Trulign™ Toric Accommodating Intraocular Lens

United States Food and Drug Administration
Ophthalmic Devices Advisory Committee

April 8, 2013

BAUSCH + LOMB

Introduction

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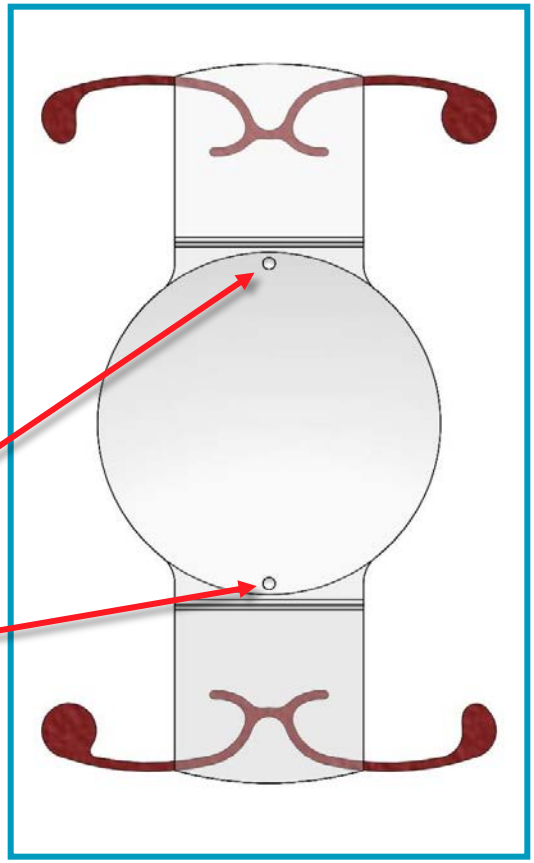
Trulign™ Toric Accommodating IOL

- >3 million US cataract surgeries annually
  - ~25% have ≥1.25 D of corneal astigmatism
- Current goal in refractive cataract surgery: residual astigmatism of ≤0.50 D
- Current Crystalens® models do not correct astigmatism
- Trulign Toric IOL
  - Safe and effective option for correction of aphakia and postoperative refractive astigmatism
  - Biconvex silicone IOL
    - Axis marks on anterior surface
    - Toric correction on posterior surface
    - No material or dimensional differences



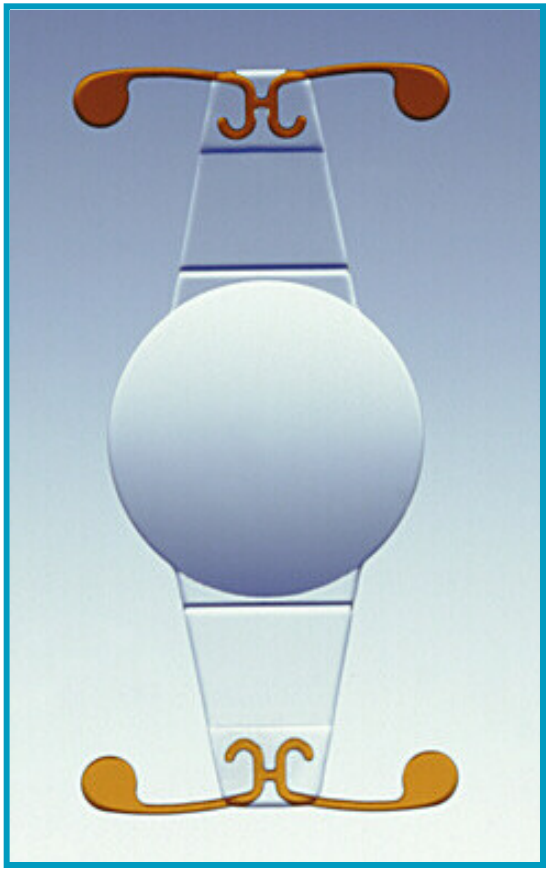
Models AT50T / AT52T

What You Will Hear Today

- Established profile of Parent IOL (Crystalens®)
- Need for safe and effective option for Crystalens patients with significant corneal astigmatism
- Pivotal Study 650: safety and effectiveness
  - Study design: US and international standards for toric IOLs
- Results: Trulign™ Toric IOL
  - Provides correction of refractive astigmatism
  - Provides improved uncorrected distance vision
  - Did not compromise intermediate and near vision
  - Did not introduce new safety or effectiveness concerns compared with Parent IOL

Crystalens® Accommodating IOL—Parent Lens

- 2000: First US eye implanted
- May 2003: Ophthalmic Devices Advisory Panel recommended approval of PMA P030002
- November 2003: FDA approval of PMA P030002
  - Model AT45



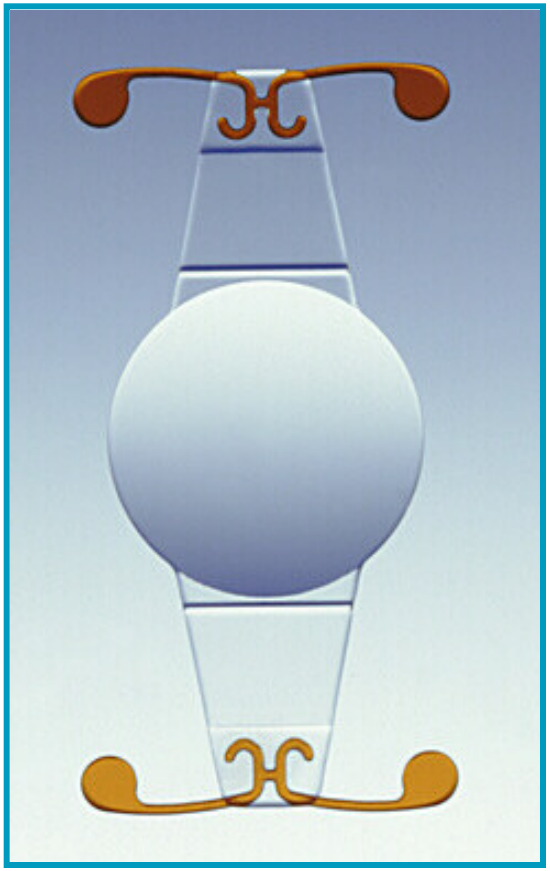
Model AT45

Subsequent FDA Approved Models of Crystalens® Accommodating IOLs

- **Level A**
  - **S04: Approved September 2005 — AT45SE**
  - **S10: Approved July 2007 — AT50SE; AT52SE**
  - **S21: Approved October 2009 — AT50 AO; AT52 AO**
  - **S20: Approved August 2011 — AT1UV/AT2UV; HD1UV/HD2UV; AO1UV/AO2UV**
- **Level B**
  - **S14: Approved June 2008 — AT45-HD 100; HD 500; HD 520**
    - **Clinical study confirming effectiveness of modification**
    - **Preserved established safety and performance of Parent IOL**

Crystalens® IOL—Parent Lens

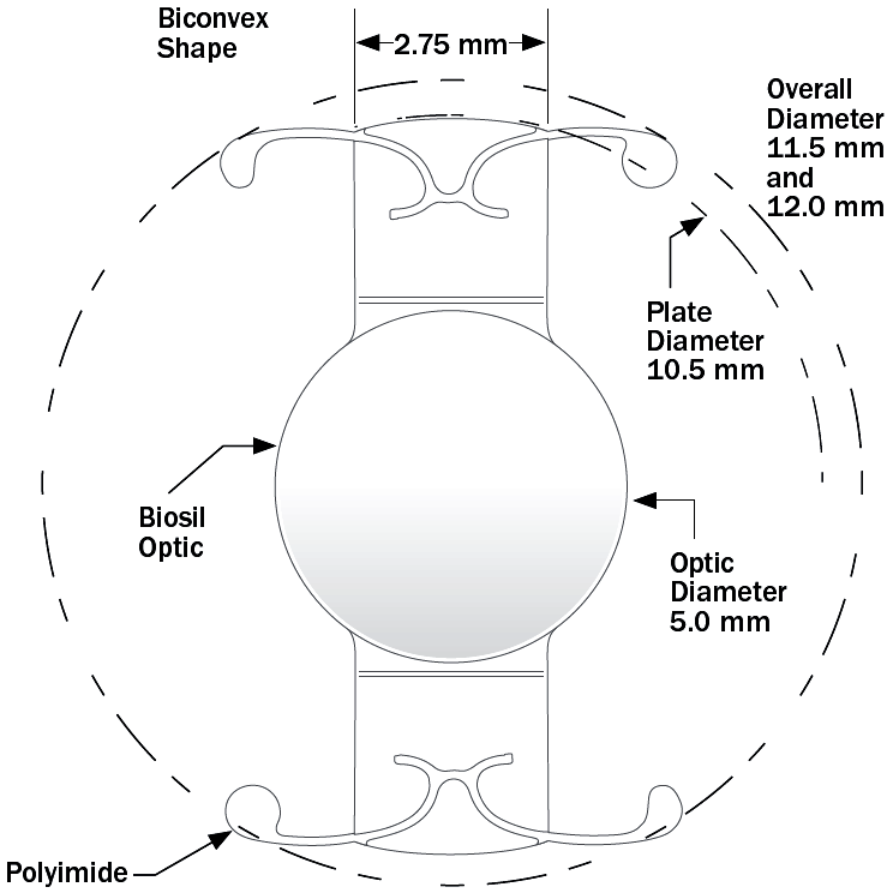
- PMA P030002
  - 6 models to date
- Approved in 69 countries
- 10+ years clinical experience
- > 315,000 lenses implanted
- Risk / benefit profile well established and understood



Model AT45

Crystalens® IOL—Key Design Features

- 5.0 mm optic body
- Biconvex shape
- Rectangular hinged haptics
- Round-to-the-right asymmetric polyimide loops
- 360° continuous posterior square edge
- Dioptric power +4.00 to +33.00 D



Models AT50SE / AT52SE

Crystalens® IOL—Indication

- **Intended for primary implantation in the capsular bag of the eye for visual correction of aphakia secondary to removal of a cataractous lens in adult patients with or without presbyopia. Provides approximately one diopter of monocular accommodation, which allows for near, intermediate, and distance vision without spectacles.**

Models AT50SE / AT52SE

Trulign™ Toric IOL—Indication

- Intended for primary implantation in the capsular bag of the eye for visual correction of aphakia and postoperative refractive astigmatism secondary to removal of a cataractous lens in adult patients with or without presbyopia who desire improved uncorrected distance vision and reduction of residual refractive cylinder. Provides approximately one diopter of monocular accommodation, which allows for near, intermediate, and distance vision without spectacles.

Models AT50T / AT52T

Trulign™ Toric IOL—
Study 650 Pivotal Clinical Trial

- Only changes to Parent IOL
  - Axis marks on anterior surface
  - Toric optic on posterior surface
- "Level B" like change to existing IOL
  - Safety and effectiveness established for Parent IOL
  - Study 650 designed to assess toric optic
    - Ability to correct astigmatism
    - No adverse impact on established Crystalens® IOL safety or effectiveness

Presentation Agenda

Clinical Landscape Design and Conduct— Study 650	Jay Pepose, MD, PhD Pepose Vision Institute Washington University
Safety—Study 650	Richard Hope, MD Medical Director, Clinical & Medical Affairs Bausch + Lomb Surgical
Effectiveness—Study 650	Jon K Hayashida, OD, FAAO Vice President, Clinical & Medical Affairs Bausch + Lomb Surgical
Evidence for Accommodation	Adrian Glasser, PhD College of Optometry, University of Houston
Clinical Perspectives	Mark Packer, MD, FACS, CPI Oregon Health & Science University

Clinical Landscape

Jay S. Pepose, MD, PhD

Founder and Medical Director
Pepose Vision Institute
Professor of Clinical Ophthalmology
Washington University School of Medicine

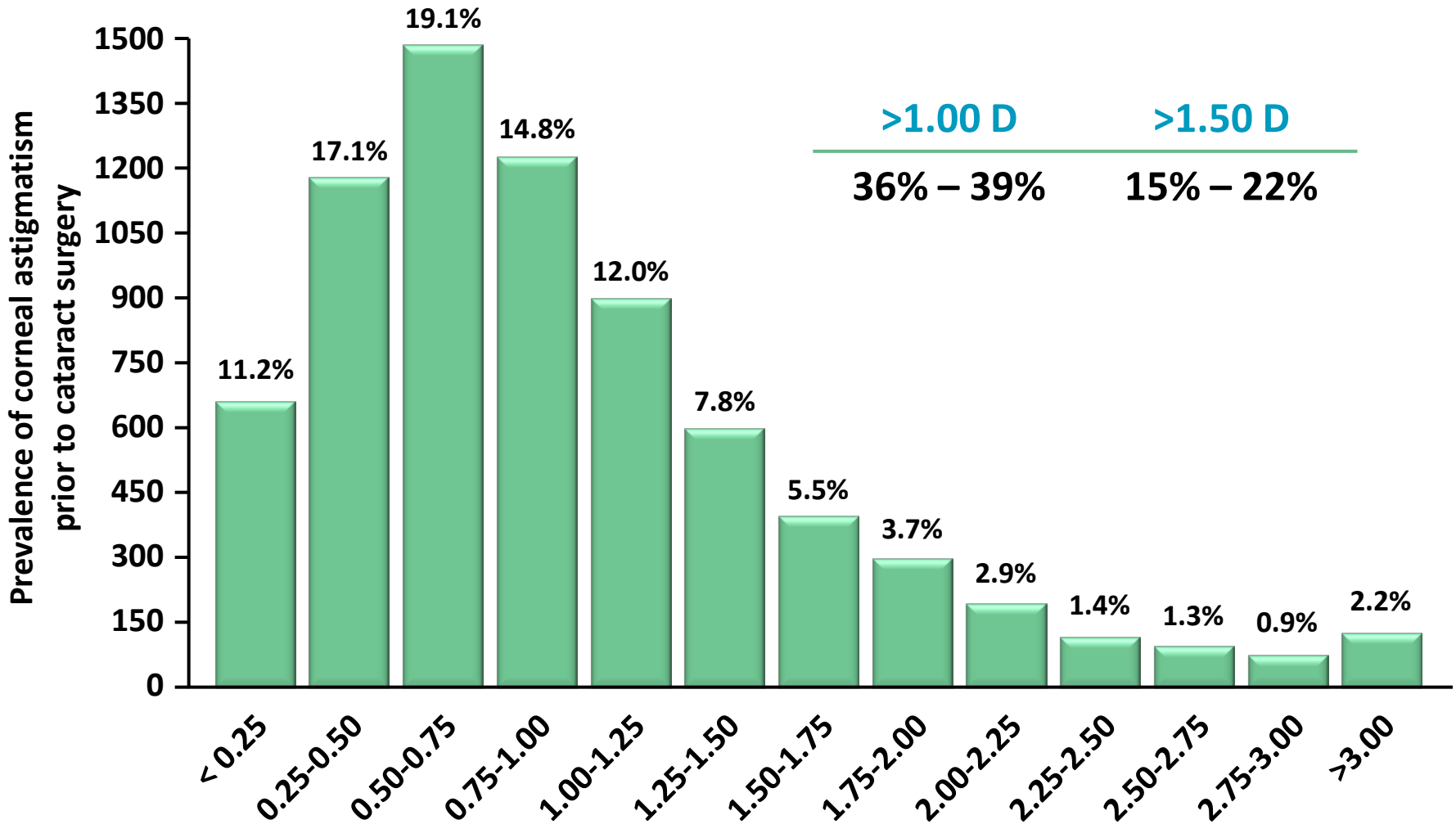
Important Unmet Clinical Needs

Visual impact of residual uncorrected astigmatism

Desire for excellent intermediate and functional near vision

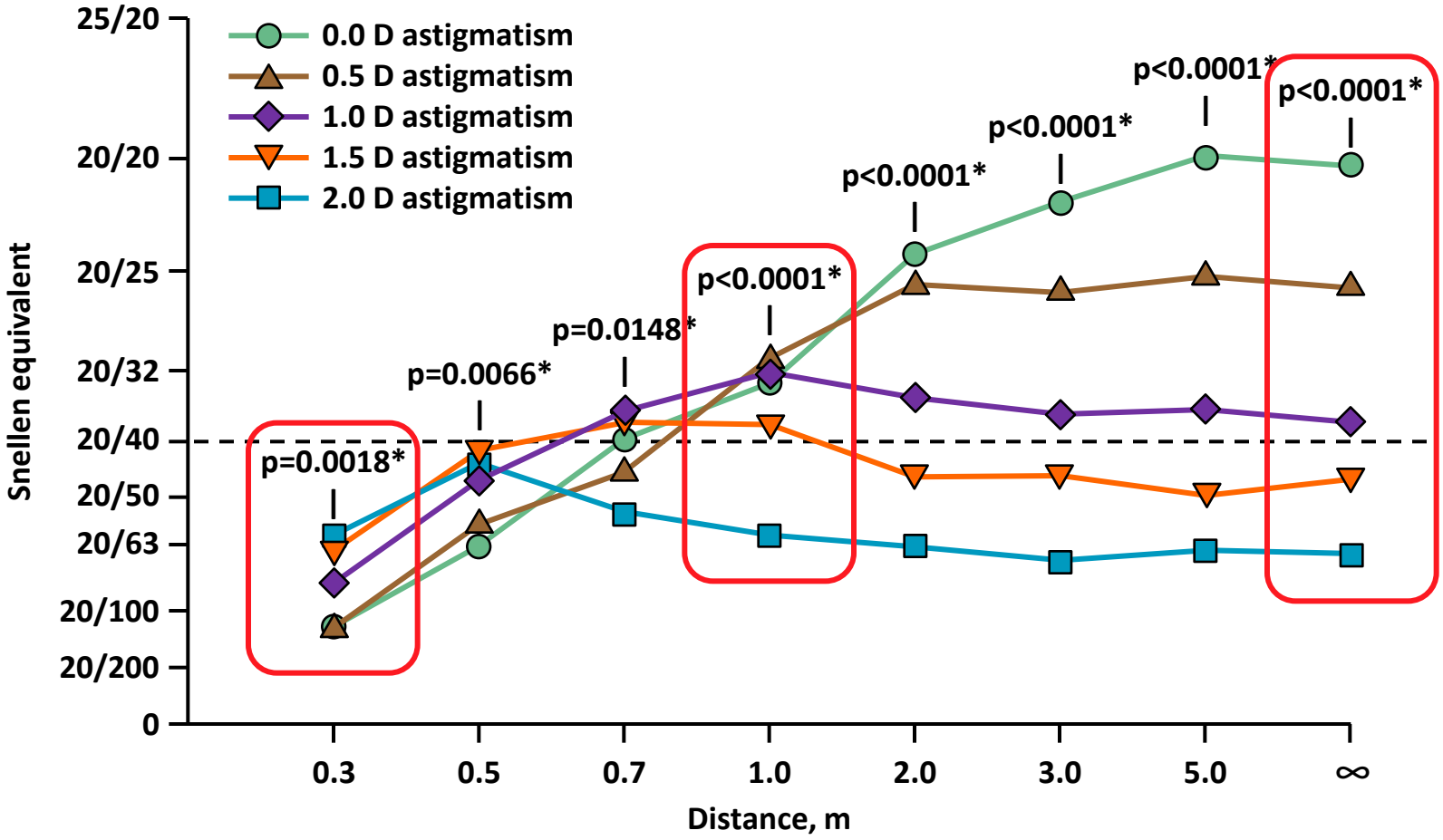
Single procedure

Cataract Patients With Corneal Astigmatism



N=6,000. Copyright 2013, Warren E. Hill, MD; keratometry database; adapted with permission.

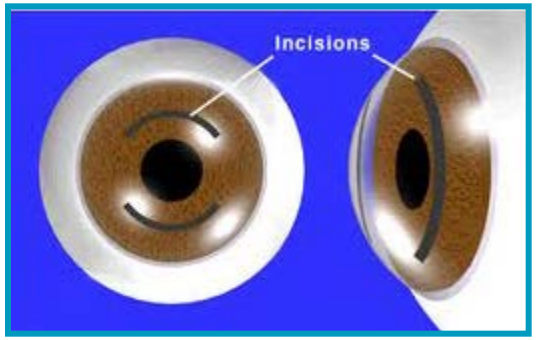
Impact of Residual Postoperative Refractive Astigmatism on Vision at Varying Vergence



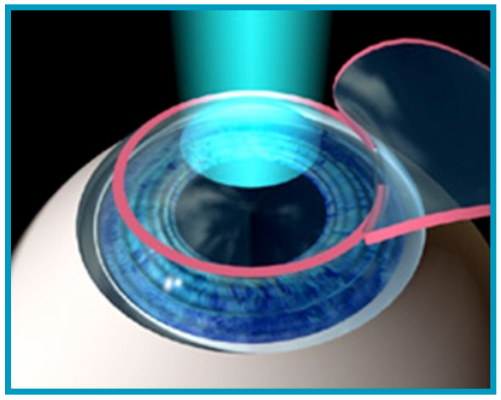
*Statistically significant difference.

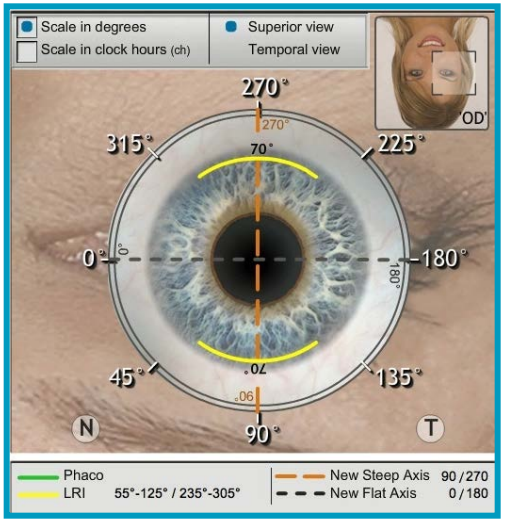
Surgical Treatment Options for Correction of Astigmatism

Astigmatic keratotomy



Excimer laser vision correction





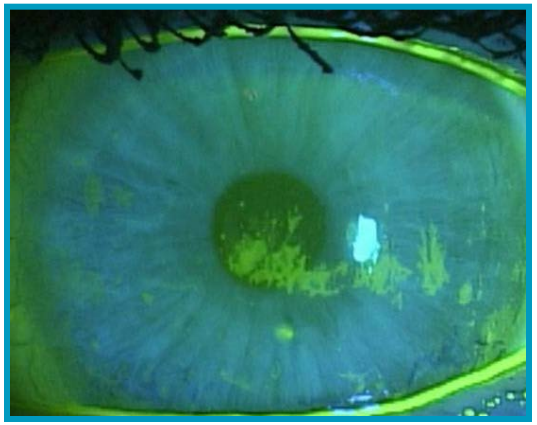
Limbal relaxing incision (LRI)

Toric IOLs

Top left image courtesy of www.lasersite.com. Top right image courtesy of Abbott Laboratories, LRI calculator; copyright 2013; all rights reserved. Lower left image courtesy of Abbott Laboratories; copyright 2013; all rights reserved. Lower right image courtesy of alconsurgical.com, all rights reserved.

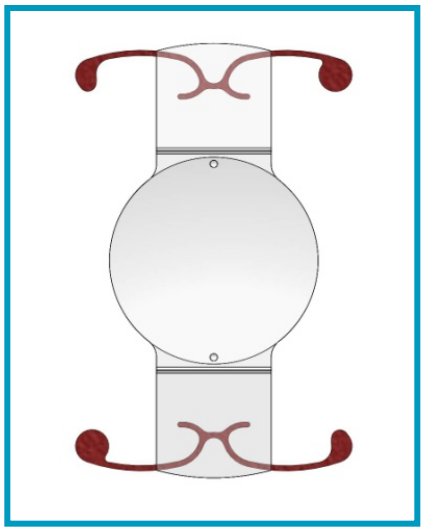
Toric IOLs

- Addresses aphakia and astigmatism in a single procedure
- Mitigates some disadvantages and potential side effects of incisional astigmatic correction
  - Variable wound healing and biomechanics
  - Corneal denervation exacerbating dry eye
  - Corneal perforation
  - Infection
  - Wound gape
  - Decreased best spectacle corrected vision due to irregular astigmatism



Key to Performance of Toric IOLs is Rotational Stability

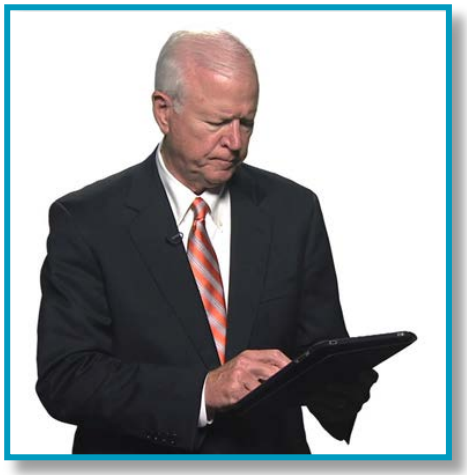
- Every 1° of misalignment of a toric IOL results in 3.3% reduction in offset of astigmatism
- A 10° misalignment means that the toric effect is reduced by a third

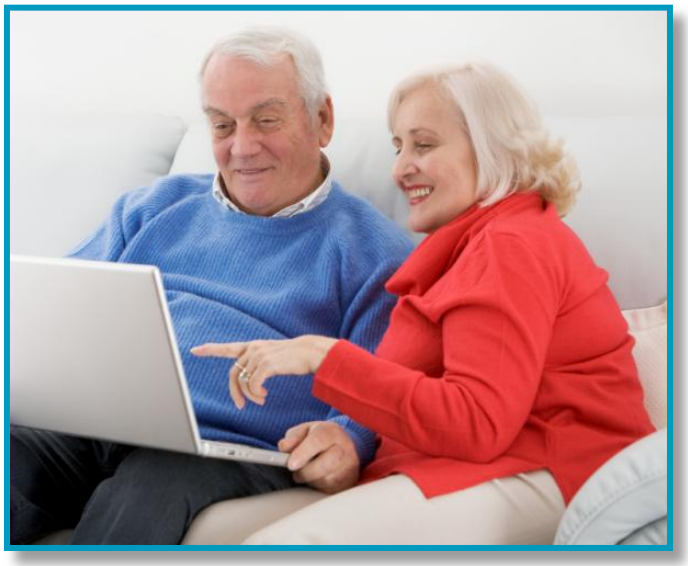


Trulign Toric Accommodating IOL

- 96.9% had ≤5.0° rotation between day of surgery and 4 – 6 months postop
- No eye had ≥10.0° of rotation
- Mean rotation between 1.35° and 1.78° for the 3 toric powers

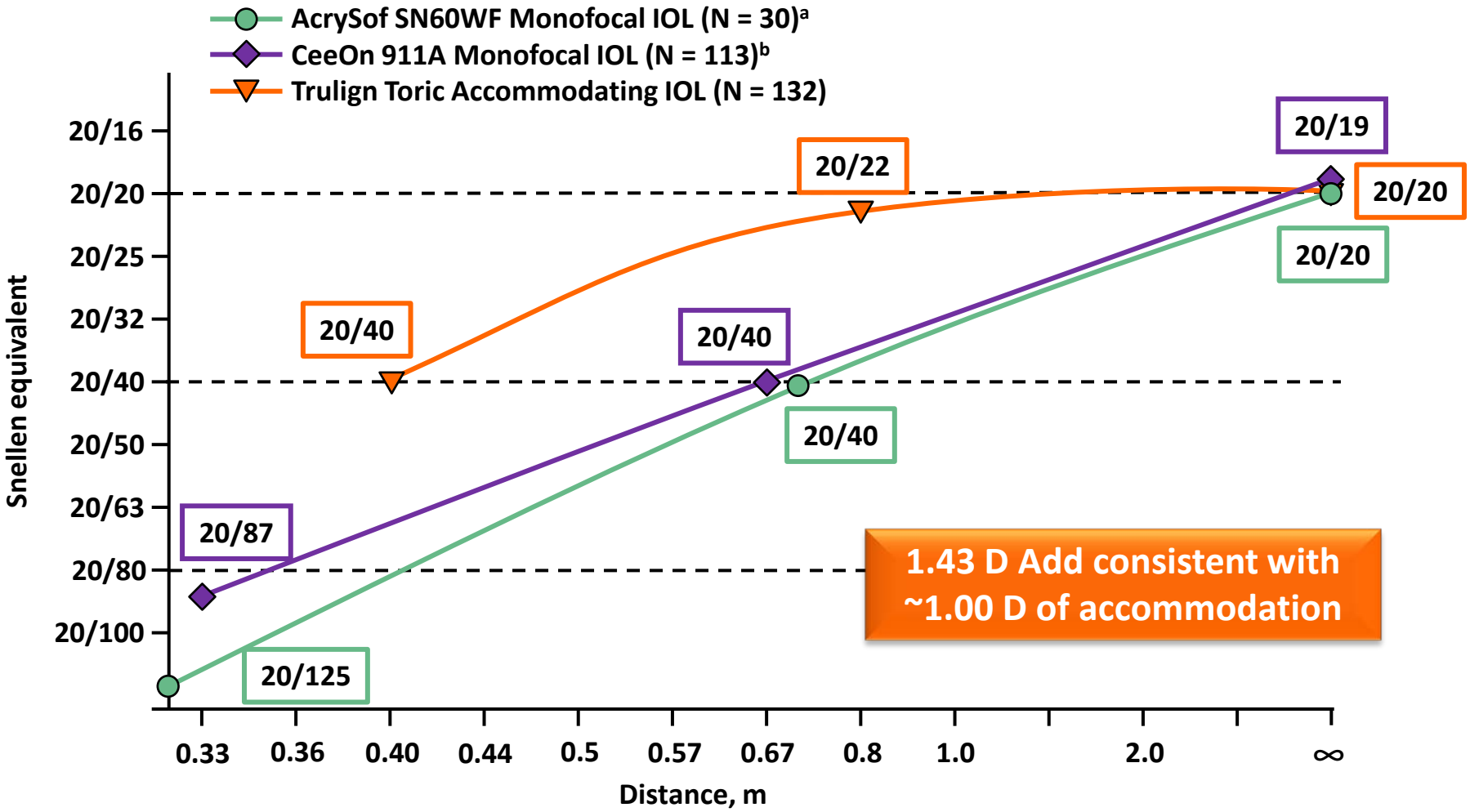
Need for Lenses That Can Address Cataract, Corneal Astigmatism, and Presbyopia





Distance Corrected Visual Acuity Accommodating vs Monofocal IOLs

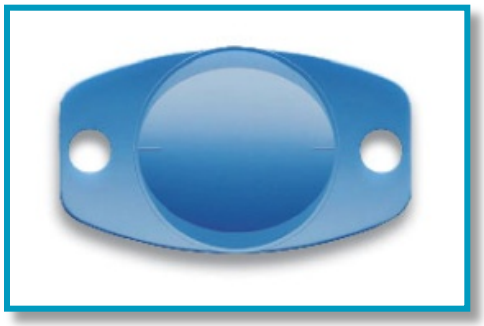
2010



[a] Hayashi K, et al. *J Cataract Refract Surg*. 2010;36:1323-1329.
[b] Packer M, et al. *Am J Ophthalmol*. 2010;149(4):577-584.

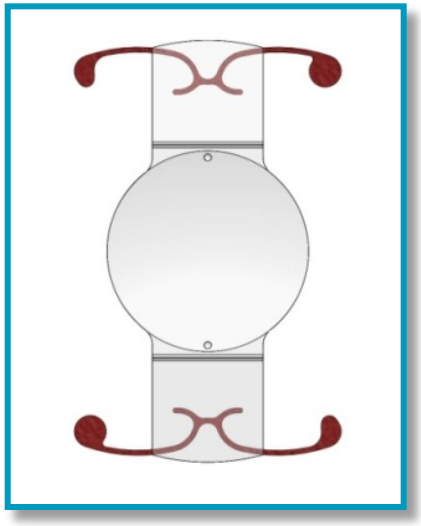
Need for Lenses That Can Address Corneal Astigmatism as Well as Pseudophakic Presbyopia

- **STAAR Elastic Toric**



- **Alcon AcrySof® Toric**

- **One way to address these needs for excellent intermediate and functional near vision is a toric accommodating IOL**



Design and Conduct—Study 650

Study Population

- Key inclusion criteria
  - Predicted postop corneal astigmatism between 0.83 and 2.50 D as determined by Toric Calculator
  - BCVA equal to or worse than 20/40 with or without glare
  - Potential for BCVA of 20/32 or better
- Key exclusion criteria
  - Conditions associated with increased risk of zonular ruptures
  - Irregular corneal astigmatism
  - Difference in corneal astigmatism between IOL master and topographer >0.50 D by vector analysis

IOL Cylinder Power and Enrollment

IOL cylinder power (D)			Enrollment	
At IOL plane	At corneal plane	Predicted postop range		
1.25	0.83	0.83 - 1.32 (Randomized 1:1)	Control (min N=72)	Toric 1.25 D (min N=72)
2.00	1.33	1.33 - 1.82	Total combined N=56	(min N=10)
2.75	1.83	1.83 - 2.50		

Examination Schedule

Form	Postop interval	
Form 0	Day 0 (surgery)	Eligibility Randomization
Form 1	Days 1 - 2	
Form 2	Days 7 - 14	
Form 3	Days 30 - 60	
Form 4	Days 120 - 180	Rotational stability Safety and effectiveness

Study Methods

- Preoperative visit
  - Vector analysis
  - Toric calculator (fixed SIA 0.50 D)
- Operative visit
  - Unilateral implantation (no binocular acuity assessments performed)
  - Incision on the steep axis
    - Preferred practice pattern
    - Minimize study variability

Study Methods

- Operative and postoperative visits
  - Lens axis misalignment and rotational stability
    - Digital slit lamp photography referencing iris and conjunctival landmarks
    - Independent reading center
      - Validated technique with repeatability of ±0.79°
  - Subjective questionnaire
    - Visual disturbances

SAP and Interim Analyses

- SAP initially provided to and approved by FDA in original study protocol
- 2 interim analyses performed using unaudited data
  - First interim analysis performed with 35 of 229 subjects available for analysis at Form 4 for planning purposes for other potential toric clinical trials
  - Second interim analysis used Form 3 (not Form 4) data to simulate format and presentation of clinical data

SAP and Interim Analyses

- Although interim analyses were conducted prior to finalization of the SAP, safety and effectiveness endpoints, and methods of analysis were unchanged
- Study sufficiently powered in that making an alpha adjustment would not impact study conclusions or overall statistical significance

Amended SAP

- SAP amended to
  - Provide further clarification of the analysis
  - Ensure alignment with required standards for toric IOLs
- SAP amended prior to primary analysis for PMA submission

SAP and Interim Analyses

- Interim analyses did not affect original planned study analyses
- Neither study conduct nor SAP revised in response to either of these interim analyses
- Study sufficiently powered so that conclusions and overall significance would not be altered by making an alpha adjustment for these 2 “looks” at the partial interim data
  - Bonferroni adjustment for interim analyses would still result in $p<0.001$

Protocol Deviations—Overview

- Bausch + Lomb reported 391 deviations
  - 14 major in 12 eyes
  - 377 minor[a]
- FDA considered implantation of 10 AT52 lenses as major deviations
- 60% of deviations occurred preoperatively

	N at Form 4	
Type of deviation	Excluding AT52 lenses	Including AT52 lenses
Major	0	10
Minor	29	29

[a] Four minor protocol deviations were reclassified to major protocol deviations during review of the submission (through amendment 4), but were not included in the information presented in the executive summary.

Effectiveness Outcomes With or Without AT52 Implanted Lenses

	With AT52			Without AT52		
Endpoint	Control	Toric 1.25 D	p-value	Control	Toric 1.25 D	p-value
Mean % cylinder reduction (SD)	46.3 (44.16)	81.1 (31.77)	<0.001[a]	45.2 (44.58)	82.3 (32.02)	<0.001[a]
MRSE within 0.5 D, %	63.6	70.4	0.468[b]	62.9	68.7	0.578[b]
Mean logMAR UCNVA (SD)	0.29 (0.14)	0.29 (0.15)	0.947[c]	0.29 (0.14)	0.29 (0.15)	0.845[c]
Mean logMAR UCIVA (SD)	0.07 (0.16)	0.04 (0.12)	0.465[c]	0.08 (0.16)	0.04 (0.12)	0.332[c]
Mean logMAR UCDVA (SD)	0.19 (0.18)	0.10 (0.13)	0.001[c]	0.19 (0.18)	0.09 (0.13)	0.006[c]

[a] T-test. [b] Fisher's exact test. [c] Wilcoxon rank-sum test.

Protocol Deviations—Statistical Impact and Conservative Imputation on Effectiveness

Analyses	Control IOL	Toric 1.25 D IOL	p-value
Current effectiveness analyses			
n	66	71	
Mean % reduction in cylinder	46.3	81.1	<0.001
Inclusive of all measured Form 4 data (including out-of-window data), regardless of the presence of protocol deviations			
n	71	75	
Mean % reduction in cylinder	46.0	80.8	<0.001
ITT analysis with conservative imputation (83% for Control and 17% for Toric) for missing data or major/minor protocol deviations[a]			
n	76	82	
Mean % reduction in cylinder	56.2	69.2	0.044
ITT analysis with conservative imputation (76% for Control and 24% for Toric) for missing data, major/minor protocol deviations, or implantation of AT52 lenses[a]			
n	76	82	
Mean % reduction in cylinder	55.9	68.8	0.042

[a] These imputation values were selected as they represent the "tipping point" for the final analyses (ie, percent reduction beyond which the p-value would have "tipped" to >0.05.

Protocol Deviations—Summary

- Included all deviations in safety cohort
  - Ensuring all safety events assessed
- Included 10 AT52 implanted lenses in effectiveness cohort
  - Exclusion or inclusion does not impact conclusions
- Excluded 14 major deviations from effectiveness cohort
  - Exclusion or inclusion with conservative imputation does not impact conclusions
- Majority occurred preoperatively, therefore, no possible effect on conclusions
- Detailed and thorough review and analysis of all deviations demonstrates integrity of data and validity of conclusions

Conclusions—Study 650

Clinical Effectiveness of a Toric IOL

- Corrects refractive astigmatism
  - Minimal residual refractive cylinder
- Demonstrates rotational stability
- Provides refractive predictability
  - Accuracy to target for MRSE

- Achievement of above criteria should yield good uncorrected distance visual acuity

Trulign Toric Accommodating IOL

- Corrects refractive astigmatism
  - 85.8% reduction of cylinder (all Toric cohort)
    - p<0.001 between 1.25 D Toric and spherical control
  - 79.7% within 0.50 D of intended (all Toric cohort)
- Demonstrates rotational stability
  - Mean <2° of IOL rotation between day of surgery and 4 – 6 mo postop
  - 96.9% of eyes ≤5° of IOL rotation
- Statistically significant improvement in uncorrected distance visual acuity vs spherical control (p=0.001)

	UCDVA	UCIVA	UCNVA
Mean visual acuity	0.10 (20/25)	0.04 (20/20)	0.29 (20/40)

Safety—Study 650

Richard Hope, MD

Medical Director, Clinical & Medical Affairs
Bausch + Lomb Surgical

Global Safety Experience—Crystalens® Accommodating IOL

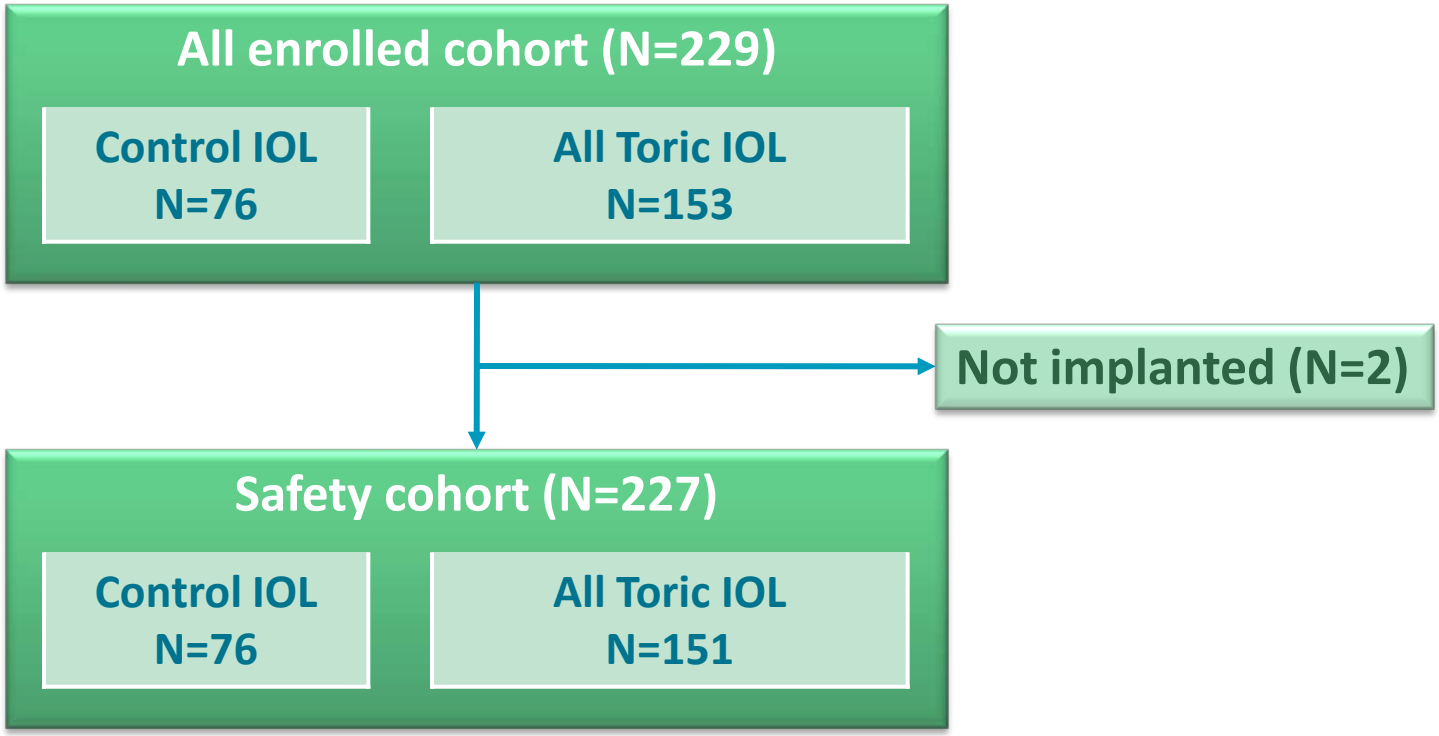
- Safety of parent Crystalens well established
  - Nearly 10 years of post-market surveillance
  - Approved in 69 countries
  - >315,000 eyes implanted
- Global adverse events rate: 1.01%

Safety Endpoints
Study 650

- **Preservation of BCDVA compared with ISO Grid**
- **Preservation of BCNVA**
- **Incidence of adverse events compared to ISO Grid**

Trulign™ Toric IOL met all safety requirements per ISO Grid of Safety and Performance Endpoints (SPE)

Safety Cohort
Study 650



Data as of January 25, 2012 database lock.

Preservation of BCDVA—Form 4 (120 - 180 Days)
Safety Cohort

	Subjects, %		
	Control IOL N=76	All Toric IOL N=151	ISO grid[a]
n	69	142	—
20/40 or better	100	97.9	92.5
Worse than 20/40	0	2.1	—

[a] ISO standard 11979-7:2006(E), Table B.3.

Preservation of BCNVA—Form 4 (120 - 180 Days)
Safety Cohort

	Subjects, %		
	Control IOL N=76	All Toric IOL N=151	ISO grid[a]
n	69	142	—
20/40 or better	100	100	92.5
Worse than 20/40	0	0	—

[a] ISO standard 11979-7:2006(E), Table B.3.

Ocular Adverse Events at Operative Visit
Safety Cohort

	Subjects, n (%)	
	Control IOL N=76	All Toric IOL N=151
Corneal abrasion from marker	1 (1.3)	0
Foreign body sensation	0	1 (0.7)
Hordeolum	0	1 (0.7)
Iris damage during surgery	0	1 (0.7)
Anterior capsule tear	2 (2.6)	0
Incorrect incision axis	0	1 (0.7)
Posterior capsule rupture	0	1 (0.7)

Ocular Adverse Events at Postoperative Visit—Cumulative Through Form 4 (120 - 180 Days)

Safety Cohort

	Subjects, n (%)	
	Control IOL N=76	All Toric IOL N=151
Allergic reaction to ocular medication	0	3 (2.0)
Anterior chamber cell	1 (1.3)	2 (1.3)
Blepharitis	2 (2.6)	5 (3.3)
Conjunctivitis	3 (3.9)	0
Corneal abrasion	1 (1.3)	2 (1.3)
Corneal edema	2 (2.6)	7 (4.6)
Dry eye/Keratoconjunctivitis sicca	9 (11.8)	14 (9.3)
Foreign body sensation in eyes	1 (1.3)	2 (1.3)
Intraocular pressure increased	2 (2.6)	1 (0.7)
Iritis	1 (1.3)	3 (2.0)
Irritation from suture	1 (1.3)	0
Nodule	1 (1.3)	0
Pinguecula	0	3 (2.0)
Punctate keratitis	2 (2.6)	5 (3.3)
Vitreous detachment	2 (2.6)	5 (3.3)
Vitreous floaters	2 (2.6)	2 (1.3)

FDA Grid Adverse Events—Cumulative Through Form 4 (120 - 180 Days)

Safety Cohort

	Subjects, % (n)		
	All Toric IOL (N=151)		
Cumulative AEs	Cumulative	SPE rate[a]	Threshold rate[a,b]
Endophthalmitis	0	0.1	3.0
Hypopyon	0	0.3	3.0
Lens dislocated	0	0.1	3.0
Macular edema	0.7 (1)	3.0	8.9
Pupillary block	0	0.1	3.0
Retinal detachment	0	0.3	3.0
Secondary surgical intervention	0.7 (1)	0.8	4.2

[a] ISO standard 11979-7:2006(E), Table B.2.

[b] Minimum rate detectable as statistically significantly different from SPE rate, based on N=100.

Ocular SAEs—Cumulative Through Form 4 (120 - 180 Days)

Study Eye (#230154-004 – Control Group)

Study arm	Control
Event	IOL malposition: inferior haptic placed in sulcus
Timing	Postop Day 1
Visual acuity	UCDVA 20/100
Treatment	Haptic repositioned in bag
Outcome	Resolved UCDVA 20/50 (at Form 4) BCDVA 20/32 (at Form 4)
Comments	Surgical complication common to all IOLs DFU specifies rotation of Crystalens® after insertion to ensure that both haptics are in the capsular bag

Ocular SAEs—Cumulative Through Form 4 (120 - 180 Days)

Study Eye (#330127-010 – Toric 2.00 D)

Study arm	Toric 2.00 D
Event	Anterior vault
Timing	Postop Day 124 (at Form 4)
Visual acuity	UCDVA 20/63 (MRSE −2.25 D, MR Cylinder +0.50 D) BCDVA 20/32 (Grade 2 PCO) 1.28 degrees IOL rotation
Factors	Subject noncompliance with postoperative anti-inflammatory medications
Treatment	IOL repositioning; no attempt to realign IOL to correct axis due to regional fibrosis and surgeon medical judgment
Outcome	Resolved with sequela (residual refractive cylinder) UCDVA 20/80 (MRSE −0.50, MR Cylinder +2.00 D) BCDVA 20/32 (Grade 2 PCO)
Comments	Surgeon did not perform preemptive YAG at first sign of capsule striae Fellow eye implanted with Crystalens® AO also exhibited early capsule striae, which was treated with YAG at 2 months with no subsequent vault DFU recommends that patients should be kept on anti-inflammatory agents for a minimum of 4 weeks

Ocular SAEs—Cumulative Through Form 4 (120 - 180 Days)

Non-Study Fellow Eye

Fellow eye	Crystalens AO
Event	Anterior vault (asymmetric)
Timing	Postop Day 132 (at Form 4)
Visual acuity	UCDVA 20/80 (MRSE −2.87, MR Cylinder +4.25 D) BCDVA 20/40 (Grade 2 PCO, mild dry AMD)
Treatment	Exchanged for another Crystalens® AO Second Crystalens vaulted intraoperatively Exchanged for monofocal IOL with haptics placed in sulcus
Factors	Cortical remnants, zonular dehiscence, capsular contraction, and progressive PCO
Outcome	Resolved UCDVA 20/50 (MRSE +0.12 D, MR Cylinder +1.75 D) BCDVA 20/40 (corneal edema; 6 months post exchange) UCDVA and BCDVA 20/32 (cornea clear; 12 months post exchange)
Comments	DFU recommends meticulous cortical cleanup DFU warns against implantation in the presence of zonular rupture

Nd:YAG Capsulotomy
Safety Cohort

	Subjects, n (%)	
	Control IOL N=76	All Toric IOL N=151
Grade 3 or 4 PCO (at Form 3 or 4)	1 (1.4)	2 (1.4)
Nd:YAG Capsulotomy (cumulative)	14 (18.4)	10 (6.6)
Days postop		
0 to 29	0	1 (0.7)
30 to 119	2 (2.6)	1 (0.7)
120 to 329	12 (15.8)	8 (5.3)

Safety—Summary
Study 650

- All safety endpoints were met
  - Preservation of BCDVA
  - Preservation of BCNVA
  - Incidence of adverse events
- Subjects with ocular SAEs retained good BCVA
- No safety events related to addition of toric optic to approved Parent IOL
  - No secondary surgical interventions related to rotational stability

Trulign™ Toric Accommodating IOL is safe for intended use

Effectiveness—Study 650

Jon K Hayashida, OD, FAAO

Vice President, Clinical & Medical Affairs
Bausch + Lomb Surgical

Effectiveness Endpoints

Primary

- % reduction in absolute cylinder
- % of eyes with cylinder reduction within 0.50 and 1.00 D of intended
- Lens axis misalignment by photographic method

Secondary

- DCIVA at 80 cm
- DCNVA at 40 cm, with and without add
- BCDVA
- UCDVA, UCIVA, and UCNVA

Other

- Manifest refraction cylinder
- Rotational stability
- MRSE
- Lens centration and tilt
- Subjective visual disturbances

Trulign Toric Pivotal Study 650—Effectiveness Outcomes

Toric IOL

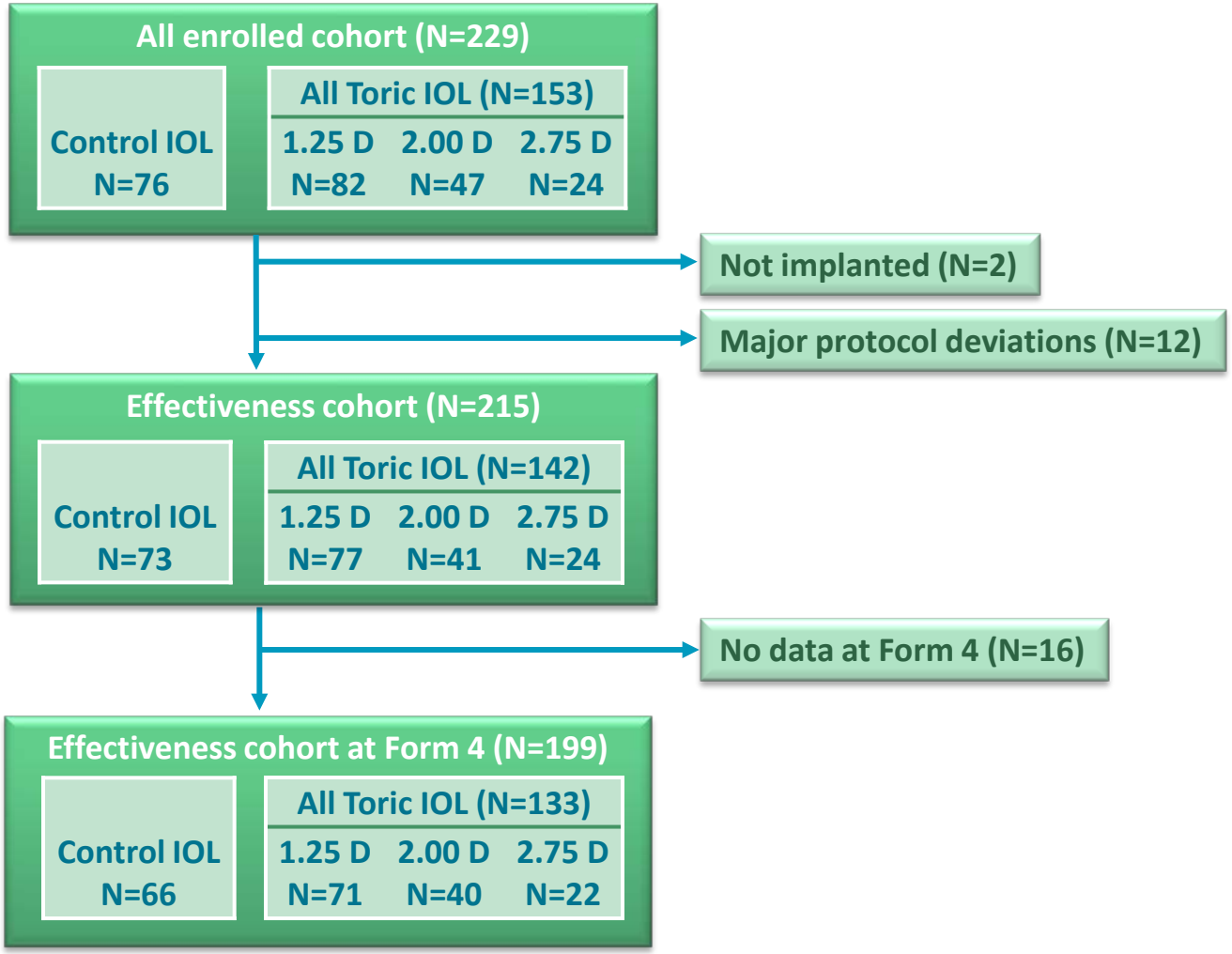
Effectiveness endpoint	Outcome
% reduction of cylinder	Toric 1.25 D superior to Control (p<0.001) All Toric: mean 85.8%
% within 0.50 & 1.00 D of intended	All Toric: 79.7% & 95.5%
Residual cylinder	Toric 1.25, 2.00, and 2.75 D: each reported mean < 0.50 D All Toric: mean 0.43 D
Lens axis misalignment	Mean < 5.0° from surgery to 4 – 6 months postop
Rotational stability	Mean < 2° from surgery to 4 – 6 months postop
Uncorrected distance visual acuity (UCDVA)	Mean 20/25 Toric 1.25 D superior to Control (p=0.004) All Toric superior to Control (p<0.001)
Visual disturbances	All Toric: 1/131 (0.8%) Resolved with Nd:YAG capsulotomy

Demographics
All Enrolled Cohort

		Toric IOL				p value	
	Control IOL N=76	1.25 D N=82	2.00 D N=47	2.75 D N=24	All Toric N=153	Control vs Toric 1.25 D	Control vs All Toric
Age, yr							
Mean (SD)	69.8 (9.2)	69.9 (8.8)	70.4 (8.4)	70.4 (10.8)	70.1 (9.0)	0.966[a]	0.817[a]
Age group, n (%)							
< 60	13 (17.1)	8 (9.8)	3 (6.4)	5 (20.8)	16 (10.5)		
60 to 69	20 (26.3)	32 (39.0)	20 (42.6)	5 (20.8)	57 (37.3)		
70 to 79	34 (44.7)	27 (32.9)	15 (31.9)	7 (29.2)	49 (32.0)		
≥ 80	9 (11.8)	15 (18.3)	9 (19.1)	7 (29.2)	31 (20.3)		
Gender, n (%)							
Male	34 (44.7)	35 (42.7)	27 (57.4)	10 (41.7)	72 (47.1)	0.873[b]	0.779[b]
Female	42 (55.3)	47 (57.3)	20 (42.6)	14 (58.3)	81 (52.9)		
Operative eye, n (%)							
OD	42 (55.3)	37 (45.1)	25 (53.2)	12 (50.0)	74 (48.4)	0.265[b]	0.331[b]
OS	34 (44.7)	45 (54.9)	22 (46.8)	12 (50.0)	79 (51.6)		

[a] T-test. [b] Fisher's exact test.

Effectiveness Cohorts

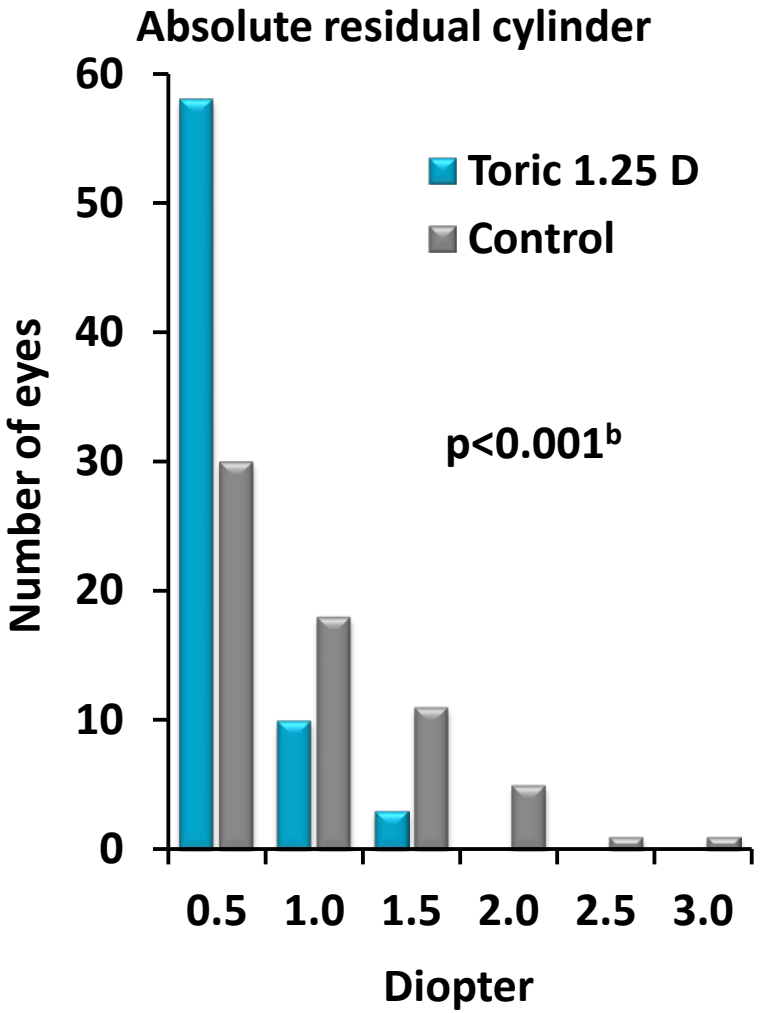


Data as of January 25, 2012 database lock.

Percent Reduction in Absolute Cylinder—Form 4 (120 - 180 Days)

Effectiveness Cohort

	Control IOL N=73	Toric IOL 1.25 D N=77	Toric IOL 2.00 D N=41	Toric IOL 2.75 D N=24	Toric IOL All Toric N=142
n	66	71	40	22	133
Mean % (SD)	46.3 (44.16)	81.1 (31.77)	87.9 (26.69)	97.2 (18.73)	85.8 (28.93)
95% CI	(35.46, 57.17)	(73.53, 88.57)	(79.35, 96.43)	(88.92, 105.53)	(80.82, 90.75)
p-value[a]		< 0.001			

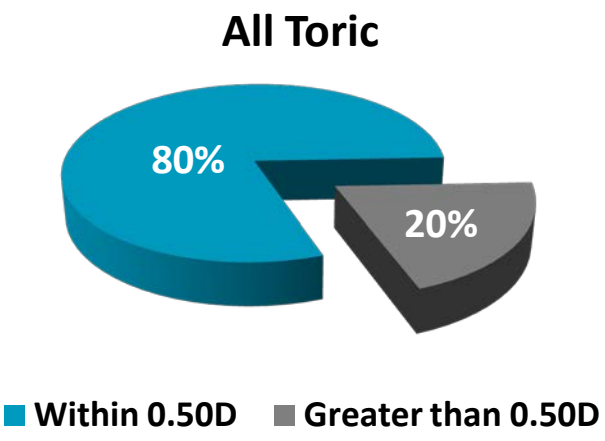


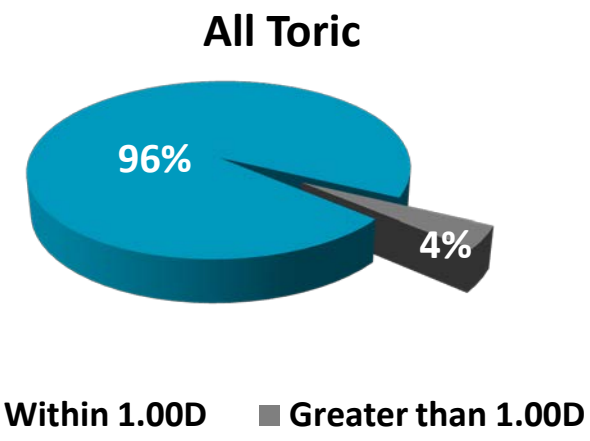
[a] 1-sided T-test. [b] T-test.

Percent of Eyes Within 0.50 and 1.00 D of Intended—Form 4 (120 - 180 Days)

Effectiveness Cohort

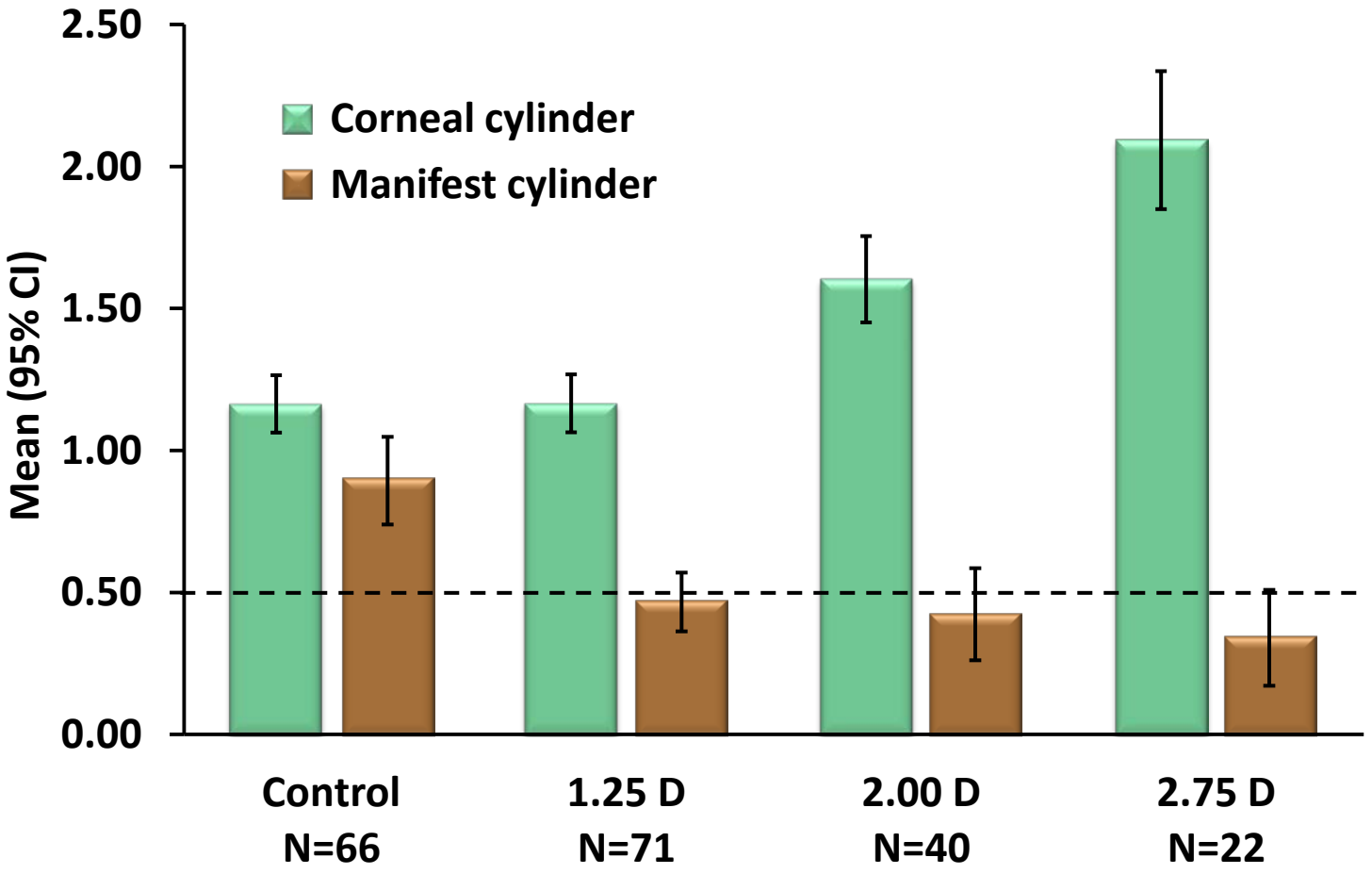
	Control IOL N=73	Toric IOL 1.25 D N=77	Toric IOL 2.00 D N=41	Toric IOL 2.75 D N=24	Toric IOL All Toric N=142
n	66	71	40	22	133
Within 0.50 D of intended, %	45.5	81.7	80.0	72.7	79.7
Within 1.00 D of intended, %	72.7	95.8	92.5	100	95.5



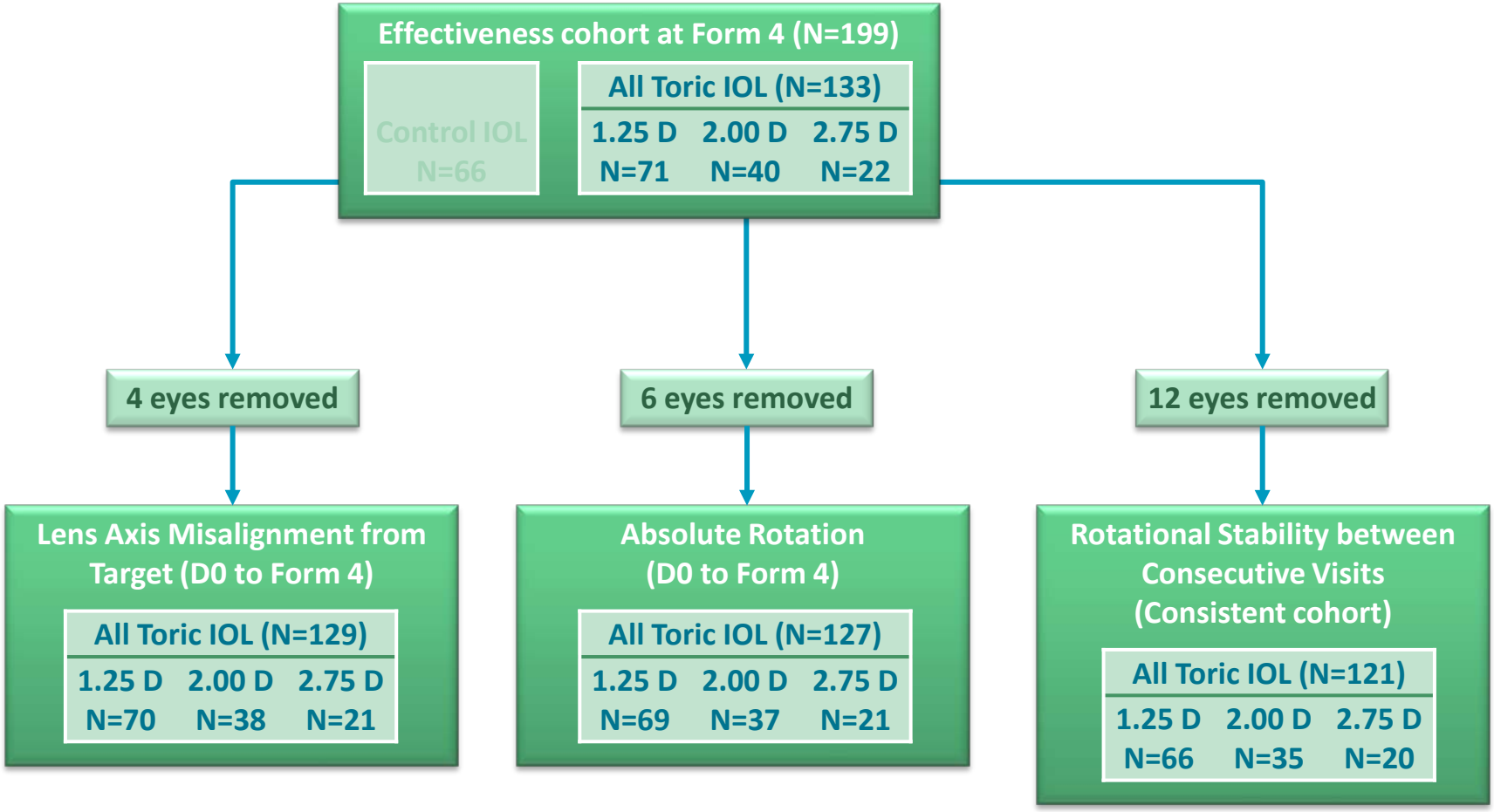


Magnitude of Corneal Cylinder vs Manifest Refractive Cylinder—Form 4 (120 - 180 Days)

Effectiveness Cohort



Effectiveness Cohorts For Rotational Stability



Lens Axis Misalignment From Target—Preop to Form 4 (120 - 180 Days)

Effectiveness Cohort

	Toric IOL			
	1.25 D N=77	2.00 D N=41	2.75 D N=24	All Toric N=142
n	70	38	21	129
Mean (SD), °	5.06 (3.862)	3.79 (2.362)	5.51 (4.650)	**4.76 (3.668)**

- **Target axis: as determined at pre-op by toric calculator**
- **Lens axis orientation at 4 - 6 mo post-op**
  - **Contributing factors include:**
    1. **Accuracy of marking the steep axis prior to surgery (surgeon)**
    2. **Accuracy of toric IOL orientation at the time of surgery (surgeon)**
    3. **Toric IOL rotational stability (IOL)**

Absolute Rotation—Implantation (Day 0) to Form 4 (120 - 180 Days)

Effectiveness Cohort

	Toric IOL			
	1.25 D N=77	2.00 D N=41	2.75 D N=24	All Toric N=142
n	69	37	21	127
Mean (SD), °	**1.78 (1.971)**	**1.35 (1.083)**	**1.68 (1.628)**	**1.64 (1.699)**
≤ 5.00°, %	**95.7**	**100**	**95.2**	**96.9**
≤ 10.00°, %	**100**	**100**	**100**	**100**

- **Mean IOL Rotation is <2°**
- **96.9% exhibited IOL rotational stability of ≤5°**

Rotational Stability Between Consecutive Visits—Form 3 (30 - 60 Days) to Form 4 (120 - 180 Days)

Consistent Cohort

	Toric IOL			
	1.25 D N=77	2.00 D N=41	2.75 D N=24	All Toric N=142
n	66	35	20	121
Mean (SD), °	**1.14 (1.081)**	**1.15 (0.941)**	**1.64 (1.316)**	**1.22 (1.086)**
≤ 5.00°, %	**98.5**	**100**	**100**	**99.2**
≤ 10.00°, %	**100**	**100**	**100**	**100**

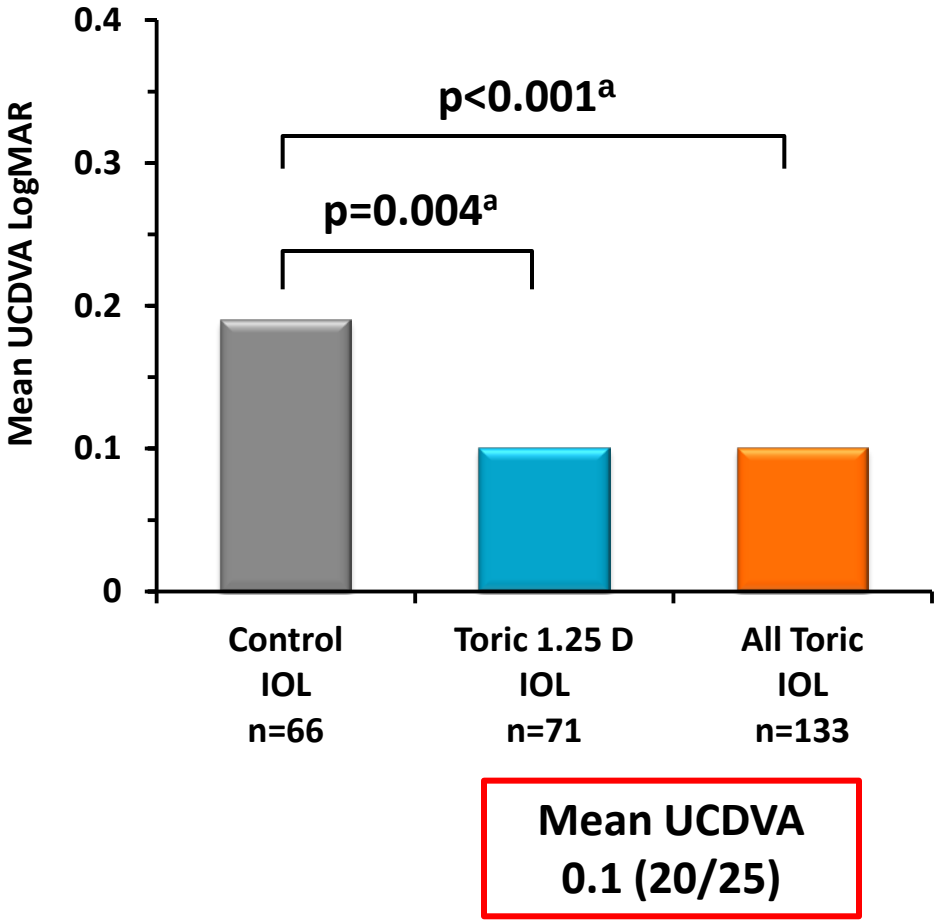
- **ANSI Guidance:**
  - **Toric IOL stability achieved when 90% of implanted lenses rotate ≤5° between 2 consecutive visits at least 3 months apart**

- **Mean IOL Rotation is <2°**
- **99.2% exhibited IOL rotational stability of ≤5°**

Refractive Predictability and Uncorrected Distance Visual Acuity (UCDVA)—Form 4 (120 - 180 Days)

Effectiveness Cohort

MRSE: accuracy to target	All Toric IOL N=142
	n=133
±0.50 D	73.7%
±1.00 D	93.2%



[a] Wilcoxon rank-sum test.

Distance Corrected Intermediate (DCIVA) and Near Visual Acuity (DCNVA)—Form 4 (120 - 180 Days)

Effectiveness Cohort

	Control IOL N=73	All Toric IOL N=142	p-value[a]
DCIVA			
Mean Snellen	20/23	20/23	
n	65	132	
Mean logMAR (SD)	0.07 (0.143)	0.06 (0.127)	0.760
DCNVA			
Mean Snellen	20/41	20/40	
n	65	132	
Mean logMAR (SD)	0.30 (0.138)	0.30 (0.144)	0.912
DCNVA with Add			
Mean Snellen	20/23	20/22	
n	66	133	
Mean (SD)	0.05 (0.073)	0.04 (0.071)	0.338
Mean Add (SD)	1.60 (0.580)	1.43 (0.505)	0.046

[a] Wilcoxon rank-sum test.

Uncorrected Distance (UCDVA), Intermediate (UCIVA), and Near (UCNVA) Visual Acuity—Form 4 (120 - 180 Days)

Effectiveness Cohort

	Control IOL N=73	Toric 1.25 D N=77	p-value	All Toric N=142	p-value[a]
UCDVA					
Mean Snellen	20/30	20/25		20/25	
n	66	71		133	
Mean (SD)	0.19 (0.181)	0.10 (0.128)	0.004	0.10 (0.130)	<0.001
UCIVA					
Mean Snellen	20/24	20/22		20/22	
n	66	71		133	
Mean (SD)	0.07 (0.155)	0.04 (0.117)	0.465	0.04 (0.129)	0.457
UCNVA					
Mean Snellen	20/40	20/40		20/40	
n	66	71		133	
Mean (SD)	0.28 (0.138)	0.29 (0.148)	0.947	0.29 (0.146)	0.725

[a] **Wilcoxon rank-sum test.**

UCDVA, UCIVA, and UCNVA *With Adjustment for MRSE*—Form 4 (120 - 180 Days)

Effectiveness Cohort

	Control IOL	Toric IOL 1.25 D	Difference	p-value[a]
logMAR UCDVA[b]				
Adjusted Mean (SE)	0.17 (0.018)	0.11 (0.017)	–0.07 (0.025)	0.007
95% CI	(0.139, 0.208)	(0.073, 0.140)	(–0.019, –0.116)	
logMAR UCIVA[c]				
Adjusted Mean (SE)	0.08 (0.015)	0.04 (0.015)	–0.04 (0.021)	0.062
95% CI	(0.047, 0.107)	(0.007, 0.066)	(–0.083, 0.002)	
logMAR UCNVA[d]				
Adjusted Mean (SE)	0.29 (0.016)	0.28 (0.016)	–0.01 (0.022)	0.579
95% CI	(0.261, 0.325)	(0.250, 0.311)	(–0.057, 0.032)	

[a] Analysis of variance.
[b] logMAR UCDVA = 0.1259 – 0.0674*Toric + 0.0122*MRSE + 0.1316*MRSE*MRSE.
[c] logMAR UCIVA = 0.0974 – 0.0405*Toric + 0.1509*MRSE + 0.0821*MRSE*MRSE.
[d] logMAR UCNVA = 0.3219 – 0.0125*Toric + 0.1546*MRSE + 0.0641*MRSE*MRSE.

Lens Decentration and Tilt—Form 4 (120 - 180 Days)

Effectiveness Cohort

		Toric IOL			
	Control IOL N=73	1.25 D N=77	2.00 D N=41	2.75 D N=24	All Toric N=142
n	65	71	40	22	133
Total decentration, mm					
Mean (SD)	0.002 (0.012)	0.014 (0.119)	0.000 (0.000)	0.000 (0.000)	0.008 (0.087)
Tilt (˚)					
Mean (SD)	0.37 (1.040)	0.44 (1.405)	0.16 (0.54)	0.09 (0.414)	0.29 (1.089)

Subjective Visual Disturbances—Form 4 (120 - 180 Days)

Effectiveness Cohort

		Toric IOL			
	Control IOL N=73	1.25 D N=77	2.00 D N=41	2.75 D N=24	All Toric N=142
n	64	71	39	21	131
Significant visual disturbance[a], n (%)	5 (7.8)	0	1 (2.6)	0	1 (0.8)
No significant visual disturbance, n (%)	59 (92.2)	71 (100)	38 (97.4)	21 (100)	130 (99.2)

- **1 subject (Toric 2.00 D cohort) reported a significant increase in visual disturbances at Form 4 (120 - 180 days)**
  - **Moderate PCO at Form 4**
  - **Post Nd:YAG capsulotomy, subject reported that visual disturbances had resolved**

[a] **A significant visual disturbance is defined as an answer of 'moderate trouble', 'severe trouble', or 'so much trouble that I did not do the activity.'**

Trulign Toric Pivotal Study 650—Effectiveness Outcomes

Toric IOL

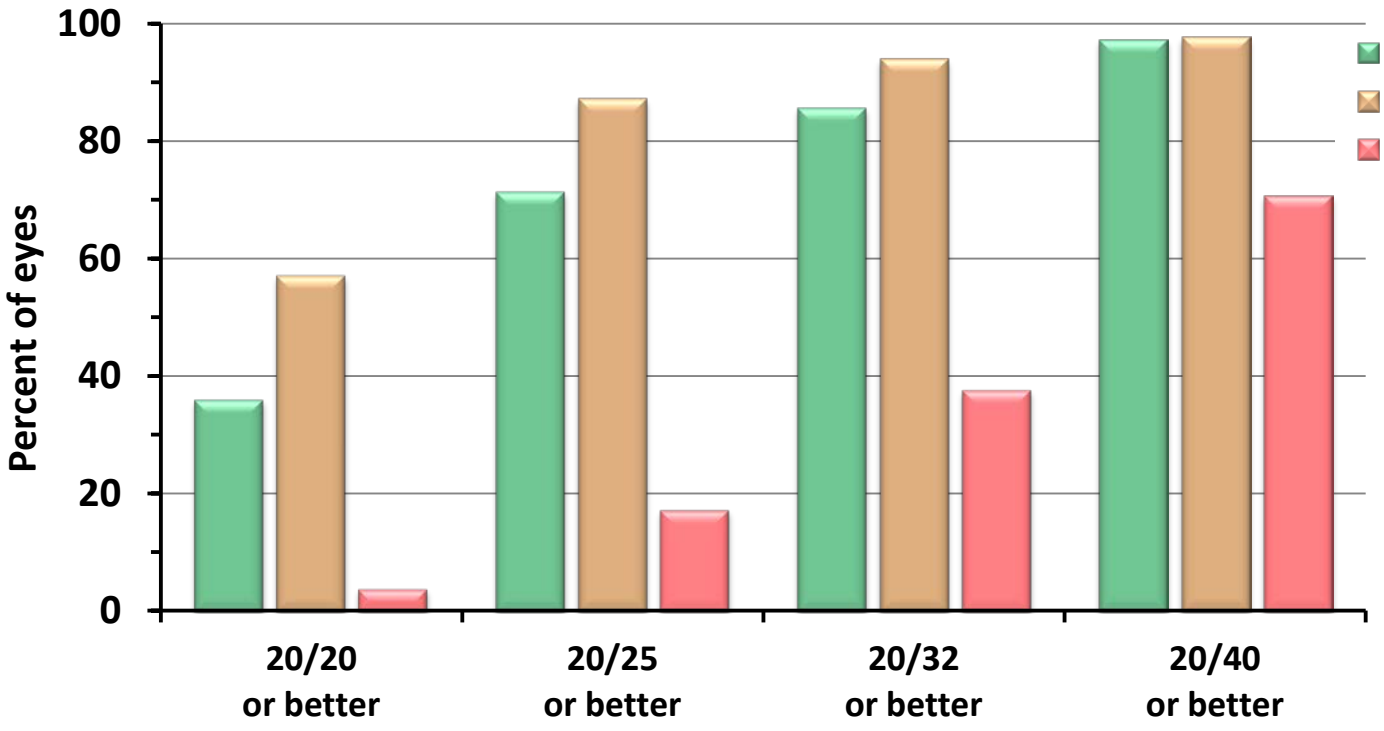
Effectiveness endpoint	Outcome
% reduction of cylinder	Toric 1.25 D superior to Control (p<0.001) All Toric: mean 85.8%
% within 0.50 & 1.00 D of intended	All Toric: 79.7% & 95.5%
Residual cylinder	Toric 1.25, 2.00, and 2.75 D: each reported mean < 0.50 D All Toric: mean 0.43 D
Lens axis misalignment	Mean < 5.0° from surgery to 4 – 6 months postop
Rotational stability	Mean < 2° from surgery to 4 – 6 months postop
Uncorrected distance visual acuity (UCDVA)	Mean 20/25 Toric 1.25 D superior to Control (p=0.004) All Toric superior to Control (p<0.001)
Visual disturbances	All Toric: 1/131 (0.8%) Resolved with Nd:YAG capsulotomy

Trulign Toric Pivotal Study 650—Effectiveness Outcomes

	Effectiveness endpoint	Outcome
Toric IOL	UCDVA	Mean 20/25 Toric 1.25 D (p=0.004) All Toric (p<0.001)
	Visual disturbances	All Toric: 1/131 (0.8%) resolved with Nd:YAG capsulotomy
Presbyopia IOL	DCIVA, DCNVA, DCNVA with Add	No compromise compared with Crystalens Control
	UCIVA	Mean 20/22, no compromise
	UCNVA	Mean 20/40, no compromise
	Add	Mean 1.43 D, no compromise

Trulign Toric Pivotal Study 650—Conclusions

Effectiveness Cohort, All Toric



Mean visual acuity
0.10 (20/25)
0.04 (20/22)
0.29 (20/40)

Trulign™ Toric Accommodating IOL is effective for intended use

Evidence for Accommodation

Adrian Glasser, PhD

Professor of Optometry and Vision Sciences
and Biomedical Engineering
Benedict/Pitts Professor
College of Optometry
University of Houston

Overview

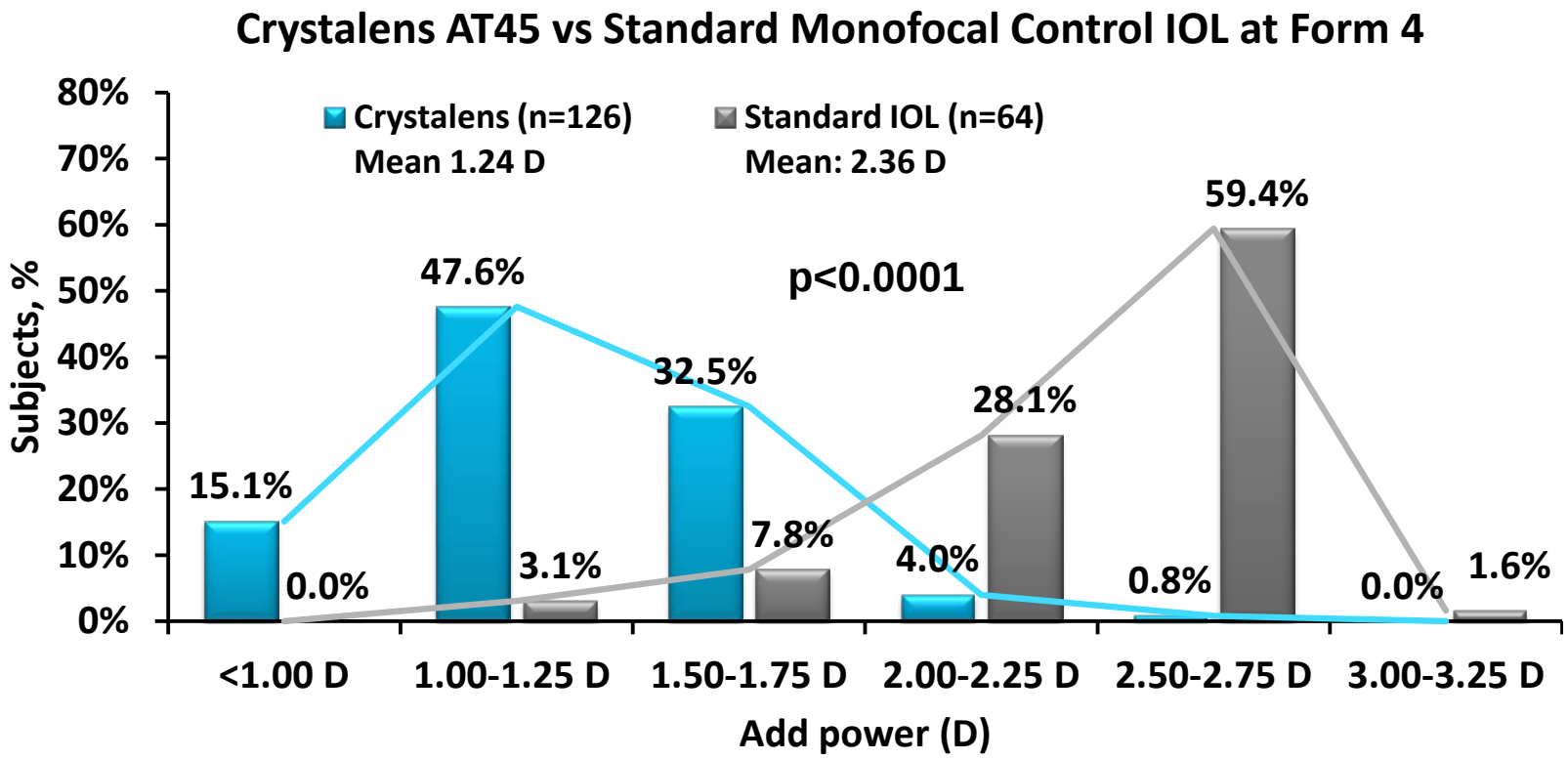
- 2003: AT45; no specified requirements for accommodation testing
  - Near add required to achieve best visual acuity
- 2003: Objective wavefront measurements
- 2006: Macsai 2006 JCRS publication
  - Dynamic retinoscopy, defocus and push-up testing
- 2007: AT45 HD-100 Level B modification
  - Drug-stimulated change in anterior chamber depth
- 2010-2012: Trulign™; no specified requirements for accommodation testing
  - Comparisons between toric and accommodating Crystalens® AT50SE/AT52SE

Accommodative Evidence—Crystalens® AT45 PMA

2003

- **November 2003: P030002 AT45**

"...intended to provide near, intermediate and distance vision without spectacles. The Crystalens® IOL provides approximately one diopter of monocular accommodation"



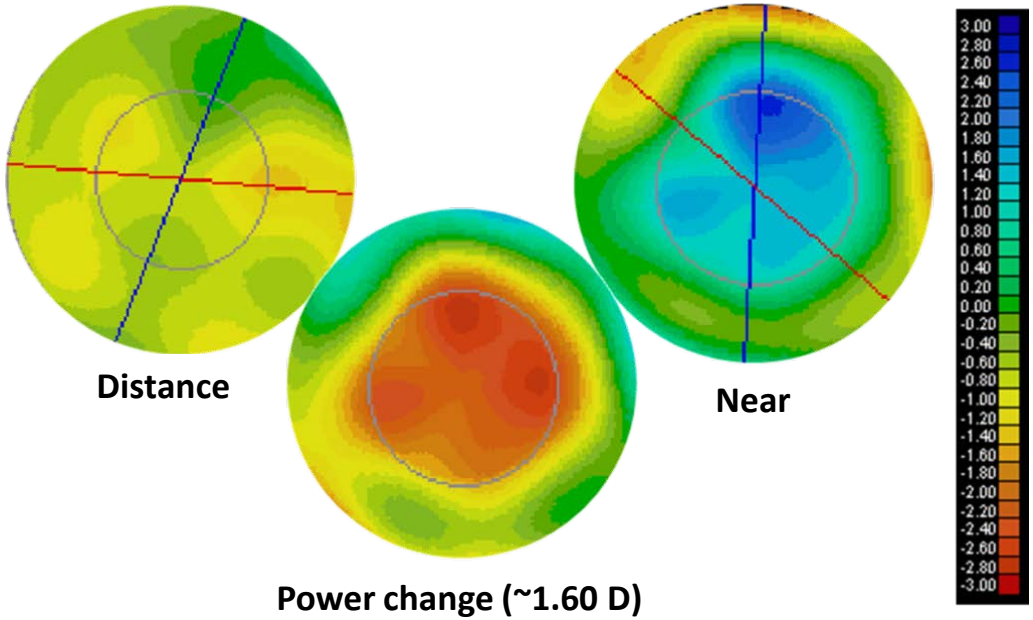
Accommodative Evidence—Crystalens® AT45 PMA

2003

- Subset of five bilateral subjects at a single site (10 eyes)
  - Near vision through distance correction

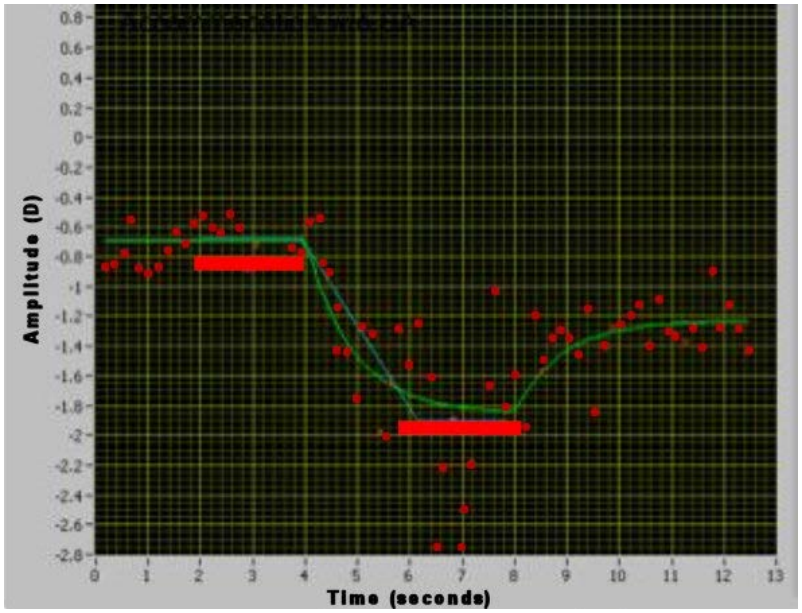
Test	Method	Results
Dynamic retinoscopy		Mean: 3.14 D Range: 2.16 D – 4.44 D
Defocus	Monocular and Binocular	Monocular: Mean: 2.42 D Range: 2.0 D – 3.25 D Binocular: Mean: 2.65 D Range: 2.0 D – 3.0 D
Power mapping	Wavefront analysis before and after cycloplegia	Range: –0.13 D – 2.93 D
ACD measurement	A scan ultrasonography • With Cyclopentolate • With Pilocarpine	Mean: 0.65 mm; SD: 0.28 Range: –0.25 D – +1.11 D

Objective Accommodation Measurement
2003



Power change (~1.60 D)

Total accommodation: 1.10 D



Spherical equivalent at distance: –0.70
Spherical equivalent at near: –1.80

Packer M. Paper Presentation, American Society of Cataract and Refractive Surgery Symposium on Cataract, IOL, and Refractive Surgery, 2004.

Adapted from Trattler, W. Oral Presentation, International Society of Refractive Surgery, 2009.

Macsai 2006 JCRS Publication on Crystalens®
2006

- N = 224 eyes
  - Crystalens AT45 (N = 112 eyes)
  - Monofocal (N = 112 eyes)
- Better UNVA in Crystalens group despite monofocal group having more myopic refraction (SE: –0.19 vs –0.45 D)
- Better UDVA with Crystalens
- More accommodation with Crystalens

Postoperative uncorrected visual acuities

Parameter	Standard monofocal	Crystalens	p-value
UDVA-monocular	0.70±0.19 (20/29)	0.85±0.30 (20/24)	<0.01
UNVA-monocular	0.35±0.12 (J6)	0.69±0.23 (J2)	<0.01
UDVA-binocular	1.01±0.14 (20/20)	1.16±0.17 (20/17)	<0.01
UNVA-binocular	0.40±0.13 (J6)	1.00±0.00 B (J1)	<0.01

Postoperative measured accommodation

Parameter	Standard monofocal	Crystalens	p-value
Dynamic retinoscopy, D	0.91±0.24	2.42±0.39	<0.01
Defocus-monocular, D	0.75±0.25	1.74±0.48	<0.01
NPA-monocular, inches (D)	34.7±9.8 (1.23)	9.5±3.1 (4.78)	<0.01
Defocus-binocular, D	0.91±0.22	1.96±0.50	<0.01
NPA-binocular, inches (D)	27.6±6.2 (1.51)	7.7±2.6 (5.79)	<0.01

NPA = near point of accommodation.

Macsai MS, et al. *J Cataract Refract Surg*. 2009;32:628-633.

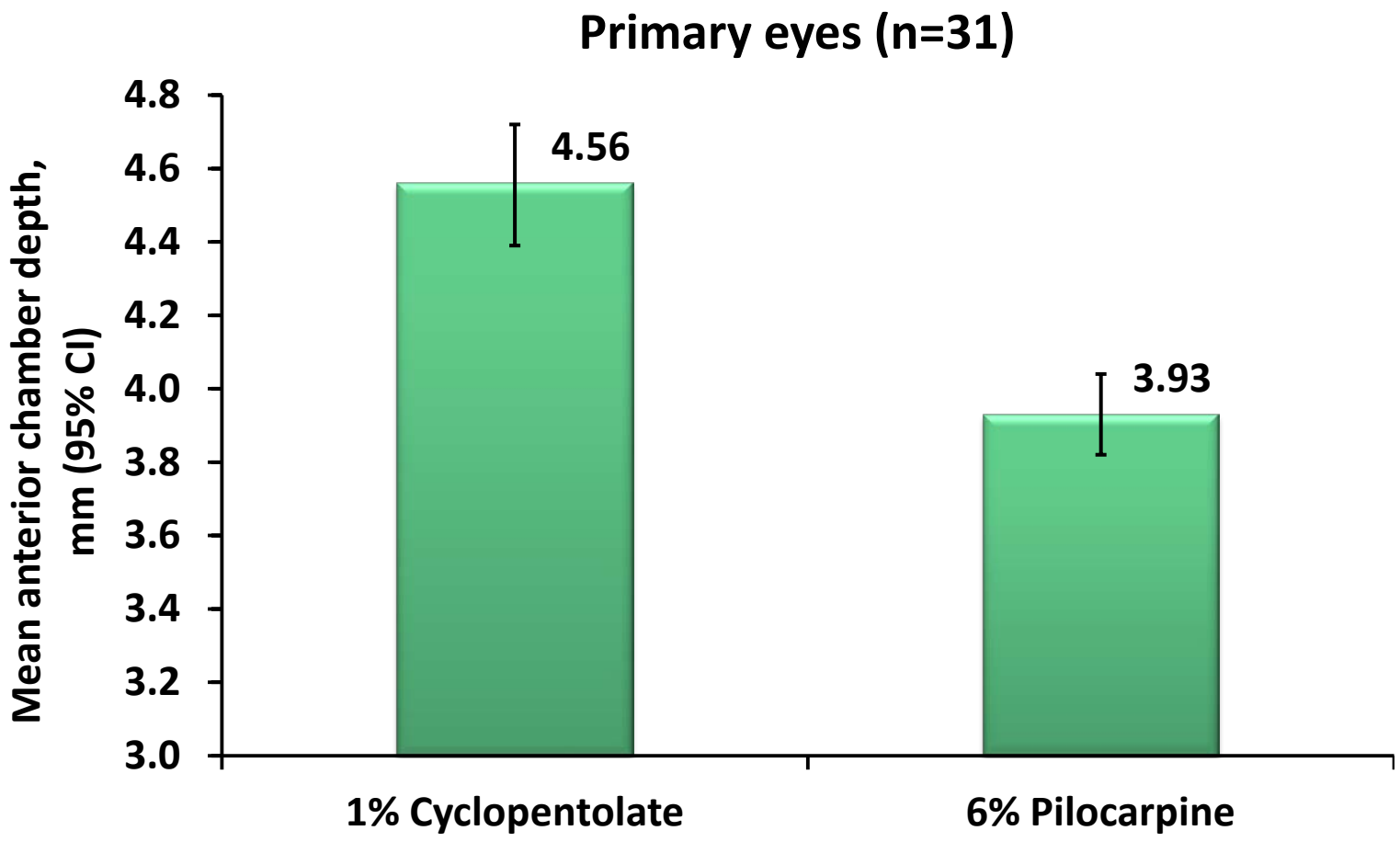
Accommodative Amplitude—Crystalens® HD-100 PMA Supplement 14

2007

Test	Method	Measure	Results
ACD measurement • 35 eyes from 2 clinical sites • ACD 45 min after drug administration • 3 weeks between agents	Immersion biometry • With 1% Cyclopentolate • With 6% Pilocarpine	Anterior chamber depth	Mean movement: 0.62 mm
Push down test • 33 eyes	Subjective measure with MN Read Card	Distance from blur	Mean: 3.93 D SD: 1.40

Change in Anterior Chamber Depth—Crystalens® HD-100 PMA Supplement 14

2007



Evidence for Accommodation—Trulign™ Pivotal Study 650

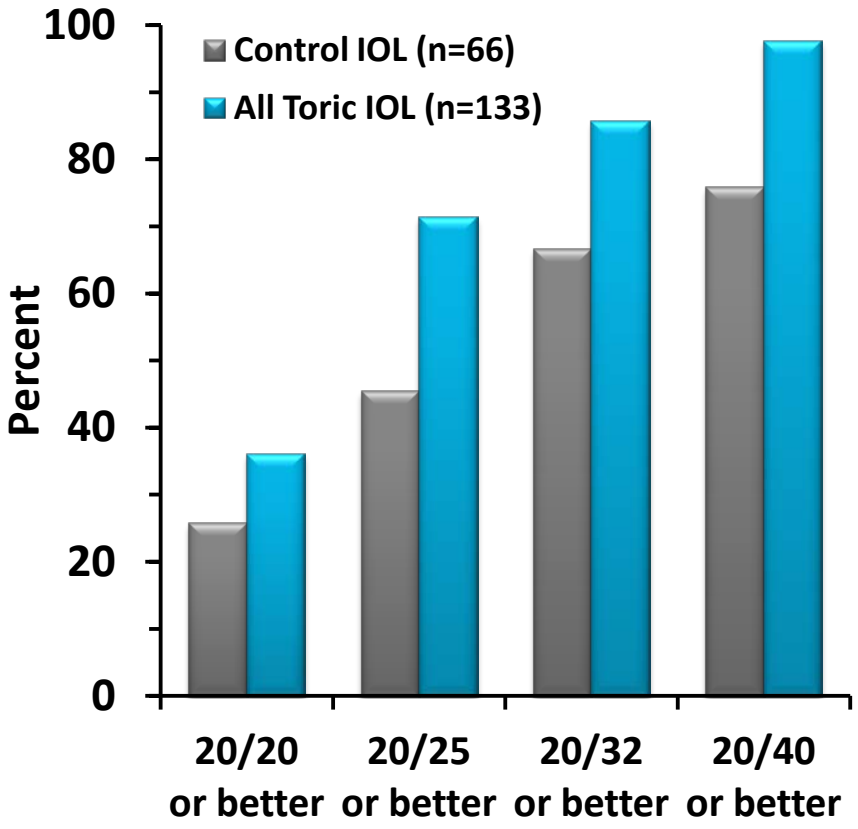
2012

- Study 650 had no specified requirements for accommodation testing
- Trulign Toric IOL is simply a modification to Parent Crystalens® Accommodating AT50SE/AT52SE IOL
- Parent Crystalens Accommodating AT50SE/AT52SE IOL served as the control IOL for Study 650
- Study 650 data support improved distance acuity and equivalent accommodative effectiveness of the Trulign Toric at intermediate and near compared with the control Crystalens

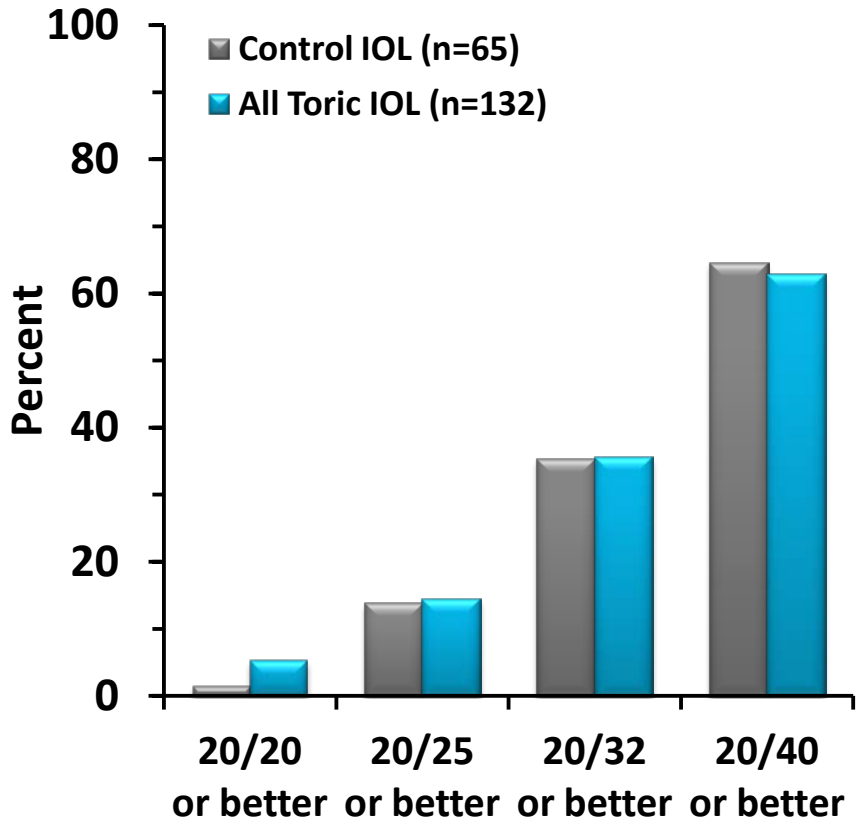
Uncorrected Distance and Distance Corrected Near Visual Acuities—Trulign™ Pivotal Study 650

2012

Uncorrected Distance Visual Acuity (UCDVA)—Form 4 (120 - 180 Days) Effectiveness Cohort

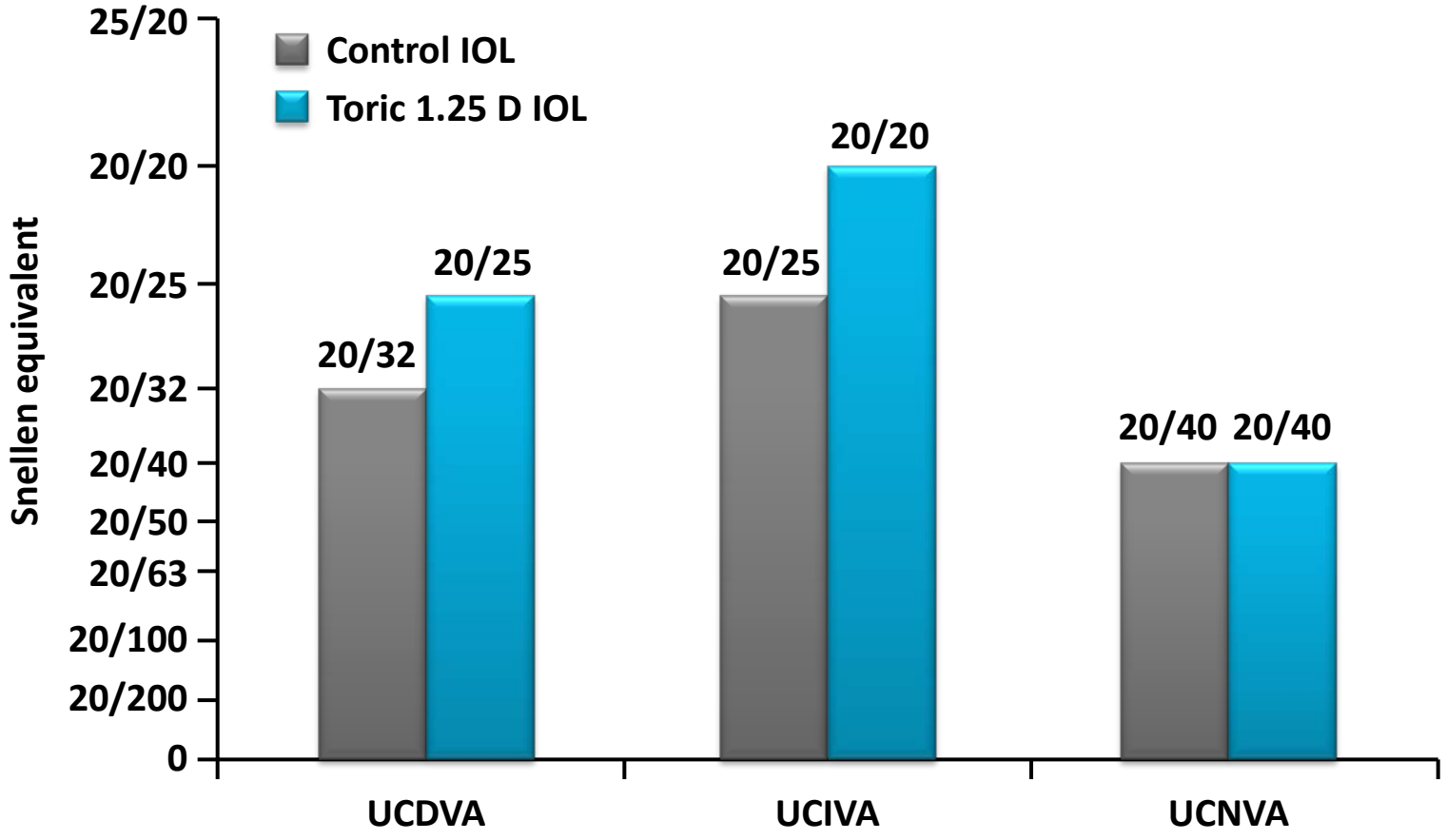


Distance Corrected Near Visual Acuity (DCNVA)—Form 4 (120 - 180 Days) Effectiveness Cohort



UCDVA, UCIVA, and UCNVA *With Adjustment for MRSE*—Trulign™ Pivotal Study 650

2012

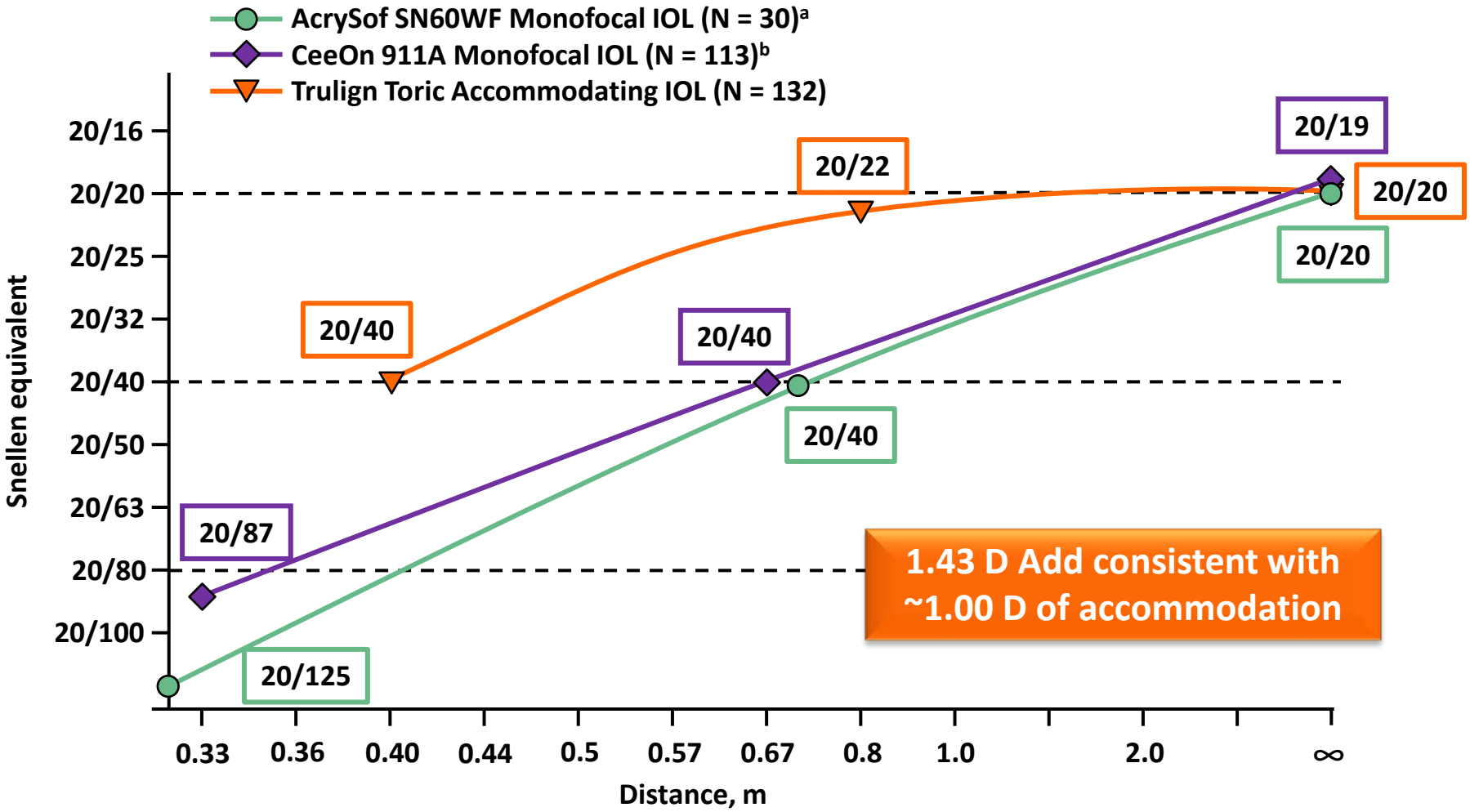


Are the Data Presented Sufficient to Support an Accommodation Claim for This Device?

- Data to support accommodation claim includes that originally presented to FDA for Parent Crystalens® AT45 IOL
- Subsequent data (both subjective and objective) support and reconfirm original accommodation claim for Parent IOL
- Pivotal Study 650 data support equivalent accommodative effectiveness for the Trulign™ Toric IOL at intermediate and near compared with the Parent Crystalens

Distance Corrected Visual Acuity Accommodating vs Monofocal IOLs

2010



[a] Hayashi K, et al. *J Cataract Refract Surg*. 2010;36:1323-1329.
[b] Packer M, et al. *Am J Ophthalmol*. 2010;149(4):577-584.

Clinical Perspectives

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Trulign™ Toric Accommodating IOL—Clinical Considerations

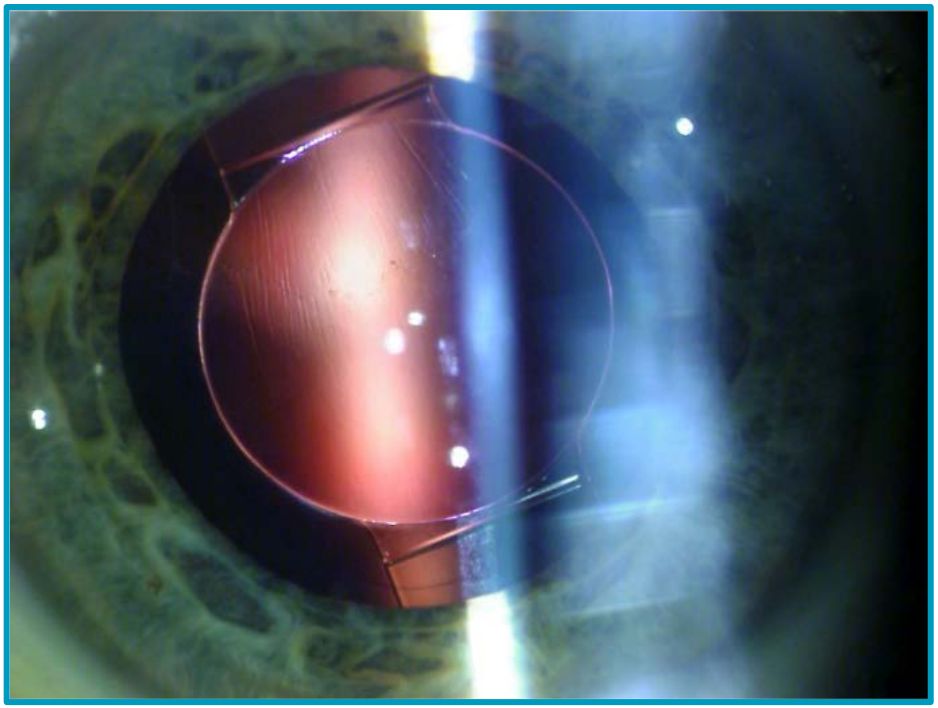
- Adding a toric optic to an established parent IOL
  - No new risks
  - Current risks already well known and understood
- Increased benefits
  - Superior uncorrected distance visual acuity
  - Reduced enhancement procedures

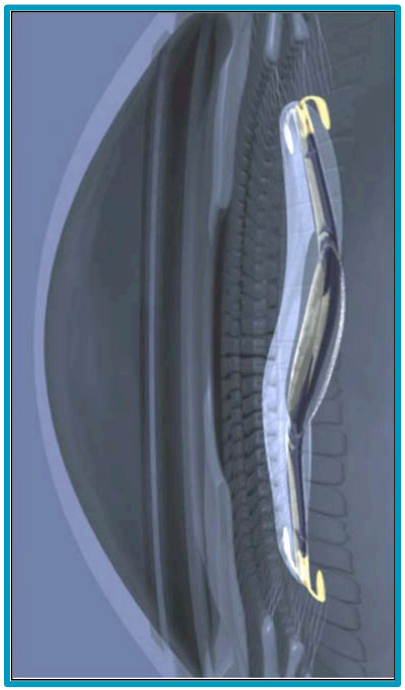
Trulign™ Toric Accommodating IOL—Clinical Considerations

- Current risks of parent platform
  - Anterior and asymmetric vault
    - Successful mitigation and treatment strategies
- Benefits
  - Distance, intermediate, and near vision
    - Presbyopia correction
  - Rotational stability
    - Astigmatism correction
  - Reduced spectacle dependence

Anterior and Asymmetric Vault

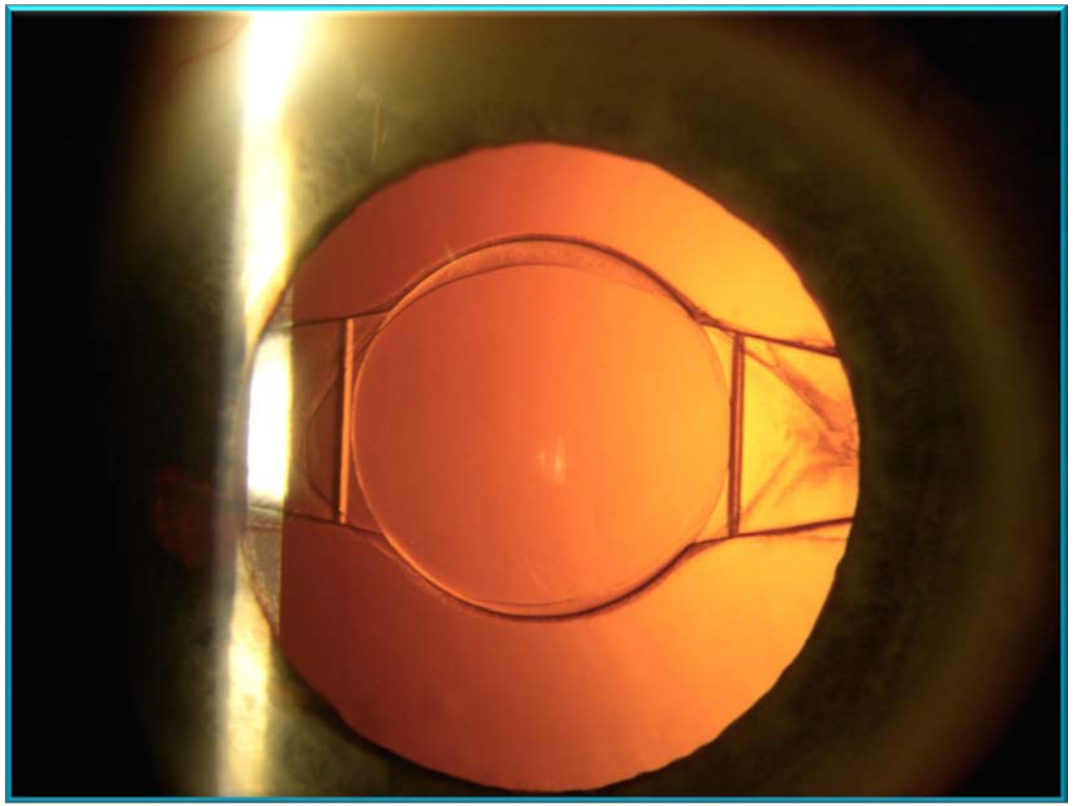
- Hinged haptics
- Capsular contraction





Anterior and Asymmetric Vault—Mitigation Strategies

- Surgical technique
  - Capsulorhexis
  - Cortical clean-up
  - Pristine capsule
  - IOL positioning
  - Watertight closure
- Medical therapy
  - Topical anti-inflammatory agents
  - Topical cycloplegic medications

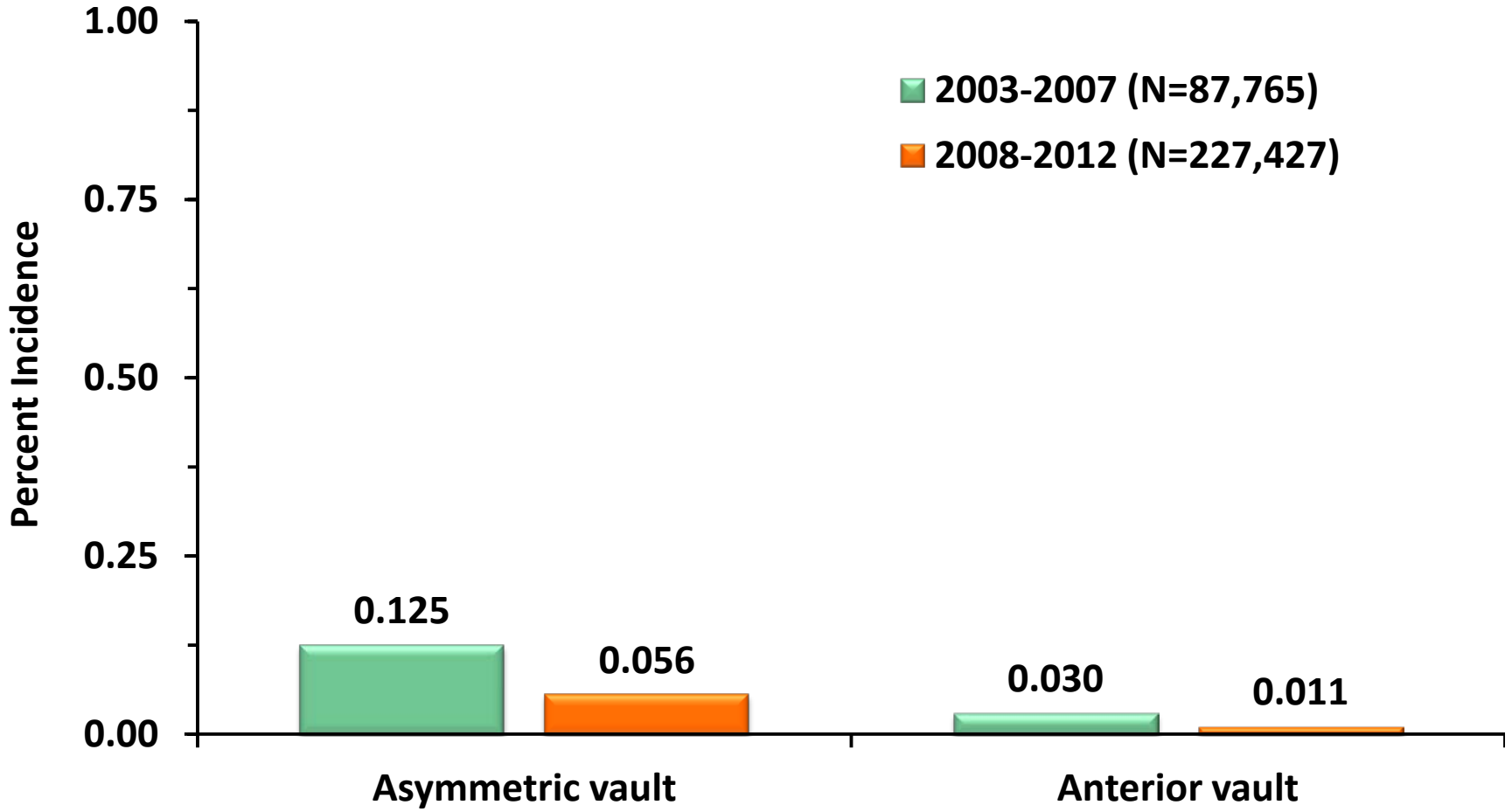


Vault—Mitigation Instructions in the DFU

Cause	Instruction for prevention per DFU[a]
Asymmetric contraction of anterior capsulotomy	Construct round, well-centered capsulorhexis, 5.5 - 6.0 mm diameter, with anterior capsule covering plate haptics
Inflammation caused by residual lens material	Meticulous clean-up of cortical material. Rotate IOL at least 90 degrees to dislodge trapped lens material
Capsular defect	Do not implant Crystalens if capsule is not intact
Zonular defect	Do not implant Crystalens if any zonular rupture
Incorrect IOL placement	Rotate IOL at least 90 degrees to ensure both haptics placed in bag Ensure optic vaulted posteriorly along normal position of posterior capsule
Inadequate control of postoperative inflammation	Reinforce patient compliance with anti-inflammatory medication for at least 4 weeks postoperative
Wound leak (Deflation Syndrome)	Careful construction of clear cornea incision Testing to ensure water tight seal. Suture as needed

[a] Crystalens Directions For Use/PN 50-0087G/4078402.

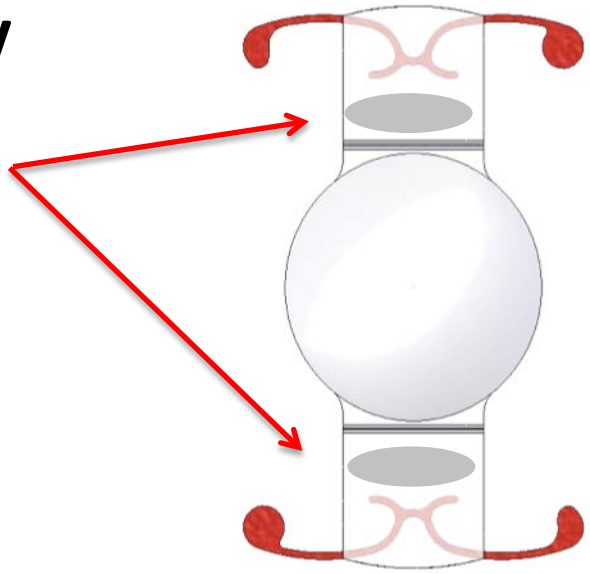
Vault—Incidence Declined Over Time



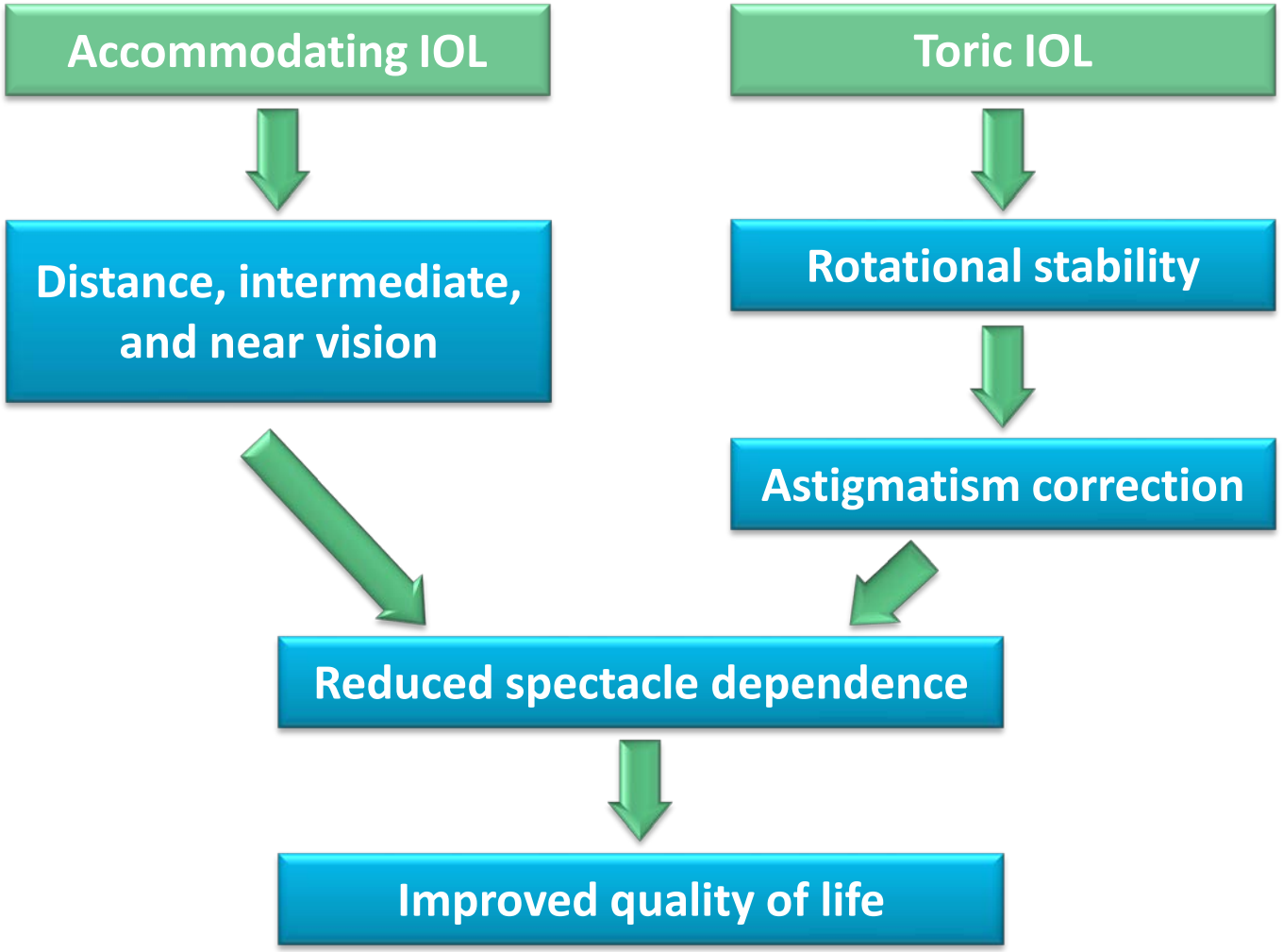
B+L data on file. CATSWeb global complaints database.

Anterior and Asymmetric Vault—Treatment Strategies

- YAG capsulotomy
  - Pre-emptive capsulotomy
  - Relaxing capsulotomies
- Repositioning/IOL exchange
  - Maintain good BCVA
- Corneal refractive procedures



Trulign™ Toric Accommodating IOL—Benefits



Crystalens®—Presbyopia Correcting Parent IOL

- Crystalens: clinically proven effectiveness
  - Superior UCIVA/UCNVA and DCIVA/DCNVA
    - Versus monofocal IOLs
  - Superior UCIVA/DCIVA and quality of vision
    - Versus multifocal IOLs
- Objective measurements support accommodative effect
- Clinical benefits reconfirmed in Pivotal Study 650
  - Equivalent effectiveness demonstrated for Trulign™ Toric IOL

Crystalens® Accommodating IOL—Versus Monofocal IOLs

Publication	Treatment(s)	Results
Macsai, et al. 2006[a]	Crystalens IOL (n=56 pts) vs Monofocal IOL (n=56 pts)	Crystalens achieved significantly better uncorrected monocular (20/25 vs 20/50; $p<0.01$) and binocular (20/20 vs 20/50) near visual acuity, and significantly more accommodation versus monofocal IOL
Marchini, et al. 2007[b]	Crystalens IOL (n=29 eyes) vs Monofocal IOL (n=21 eyes)	Crystalens group demonstrated significantly better monocular DCNVA ($p<0.001$) and less add power to achieve BCNVA. Mean monocular DCNVA at 40 cm was J4 (20/32) in the Crystalens group
Patel, et al. 2008[c]	Crystalens IOL (n=18 eyes) vs Monofocal IOL (n=17 eyes)	Crystalens achieved significantly better monocular UCNVA compared with monofocal IOL (0.51 vs 0.30; $p<0.05$)
Beiko. 2013[d]	Crystalens IOL (n=10 pts) vs Monofocal IOL (n=11 pts)	Crystalens group achieved near visual acuity that was 1.5 lines better than the monofocal mini-monovision IOL group

[a] Macsai MS, et al. *J Cataract Refract Surg*. 2006;32:628-33; [b] Marchini G, et al. *Ophthalmology*. 2007;114:2038-43; [c] Patel S, et al. *J Refract Surg*. 2008;24:294-9; [d] Beiko GH. *J Cataract Refract Surg*. 2013;39:48-55.

Crystalens® Accommodating IOL—Versus Multifocal IOLs

Publication	Treatment(s)	Results
Pepose, et al. 2007[a]	49 pts received either bilateral Crystalens IOLs, bilateral ReSTOR or ReZoom multifocal IOLs, or combinations thereof	4 to 6 months postoperatively, eyes with Crystalens achieved statistically better best-spectacle corrected distance, uncorrected and distance-corrected intermediate, and best-corrected near vision, and better contrast sensitivity versus multifocal IOLs

[a] Pepose JS, et al. *Am J Ophthalmol*. 2007;144:347-57.

Crystalens® Accommodating IOL

Publication	Treatment(s)	Results
Marchini, et al. 2004[a]	Crystalens IOL (N=20 eyes)	All eyes achieved DCNVA at 30 cm of J5 (20/40) or better and needed an add power <1.25 D to achieve J1 (20/20) near visual acuity at 30 cm
Alio, et al. 2004[b]	Crystalens IOL (N=12 pts)	Significant 12-month post-operative improvement in UCNVA (p=0.14), BCNVA (p<0.001), and DCNVA (p=0.04); mean binocular DCNVA of 20/25 at 40 cm
Hantera, et al. 2010[c]	Crystalens IOL (N=25 eyes)	Good monocular UCDVA (mean, 20/25) and DCNVA at 35 cm (62% achieved J3 or better)
Szigeti, et al. 2012[d]	Crystalens IOL (N=17 eyes) with either 5.5 or 6.0 mm capsulorhexis diameters	Mean DCNVA at 35 cm was 0.60 (20/33), and 13 of 17 eyes (76%) achieved DCNVA of J3 or better

[a] Marchini G, et al. *J Cataract Refract Surg*. 2004;30:2476-82; [b] Alio JL, et al. *J Cataract Refract Surg*. 2004;30:2494-503; [c] Hantera MM, et al. *J Cataract Refract Surg*. 2010;36:1167-72; [d] Szigeti A, et al. *J Refract Surg*. 2012;28:609-13.

Meta-Analysis of Accommodating IOLs Supports Greater Anterior Displacement Versus Monofocal Controls

- Pilocarpine stimulation
  - Generally anterior movement, up to 0.84 mm[a-c]
  - Heterogeneous results, with some posterior movement[d]
    - Effects of pilocarpine vary with iris color
    - Primate studies have shown spurious results compared with stimulation of the Edinger-Westphal nucleus[e]
- Stimulation of accommodation
  - 0.33 mm anterior IOL movement,[f] consistent with *in vitro* studies[g]
- Axial movement of Crystalens appears to constitute a component of its mechanism of action

[a] Takakura A, et al. *J Cataract Refract Surg*. 2010;36:380-388. [b] Dick HB, Dell S. *Ophthalmol Clin N Am*. 2006;19:107-124.
[c] Stachs O, et al. *J Refract Surg*. 2006;22:145-150. [d] Koeppl C, et al. *J Refract Surg*. 2005;31:1290-1297.
[e] Glasser A. *Ophthalmol Clin N Am*. 2006; 19:1-12. [f] Marchini G, et al. *J Cataract Refract Surg*. 2004;30:2476–2482.
[g] Stachs O, et al. *J Refract Surg*. 2005;21:37–45.

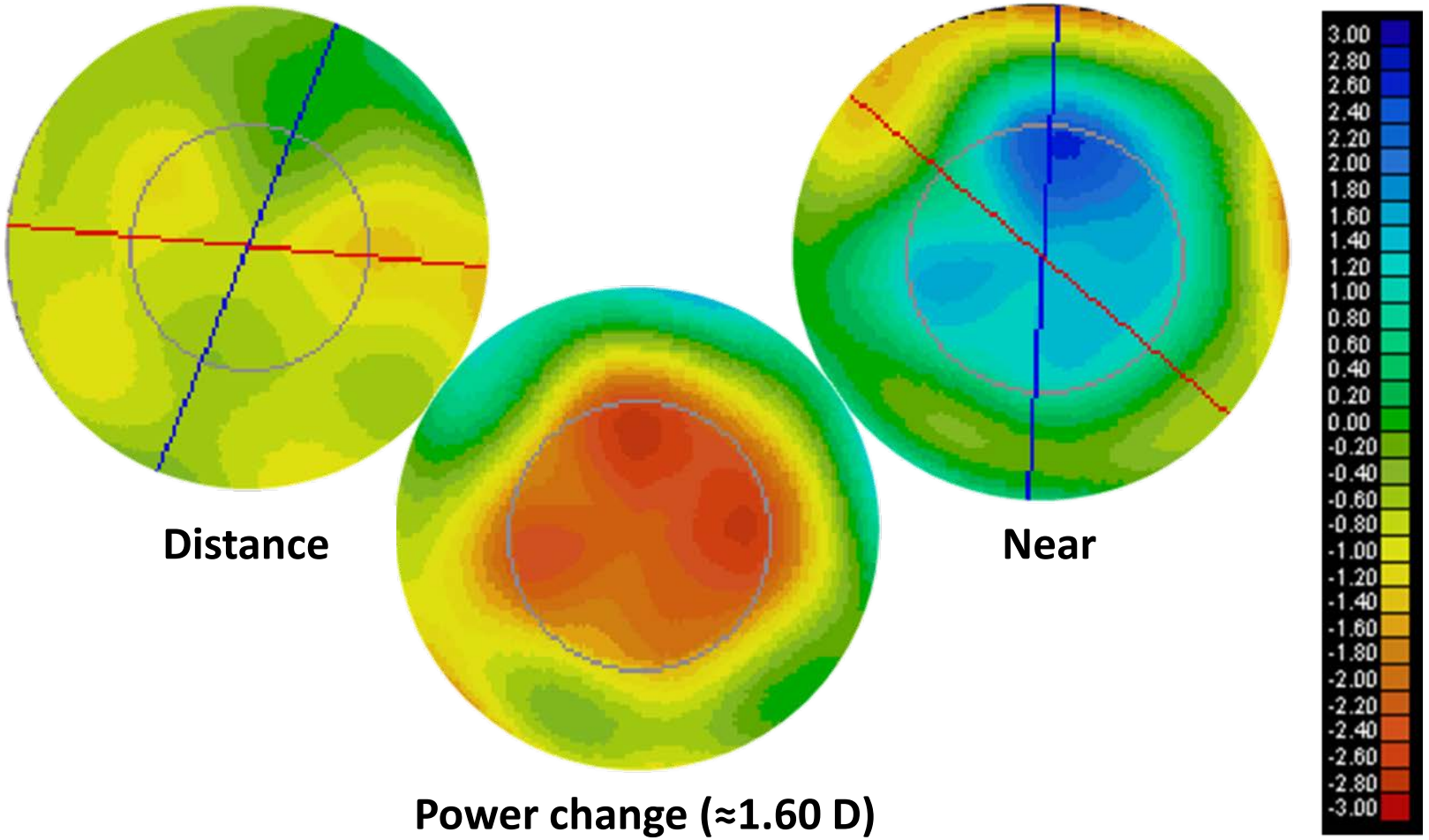
Objective Measurement of Accommodation

- iTrace (Tracey Technologies)
  - Validated ray-tracing wavefront aberrometer[a]
  - ANSI recommended for measure of accommodation

[a] Win-Hall DM, Glasser A. *J Cataract Refract Surg*. 2006; 34:774-784.

Image courtesy of Tracey Technologies; used with permission.

Objective Measurement of Accommodation



Packer M. Paper Presentation, American Society of Cataract and Refractive Surgery Symposium on Cataract, IOL, and Refractive Surgery, 2004.

Distance Corrected Near Visual Acuity (DCNVA)—Trulign™ vs Monofocal and Multifocal IOLs

	CeeOn 911A[a] Monofocal 33 cm (N=113)	Crystalens® Control 40 cm (N=65)	Trulign Toric 40 cm (N=132)	Tecnis[a] Multifocal 33 cm (N=116)
DCNVA (Snellen)				
Mean	20/87	20/40	20/40	20/28

[a] Packer M, et al. *Am J Ophthalmol*. 2010;149(4):577-584.

Uncorrected Intermediate Visual Acuity (UCIVA)—Trulign™ vs Multifocal IOLs

	Trulign Toric (N=133)	ReSTOR[a] 3.0 Multifocal (N=50)	Tecnis[a] Multifocal (N=44)
UCIVA (Snellen), %			
20/20 or better	57.1	10.0	18.2
20/25 or better	87.2	30.0	40.9
20/32 or better	94.0	58.0	54.5
20/40 or better	97.7	74.0	75.0
Worse than 20/40	2.3	26.0	25.0

[a] Pepose JS and Qazi MA. A prospective, randomized evaluation of bilateral implantation of 3 FDA-approved presbyopia-correcting IOLs. Hawaiian Eye. January 20-25, 2013.

UCIVA/UCNVA Versus DCIVA/DCNVA—Form 4 (120 - 180 Days)

Study 650—Effectiveness Cohort, All Toric

- **Performance at intermediate and near**
  - **Not due to targeting myopia or "mini-monovision"**

	Visual acuity			
Mean acuity	Uncorrected intermediate	Distance corrected intermediate	Uncorrected near	Distance corrected near
logMAR (SD)	0.04 (0.129)	0.06 (0.127)	0.29 (0.146)	0.30 (0.144)
p value	0.0973		0.3281	

- **Expect one line improvement with binocular summation**

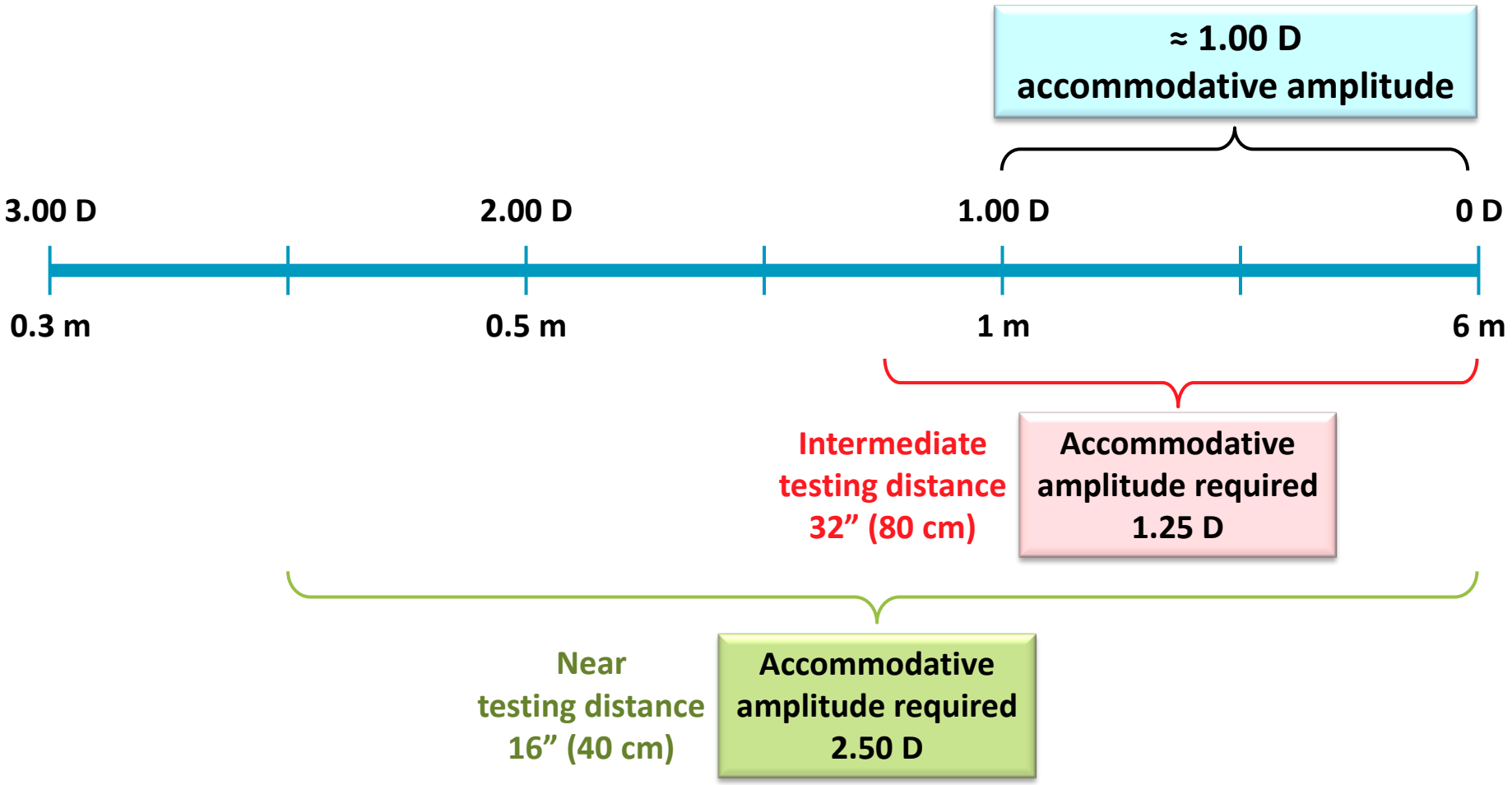
UCDVA, UCIVA, and UCNVA *With Adjustment for MRSE*—Form 4 (120 - 180 Days)

Study 650—Effectiveness Cohort

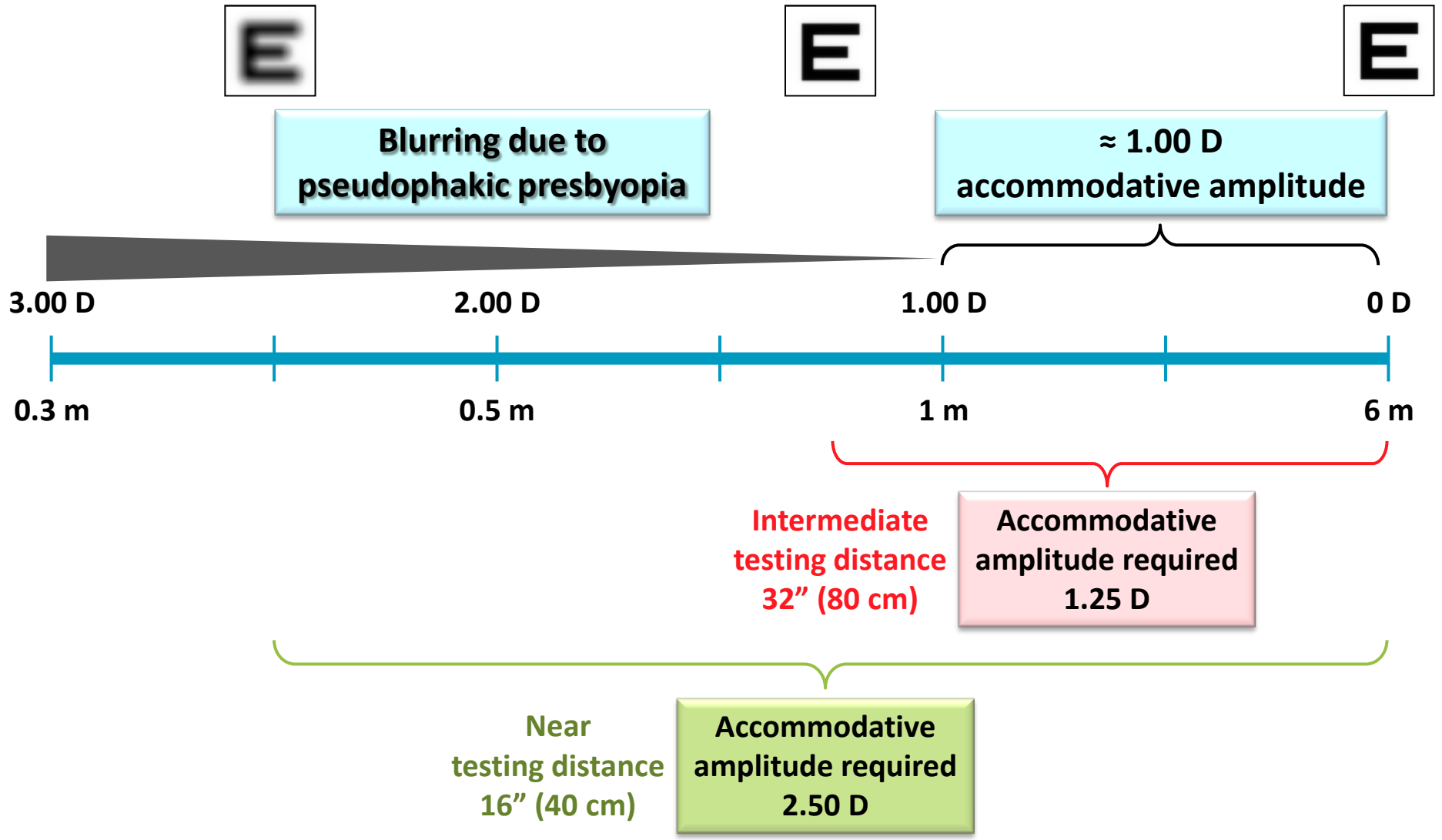
	Crystalens® Control	Trulign™ Toric 1.25 D	Difference	p-value[a]
UCDVA (logMAR)[b]				
Adjusted mean (SE)	0.17 (0.018)	0.11 (0.017)	–0.07 (0.025)	0.007
95% CI	(0.139, 0.208)	(0.073, 0.140)	(–0.019, –0.116)	
UCIVA (logMAR)[c]				
Adjusted mean (SE)	0.08 (0.015)	0.04 (0.015)	–0.04 (0.021)	0.062
95% CI	(0.047, 0.107)	(0.007, 0.066)	(–0.083, 0.002)	
UCNVA (logMAR)[d]				
Adjusted mean (SE)	0.29 (0.016)	0.28 (0.016)	–0.01 (0.022)	0.579
95% CI	(0.261, 0.325)	(0.250, 0.311)	(–0.057, 0.032)	

[a] Analysis of variance.
[b] logMAR UCDVA = 0.1259 – 0.0674*Toric + 0.0122*MRSE + 0.1316*MRSE*MRSE.
[c] logMAR UCIVA = 0.0974 – 0.0405*Toric + 0.1509*MRSE + 0.0821*MRSE*MRSE.
[d] logMAR UCNVA = 0.3219 – 0.0125*Toric + 0.1546*MRSE + 0.0641*MRSE*MRSE.

Intermediate and Near Testing Distances



Residual Presbyopia



Residual Astigmatism

- Residual astigmatism in control group benefits uncorrected near visual acuity[a]
- Effectiveness of toric correction reduced when the IOL shifts into an accommodated position
  - Toric power calculated to correct corneal astigmatism when the IOL is in distance focus position

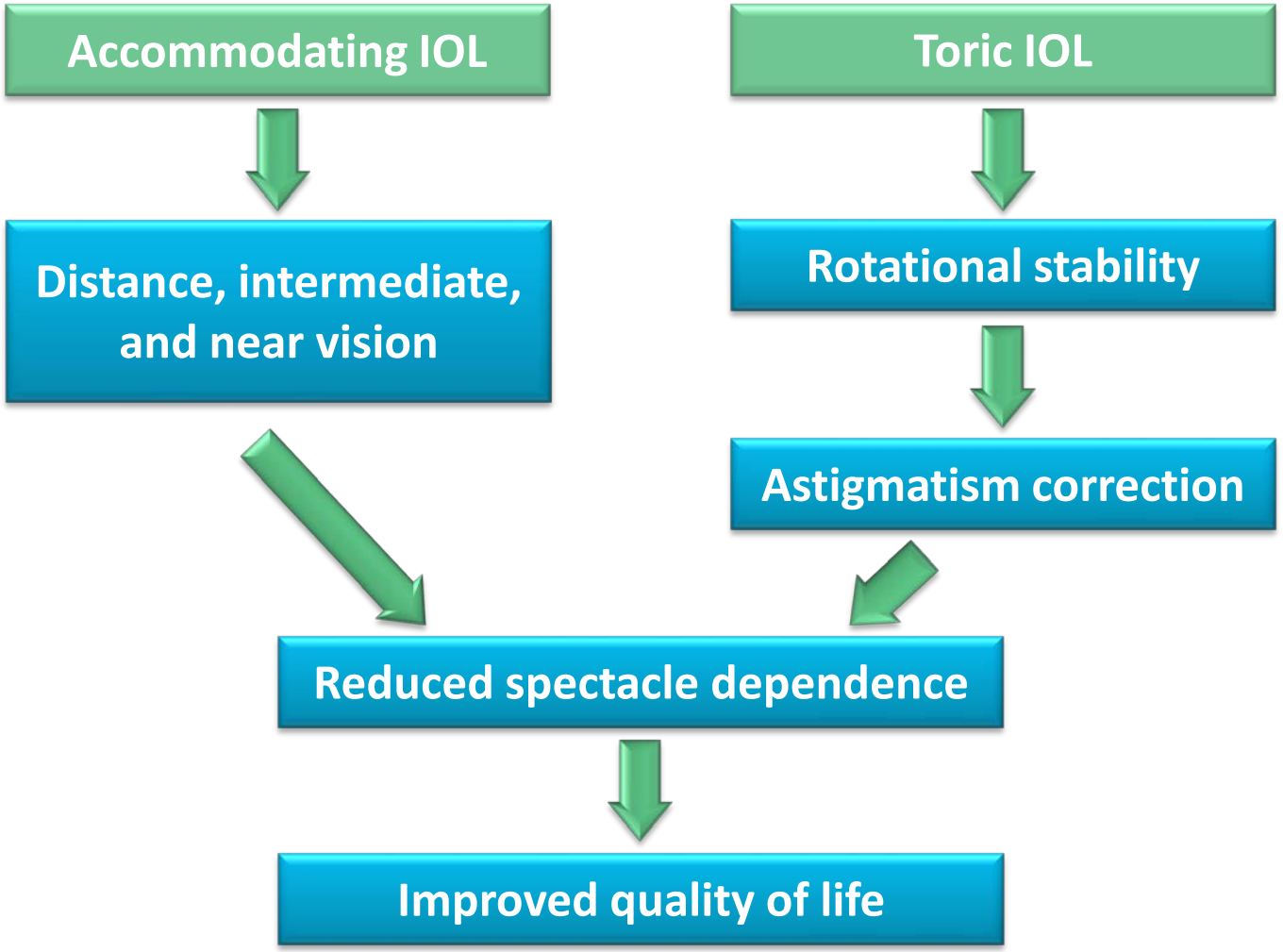
[a] Trindade F, et al. *J Cataract Refract Surg*. 1997;23:82-85.

Performance Expectations

- Approved labeling: ≈ 1.00 D of accommodation
  - Continuous best visual acuity from distance to within 1 meter
- Clinical experience:
  - Outperforms labeling
    - 20/22 at intermediate
    - Parent IOL: 80.6% use computer without spectacles[a]
  - Low power (1.25 – 1.50 D) OTC readers prn at near

[a] Note: Summary of Safety and Effectiveness Data, Model AT45

Trulign™ Toric Accommodating IOL—Benefits



Lens Axis Misalignment From Target—Preop to Form 4 (120 - 180 Days)

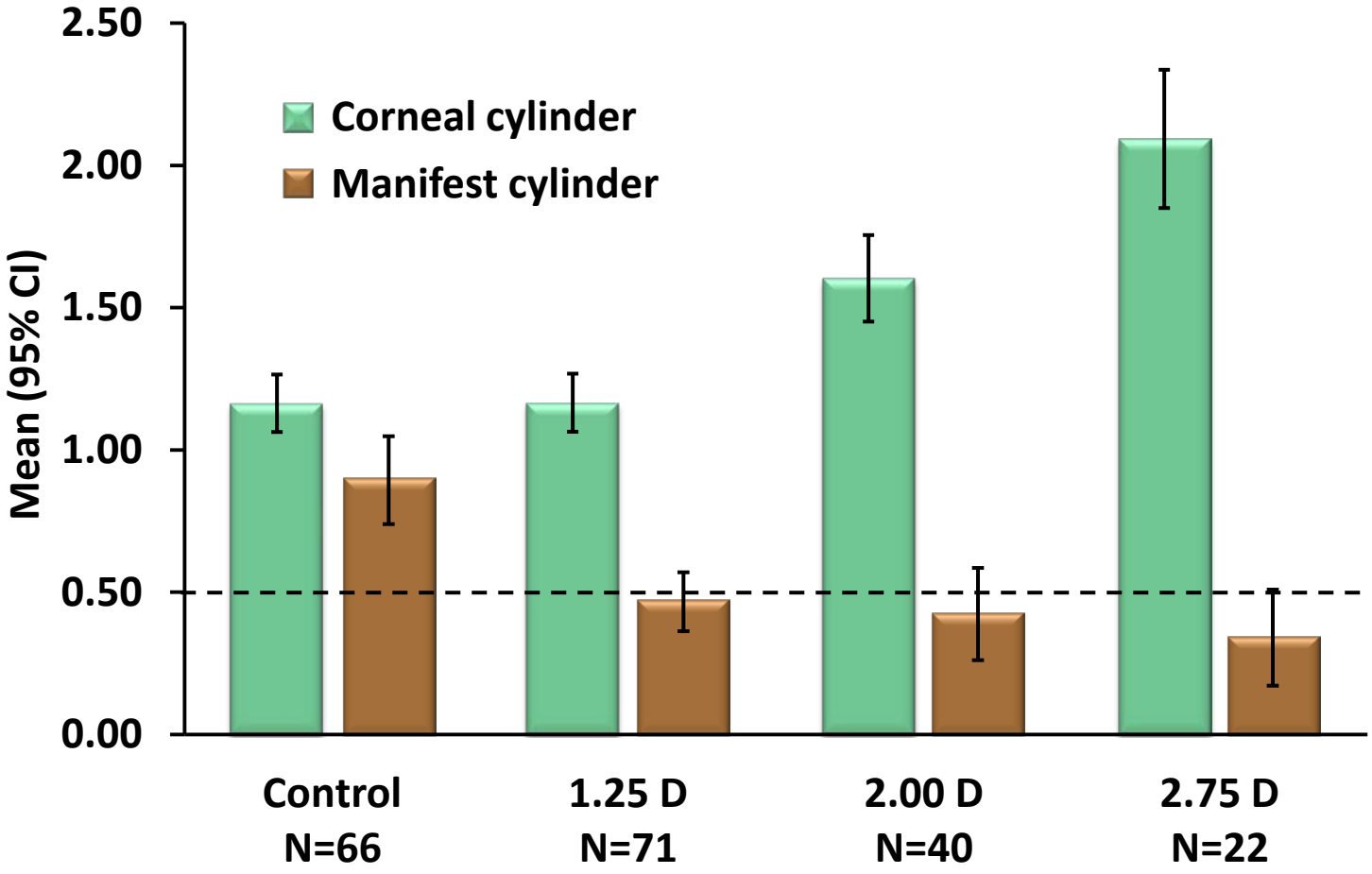
Study 650—Effectiveness Cohort

	Toric IOL			
	1.25 D N=77	2.00 D N=41	2.75 D N=24	All Toric N=142
n	70	38	21	129
Mean (SD), °	5.06 (3.862)	3.79 (2.362)	5.51 (4.650)	4.76 (3.668)

Magnitude of Corneal Cylinder vs Manifest Refractive Cylinder—Form 4 (120 - 180 Days)

Study 650—Effectiveness Cohort

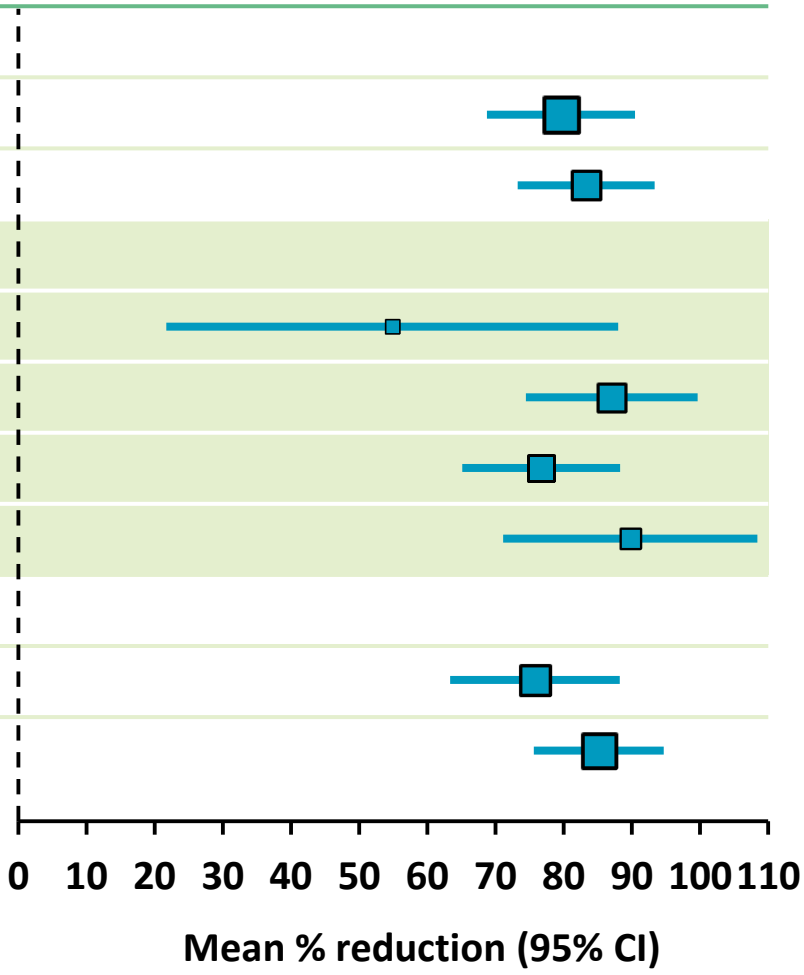
- **All Toric Cohorts demonstrated good mean residual cylinder**



Effect of Age

Study 650—Effectiveness Cohort, Toric 1.25 D

	Mean	n	95% CI
Gender			
Female	79.596	43	68.734, 90.457
Male	83.289	28	73.244, 93.335
Age, yr			
<60	54.846	7	21.703, 87.988
60-69	87.045	27	74.450, 99.641
70-79	76.694	23	65.116, 88.271
80+	89.759	14	71.112, 108.406
Eye			
OD	75.778	31	63.337, 88.220
OS	85.140	40	75.611, 94.669



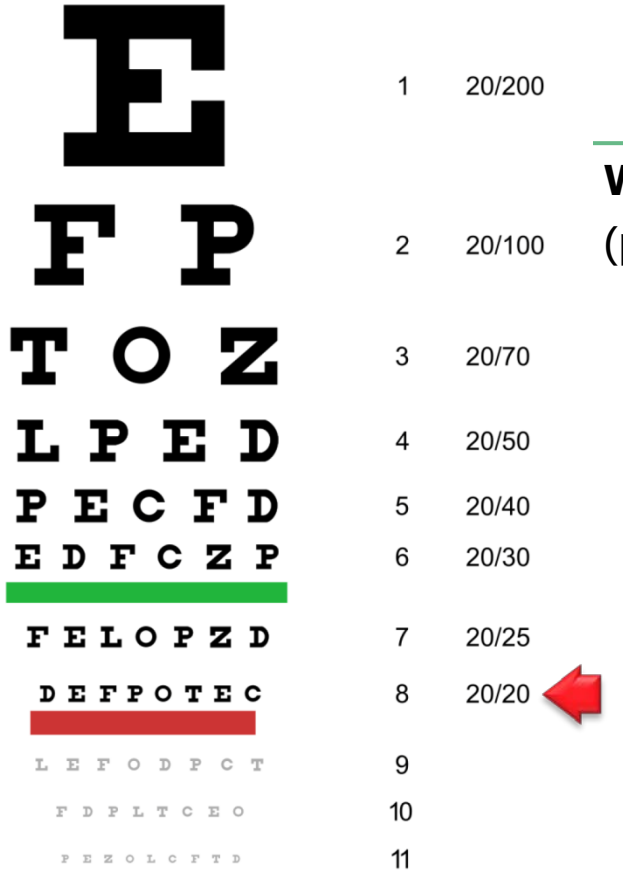
Uncorrected Distance Visual Acuity (UCDVA)—Trulign™ vs AcrySof® Toric IOL

	Trulign Toric (N=133) Form 4 (120 – 180 days)	AcrySof[a] (N=243) 1 year postoperative
UCDVA (Snellen), %		
20/20 or better	36.1	40.7
20/25 or better	71.4	63.4
20/32 or better	85.7	79.0
20/40 or better	97.7	92.2
Worse than 20/40	2.3	7.8

[a] Holland E, et al. *Ophthalmology*. 2010;117:2104–2111.

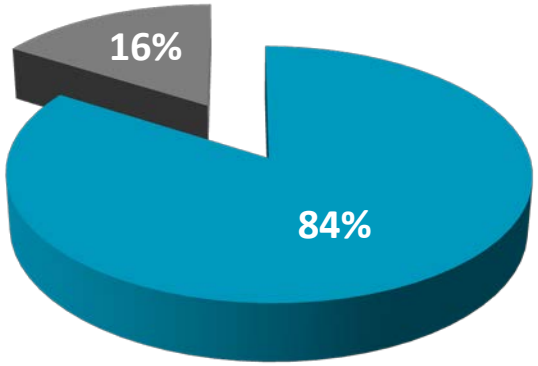
UCDVA Within 2 Lines of BCDVA—Form 4 (120 - 180 Days)

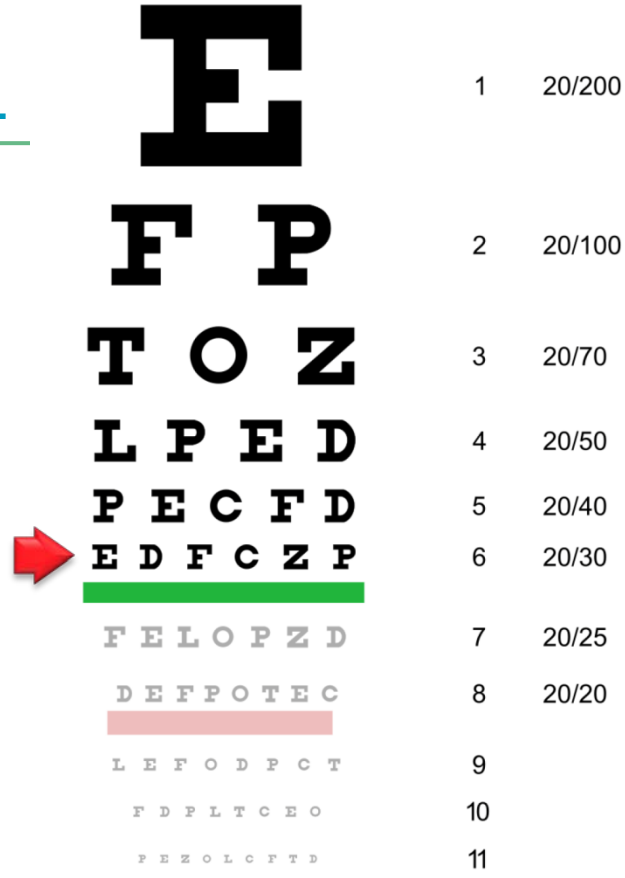
Study 650—Effectiveness Cohort, All Toric



All Toric IOL	
Within 2 lines (paired analysis)	**84.2%**

UCDVA vs BCDVA within 2 lines



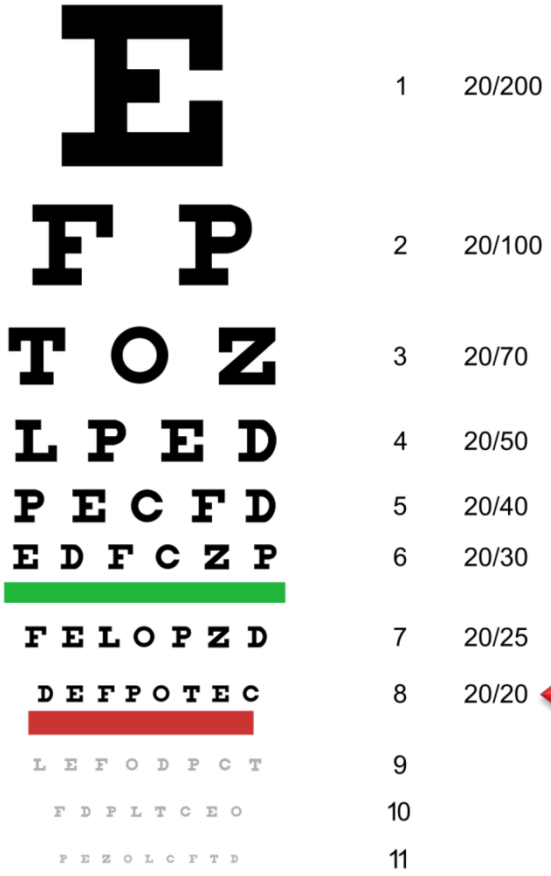


With glasses (BCDVA)
Mean logMAR 0.01 (20/20)

Without glasses (UCDVA)
20/32 or better (85.7%)

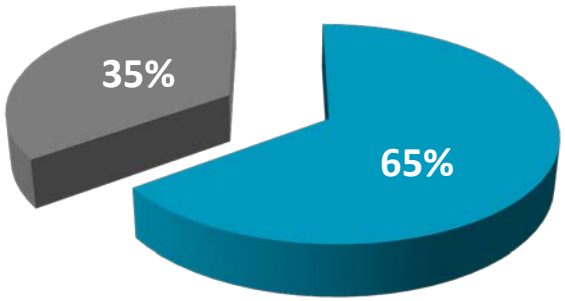
UCDVA Within 1 Line of BCDVA—Form 4 (120 - 180 Days)

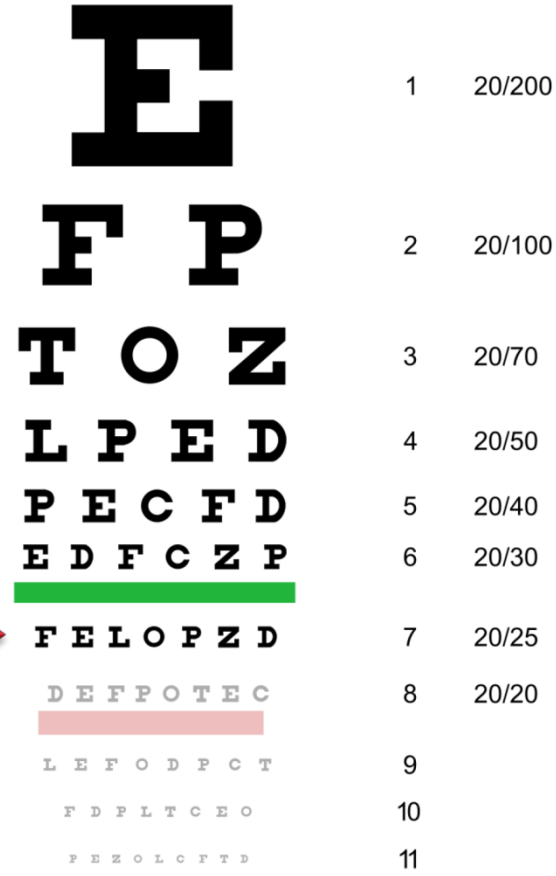
Study 650—Effectiveness Cohort, All Toric



All Toric IOL	
Within 1 line (paired analysis)	**64.7%**

UCDVA vs BCDVA within 1 line



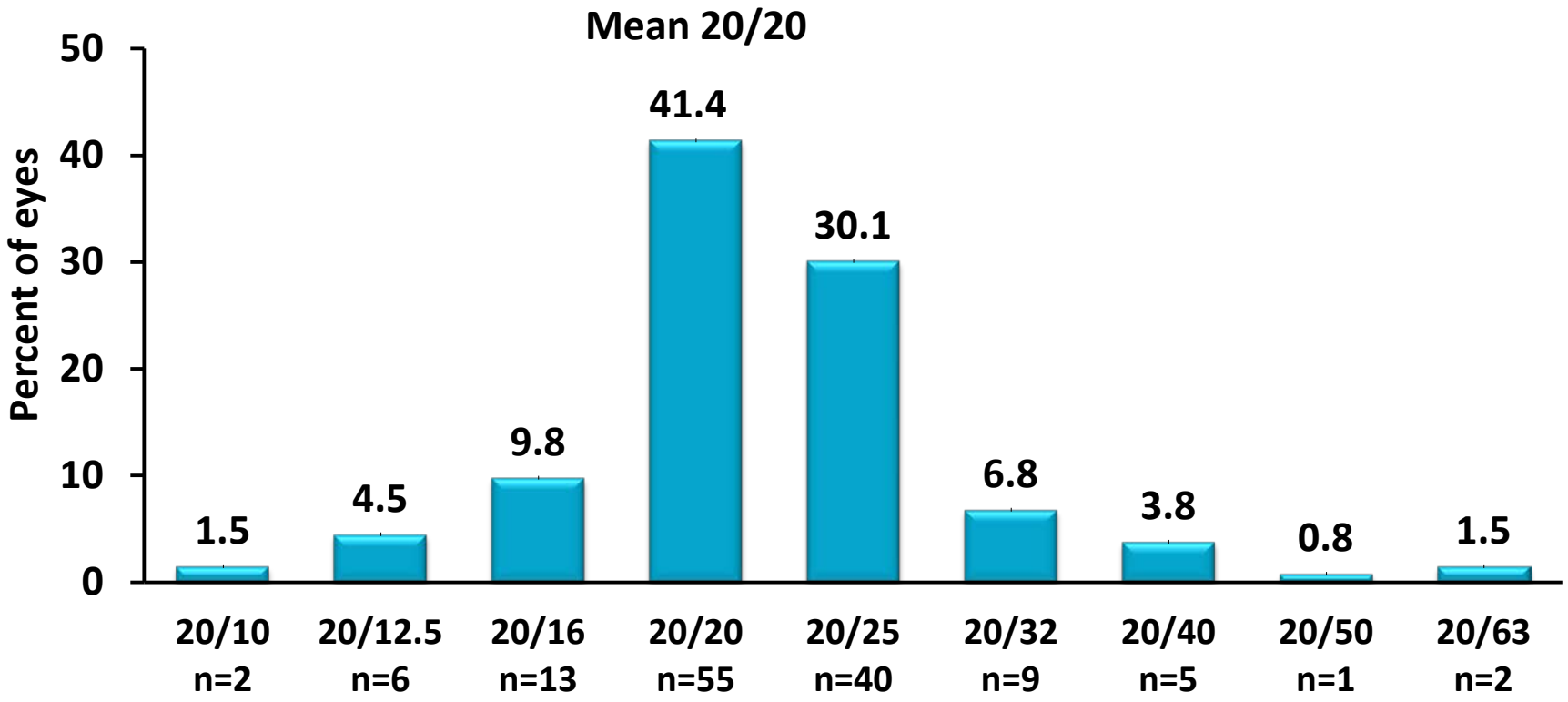


With glasses (BCDVA)
Mean logMAR 0.00 (20/20)

Without glasses (UCDVA)
20/25 or better (71.4%)

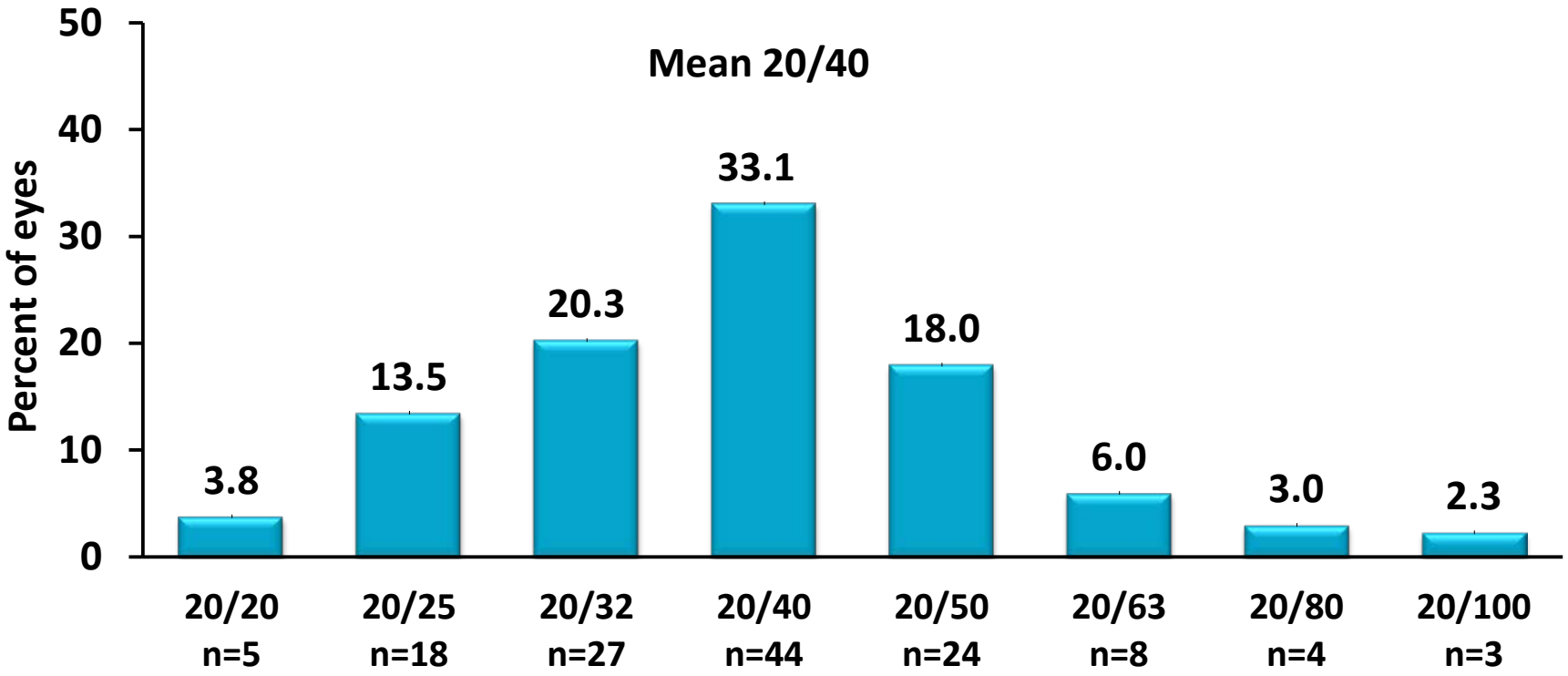
Uncorrected Intermediate Visual Acuity (UCIVA)—Form 4 (120 - 180 Days)

Study 650—Effectiveness Cohort, All Toric



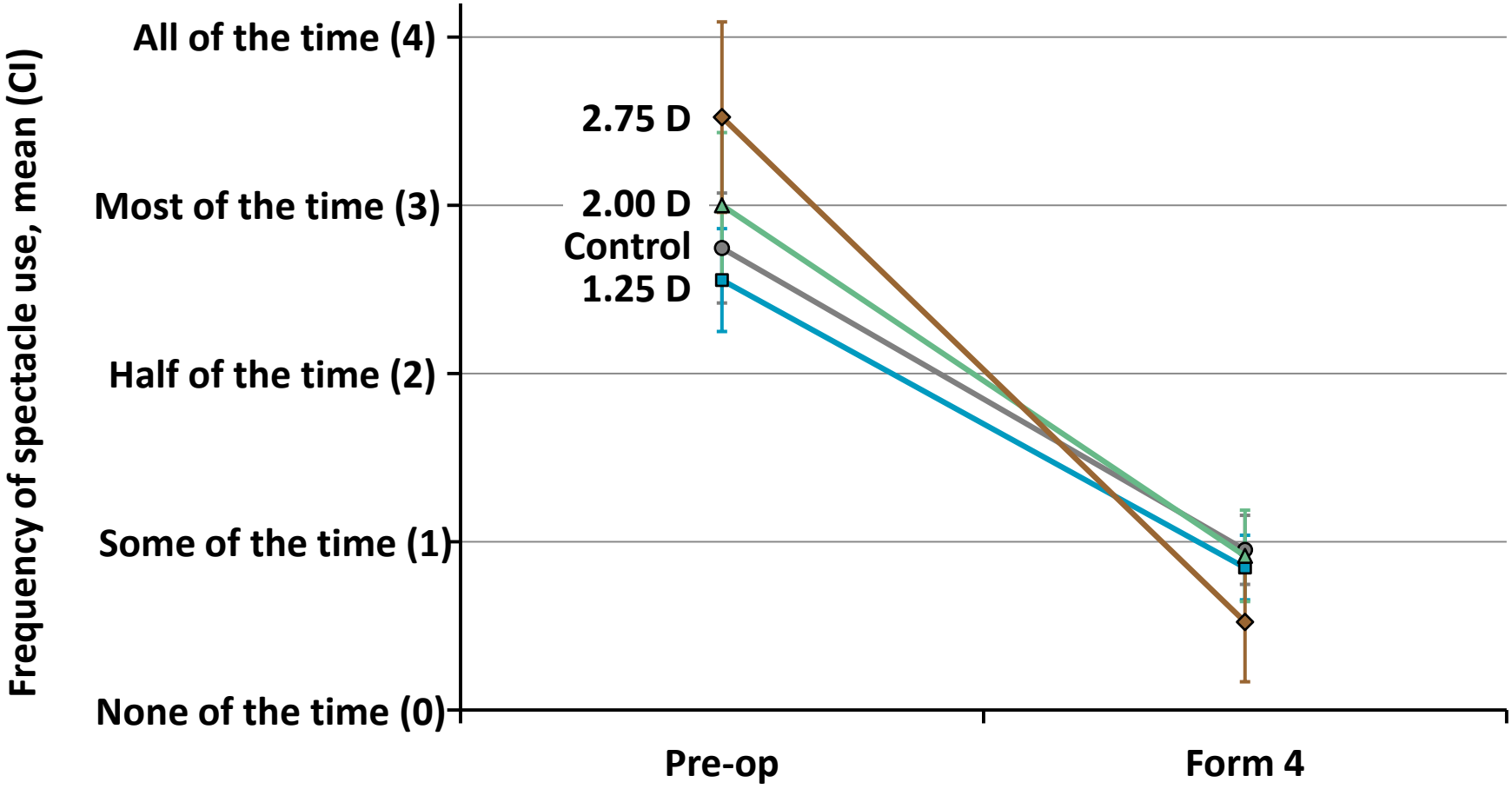
Uncorrected Near Visual Acuity (UCNVA)—Form 4 (120 - 180 Days)

Study 650—Effectiveness Cohort, All Toric



Change in Spectacle Use—Preop to Form 4 (120 - 180 Days)

Study 650—Effectiveness Cohort



Real-World Examples of Visual Acuity at Near

20/200

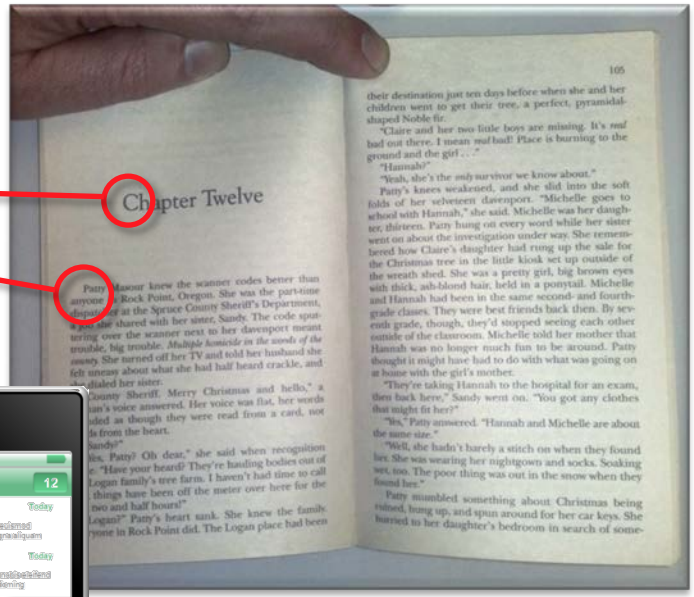
20/160

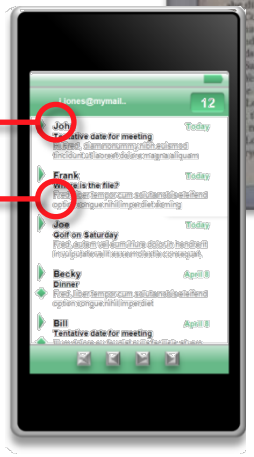
20/80

20/63

20/50

20/40





Correlates to MN Read Card at 16” (40 cm)

Refractive Correction with Cataract Surgery

- **“Would you like to reduce your need for eyeglasses?”**

Intraocular Lens Options

- Monovision
  - Can be great for an experienced contact lens wearer
  - May have reduced stereopsis or need driving glasses
- Multifocal IOLs
  - High degree of freedom from glasses
  - Compromised contrast sensitivity, dysphotopsia
  - Contraindicated in macular degeneration, glaucoma, etc.
- Trulign™ Toric Accommodating IOL
  - Superior distance and intermediate visual acuity
  - No compromise on quality of vision
  - Functional near vision

Trulign™ Toric Accommodating IOL—Clinical Considerations

- No new risks introduced by adding a toric optic
  - Current risks already well known and understood
    - Cataract/IOL surgery in general
    - Parent platform – over 10 years experience
- Increased benefits from correcting astigmatism
  - Superior uncorrected distance vision
  - Reduced need for secondary surgical procedures for residual astigmatism
- Enhanced quality of life

Trulign™ Toric Accommodating IOL

- **Thank you**

Trulign™ Toric Accommodating IOL

Safety	• Meets ISO Standards/FDA Grid
Effectiveness	• Meets all endpoints
	• Mean UCDVA 20/25, p=0.004, p<0.001 • 85.8% reduction of cylinder, p<0.001 • 79.7% and 95.5% within 0.50 and 1.00 D of intended • <0.50 D mean residual cylinder, p<0.001
	• Objective measurements of axial movement • Clinical comparisons to non-accommodative IOLs • Mean minimal required spectacle Add 1.43 D
	• 84.2% UCDVA within two lines of BCDVA • 64.7% UCDVA within one line of BCDVA • Mean UCDVA 20/25, UCIVA 20/22, UCNVA 20/40

A Lens That Addresses Cataract, Corneal Astigmatism, and Presbyopia