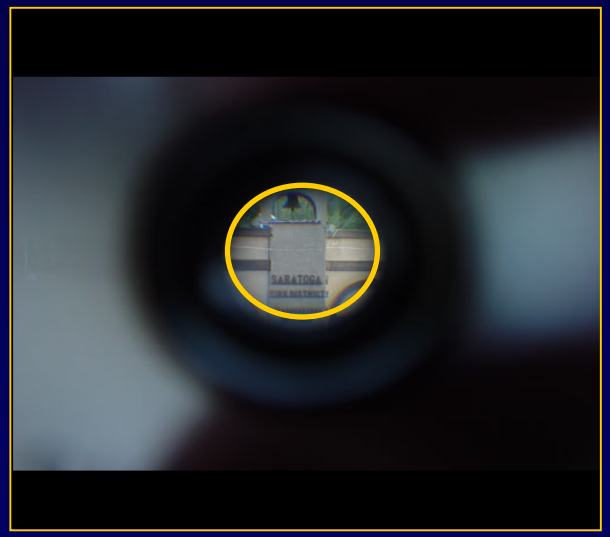
Enlargement of Retinal Image

- Enlarges retinal image 2.2x or 2.7x
- Reduces relative size of scotoma
- Enlarges and positions relevant information on seeing retina



Field of View
External vs Implantable Telescopes

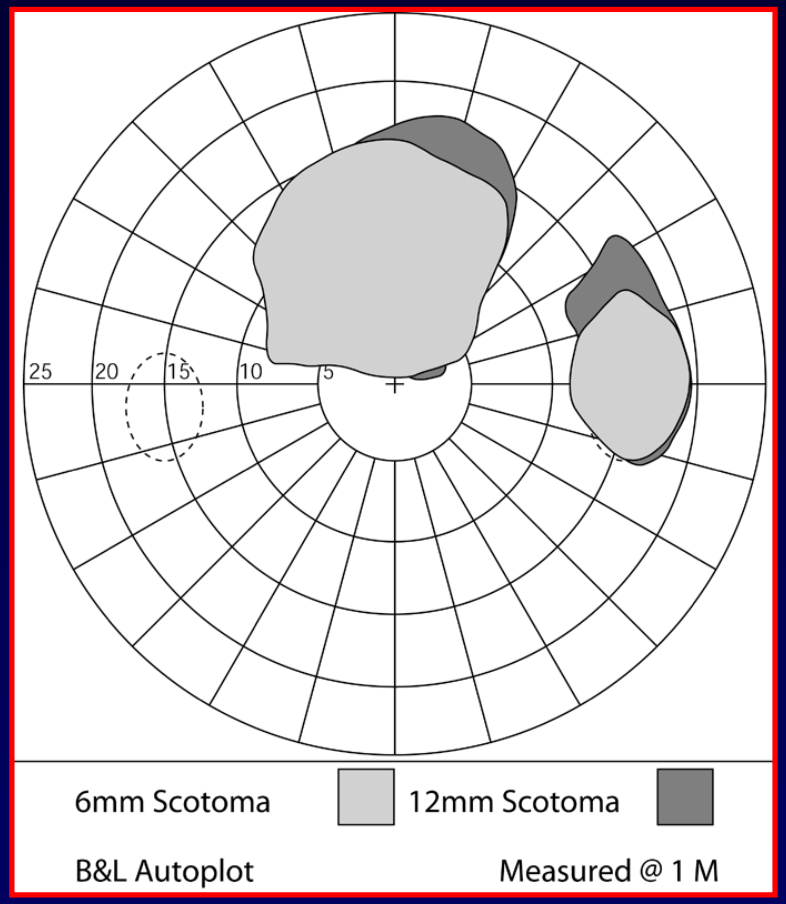
Magnification	External Telescope on Spectacles	Wide Angle Implantable Telescope
2.2x	13°	24°
3.0x, 2.7x	5-6°	20°



3.0x External Telescope

WA 3.0x Implantable Telescope

Preoperative Measurement of Scotoma and Simulation of Effect in Study Subject



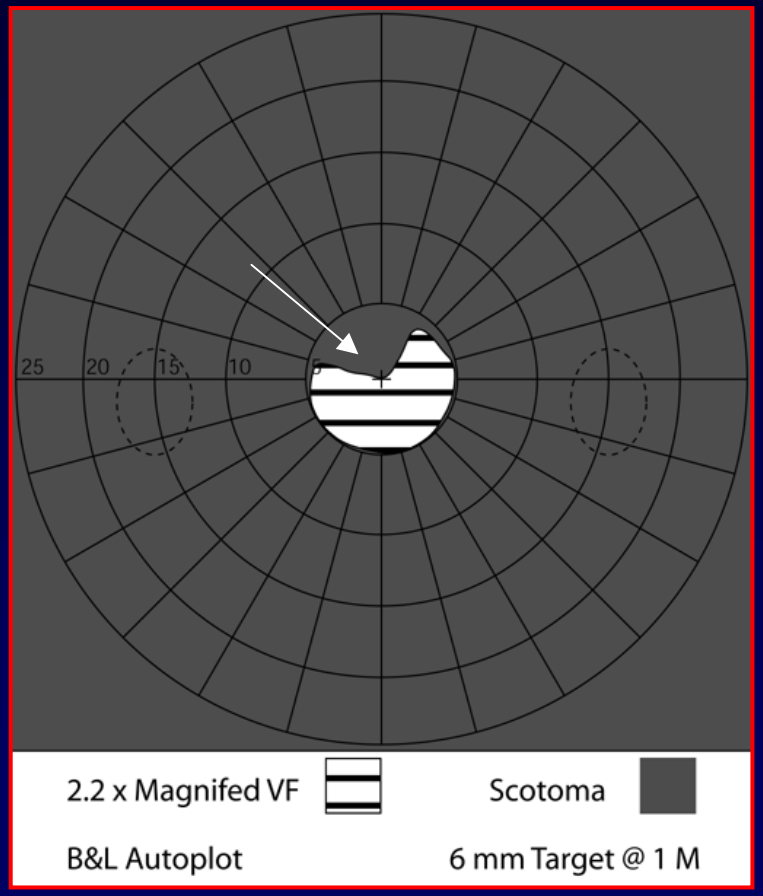
Measurement of Scotoma at Baseline

Simulation

Eli Peli, OD
Schepens Eye Institute

Preoperative of the Field of View and Scotoma through an External Telescope in Study Subject

10° Field of View, Restricted Superiorly by Scotoma



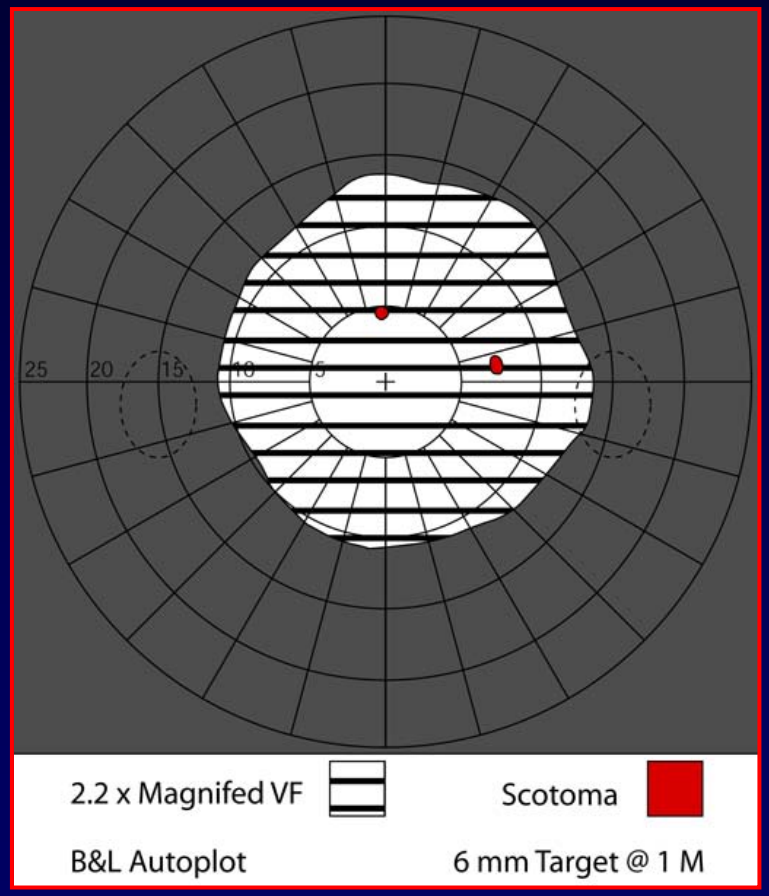
Simulation

Measurement of Magnified Field of View and Scotoma through a 2.2X External Telescope

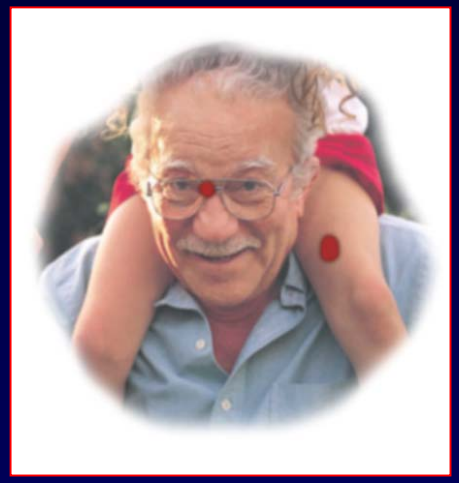
Eli Peli, OD
Schepens Eye Institute

Postoperative View Through the Implanted Telescope in Study Subject

25° Field of View and Relative Reduction in Scotoma



Measurement of Magnified Field of View and Scotoma through IMT



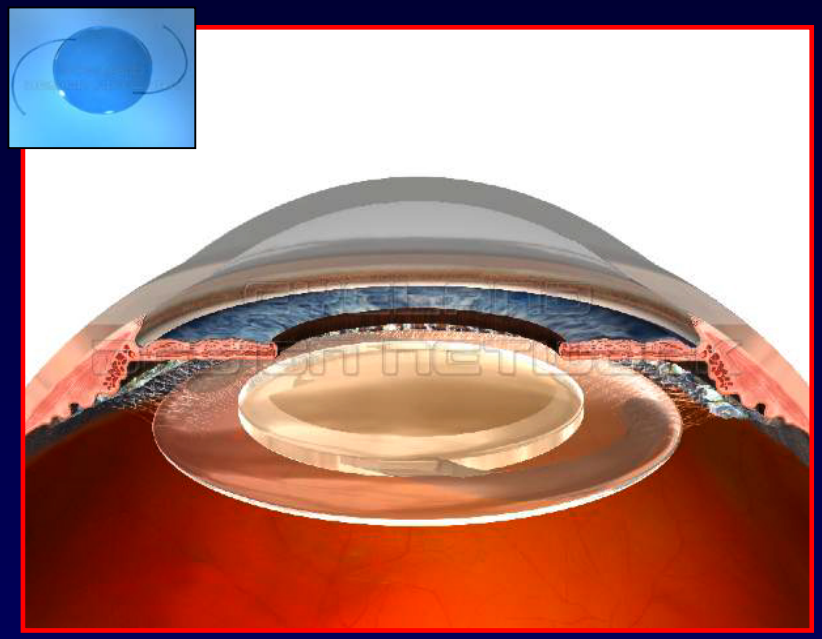
Simulation

Eli Peli, OD
Schepens Eye Institute

Surgical Procedure

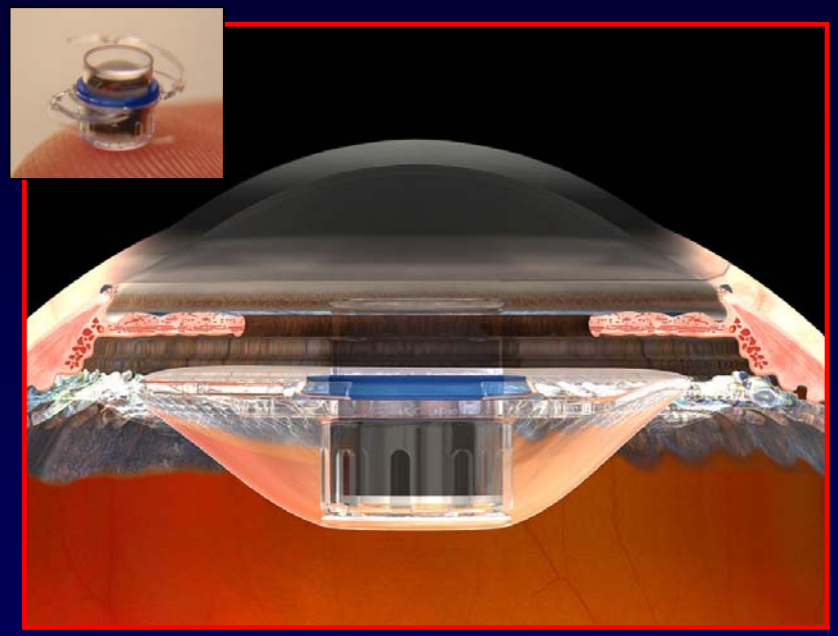
Stephen Lane, MD
Medical Monitor, Anterior Segment
Clinical Investigator

Unique Geometrical and Surgical Considerations for the Implantable Telescope



Standard IOL

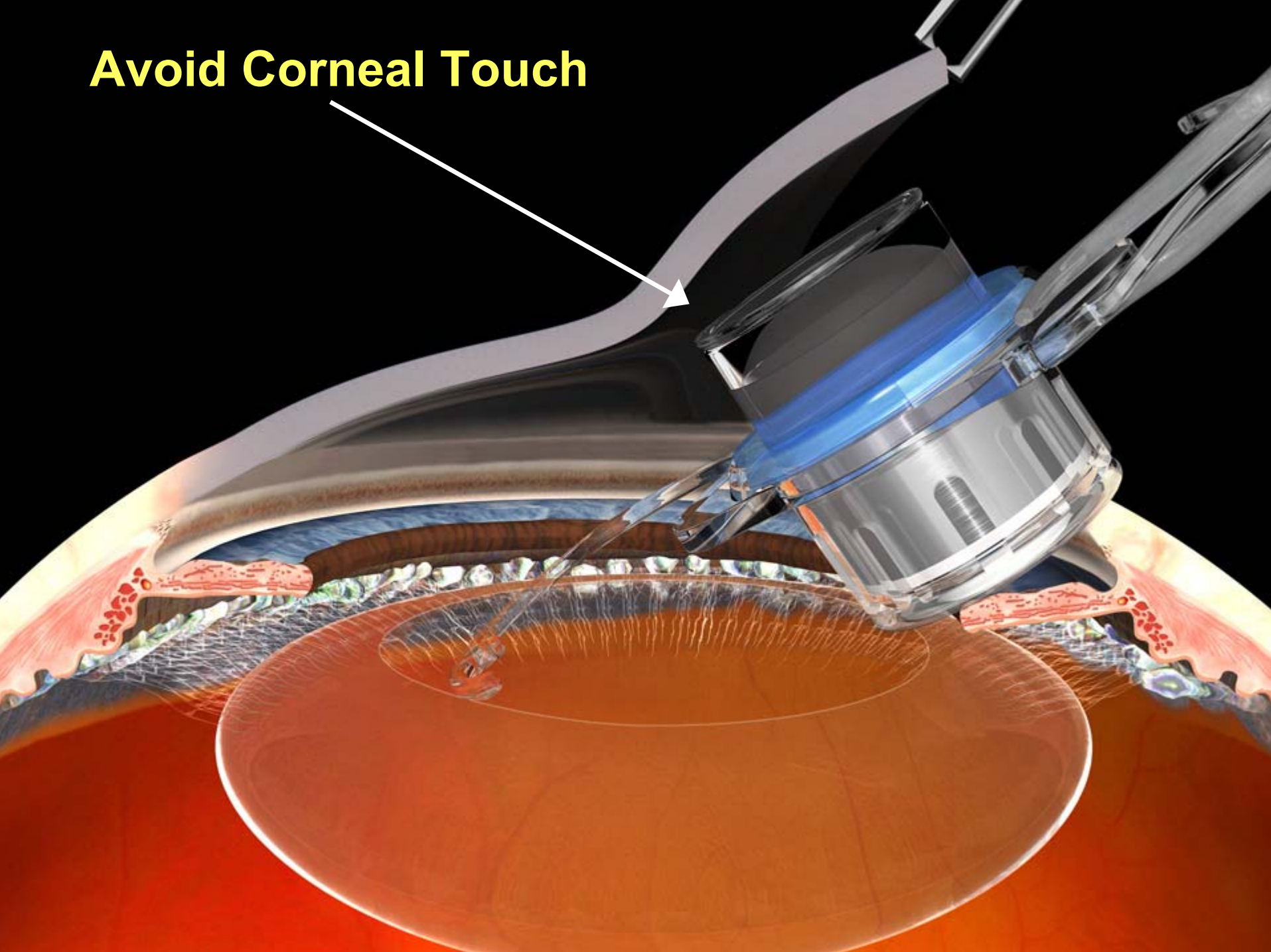
- ECCE represented an improvement over ICCE, with decreased endothelial cell loss
- Phacoemulsification and small incision surgery further reduced surgical trauma, loss of ECD



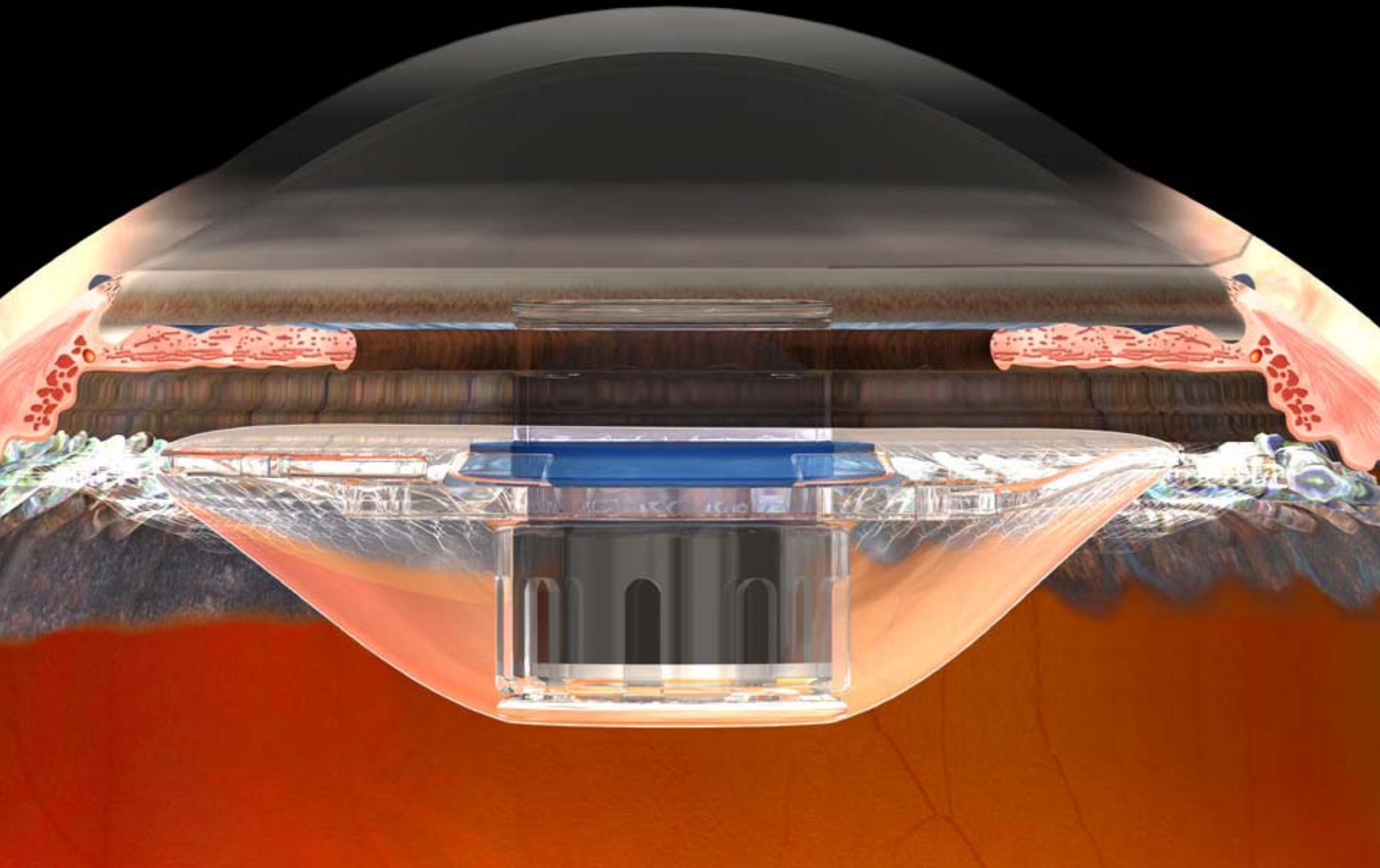
Implantable Telescope

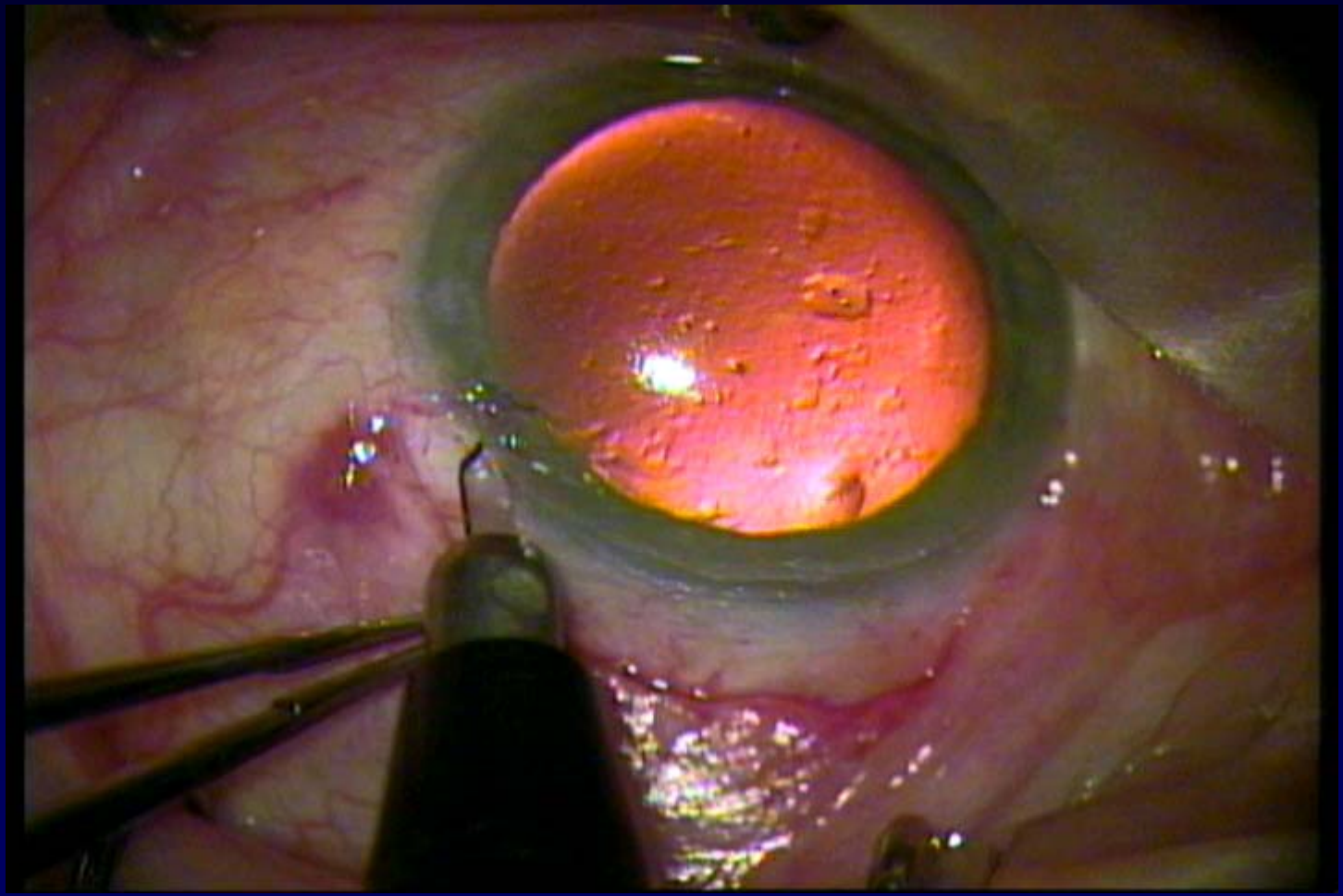
- Requires large incision, results in greater endothelial cell loss
- Careful handling of the cornea and adequate use of ophthalmic viscosurgical devices (OVD) are key

Avoid Corneal Touch



Both Loops in the Capsular Bag

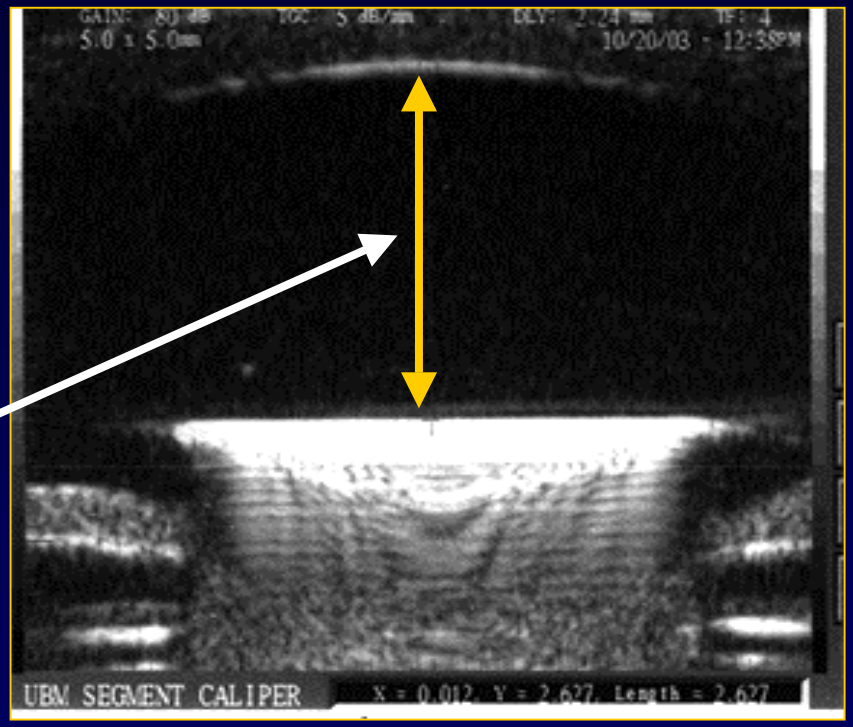




Corneal Clearance

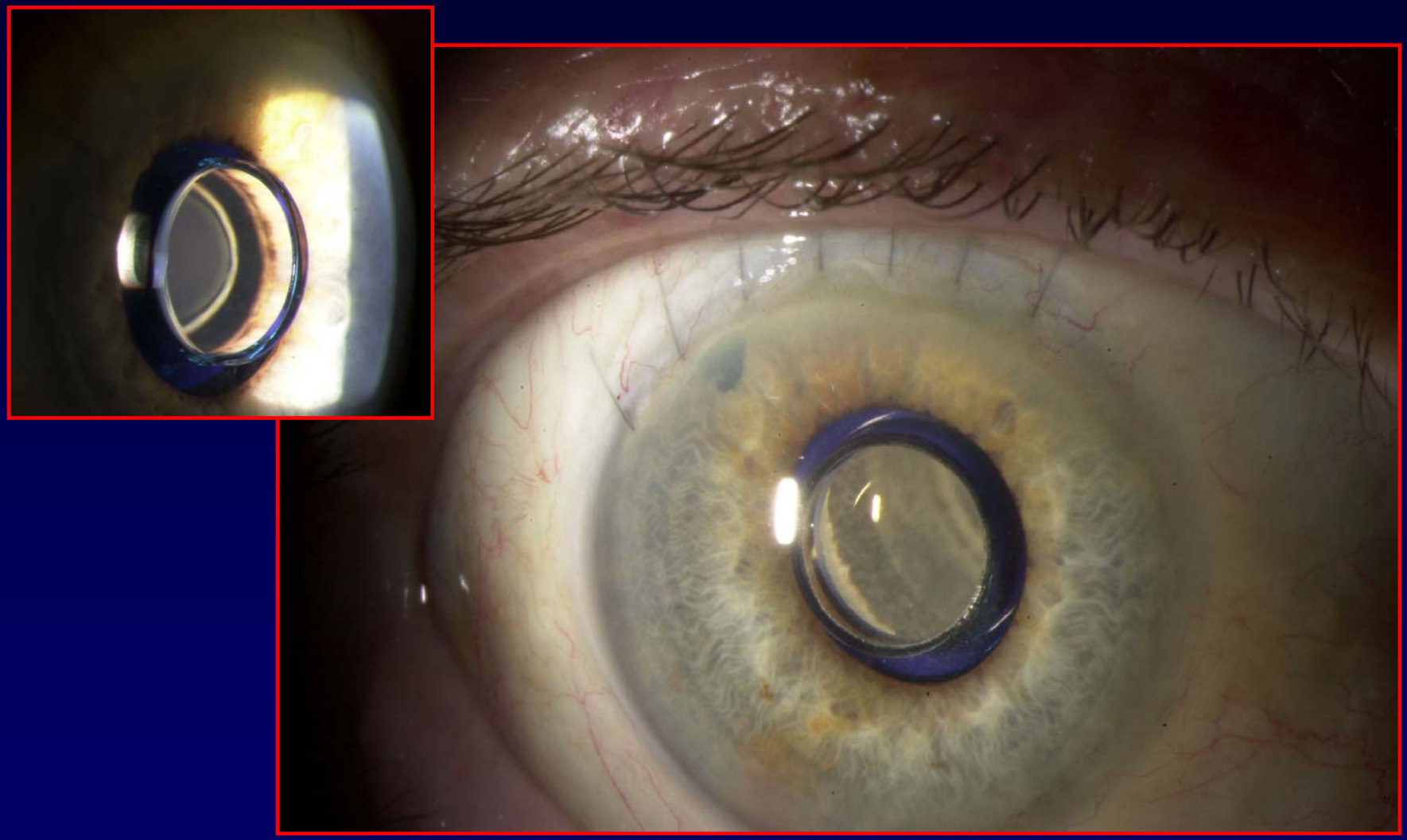
Ultrasound indicates good postoperative clearance to cornea

- Images obtained for 7 eyes implanted at Kellogg Eye Center, University of Michigan
- Average 2.54 mm clearance between anterior surface of telescope and cornea
- Well centered in capsular bag

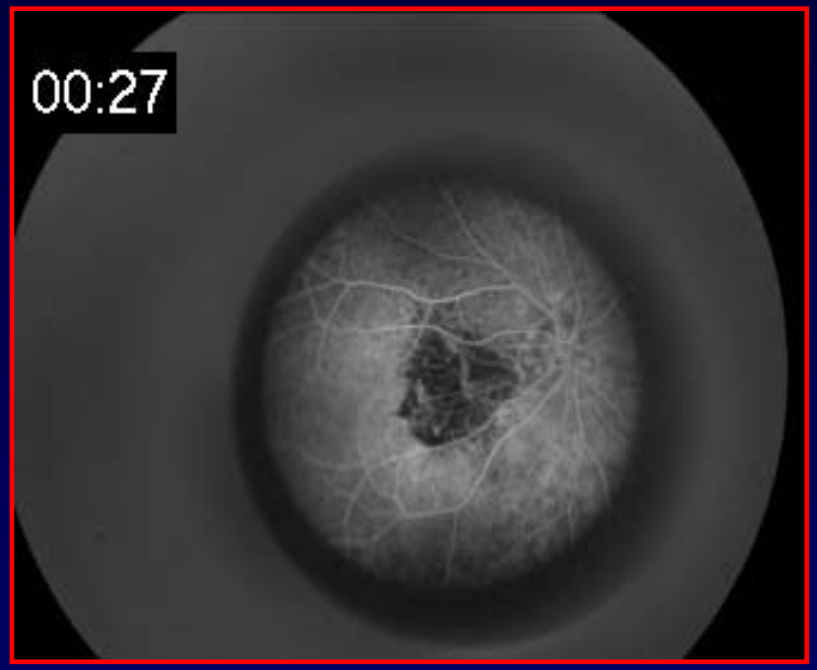


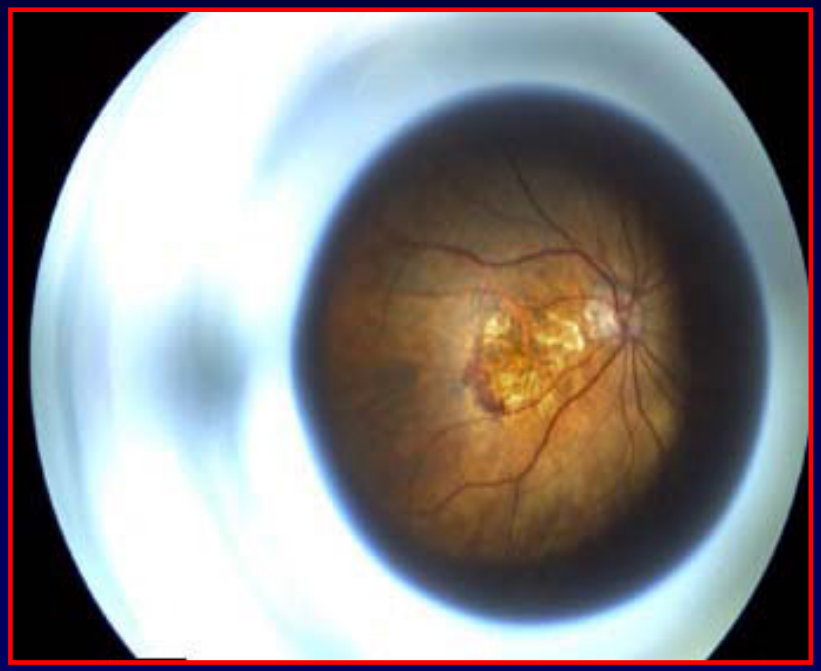
Source: not in PMA

Appearance of Implantable Telescope in the Eye 6 Weeks Postoperative



Visualization of Retina through the Implantable Telescope





Protocol IMT-002

A Prospective, Multicenter Clinical Trial of the Implantable Miniature Telescope (IMT™ by Dr. Isaac Lipshitz) in Patients with Central Vision Impairment Associated with Age Related Macular Degeneration

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Study Design

Stephen Lane, MD

Clinical Study Investigators

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Protocol IMT-002 - Study Design

- Patients screened using external telescope in office and home environment
  - Gain ≥5 letters BCDVA with telescope was required to qualify for enrollment
- Monocular implantation
  - In worse seeing eye if one or both eyes better than 20/200
  - Doctor/patient select if both eyes less than 20/200
- Visit schedule
  - Day 1, Week 1, Months 1, 3, 6, 9, 12, 18, 24
- Vision training
  - Weeks 1, 2, 4, 6, 10 and 12

Key Eligibility Criteria

- Bilateral, stable, untreatable AMD on fluorescein angiography
- Distance BCVA of 20/80 to 20/800
- Adequate peripheral vision in fellow eye to allow for navigation
- Improvement in BCDVA of $\geq$ 5 letters on ETDRS chart with the external telescope in the eye scheduled for surgery
- Anterior chamber depth of $\geq$ 2.5mm on A-scan
- Endothelial cell density $\geq$ 1600 cells/mm^2
- Manifest sphere between +4.0 to -6.0 D
- Axial length $\geq$ 21 mm
- Schaffer grade $\geq$ 2
- Controlled glaucoma
- No corneal stromal or endothelial dystrophies or disorders, inflammatory ocular disease, zonular weakness, pseudoexfoliation, retinal pathology other than stable end-stage AMD

Study Methods

- Distance visual acuity (BCDVA) – all study visits
  - Measured with standard ETDRS charts (C110 and C105) with retro-illuminated box; LogMAR computed
- Near visual acuity (BCNVA) – all study visits
  - Measured with ETDRS chart (Precision Vision Chart 2000); LogMAR computed
- VFQ-25 and Activities of Daily Living (ADL) Questionnaires – baseline through 12 months
  - Administered by trained study personnel
- Specular microscopy – baseline through 24 months
  - Images analyzed by central reading center (H. Edelhauser, B. McCarey, Emory University)

Vision Training/Rehabilitation Protocol

- Goal to provide patients with the skills to adjust to the IMT and achieve optimal functionality
- Conducted by low vision professionals at each clinical site
- Five fundamental skills
  - **Localizing** - locating an object of interest in the IMT field of view. If difficult, the patient first looked at the object with both eyes, then obscured the fellow eye and tried again with implanted eye
  - **Fixating** – performed by the implanted eye to enable object identification
  - **Scanning** –natural eye movement performed by the implanted eye
  - **Tracing** – following a path between objects of interest
  - **Tracking** - ability to follow a moving object
- Training for distance activities, intermediate distance, reading and writing, static and dynamic environments
- IMT bi-ocular function: initial training performed with the fellow eye patched to promote use of the IMT
  - Fellow eye patched for training in static vision
  - Implanted eye patched for motility training

Protocol IMT-002
Safety and Effectiveness Endpoints

Effectiveness Parameters

- Change in lines of best corrected visual acuity
- Quality of life - VFQ-25 and ADL questionnaires

Safety Parameters

- Preservation of best corrected visual acuity
- Endothelial cell loss
- Adverse events and complications

Protocol IMT-002

Baseline Information and Effectiveness Data

Jeffrey Heier, MD

Patient Accountability

Enrolled N = 218

→ **1 patient withdrawal**

IMT Surgery N = 217

→ **11 eyes not implanted**

- **7 eyes with posterior capsular rupture**
- **2 eyes with choroidal detachment (increased posterior pressure)**
- **1 eye with choroidal hemorrhage**
- **1 eye with loss of zonular support**

Implanted N = 206

→ **Model WA2.2X – 115 patients**
Model WA3.0X – 91 patients

Accountability
Original PMA

6 Months	100.0% (202/202)
12 Months	97.5% (194/199)
18 Months	91.4% (180/197)
24 Months	95.5% (148/155)

→ Complete 24-Month Safety Data
92.6% (N = 174/188)

Source: PMA Table A2

Demographic and Baseline Information

Age (years)

Mean (SD)	75.4 (7. 2)
Range	55 - 93

Gender

Female	98	47.6%
Male	108	52.4%

Race

Caucasian	198	96.1%
Black	3	1.5%
Hispanic	4	1.9%
Asian	1	0.5%

Best Corrected Visual Acuity (mean, range)

Mean BCDVA	20/312
Range	20/80 to 20/800

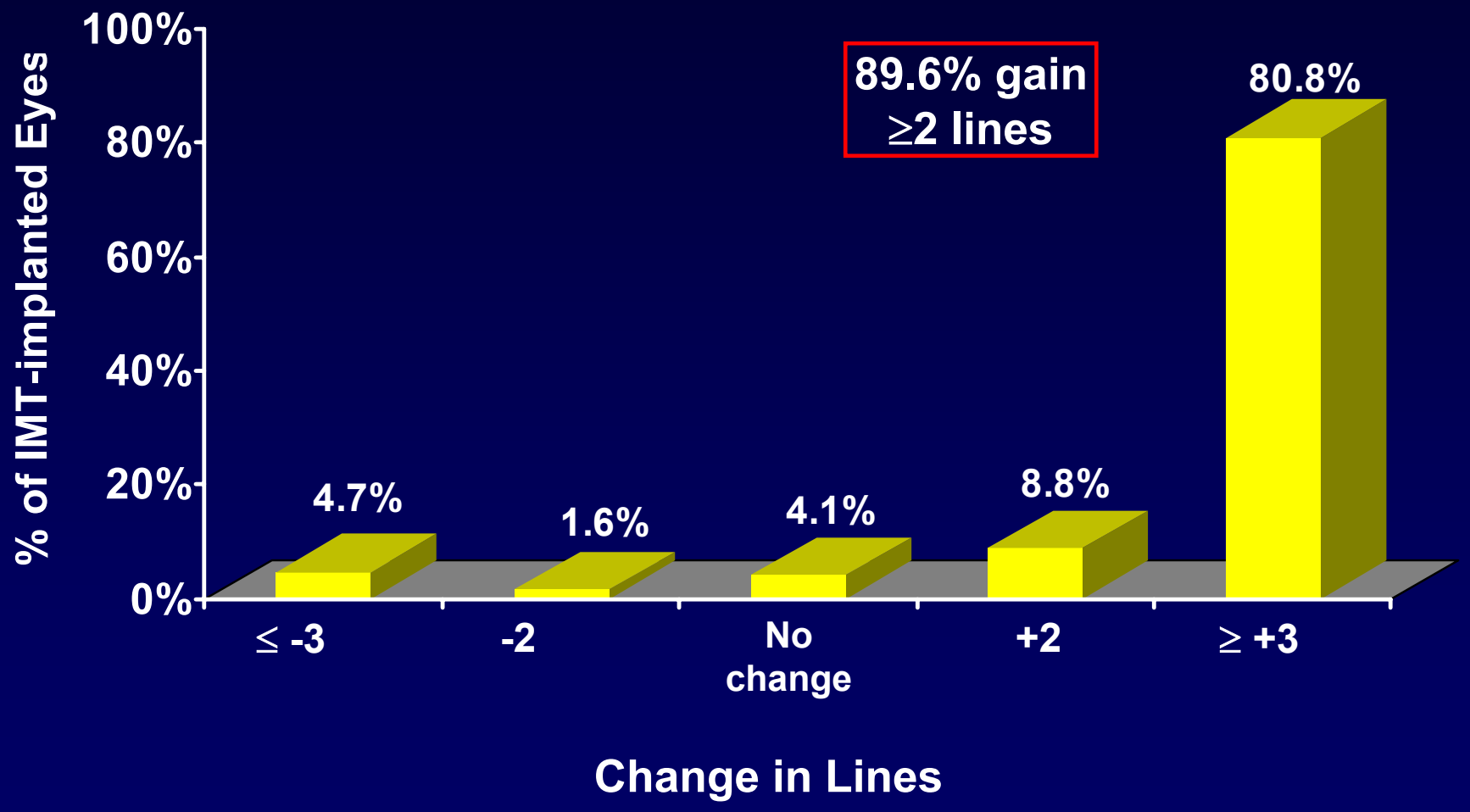
Source: PMA Table A3

Effectiveness Outcomes

Visual Acuity

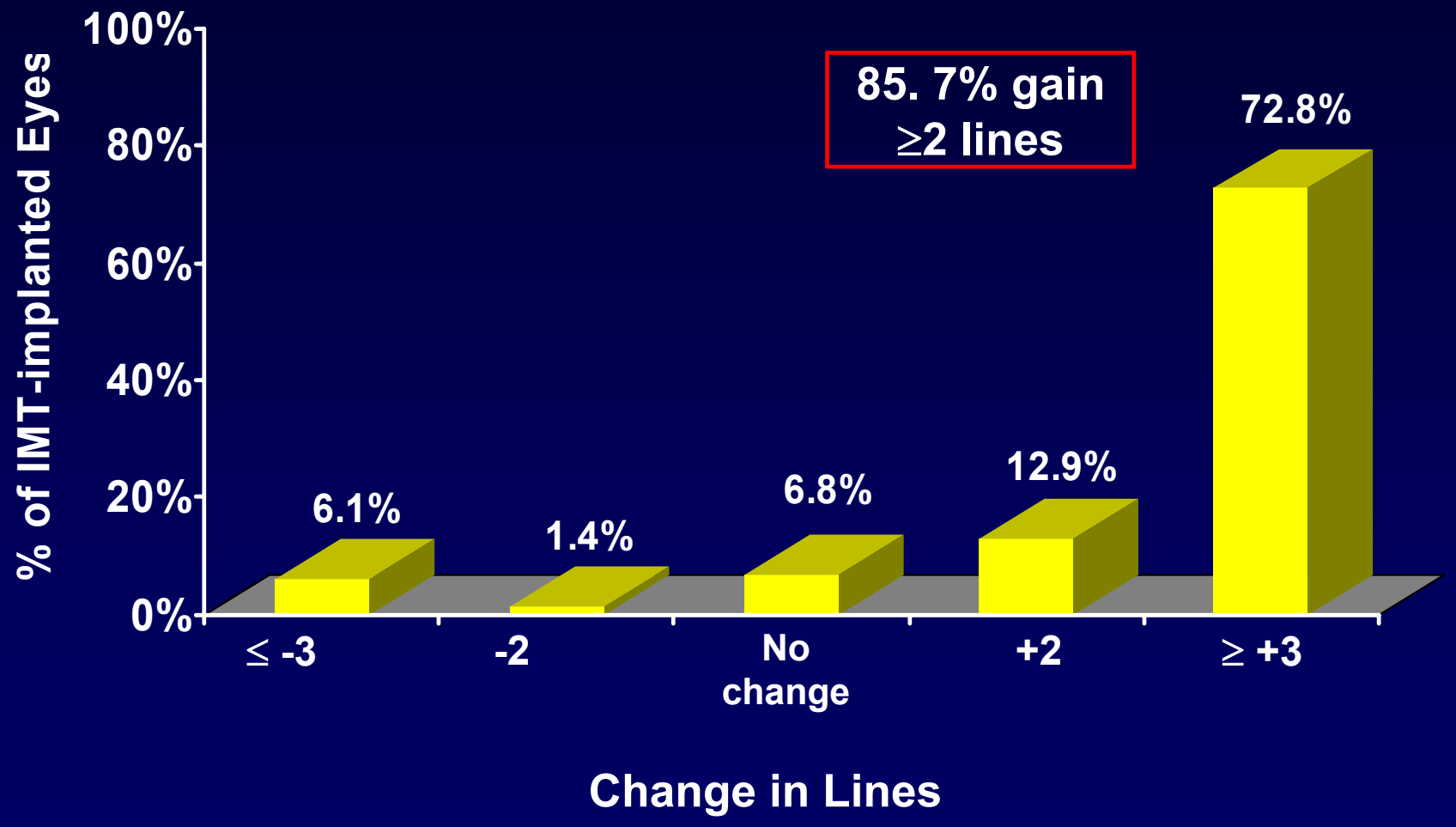
NEI VFQ-25, ADL

Improvement in Distance or Near Vision at 12 Months (N = 193)



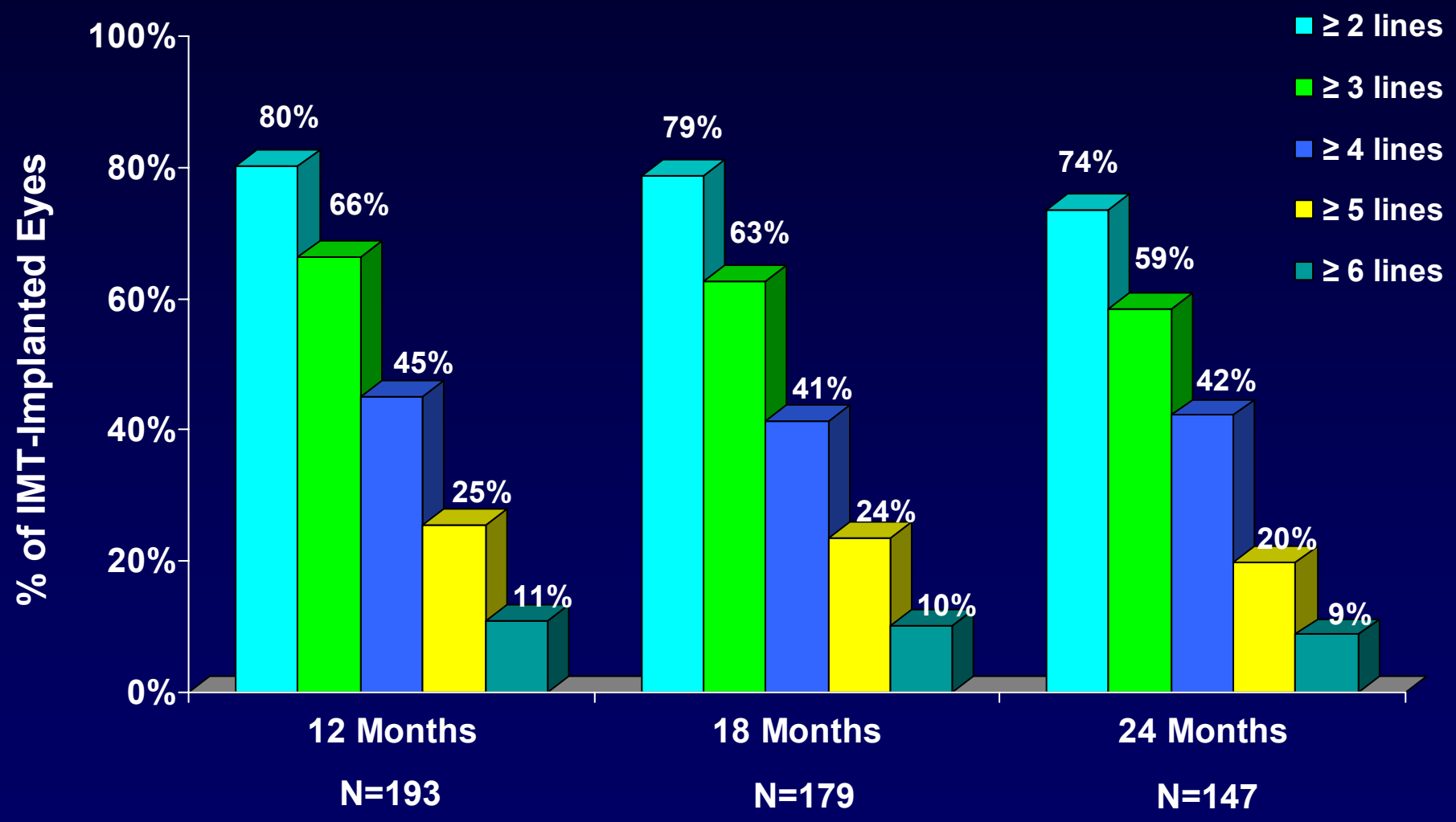
Source: PMA Table A11

Improvement in Distance or Near Vision at 24 Months (N = 147)



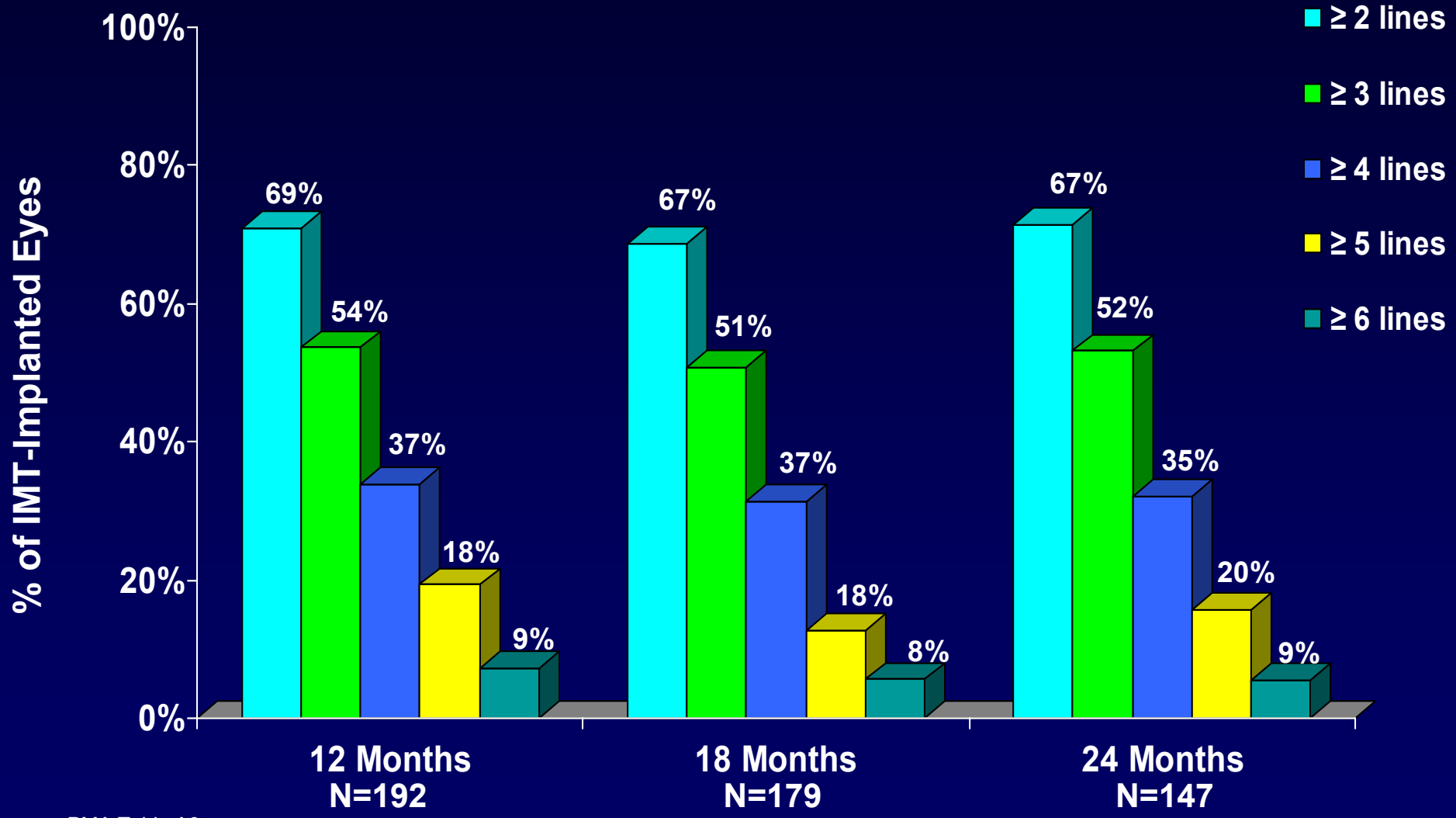
Source: PMA Table A13

Improvement in Distance Vision



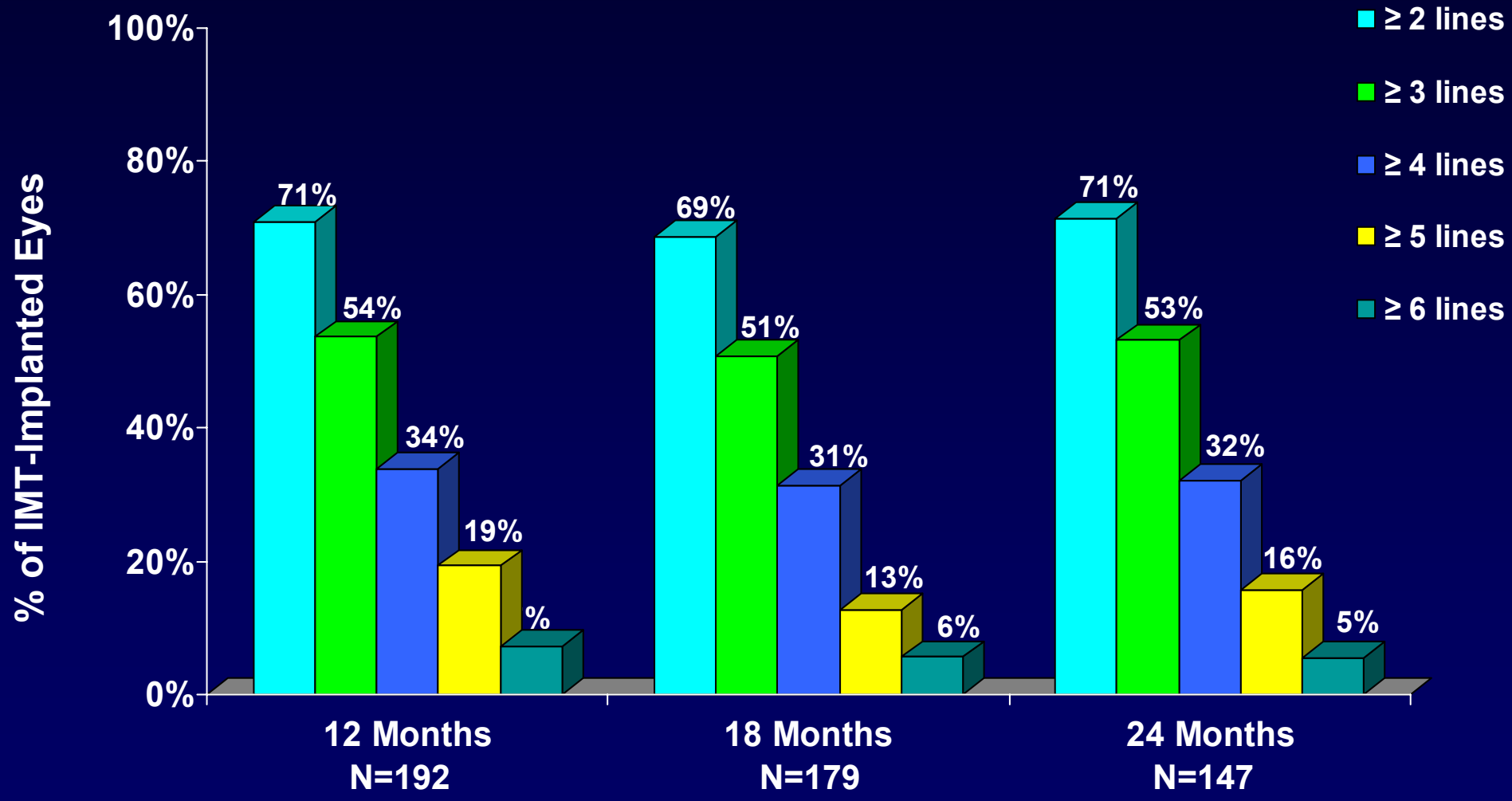
Source: PMA Table A7

Improvement in Near Vision at 8” (20 cm)



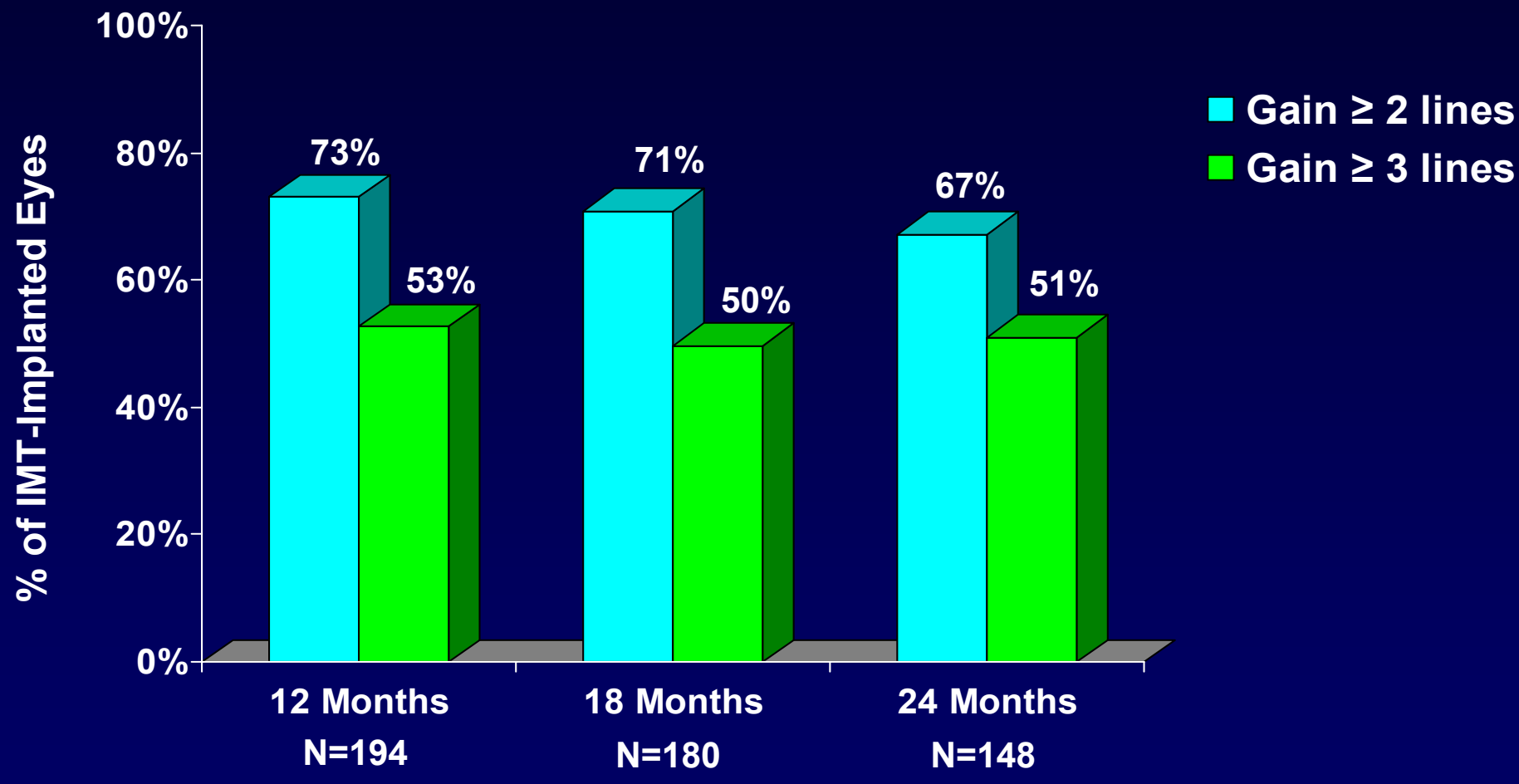
Source: PMA Table A8

Improvement in Near Vision at 16” (40 cm)



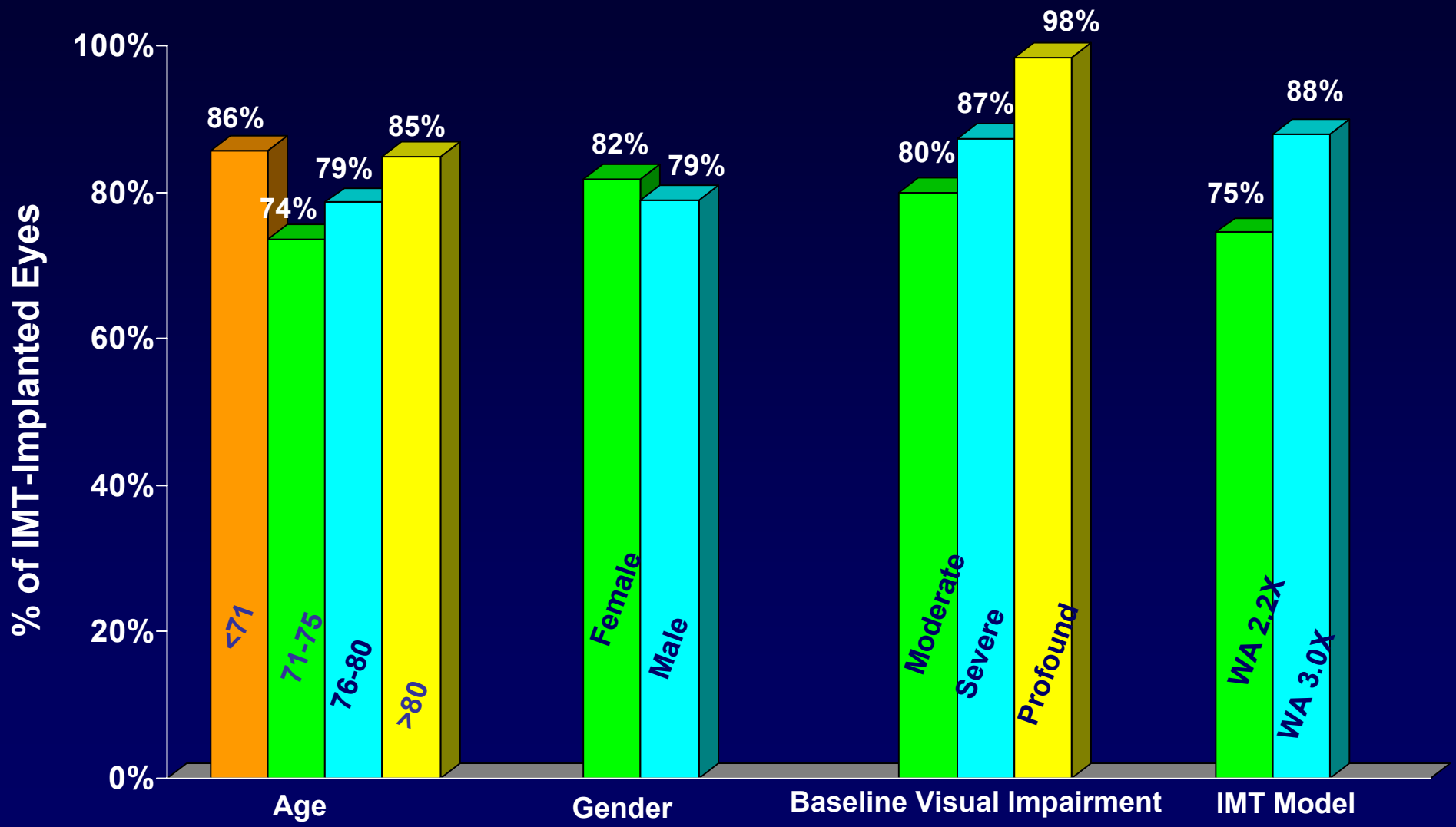
Source: PMA Table A9

Improvement in Distance and Near Vision



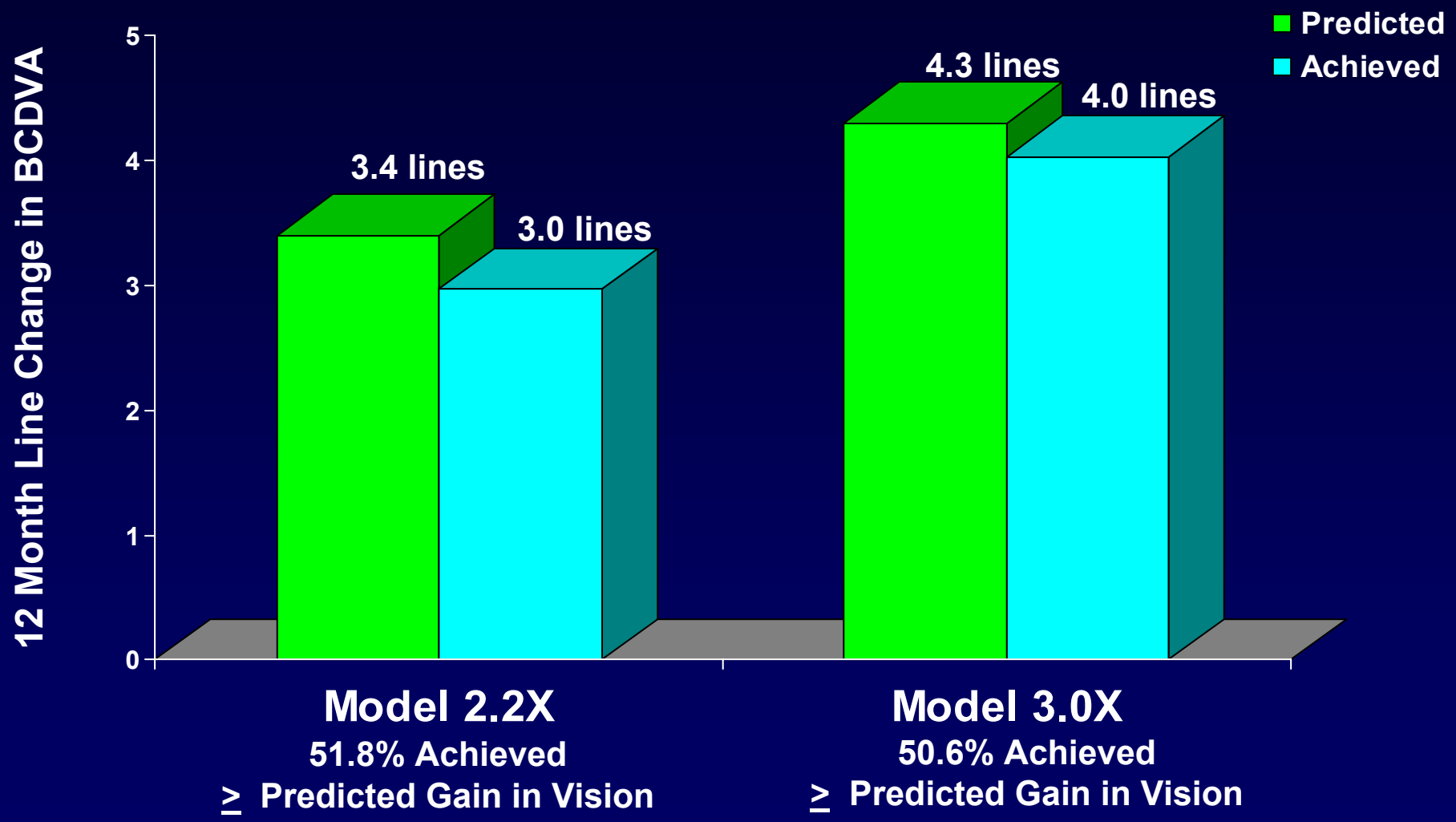
Source: PMA Table A11, A12, A13

Gain ≥ 2 Lines in Distance Vision at 12 Months Stratified by Age, Gender, Baseline Visual Impairment, Model



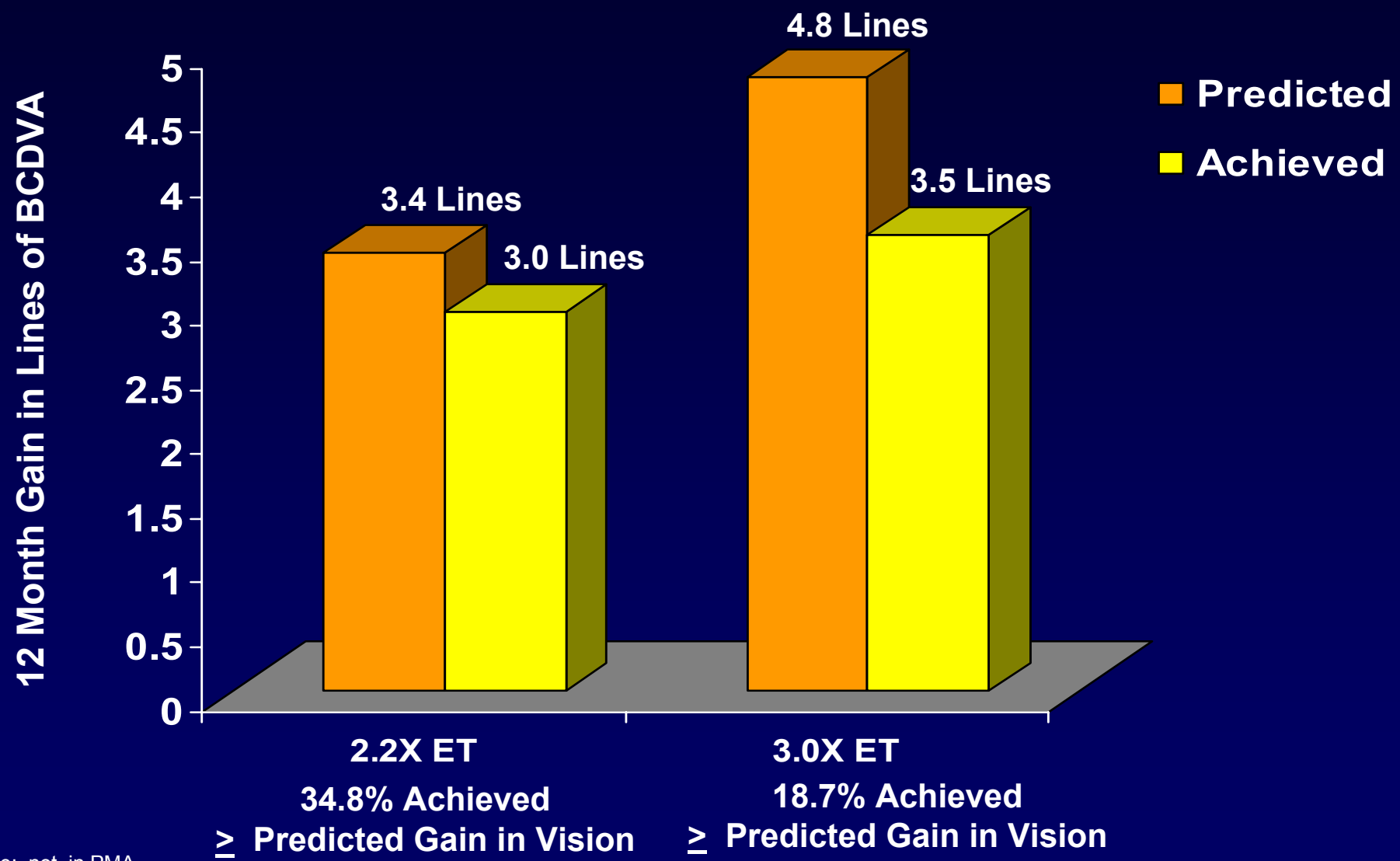
Source: PMA Table A7a.1, A7b.1, A7c.1, A7d.1

Mean Gain in Distance Vision at 12 Months vs Expected Benefit from Magnification



Source: not in PMA

Mean Gain in Distance Vision at Baseline vs Expected Benefit from Magnification with External Telescope



Source: not in PMA

National Eye Institute VFQ-25

- Validated quality of life questionnaire developed by Mangione et al[1,2] sponsored by NEI
- Assesses vision-targeted functioning[3] by measuring impact of vision problems on health-related QOL in many eye diseases
- Patient reported outcomes, reflects effect of improvement in vision on functionality, quality of life
- Validated instrument, employed in numerous clinical trials
- DHHS, Agency for Healthcare Research and Quality, Technology Assessment Program, Vision Rehabilitation for Elderly Individuals with Low Vision or Blindness, Oct. 2004, pg 58, QOL

"This outcome measure may be the most meaningful of all measures. This is because an individual's ability to perform activities of daily living, mood, psychological status, and any adverse events associated with the intervention should – if these changes are meaningful – be reflected by changes in the individual's quality of life."

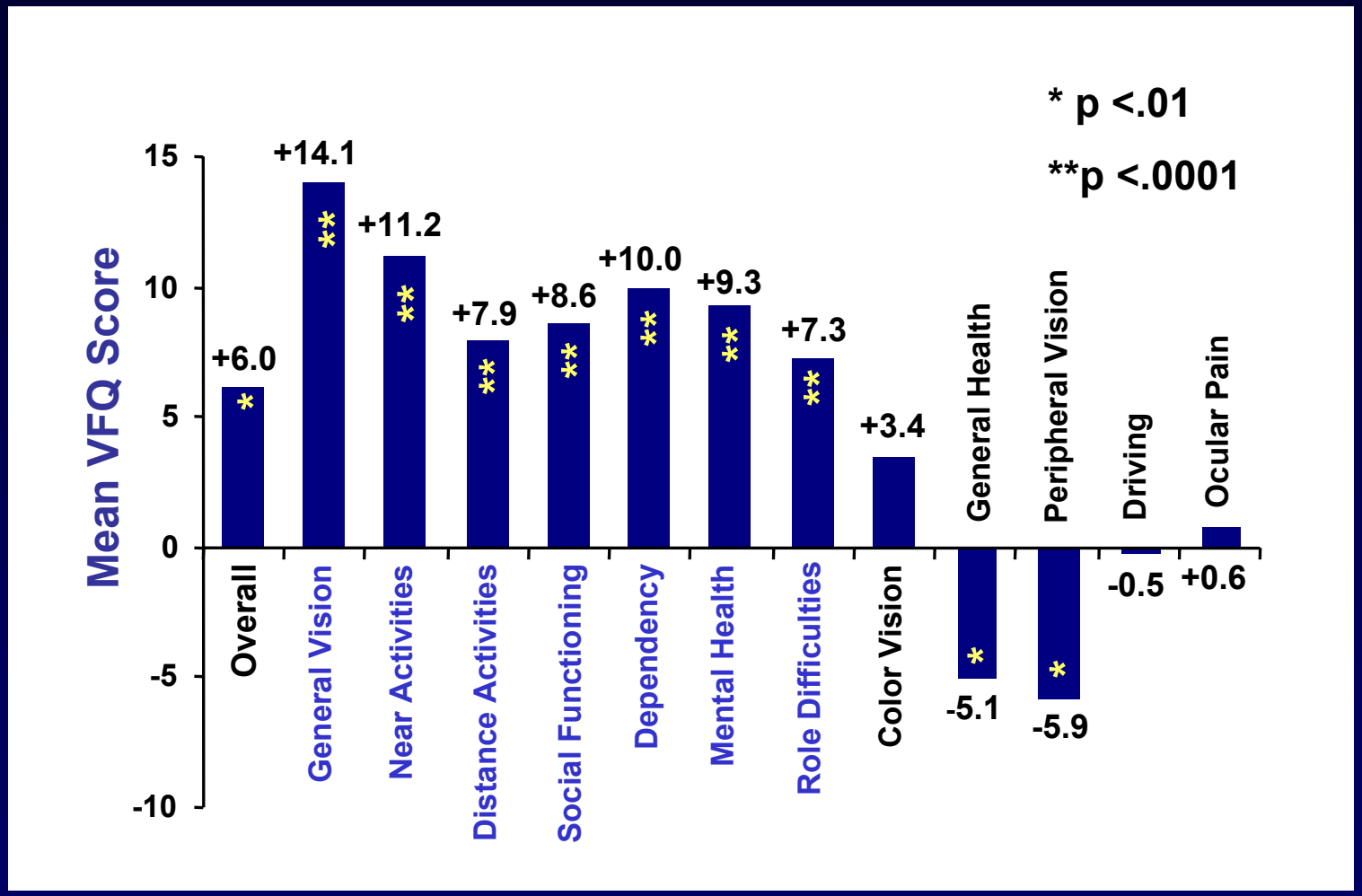
[1] Mangione et al. Arch Ophthalmol 2001:119:1050-8
[2] Mangione et al. Arch Ophthalmol 1998;116:1496-1504
[3] Clemons et al. Arch Ophthalmol 2003;21:211-7

NEI VFQ-25

- A total of 25 items representing 12 subscales
  - General vision - 1 item
  - Near activities - 3 items (newsprint, up close, objects on shelf)
  - Distance activities - 3 items (movies, stairs, street signs)
- 100 point scale, 0 = worst, 100 = best
- Clinical relevance established - 5-10 point change corresponds to a 2 to 3 line change in vision[1]
- Defined scoring algorithm

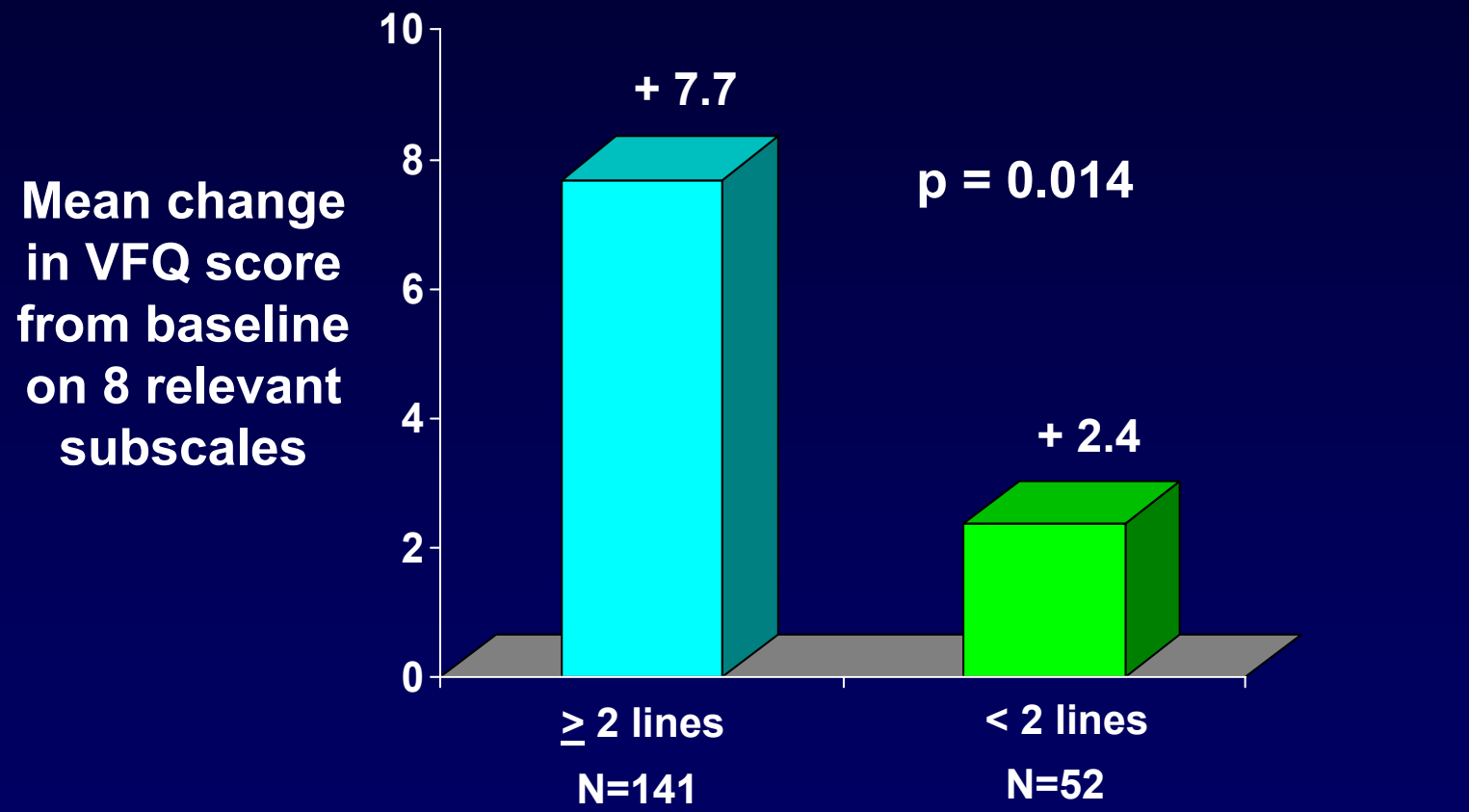
[1] Globe et al. Ophthalmol 2004;111:1141-9

Change from Baseline on VFQ-25 Subscales at 12 Months



Source: PMA Table A15; A002 Table Q29

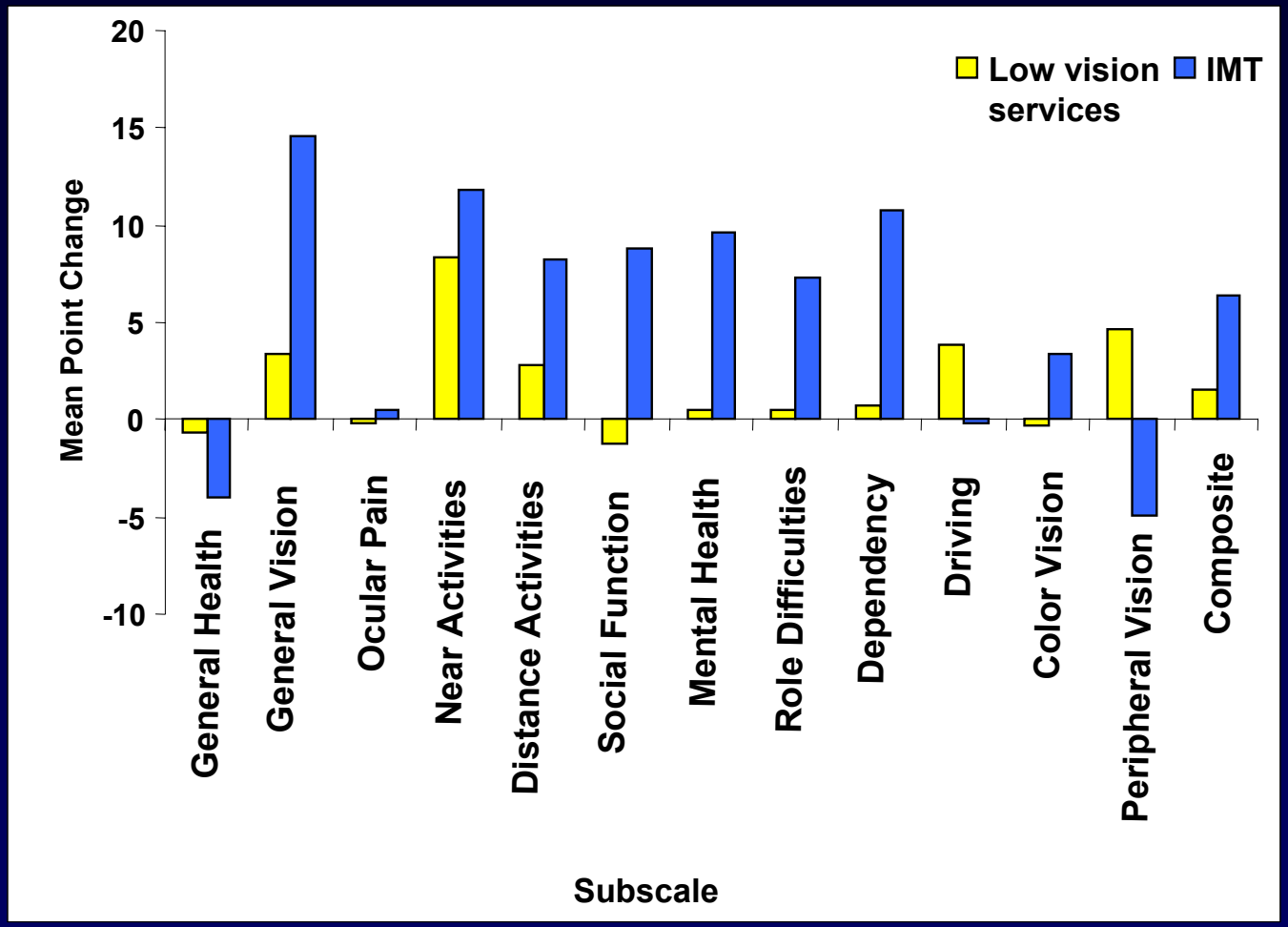
Relationship between Visual Acuity and VFQ



Distance *and* Near Vision in IMT-Implanted Eye

Source: not in PMA

Change from Baseline on VFQ-25 Subscales IMT vs Low Vision Services



Scott et al. AJO 1999*

- 156 patients
- Bascom Palmer
- 55% AMD patients
- BCVA 20/200 (mean)
- 1 'device or service' per patient
- VFQ measured at 3 months

*Scott IU, et al. Quality of life of low-vision patients and the impact of low-vision services. AJO 1999;128:54-62

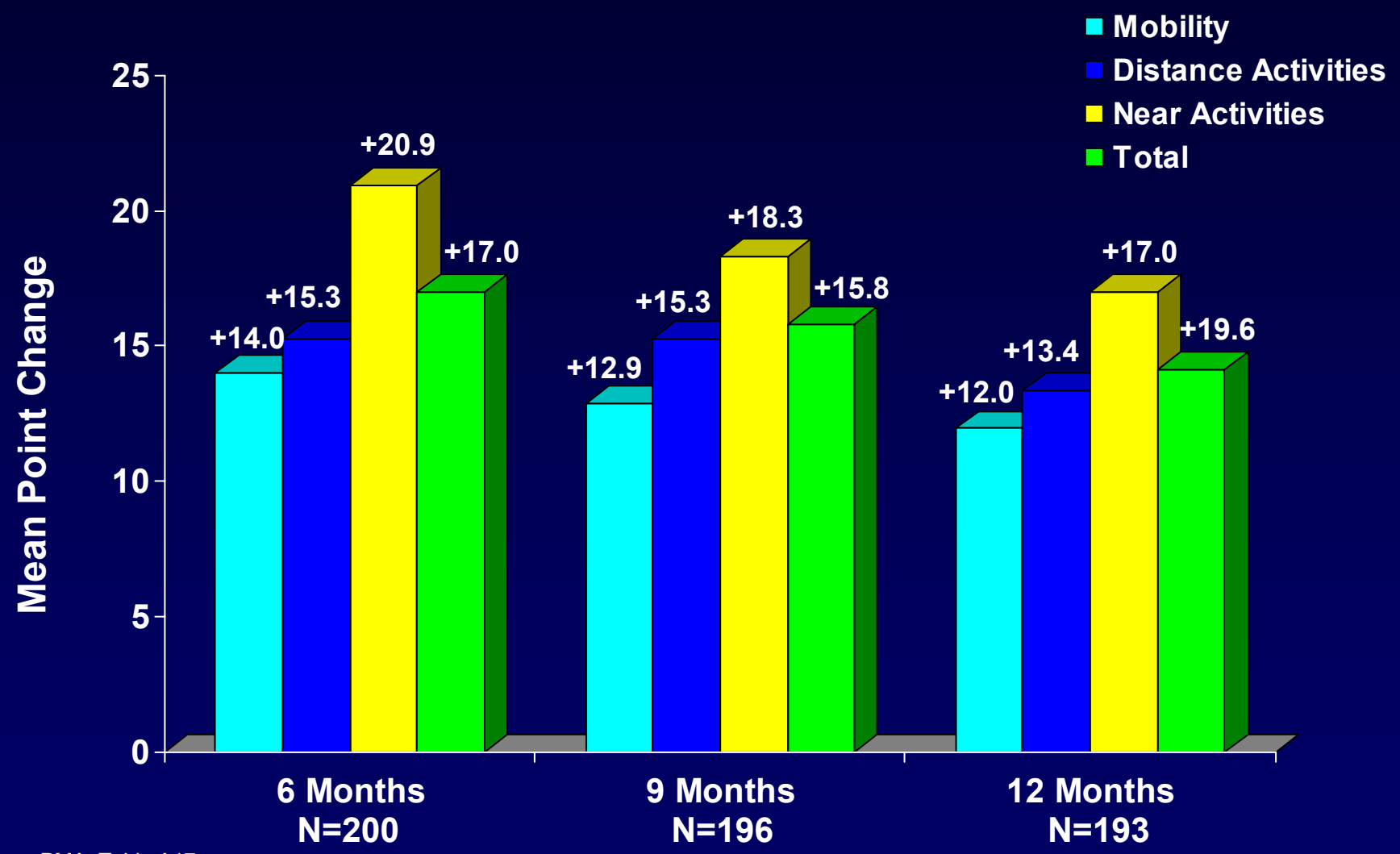
Source: not in PMA

Distribution of Outcomes on VFQ-25 at 12 Months for Subjects Reporting Extreme Difficulty at Baseline Questions 5 through 9

	VFQ5 Reading Newspaper	VFQ6 Hobbies	VFQ7 Finding on Crowded Shelf	VFQ8 Street Signs and Stores	VFQ9 Stairs, or Curbs in Dim Light
BASELINE					
Patients who stopped activity or had extreme difficulty	**N = 185**	**N = 112**	**N = 101**	**N = 144**	**N = 71**
12 MONTHS					
Stopped activity	59%	17%	2%	23%	12%
Had extreme difficulty	26%	27%	37%	29%	28%
Moderate difficulty	9%	41%	43%	29%	41%
No or little difficulty	5%	15%	18%	19%	18%

Source: not in PMA

Activities of Daily Living
Change in Subscales from Baseline



Source: PMA Table A17

Summary of Effectiveness

- Protocol target for effectiveness significantly exceeded
  - 85% gain ≥ 2 lines distance or near
  - 60% gain ≥ 3 lines distance or near
  - 50% gain ≥ 3 lines distance and near
- IMT performed as intended, with study subjects on average achieving the predicted gain in vision based on magnification
- Significant relationship between gain in BCVA and improvement in VFQ-25

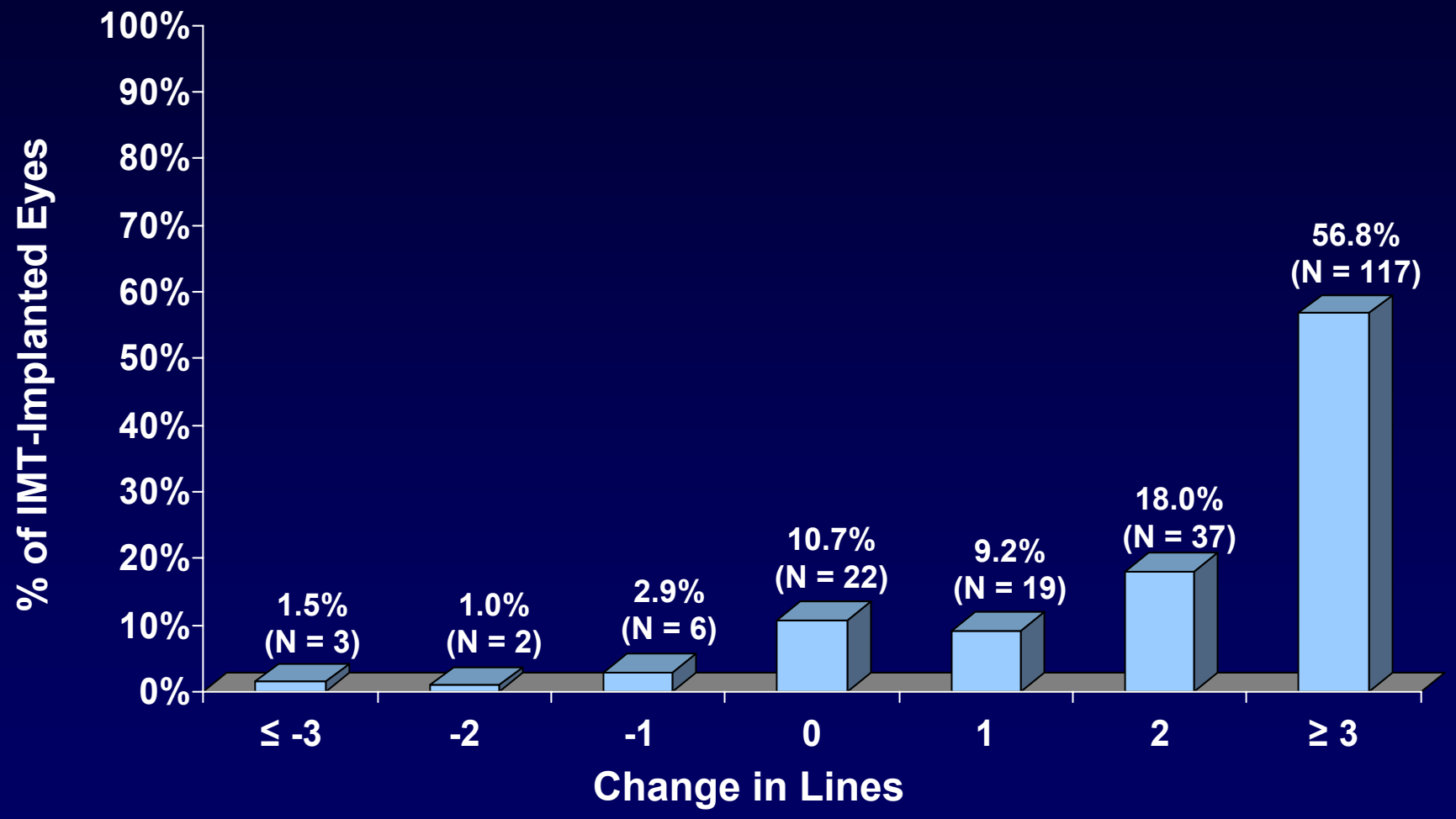
Safety Outcomes

Doyle Stulting, MD, PhD

Safety Parameters

- Loss of lines of acuity
- Intraocular pressure
- Complications
- Adverse events
- Endothelial cell density (ECD)

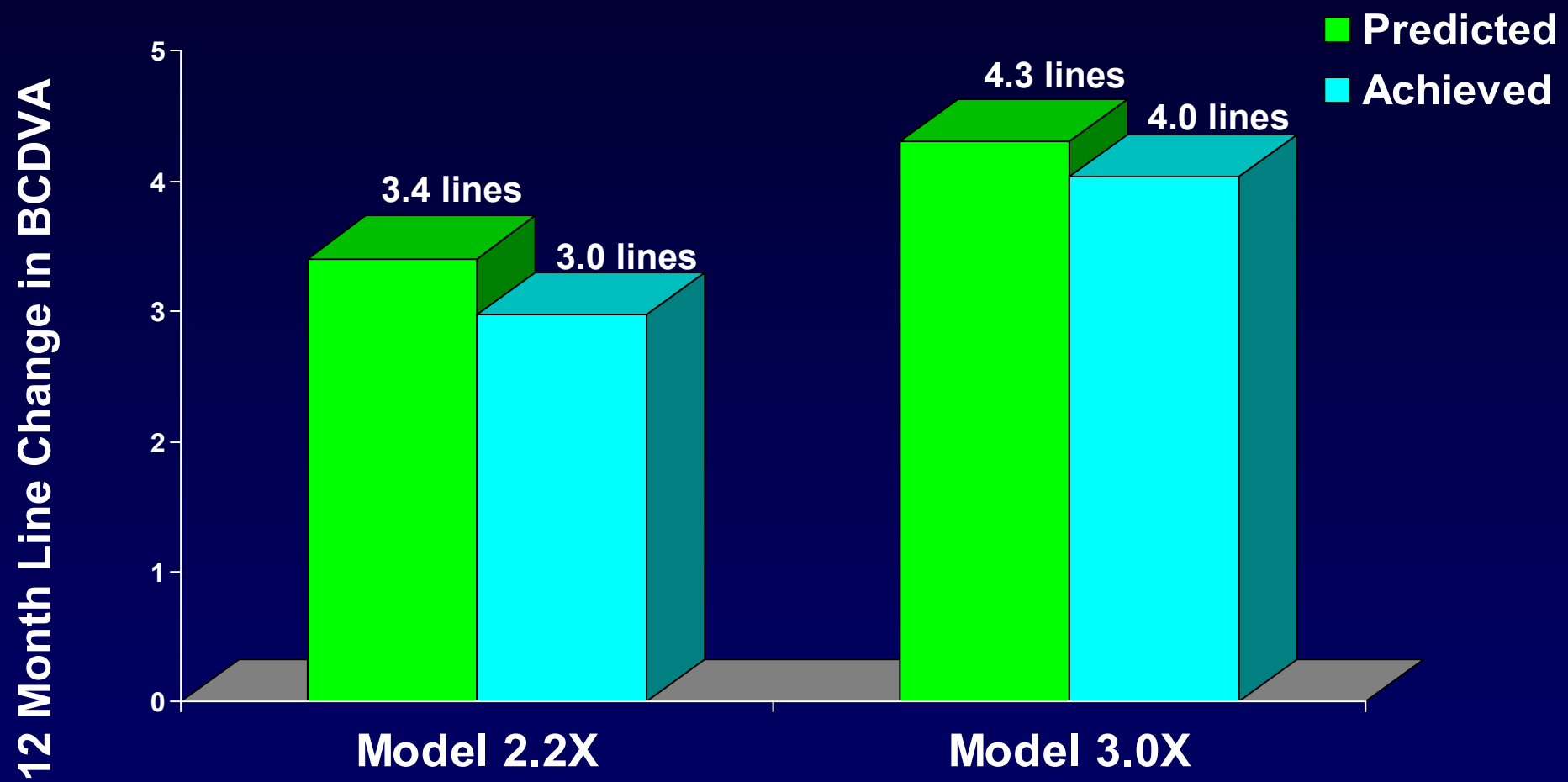
Change in Distance Vision
Baseline to Last Available Visit



Source: not in PMA

Mean Gain in BSCVA

Expected Change from Magnification



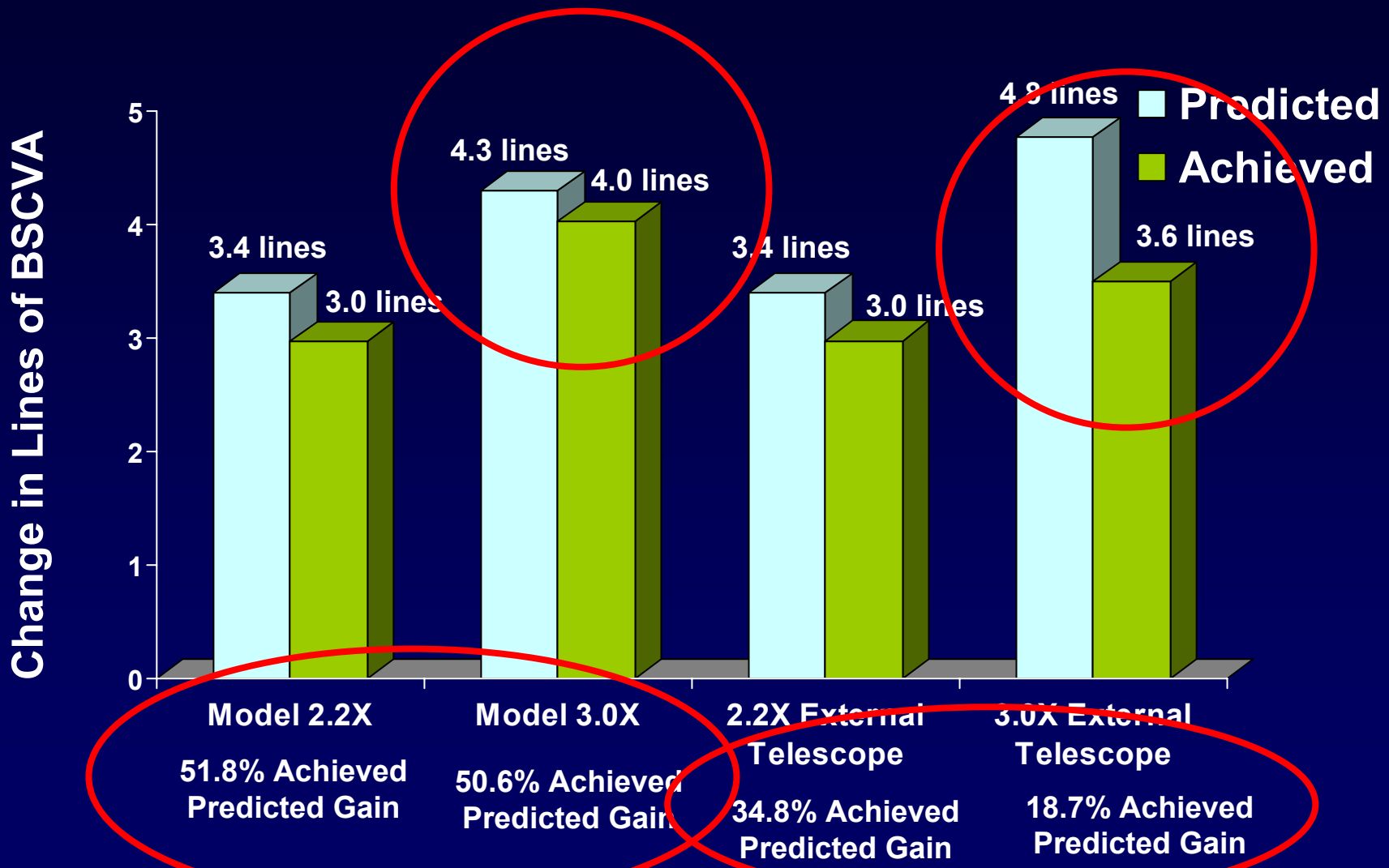
51.8% Achieved
≥ Predicted Gain in Vision

50.6% Achieved
≥ Predicted Gain in Vision

Source: not in PMA

Mean Gain in BSCVA

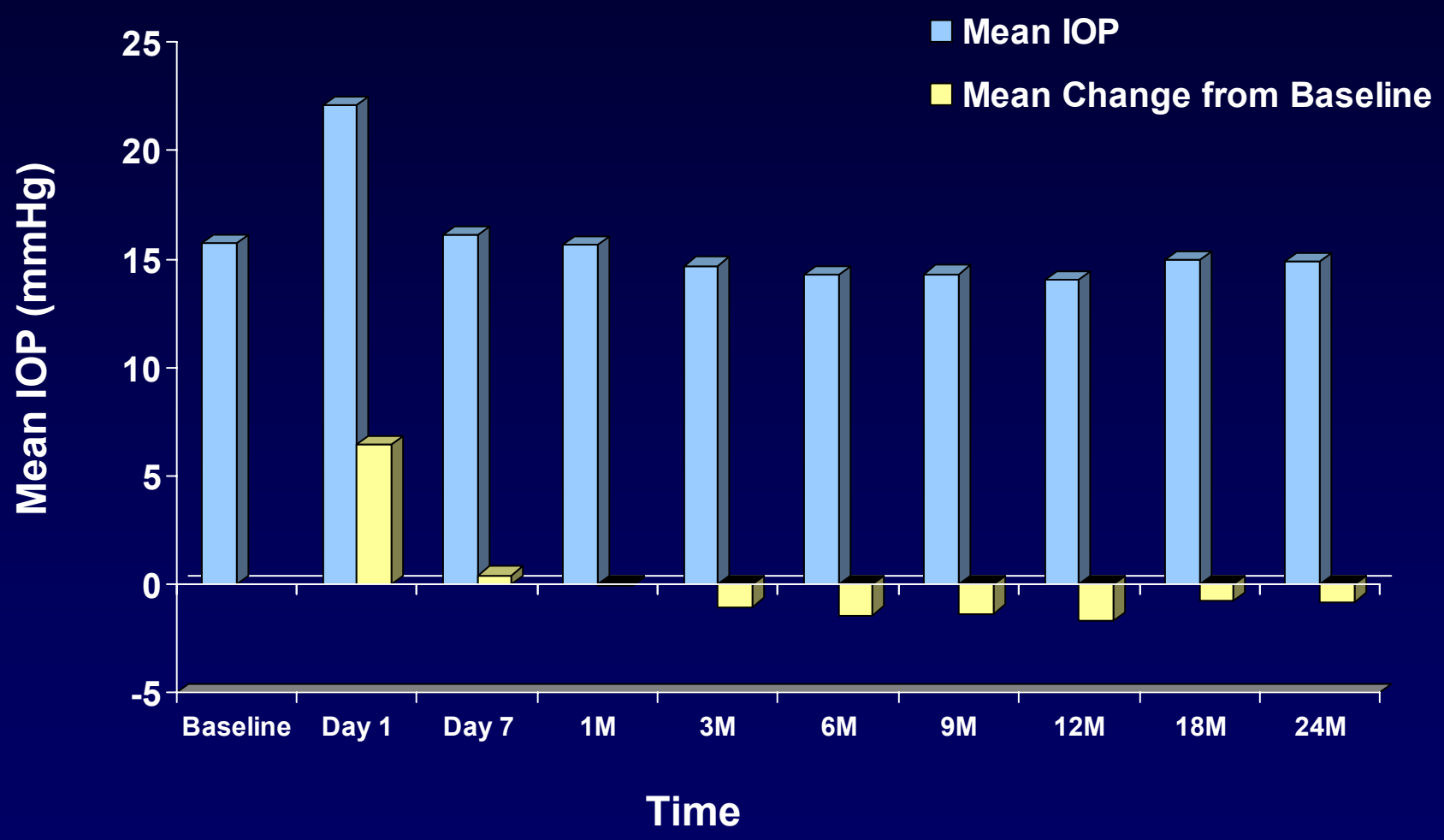
Expected Change from Magnification



Source: not in PMA

Intraocular Pressure

Mean, Change from Baseline



Source: PMA Table A25

Operative and Perioperative Complications Cumulative Incidence ≥ 1%

All Eyes – Implanted (N = 206) and Non-Implanted (N = 11)

Corneal abrasion	11 eyes	5.1%
Corneal edema	14 eyes	6.5%
Descemet's membrane separation	3 eyes	1.4%
Hyphema	14 eyes	6.5%
Increased IOP	62 eyes	28.6%
Iris atrophy	4 eyes	1.8%
Iris damage	8 eyes	3.7%
Iris incarceration	3 eyes	1.4%
Iris prolapse	12 eyes	5.5%
Posterior capsule rupture	10 eyes	4.6%
Posterior capsule opacification	8 eyes	3.7%
Vitreous in anterior chamber	3 eyes	1.4%
Wound leak	3 eyes	1.4%

Source: A004 Table 46, 48; A003 Table 46 rev., 14.2-14.6

Ocular Adverse Events
Cumulative Incidence <5% (N = 206)

Anterior ischemic optic neuropathy	1 eye	0.5%
Choroidal neovascularization	3 eyes	1.5%
Choroidal hemorrhage	1 eye	0.5%
Corneal edema onset > 30 days postop	6 eyes	2.9%
Corneal decompensation	2 eyes	1.0%
Cyclitic membrane/phthisis	1 eye	0.5%
Cystoid macular edema	1 eye	0.5%
Device failure and removal	2 eyes	1.0%
Diplopia	3 eyes	1.5%
Distorted pupil	7 eyes	3.4%
Patient dissatisfaction and removal	4 eyes	1.9%
IMT dislocation	2 eyes	1.0%
Inflammatory membrane on IMT	1 eye	0.5%
Increased IOP requiring treatment	7 eyes	3.4%
Iris atrophy	7 eyes	3.4%
Obstructed iridectomy	1 eye	0.5%
Subretinal hemorrhage	2 eyes	1.0%
Synechiae	1 eye	0.5%
Vitreous hemorrhage	3 eyes	1.5%

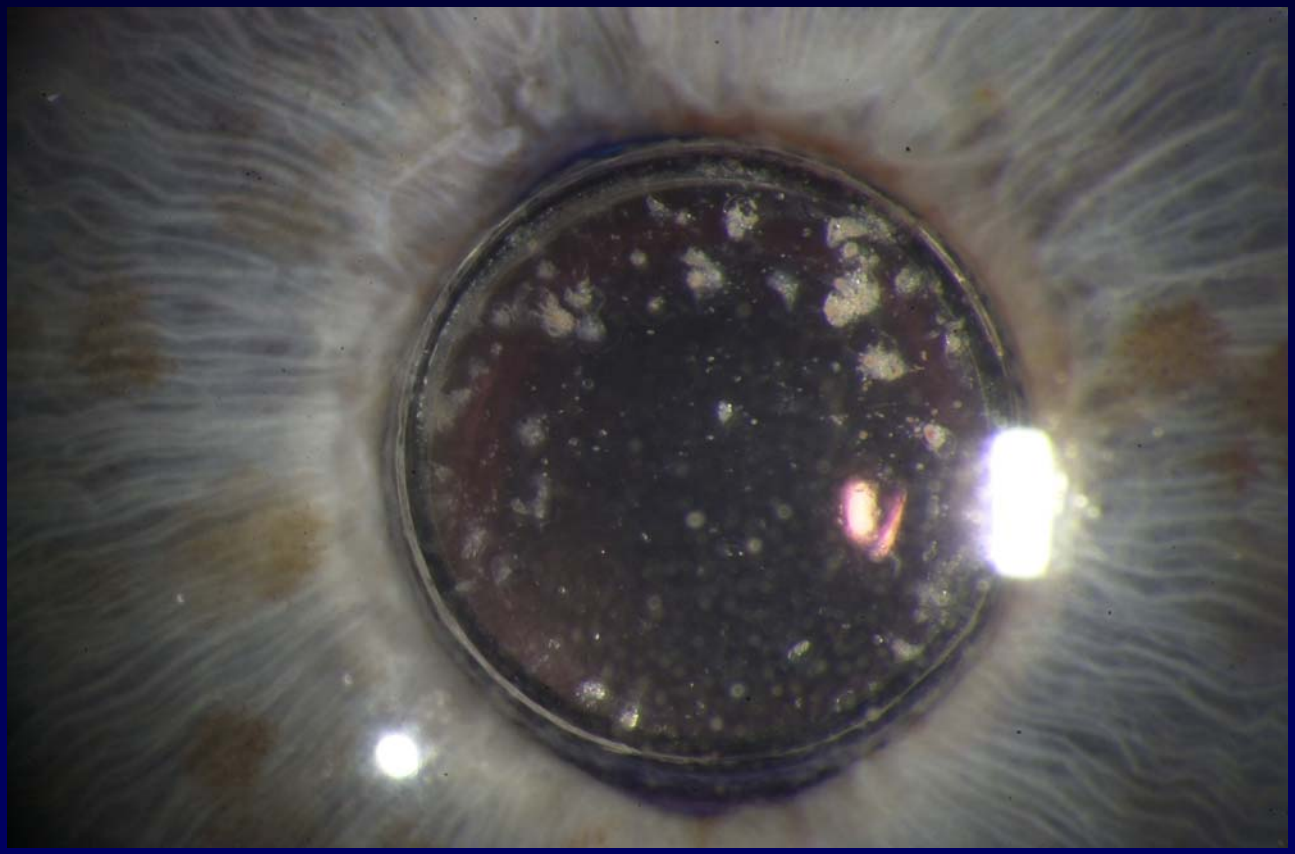
Source: A004 Table 46, 48; A003 Table 46 rev., 14.2-14.6

Ocular Adverse Events with Incidence ≥ 5% (N = 206)

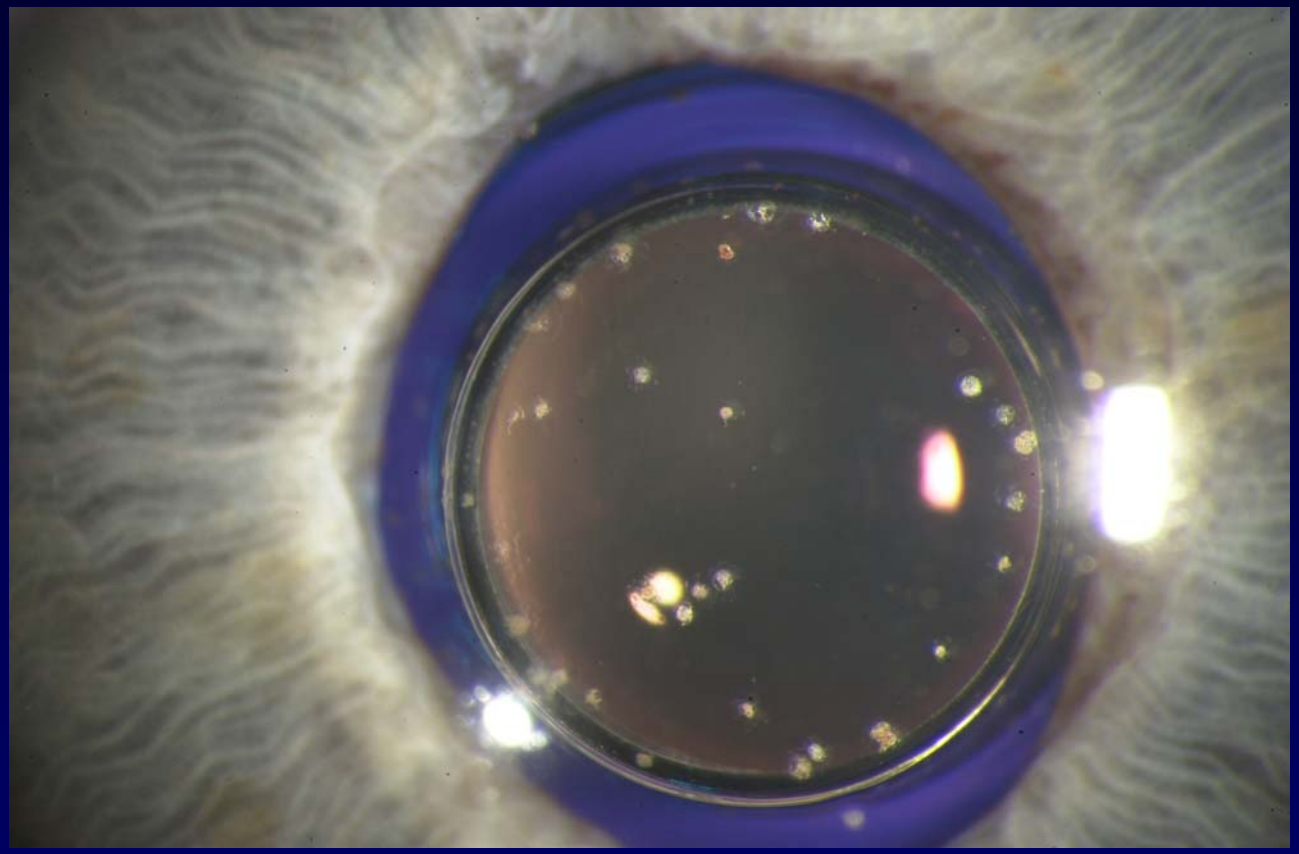
	Cumulative	Persistent (≥ 1 Year)
Iris transillumination defects	11 eyes (5.3%)	10 eyes (5.1%)
Iritis	12 eyes (5.8%)	0 eyes (0%)
Posterior synechiae	15 eyes (7.3%)	9 eyes (5%)
Guttae	16 eyes (7.8%)	15 eyes (7.6%)
Pigment deposits on IMT	23 eyes (11.2%)	15 eyes (7.6%)
Inflammatory deposits on IMT	51 eyes (24.8%)	32 eyes (16.2%)

Source: A004 Table 46, 48; A003 Table 46 rev., 14.2-14.6; persistent AE not in PMA

Inflammatory Deposits on IMT



Inflammatory Deposits on IMT



IMT Removals
(N = 8)

- Device failures (N=2)
- Dissatisfaction with outcome (N=4)
- Corneal decompensation (N=2)

IMT Removal Due to Device Failure
(N = 2)

- Condensation in the telescope
- Cracks in lateral wall of the telescope
- No recurrences after
  - Physician training on handling of the IMT
  - Overall improvement in manufacturing process since early devices were fabricated

IMT Removal Due to Dissatisfaction
(N = 4)

- Four subjects dissatisfied with outcome
  - Three subjects requested removal of the IMT based on complaints of glare in bright light
  - One subject complained of haze, loss of peripheral vision in implanted eye, loss of depth perception

IMT Removal Due to Corneal Decompensation (N = 2)

- Operative complications
  - In both eyes, positive vitreous pressure during implantation resulted in iris prolapse and shallowing of the anterior chamber, and significant early endothelial cell loss
  - In one of the two cases, one haptic was placed in the capsular bag and the other, in the sulcus
- Corneal transplantation and IOL exchange was performed

Major Non-Ocular Adverse Events
(N = 206)

Arrhythmia	7 subjects	3.4%
Cancer	12 subjects	5.8%
CVA/TIA	5 subjects	2.4%
Death	10 subjects	4.9%
Falls	3 subjects	1.5%
Fractures	5 subjects	2.4%
Infection	19 subjects	9.2%
Myocardial Infarction	5 subjects	2.4%

Source: PMA Table A49

Major Non-Ocular Adverse Events
(N = 206)

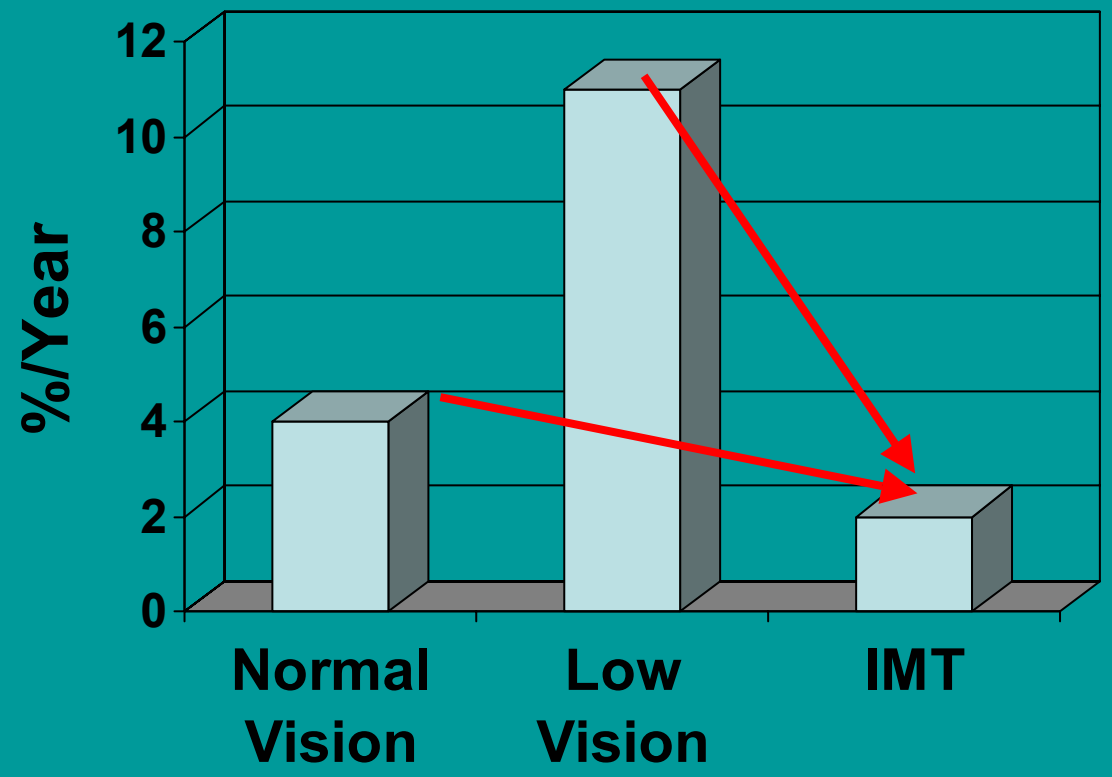
Arrhythmia	7 subjects	3.4%
Cancer	12 subjects	5.8%
CVA/TIA	5 subjects	2.4%
Death	10 subjects	4.9%
Falls	3 subjects	1.5%
Fractures	5 subjects	2.4%
Infection	19 subjects	9.2%
Myocardial Infarction	5 subjects	2.4%

Source: PMA Table A49

Fractures/Falls (N = 8)

Patient ID	Description of Event	Relationship to IMT (Per Investigator)
008-213 63-year-old male	Patient slid off ladder and fractured heel bone	Not Related
010-209 61-year-old female	Patient fell 4 weeks after knee replacement, required right knee repair	Not Related
014-202 75-year-old male	Fracture of the femur from a fall from a chair while attempting to pick up an object	Not Related
014-204 83-year-old female	Patient hurriedly stood up to see across the street, tripped, fell, fractured wrist	Not Related
019-204 73-year-old female	Patient fell out of bed	Not Related
023-204 88-year-old female	Patient lost balance and fell	Not Related
023-212 78-year-old female	Patient was sexually assaulted and, in addition to other trauma, fractured toe	Not Related
026-207 85-year-old female	Patient stumbled backwards over her slipper, fell and fractured her hip	Not Related

Falls in the Elderly



Source: Beaver Dam Eye Study

Endothelial Cell Density

Specular Microscopy Methods

- Images analyzed at Emory University Specular Microscopy Reading Center (H Edelhauser, B McCarey)
- Endothelial images were scanned and then analyzed with Konan KSS-300 software
- 3 images per eye (implanted eye and fellow) for each visit were analyzed and the mean was calculated
- Specular images were difficult to obtain in the study population
  - At baseline, some difficulty fixating due to scotoma
  - Glare and reflection from the anterior surface of the IMT

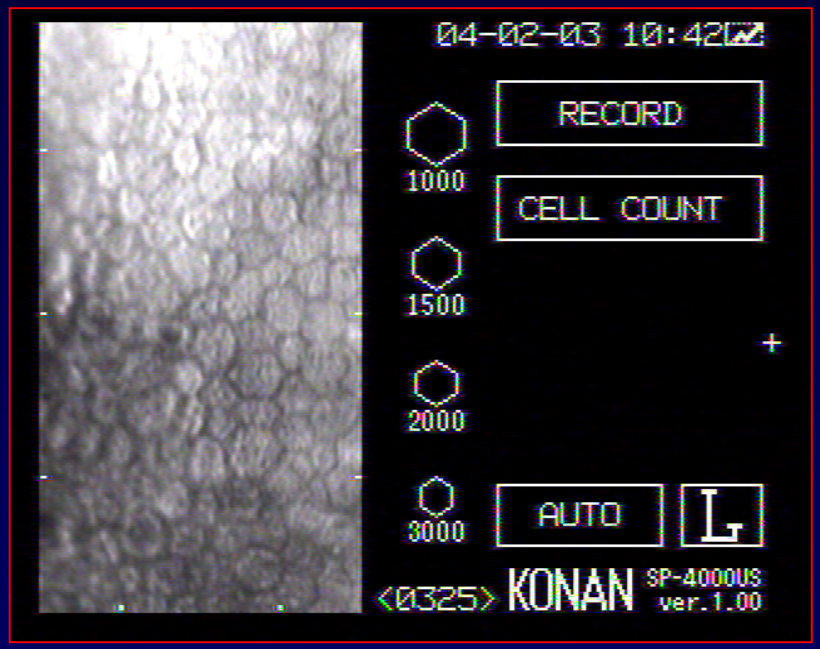
Specular Microscopy
Estimates of Precision

- Best case - 2% SD (47 cells) for a single clinical site, single photographer imaging his own eye, and a single reader[1]
- For multicenter study, precision varies from 8% to 10% with a single reader

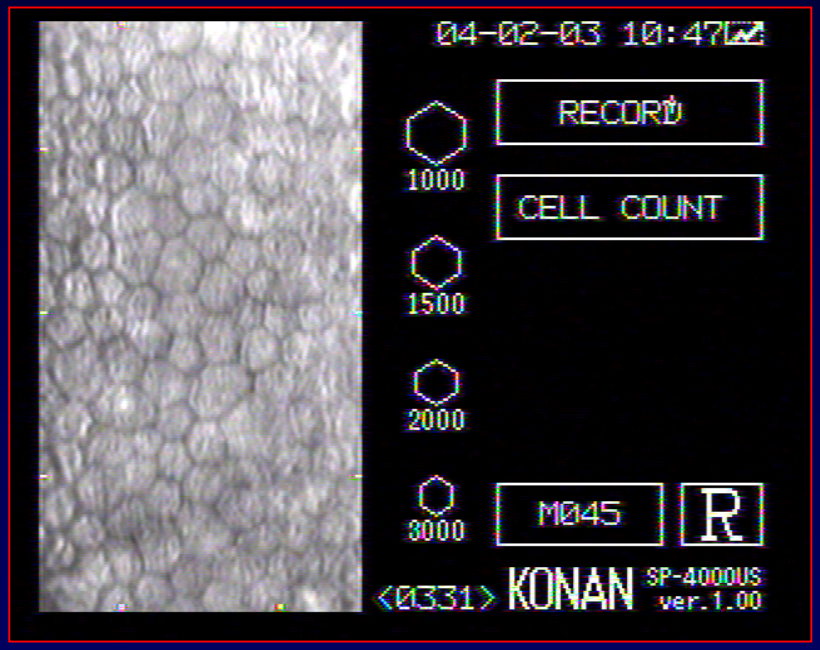
[1]Jones SS et al. Effect of laser *in situ* keratomileusis on the corneal endothelium. AJO 1998;125:465-71

Specular Images from Subject 23-201

Male, 79 Years of Age, Pseudophakic Fellow Eye



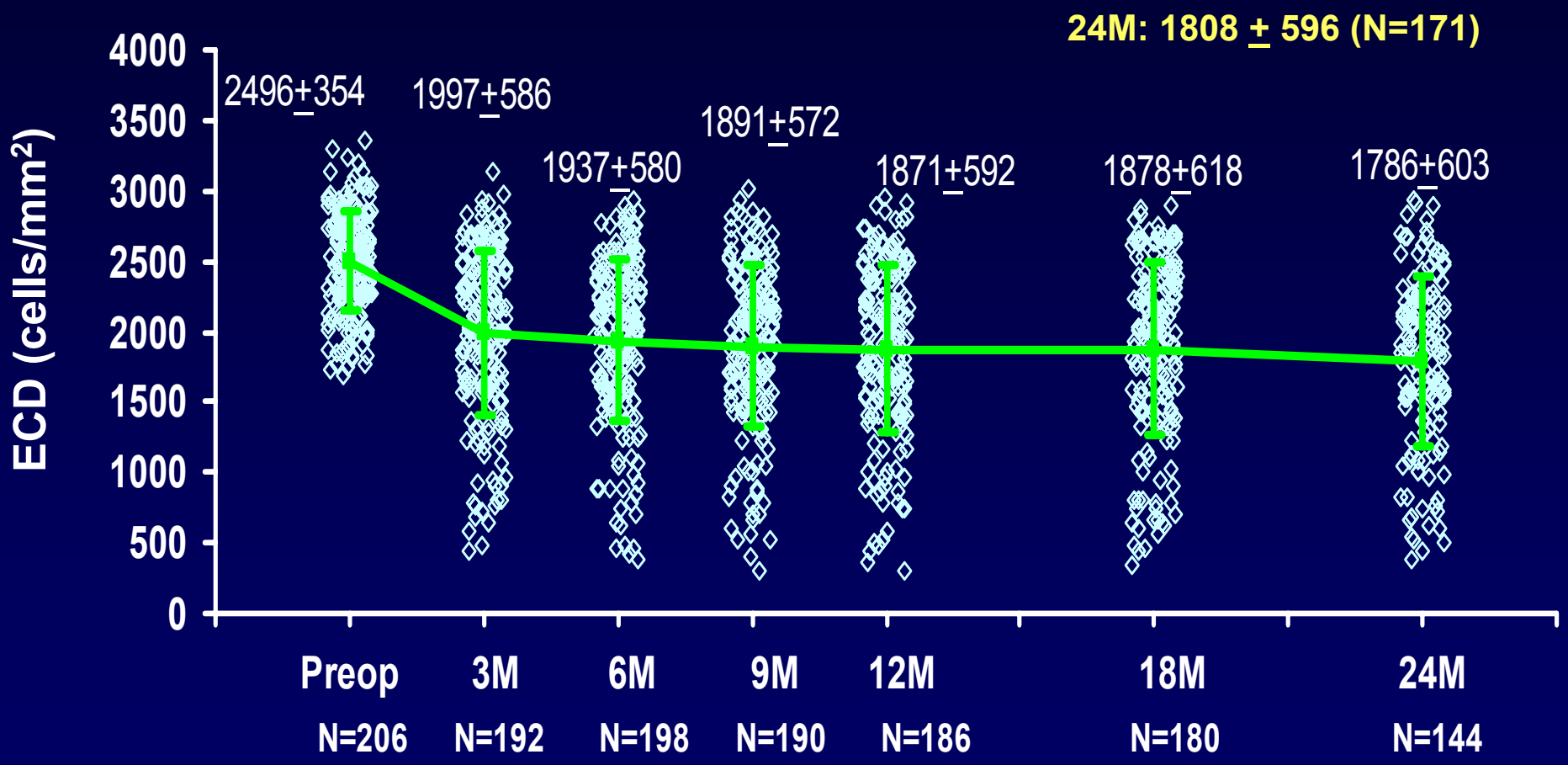
OS - IMT-Implanted Eye at 3 Months
1805 cells/mm^2



OD - Fellow Eye at 3 Months
1798 cells/mm^2 (pseudophakic)

Results of Specular Microscopy

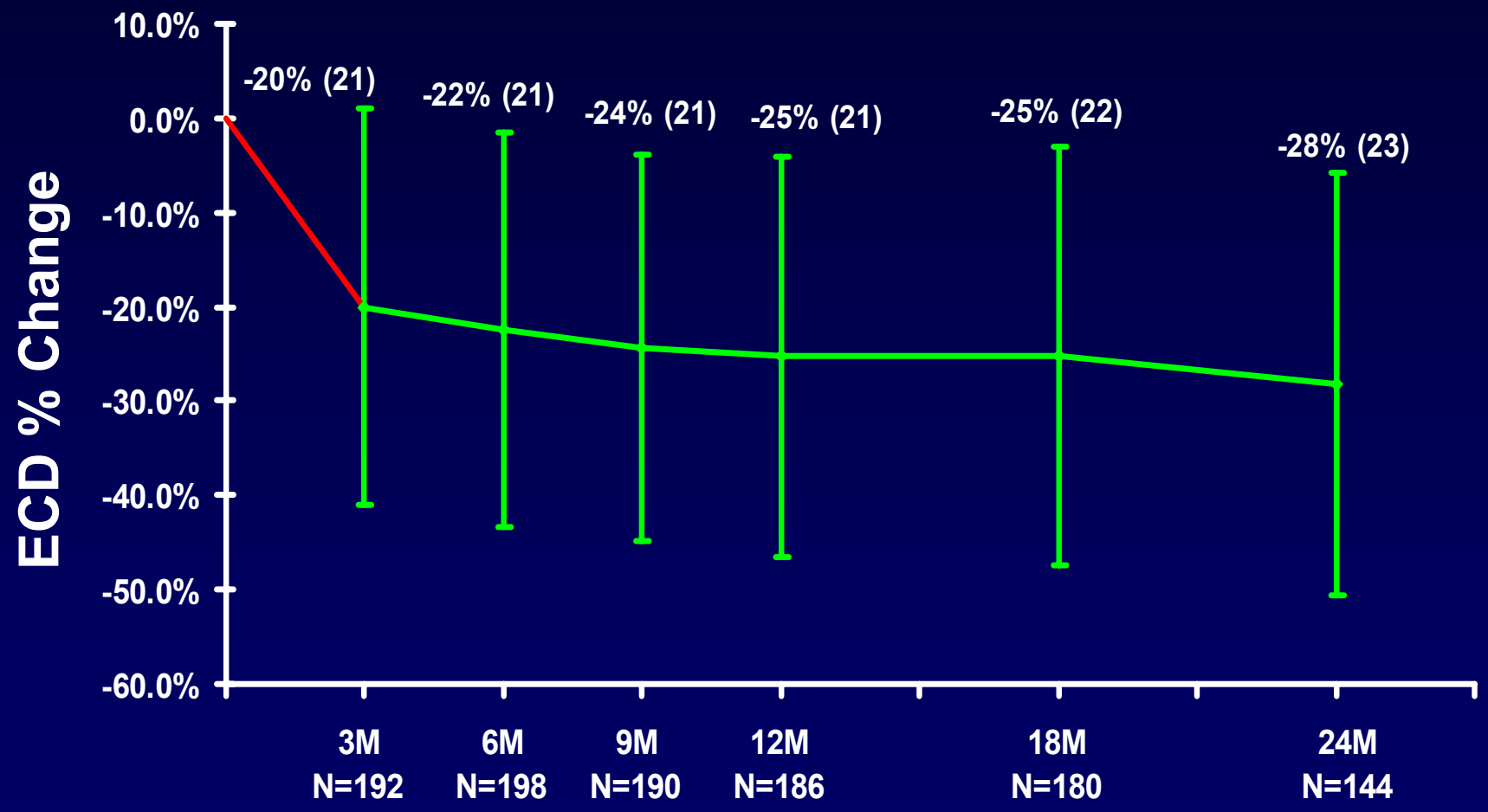
Endothelial Cell Density
IMT-Implanted Eyes (mean, SD)



Source: PMA Figure 11

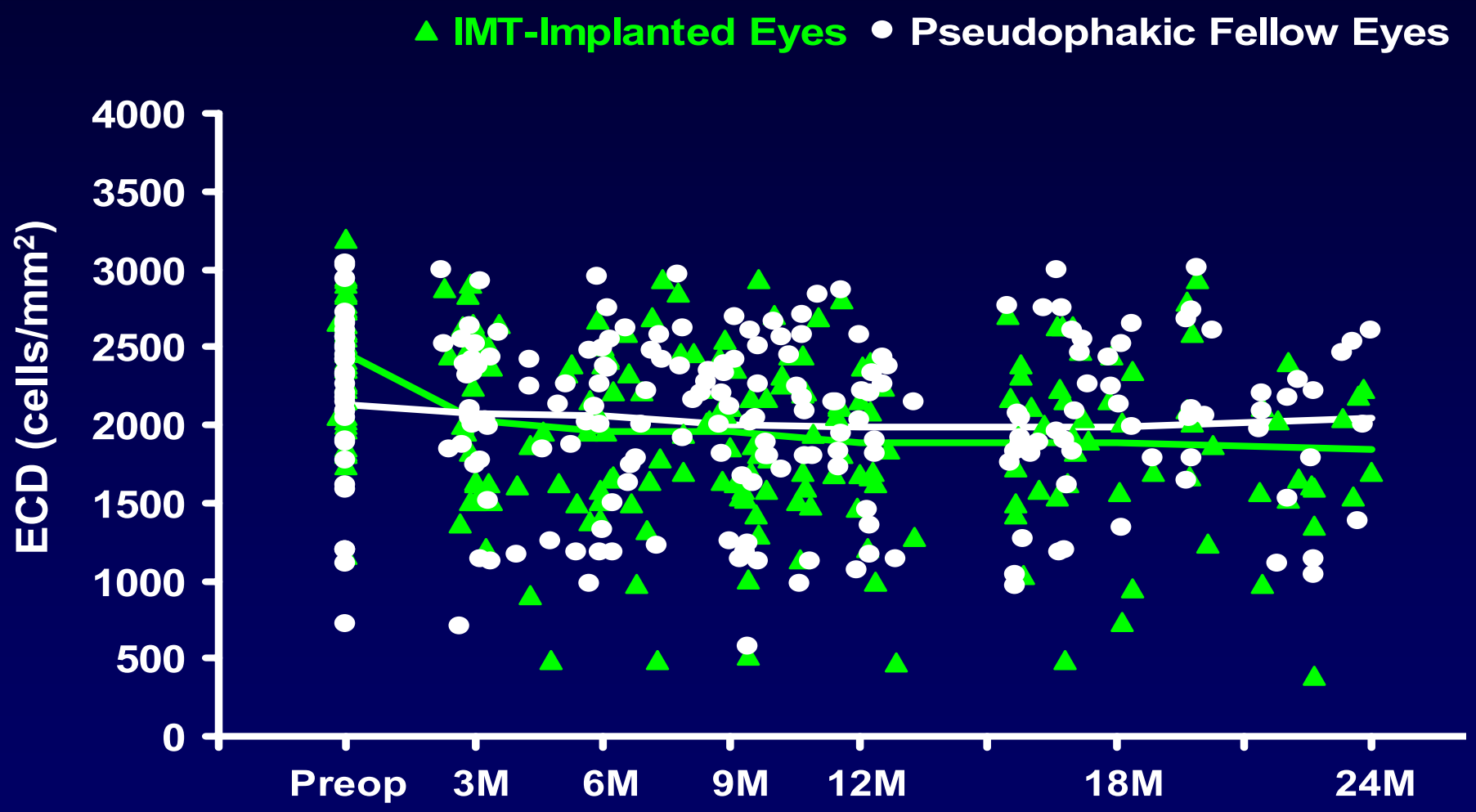
Percentage Change in ECD from Baseline

IMT-Implanted Eyes (mean, SD)



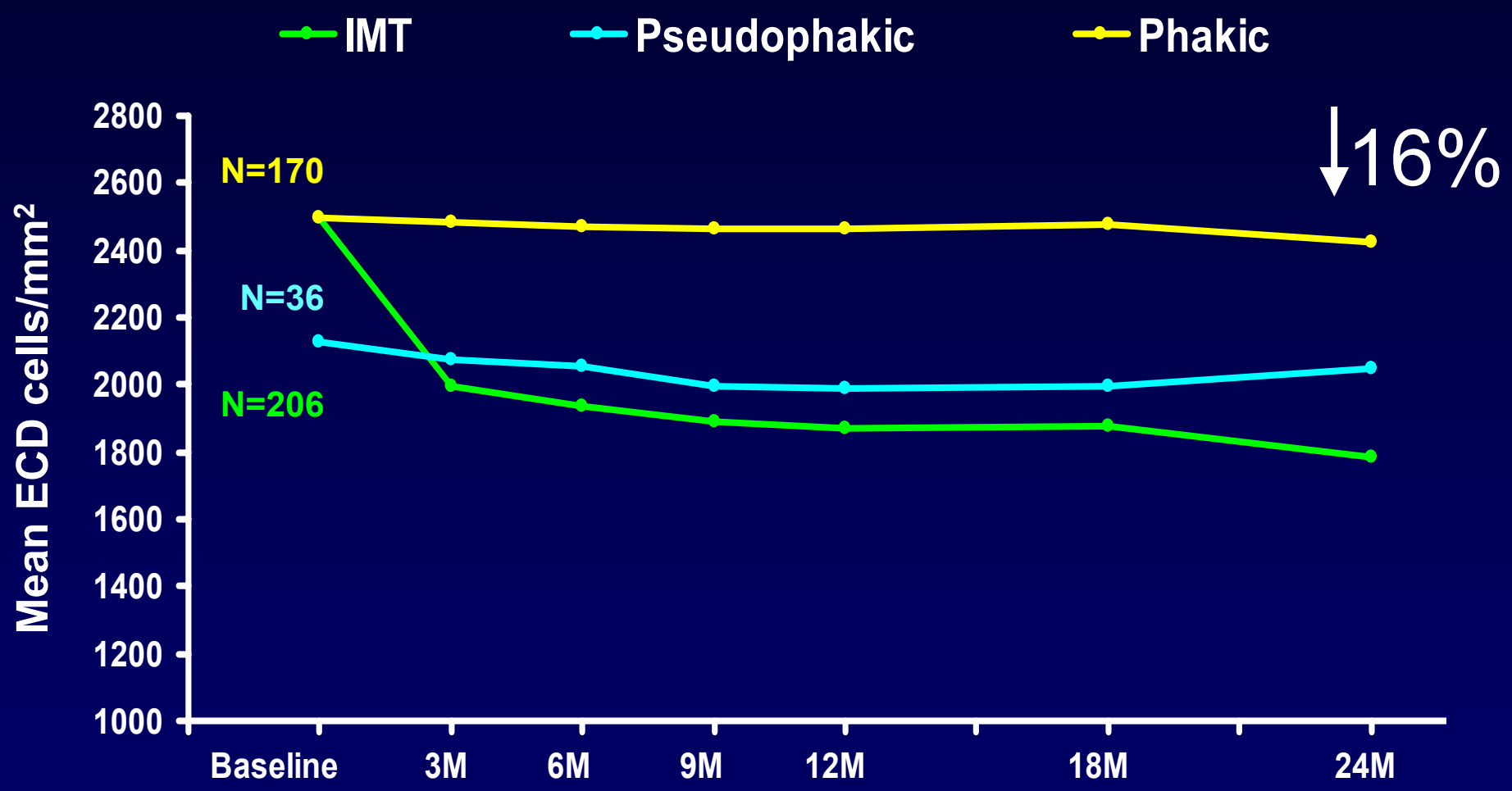
Source: PMA Table A29

ECD In Subjects With Pseudophakic Fellow Eyes



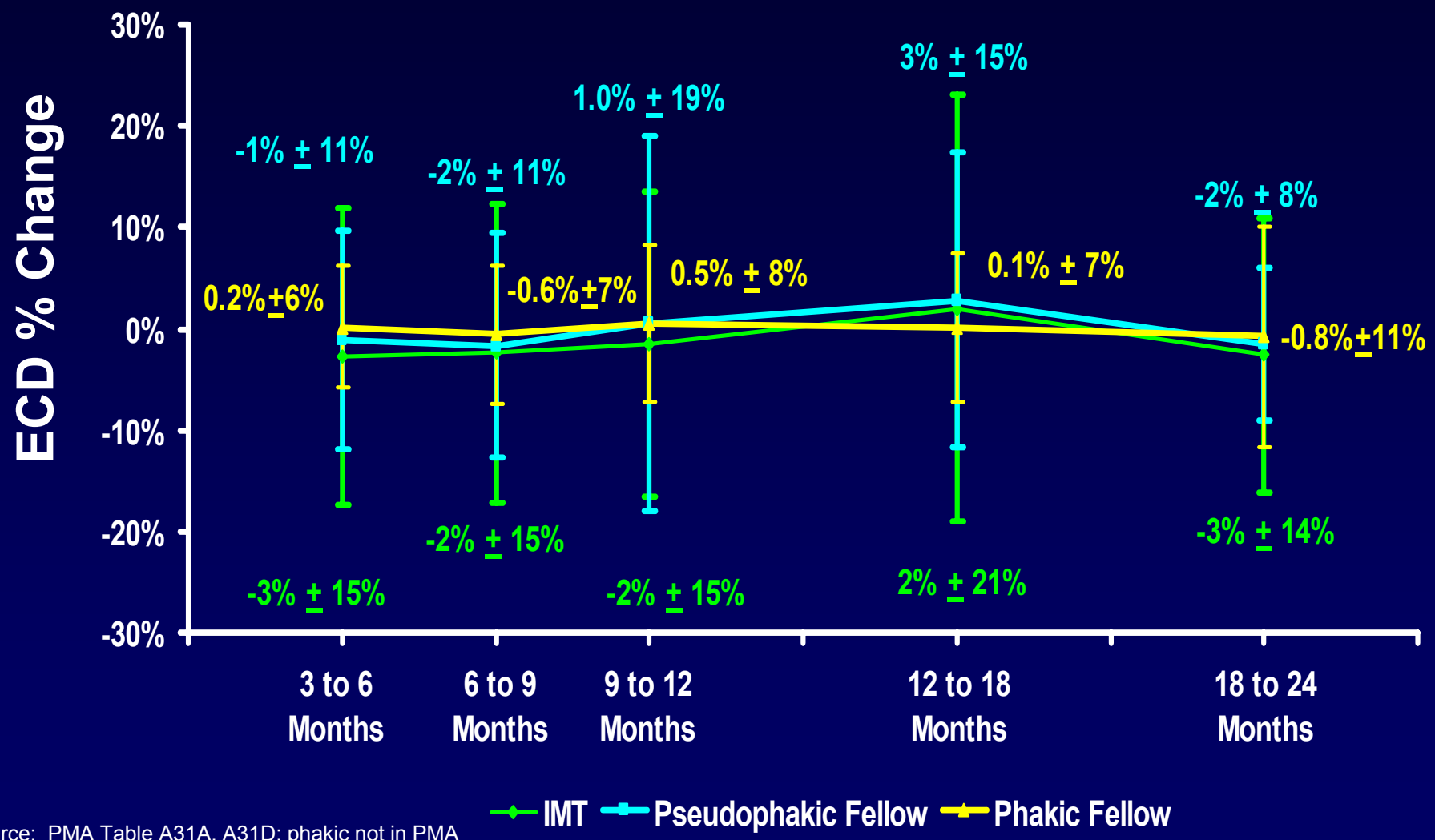
Source: not in PMA

ECD (mean, SD) for IMT-Implanted Eyes, Pseudophakic and Phakic Fellow Eyes



Source: PMA Table A27; (pseudo)phakic not in PMA

Percentage Change (mean, SD) in ECD Between Consecutive Visits IMT-Implanted Eyes vs Pseudophakic & Phakic Fellow Eyes



Source: PMA Table A31A, A31D; phakic not in PMA

How does the loss in ECD following IMT implantation compare to published data on conventional cataract surgery?

Percentage ECD Loss Following Cataract Surgery

Publication or Study	3 Months	12 Months	24 Months	36 Months
Protocol IMT002 - IMT-Implanted Eyes (N=206)	20%	25%	28%	
Protocol IMT002 - Pseudophakic fellow eyes (N=34)		16%	16%	
Bourne WM et al. Arch Ophthalmol 1981;99:1375-1376				
Intracapsular (N=99)	17%			
Extracapsular (N=99)	14%*			
Liesegang TJ et al. Am J Ophthalmol 1984;97-32-39				
Intracapsular, no IOL (N=20)	13%	16%	22%	
Intracapsular, IOL (N=96)	16%	22%	26%	
Extracapsular, no IOL (N=83)	11%	9%	11%	
Extracapsular, IOL (N=393)	14%	17%	19%	
Bourne WM et al. Ophthalmology 1994;101:1014-1022 N=50	19%	20%		27%
Beltrame G et al. J Cataract Refrac Surg 2002;22:118-125				
3.5mm CCI (N=27)	17%	20%		
5.5mm CCI (N=27)	22%	24%		
Scleral Tunnel (N=27)	17%	19%		
Bourne RA et al. Ophthalmology 2004;111:679-685				
Overall (N = 433)	7%	10%		
Phaco (N=223)		11%		
ECCE (N=210)		9%		

What factors contributed to the acute and the overall reduction in ECD?

Candidate Predictive Factors

- Day 1 corneal edema
- ACD
- Surgical Order
- Incision Type
- Incision Size
- Age at implantation
- Preoperative ECD
- Surgeon
- Axial Length
- Use of Healon V

Factors Affecting Change in ECD Final Models

3 Month Change in ECD

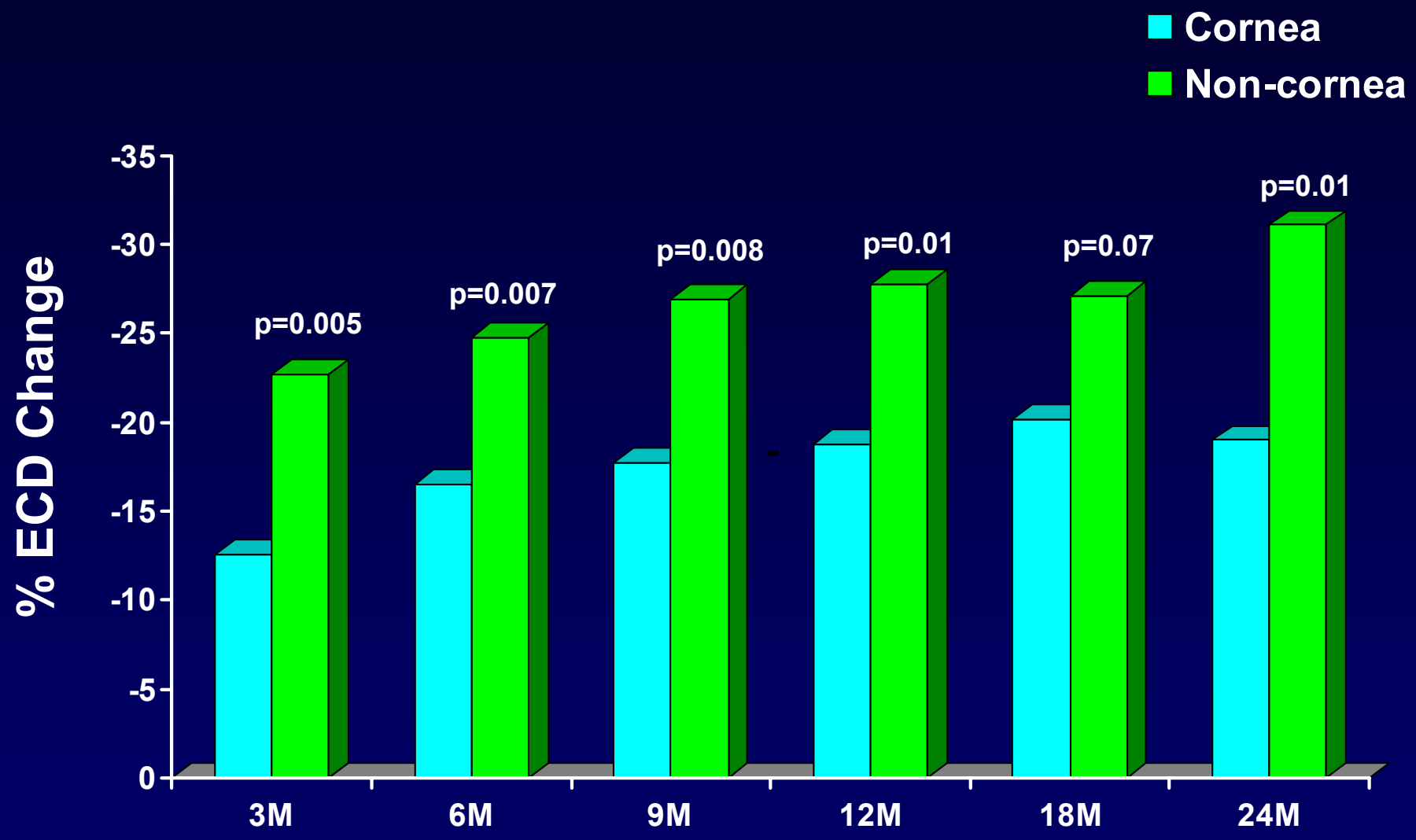
Day 1 Corneal Edema	<.0001
Surgeon's Specialty	0.0336

Total Change in ECD

Day 1 Corneal Edema	<.0001
Surgeon's Specialty	0.0336
Surgical Order	0.0023
Day 1 Corneal Edema and Surgical Order Interaction	0.0679

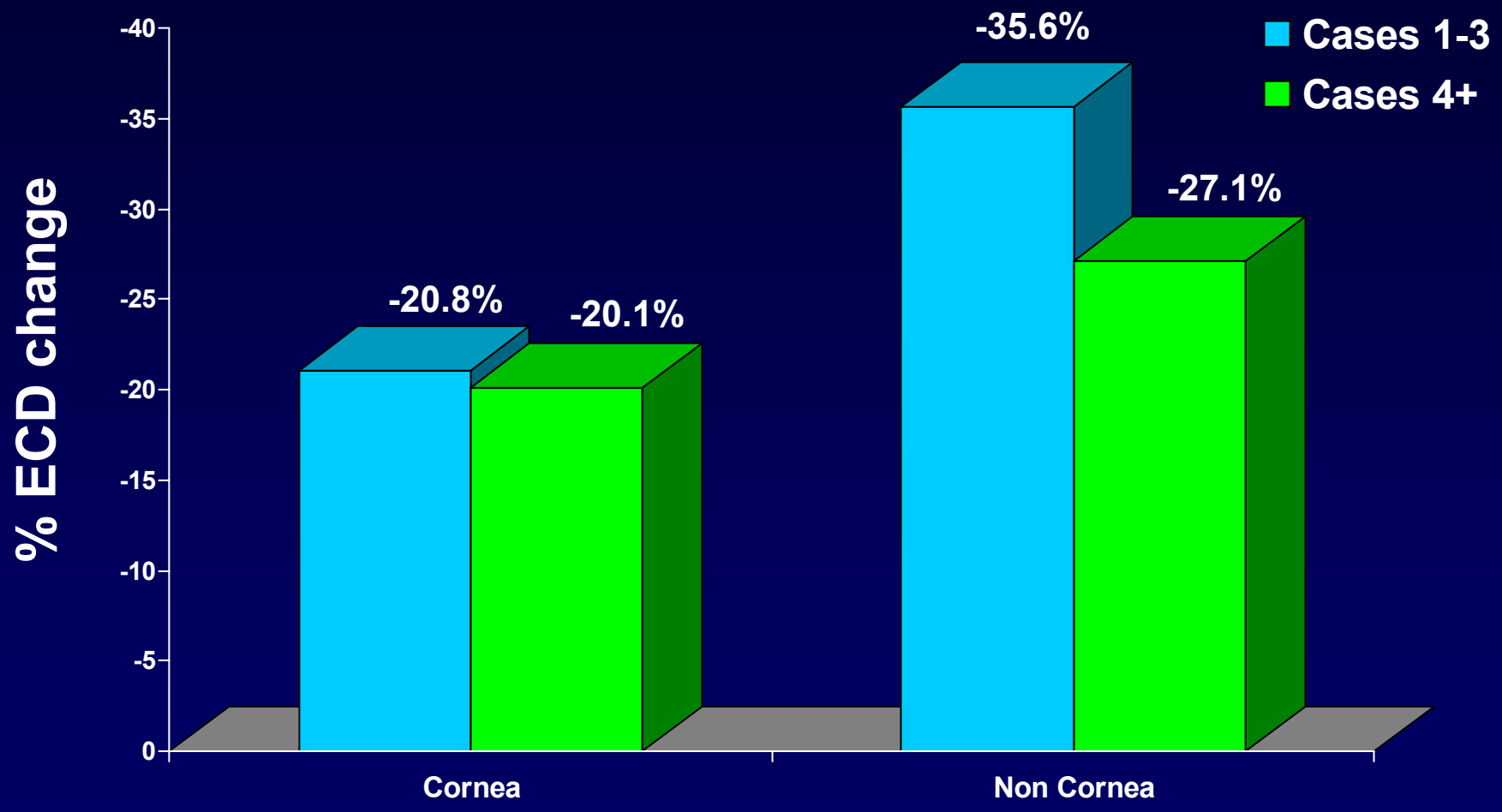
Source: PMA Table A39; A002 Table Q3.5.9

Percentage Change in ECD Stratified by Surgeon's Specialty



Source: PMA Table A29F

Percentage Change in ECD Stratified by Surgeon's Specialty and Surgical Order



Source: not in PMA

Effect of Anterior Chamber Depth on Change in ECD

- Linear effect on % change in ECD for surgical order $\leq$ 3 cases
  - p=0.01 for baseline to 3 months
  - p=0.03 for baseline to 24 months
- No effect for surgical order $\geq$ 4 cases
  - p=0.20 for baseline to 3 months
  - p=0.13 for baseline to 24 months
- Predictive power (coefficient of determination or R^2) is low
  - 0.05 for baseline to 3 months
  - 0.07 for baseline to 24 months

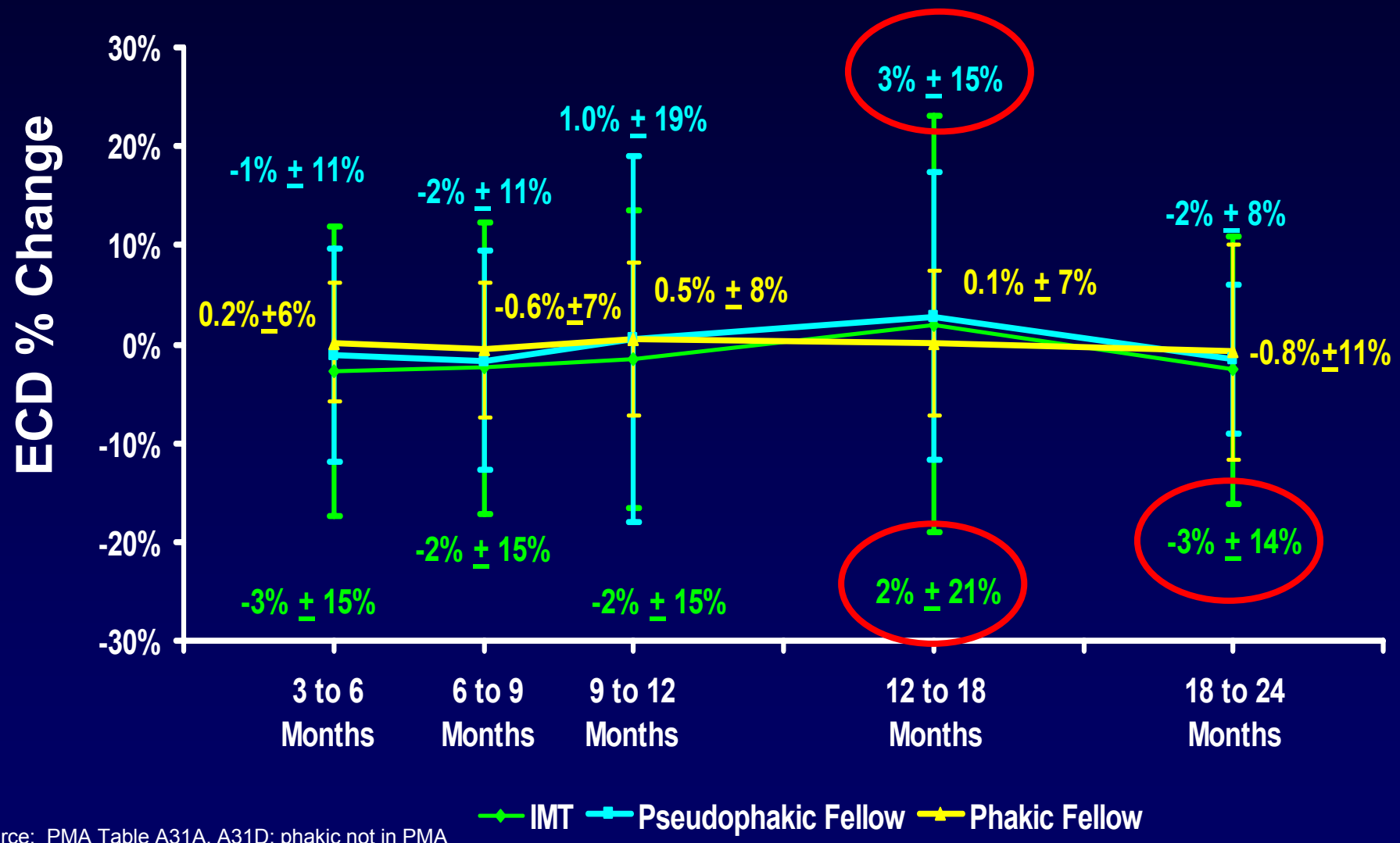
Source: A003 Table 3.1A, 3.3A

How can we mitigate these contributors to endothelial cell loss?

- Surgeon training
  - Extensive training program described in PMA
  - Meticulous attention to surgical detail to avoid iris prolapse, flat anterior chamber and Day 1 corneal edema
- Suggest high ECD and deep ACD for first 5 cases for each surgeon

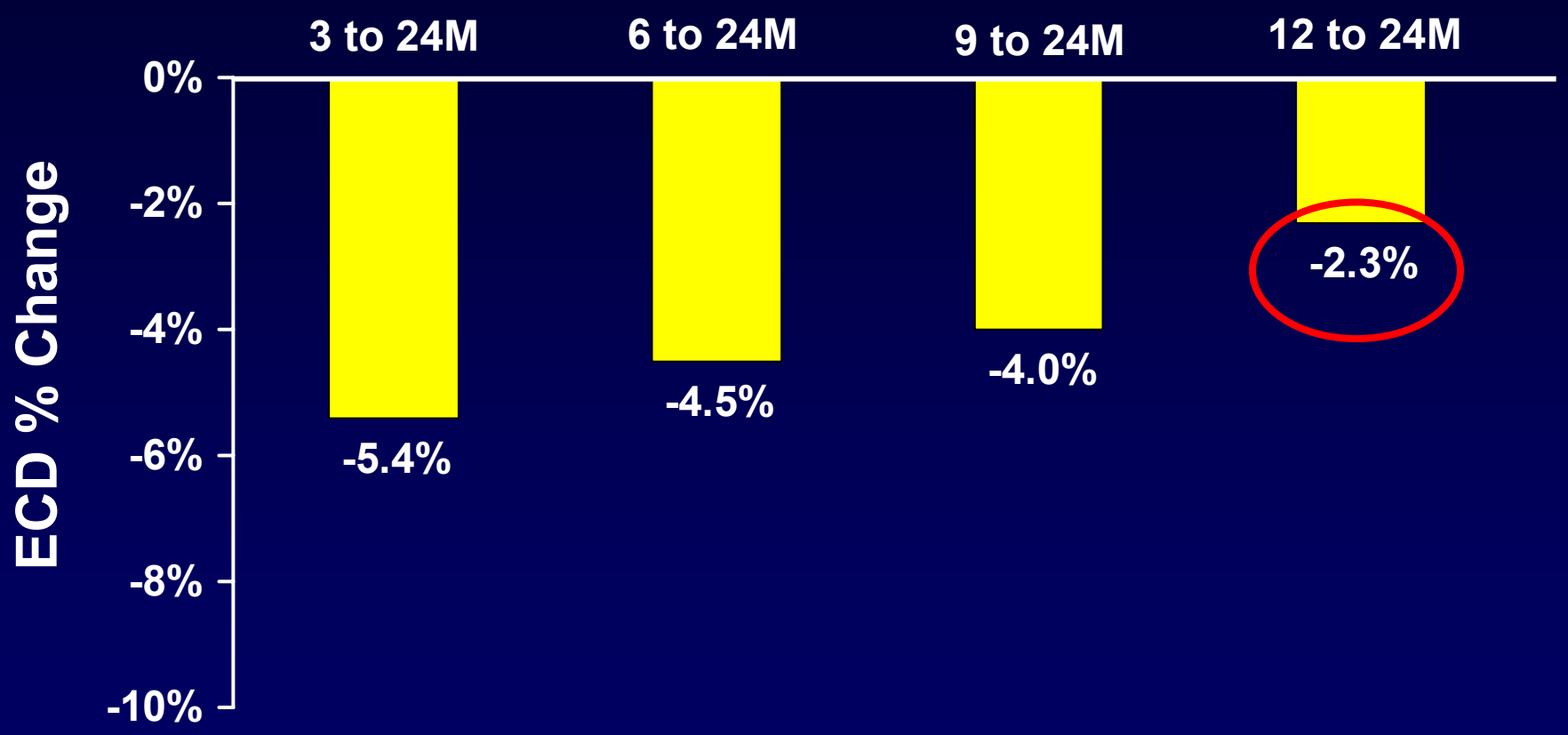
Following the initial surgical loss, does the rate of ECD loss decrease over time?

Percentage Change (mean, SD) in ECD Between Consecutive Visits IMT-Implanted Eyes vs Pseudophakic & Phakic Fellow Eyes



Source: PMA Table A31A, A31D; phakic not in PMA

Annual Percentage Change in ECD



Source: PMA Table A37; A002 Table Q6.6

Relationship Between Early Loss of ECD and Later Loss of ECD

- ECD at 3 months is not predictive of the rate of ECD loss at later time points
  - No difference in corneas with 3-month loss of ECD $\leq$ 20% vs loss of ECD > 20%
  - No difference in corneas with 3-month loss of ECD $\leq$ 1000 cells/mm^2 vs ECD > 1000 cells/mm^2

Source: PMA Table A37; A002 Table Q6.6

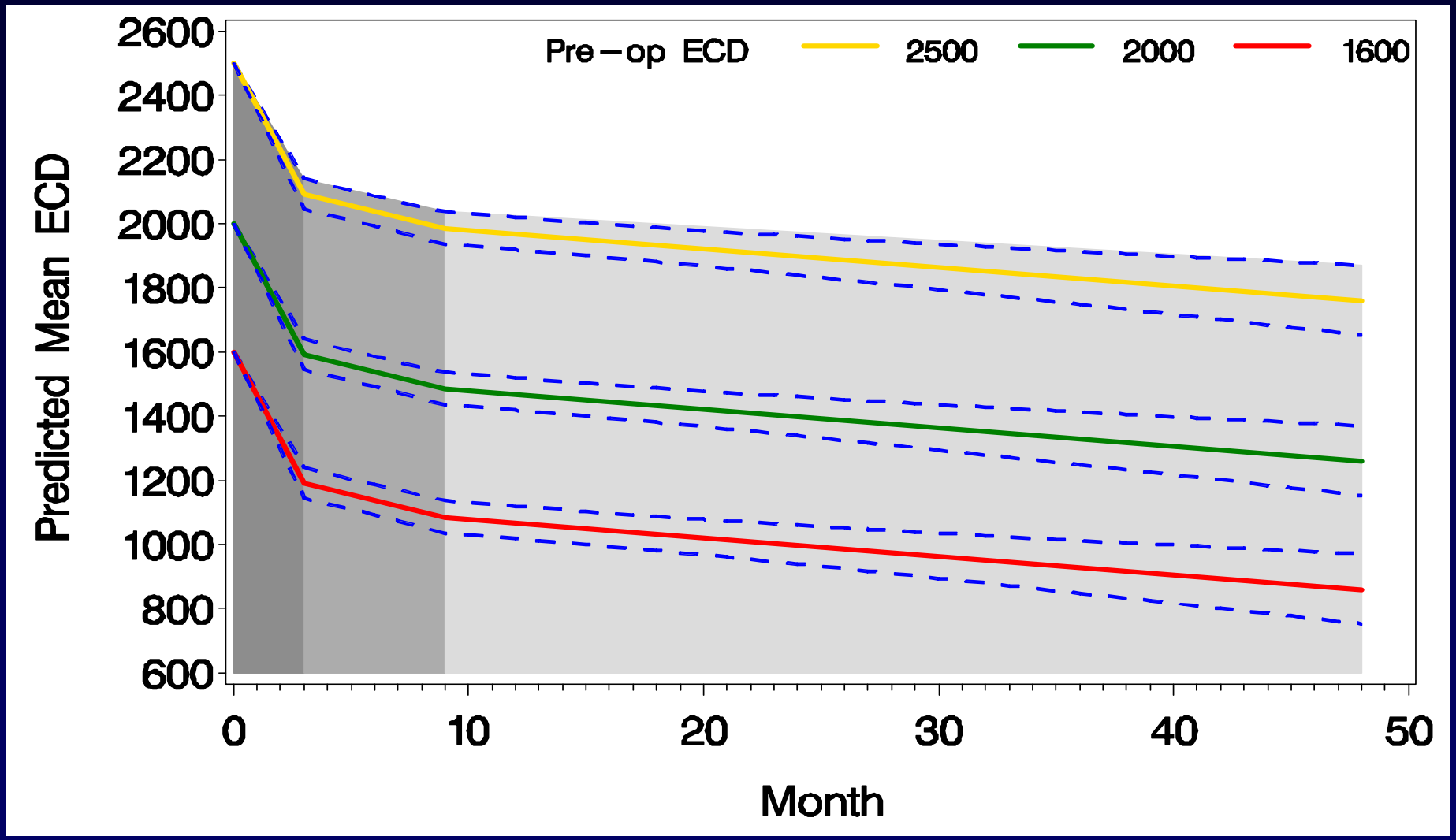
What is the rate of ECD loss more than two years after implantation?

Three-Piece Regression Model

- Change in rate of endothelial cell loss at 3 and 9 months
- Consistent with pathophysiology of endothelial cell loss after intraocular surgery
  - Acute loss at time of surgery
  - Endothelial cell migration
  - Continuing, long-term loss

Chronic Change in ECD

Baseline ECD 1600, 2000 and 2500 cells/mm^2 and ACD 3.0 mm
Piecewise Regression Model (3-Piece)



Source: A004 Table B

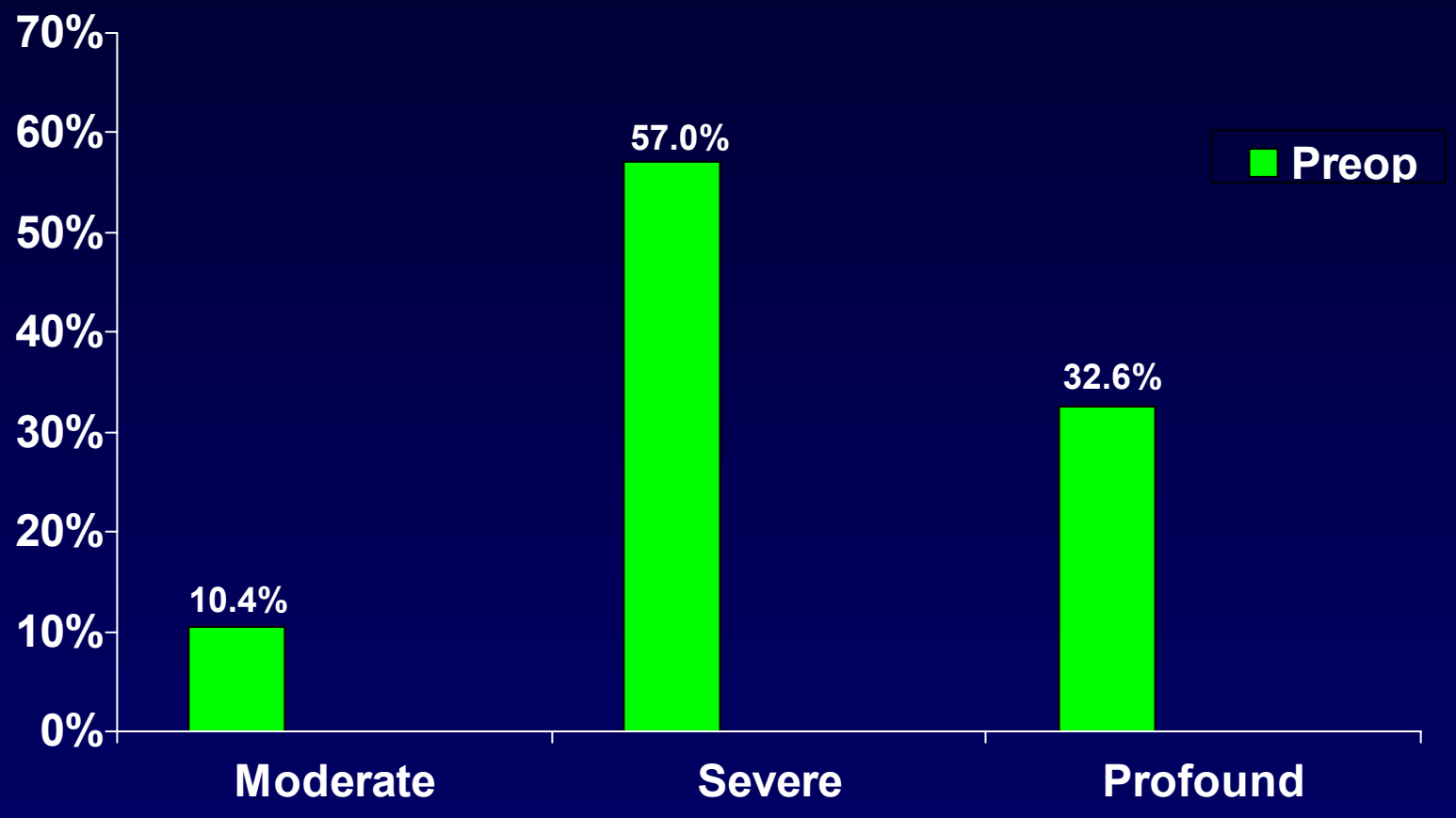
How can the corneal endothelium be protected?

Recommendations

- Establish a minimum endothelial cell density based on age and life expectancy
- High ECD and deep ACD for the first 5 cases
- Comprehensive surgeon training program

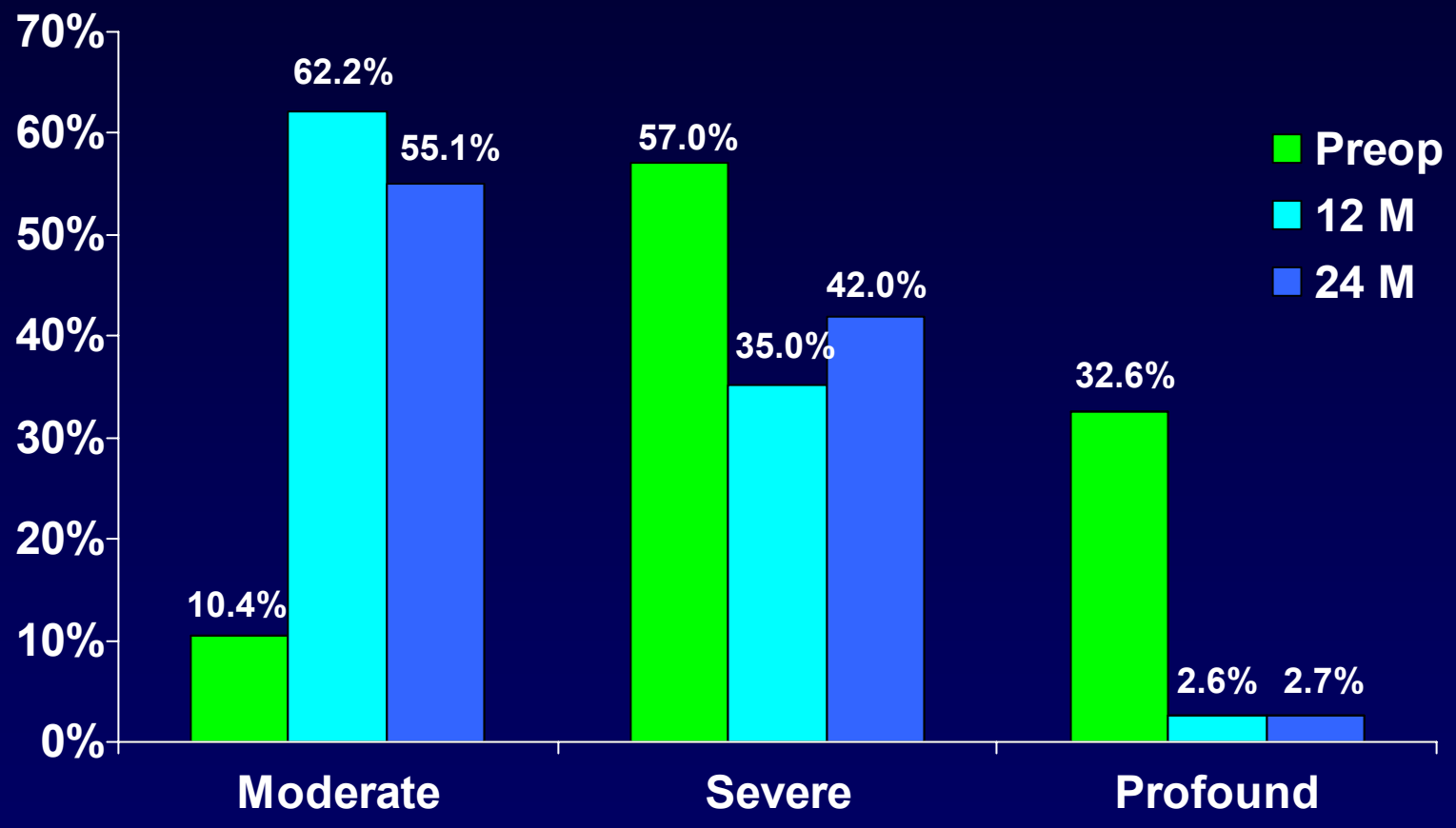
How can the loss in ECD be balanced against the significant improvement in vision and quality of life?

Change in ICD-9-CM Categories for Visual Impairment in IMT-Implanted Eyes



Source: not in PMA

Change in ICD-9-CM Categories for Visual Impairment in IMT-Implanted Eyes



Source: not in PMA

Risk vs Benefit Considerations

- Patient benefit: Improvement in vision, VFQ-25
- Patients with AMD place high value on vision
  - Brown et al[1] identified utility value of approximately 0.5 for severe macular degeneration, i.e., patients would give up half of remaining years of life for normal vision
- Endothelial cell loss
  - Acute
  - Not substantially different from that seen after traditional cataract extraction with IOL implantation
  - Can be reduced by training

[1]Brown et al. Utility values associated with age-related macular degeneration. Arch Ophthalmol 2000;118:47-51

Implantable Miniature Telescope

- Defined risk, not substantially different from that of routine, modern, cataract surgery
- Risk is manageable by
  - Training
  - Appropriate selection of subjects
  - Informed consent
  - Multidisciplinary approach, including postoperative visual rehabilitation
- Substantial improvement in functional vision for an under-served population with limited treatment options