

The Role of Corneal Cross Linking in LVC

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What Is Corneal Cross-Linking?

- Collagen cross-linking (CXL) using UVA light and riboflavin (vitamin B2)
- Stabilizes the cornea by inducing cross-links within and between collagen fibers
- CXL has been investigated extensively and has been shown clinically to arrest the progression of **Keratoconus** or **post-LASIK ectasia**

Background : CXL

- Collagen I is the major macromolecular constituent of the corneal stroma (Types III, V, AND VI also represented)
- Light transmission through the cornea is the result of a particular, cornea-specific arrangement of collagen fibrils.
- Corneal collagen uniquely forms small (32 nm), uniformly spaced fibrils
- Organized as larger bundles or fibers (termed corneal lamellae) of varying thickness (1-2 μm) and width (5–100 μm) that are arranged in interweaving orthogonal layers throughout the stroma

Background: CXL cont'd

- Collagen is synthesized by keratocytes in the form of its precursor molecule, called procollagen
- Specialized enzymes known as procollagen proteinases process the procollagen into fibrils and form fibers in the extracellular space
- This process involves the enzyme lysyl oxidase and results in oxidation of the amino acids lysine and hydroxylysine into their respective aldehydes, which condense with other aldehydes to form intra- and intermolecular cross-links.

Background: CXL cont'd

- Another mechanism influencing the strength of the fibers involves non-enzymatic glycation
- This phenomenon is related to the reduced metabolic turnover of collagen and occurs through the reaction of collagen with glucose and its oxidation products
- Hence Keratoconus progression slows with age and is uncommon in diabetic patients related to collagen cross-linking via non-enzymatic glycation

Mechanism of CXL

- Riboflavin (B2) is an essential constituent of living cells and is non-cytotoxic
- It acts as photo-mediator, considerably increasing the absorption of UVA light on exposure to corneal stroma
- Following exposure, riboflavin is excited into a triplet state
- Generating reactive oxygen species: singlet oxygen and superoxide anions then react with available groups nearby.
- Creating additional chemical bonds between histidine, hydroxyproline, hydroxylysine, tyrosine, and threonine amino-acid residues

Preventive Indications for CXL

- Provides an extra safety element for thin or marginal corneas, or high degrees of correction necessitating a greater amount of tissue removal
- High risk of corneal instability or ectasia after LASIK or PRK
- High myopic and hyperopic pts who have a greater tendency to regress
- Young patients, especially women of child bearing age, with high correction or high astigmatism and anisometropia may also be higher risk
- Those with worrisome, but not frankly contraindicative, topography
- Strengthening the cornea with concurrent CXL may be beneficial for the long-term stability of the refractive result and ultimate predictability of the procedure

Why FemtoSBK ?

- “Best of both worlds” per Dr. John Marshall PhD
- PRK downside is the well-known problems of haze and pain
- In LASIK, there is no haze and no pain, but biomechanically it can result in an unstable system
- SBK cut at around 40 microns below Bowman’s membrane removes only about 10 – 14 per cent of the total strength
- Studies show earlier visual recovery with sub-Bowman’s Keratomileusis

Advantages of FemtoSBK Xtra

- FemtoSBK Xtra (SBK with CXL) may improve the long-term stability and ultimate predictability of the procedure
- Dr. Jerry Tan (Singapore) compared 72 highly myopic eyes (> -8.00 D) treated with adjunctive CXL and 62 eyes that underwent LASIK alone
- Predictability and visual acuity results were found to be better in the combined treatment group

- Tan J, Lytle GE, Marshall J. Consecutive laser in situ keratomileusis and accelerated corneal crosslinking in highly myopic patients: preliminary results. Eur J Ophthalmol. 2014;5:0.

FemtoSBK Xtra Studies

- Kanellopoulos compared LASIK Xtra (65 eyes) to standard LASIK (75 eyes) for high myopic corrections (mean correction, -6.00 D)
- Combined treatment group, 91% of eyes achieved a distance UCVA of 20/20 or better, and 95% achieved a distance UCVA of 20/25 or better
- LASIK only group, 85% of eyes achieved a distance UCVA of 20/20 or better, and 89% achieved a distance UCVA 20/25 or better

Kanellopoulos AJ, Asimellis G. Epithelial remodeling after femtosecond laser-assisted high myopic LASIK: comparison of Stand-alone with LASIK combined with prophylactic high-fluence cross-linking. *Cornea*. 2014;33:463-469.

Tamayo GE. Predictable visual outcomes with accelerated corneal cross-linking concurrent with laser in situ keratomileusis. *J Cataract Refract Surg*. 2012;38(12):2206

Hyperopic FemtoSBK Xtra

- Hyperopes of greater concern with regression
- Epithelial remodeling and hyperplasia over the area of ablation
- Regression may be related to biomechanical changes induced by the mid-peripheral tissue removal of the hyperopic ablation
- Kanellopoulos found mean regression from treatment of $+0.22 \pm 0.31$ D in eyes with Xtra, whereas eyes that underwent LASIK alone showed greater regression of $+0.72$ D, suggesting a benefit of LASIK with adjunctive CXL for this population

- Kanellopoulos AJ, Khan J: Topography-guided hyperopic LASIK with and without high irradiance collagen cross-linking: Initial comparative clinical findings in a contralateral eye study of 34 consecutive patients. J. Refract. Surg. 2012;28 (11 suppl):S837-40.

Summary FemtoSBK Xtra

- FemtoSBK Xtra is designed to increase surgical safety and refractive stability in eyes that have thin corneas or require high degrees of correction
- SBK Xtra may be particularly beneficial for hyperopia and certain forms of astigmatism, increasing the long-term stability of the refractive result
- Our experience has been that there is no nomogram adjustment needed when the procedure is combined with CXL nor is there any increased risk of infection, inflammation, and corneal haze

Prescriptive Indications for CXL without LVC: Keratoconus

- Decreased corneal rigidity in keratoconus has been attributed to reductions in collagen cross-links and in molecular bonds between neighboring stromal proteoglycans
- Cross-link induction in the corneal stroma by photo polymerization was proposed as a means of stiffening the cornea and hence of slowing disease progression
- By actively increasing the degree of covalent bonding between and within the molecules of extracellular matrix, such as collagen type I and proteoglycans, therapeutic cross-linking enhances corneal rigidity and slows or even arrests the progression of keratoconus and ectasia disorders

Topography Guided PRK with CXL

- CXL in combination with a topography-guided laser treatment in the case of frank keratoconus
- The object is to halt or decrease the progression of keratoconus via CXL, and reduce the irregularity and asymmetry of the corneal optics with topography-guided PRK
- Kanellopoulos and colleagues reported improved distance BCVA and UCVA in 27 of 32 eyes after combined CXL and PRK
- Same-day CXL combined with topography-guided PRK was superior to sequential procedures for visual rehabilitation

Kanellopoulos AJ, Binder PS. Management of corneal ectasia after LASIK with combined, same-day, topography-guided partial transepithelial PRK and collagen cross-linking: the athens protocol. J Refract Surg. 2011;27:323-31

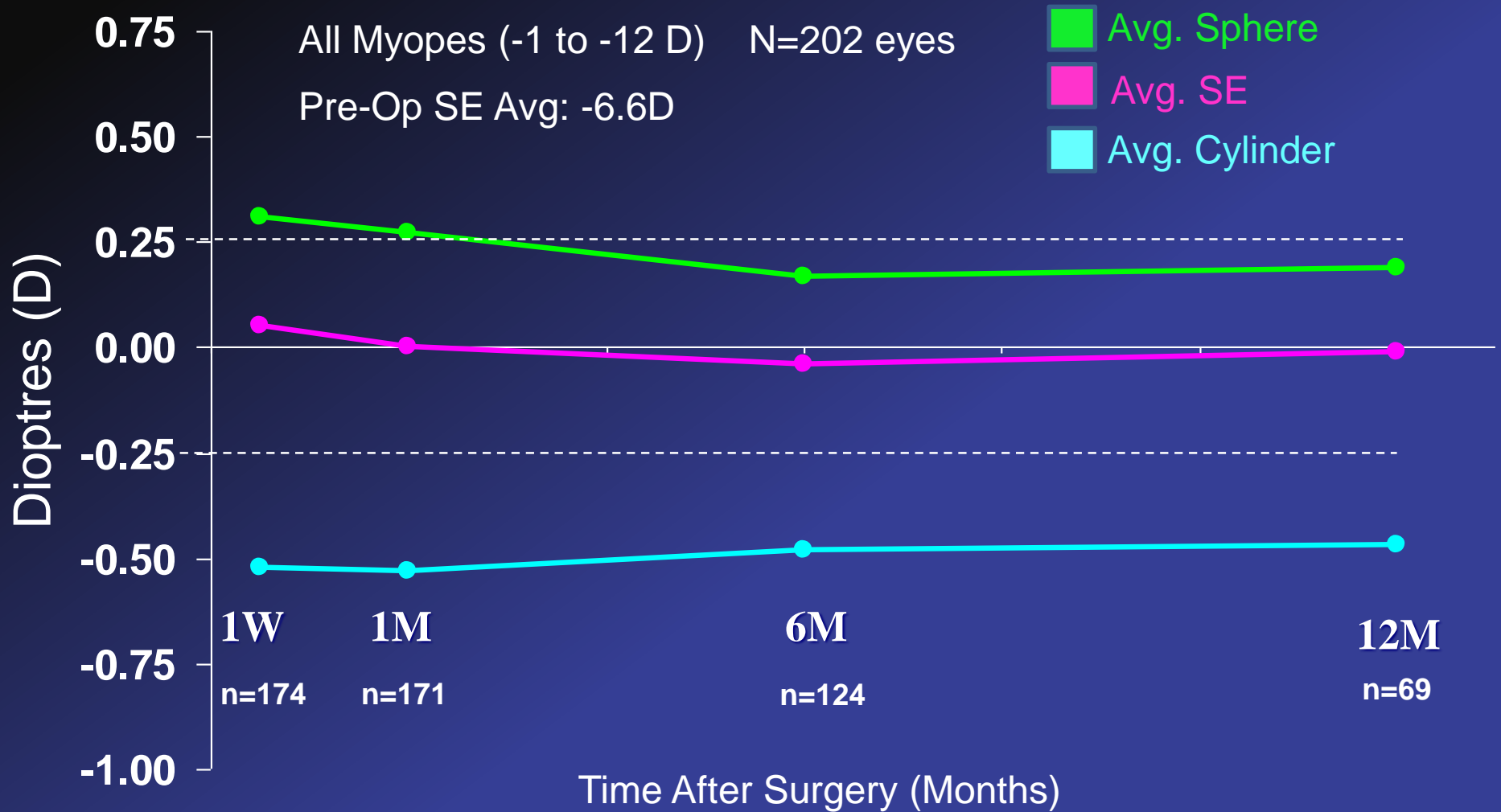
Limited PRK with CXL

- Reduces corneal irregularity caused by Keratoconus or other ectatic condition
- Improves the refractive error to enable better contact lens fitting/ glasses
- Is NOT a full refractive correction, limited by the patient's corneal thickness

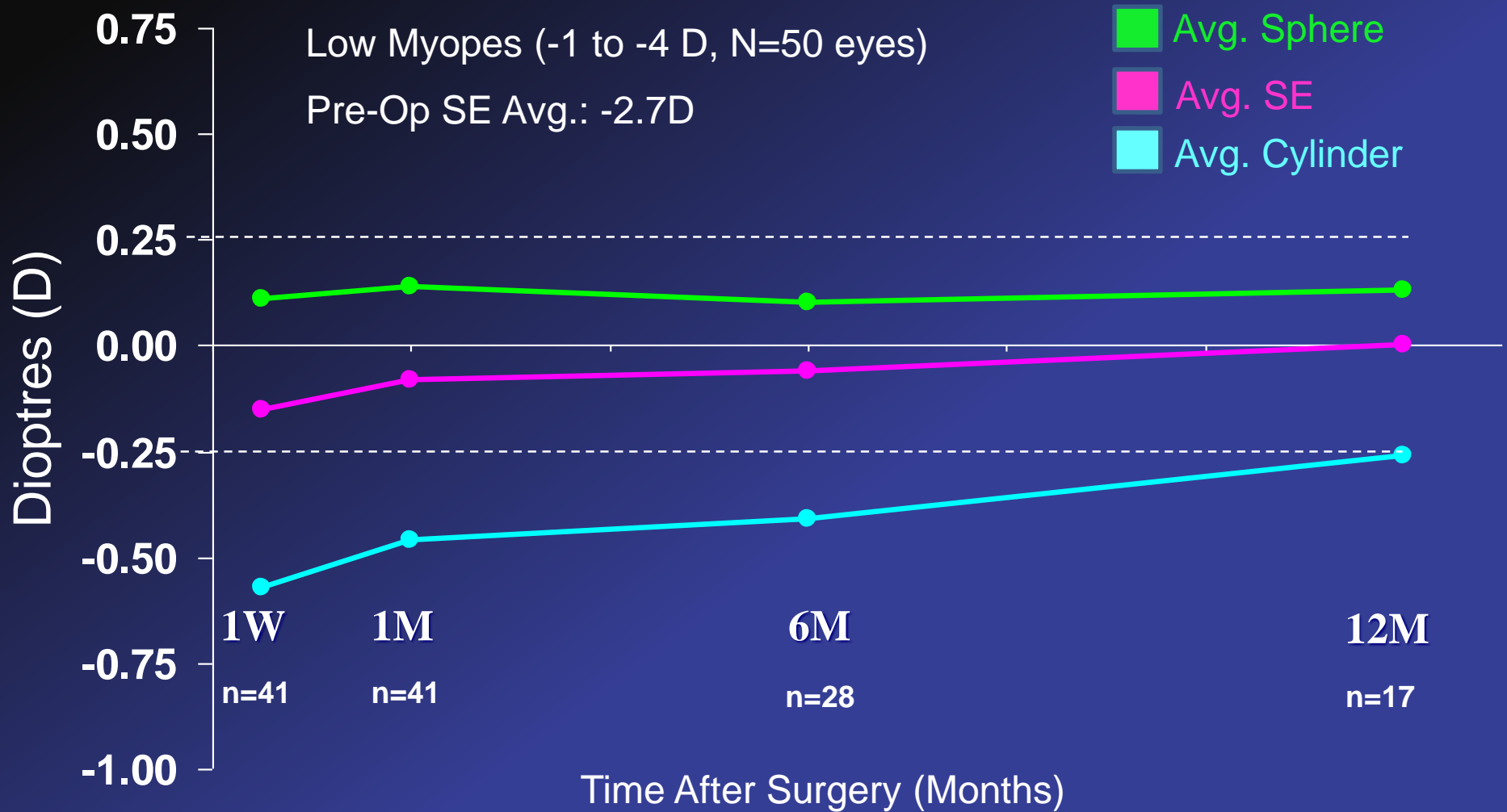
Calgary Focus Eye Centre Data Analysis: SBK Xtra



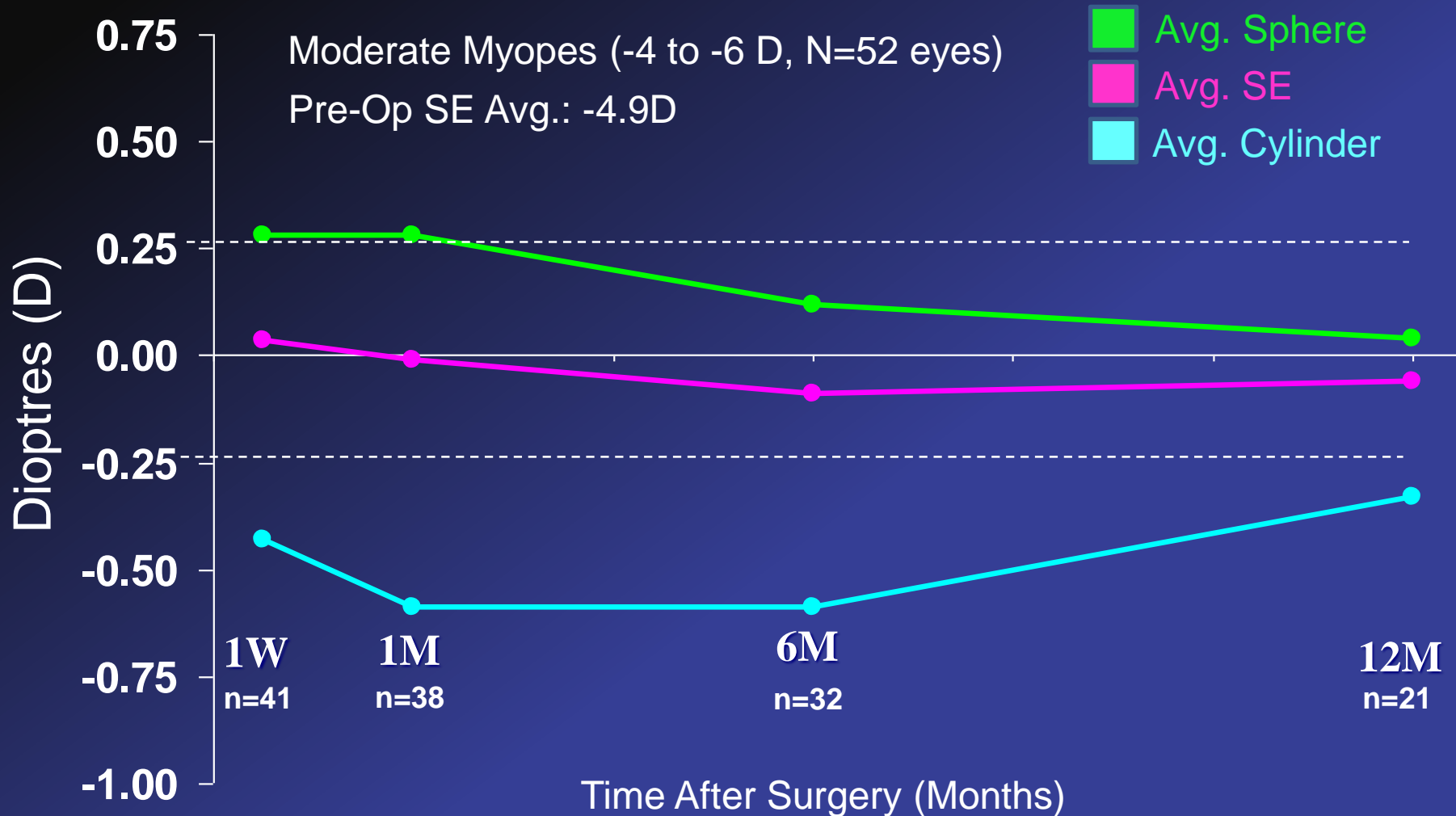
Avg Sph & Cyl (D) over Time



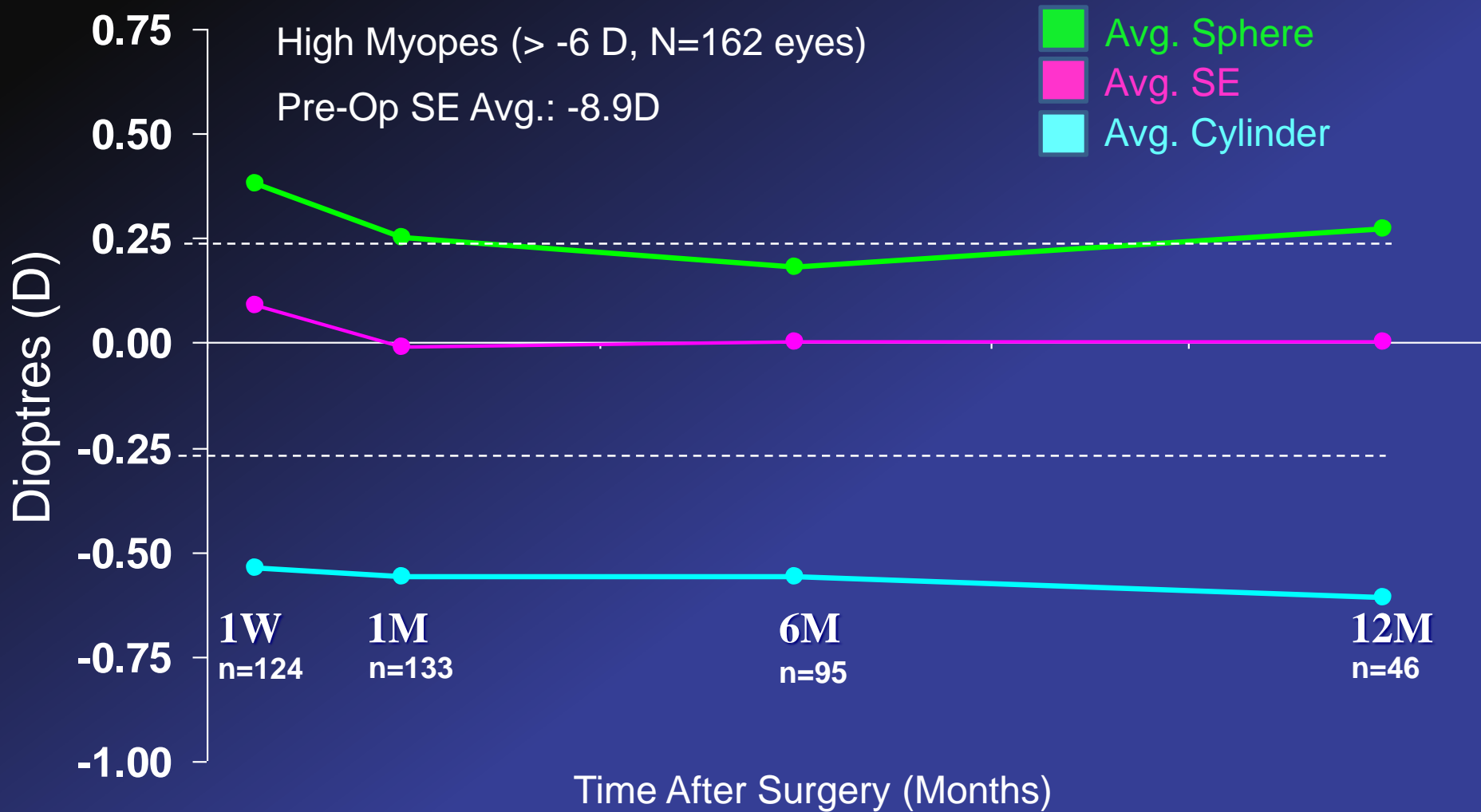
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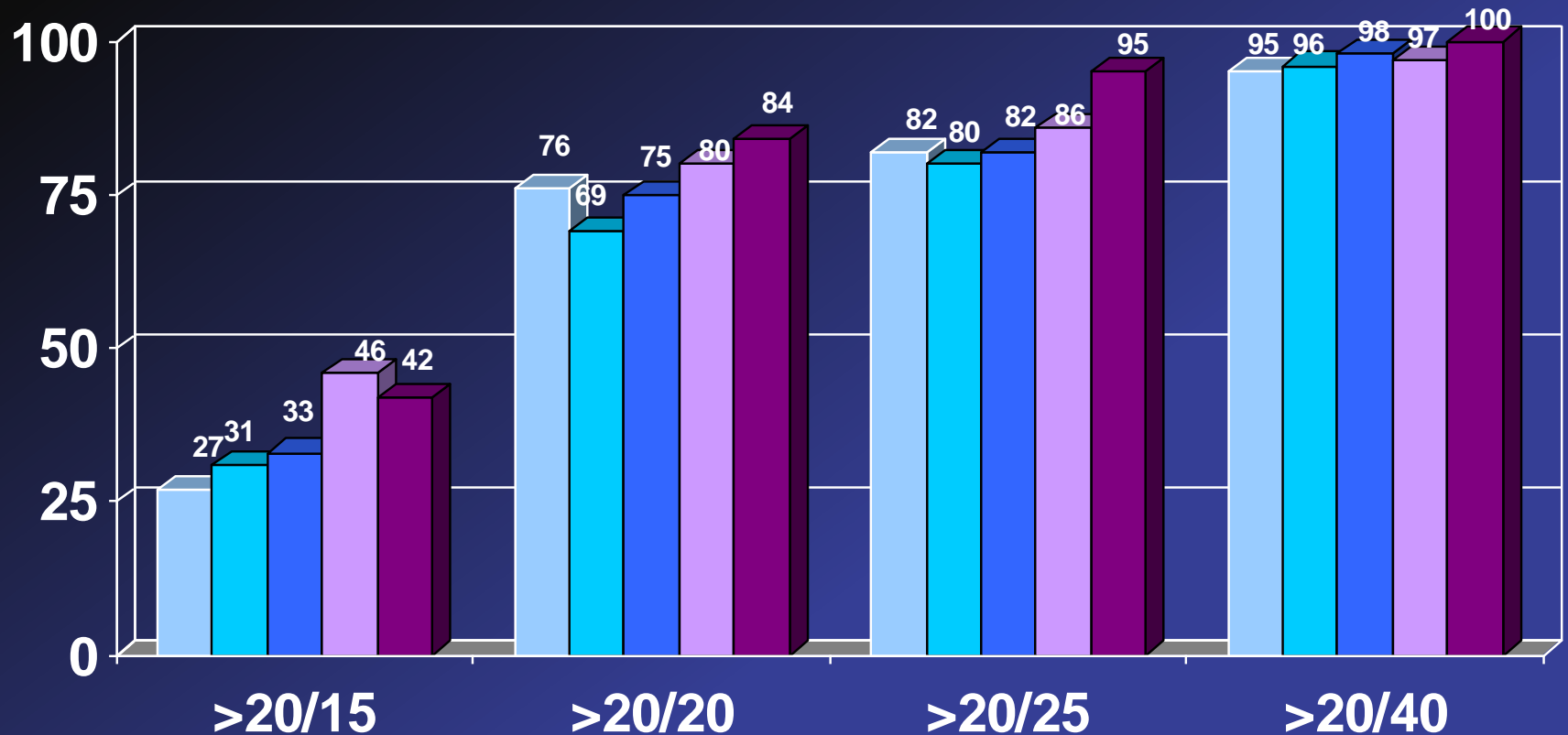
Avg Sph & Cyl (D) over Time



Avg Sph & Cyl (D) over Time



SBK Xtra UCVA (-1 to -4D SE)



1 Day 1 Week 1 Month 6 Months 1 Year

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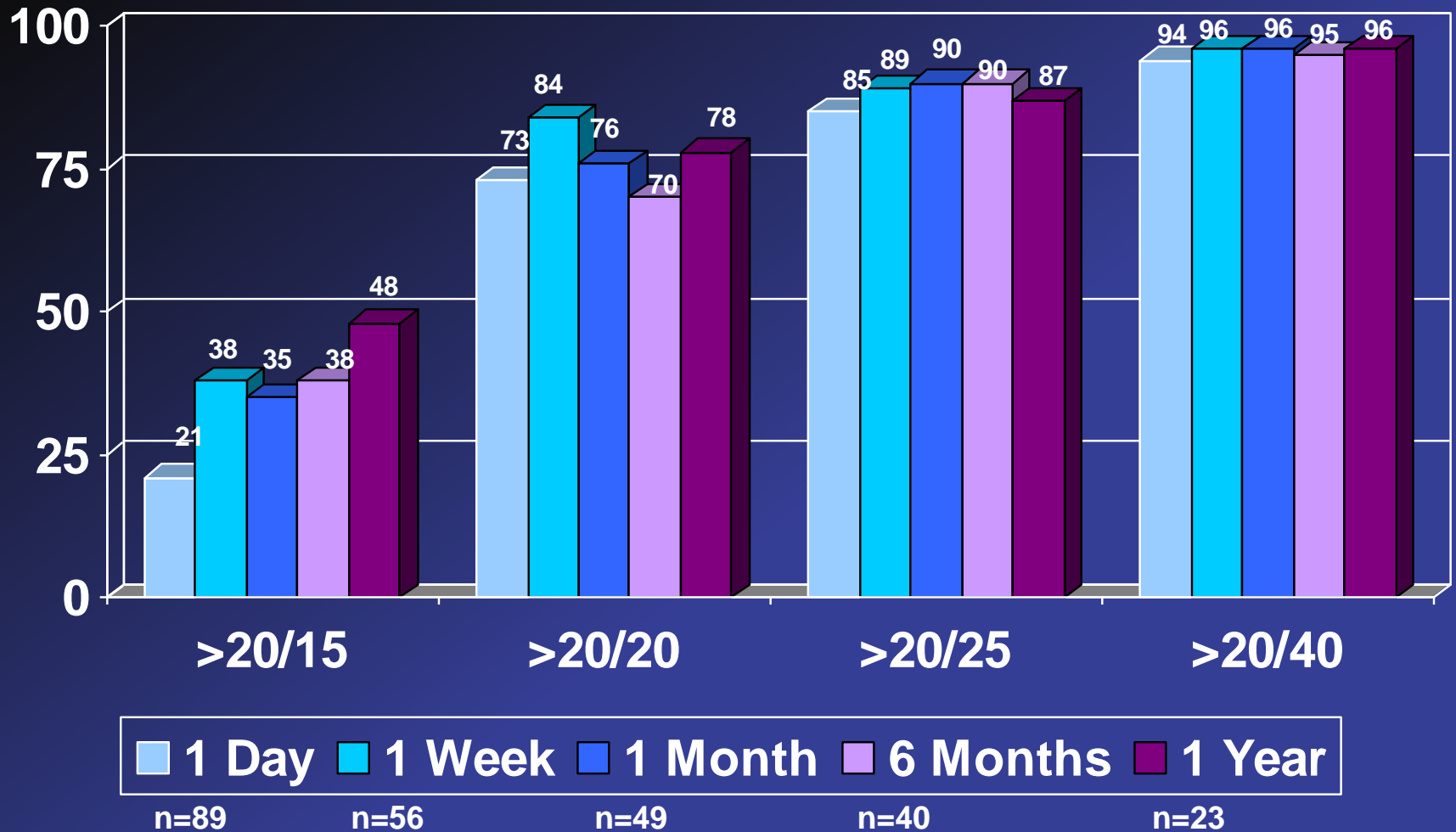
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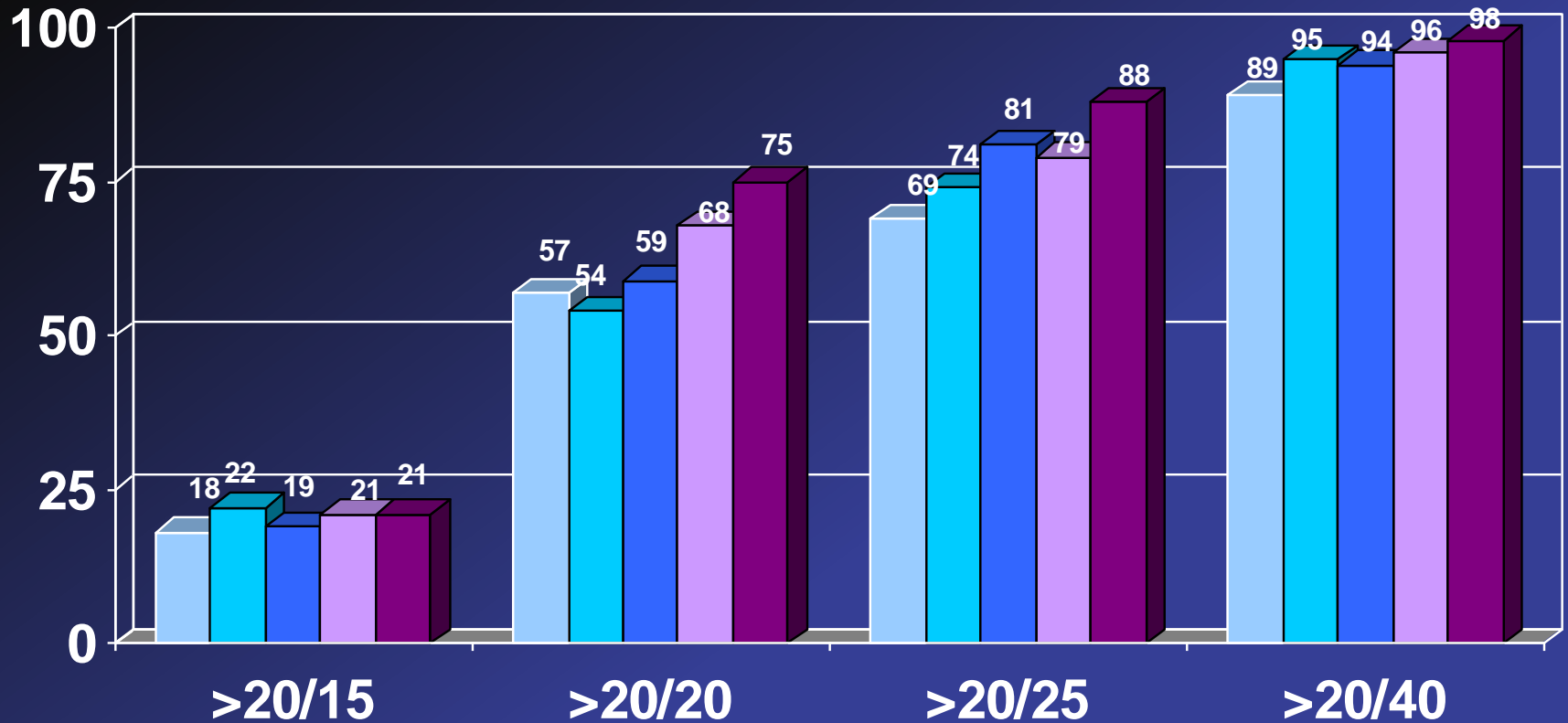
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SBK Xtra UCVA (-4 to -6D SE)



SBK Xtra UCVA (>-6D SE)



1 Day 1 Week 1 Month 6 Months 1 Year

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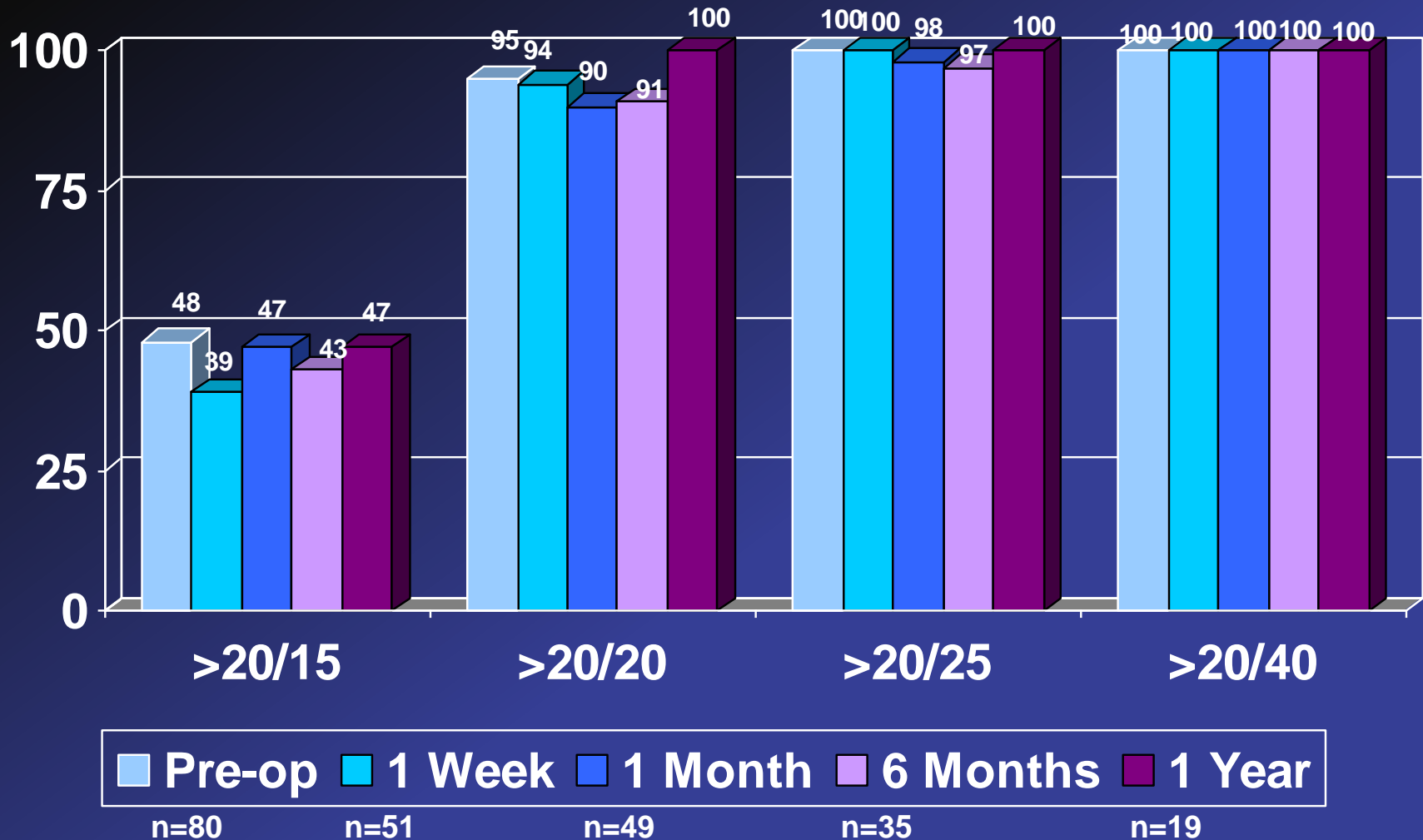
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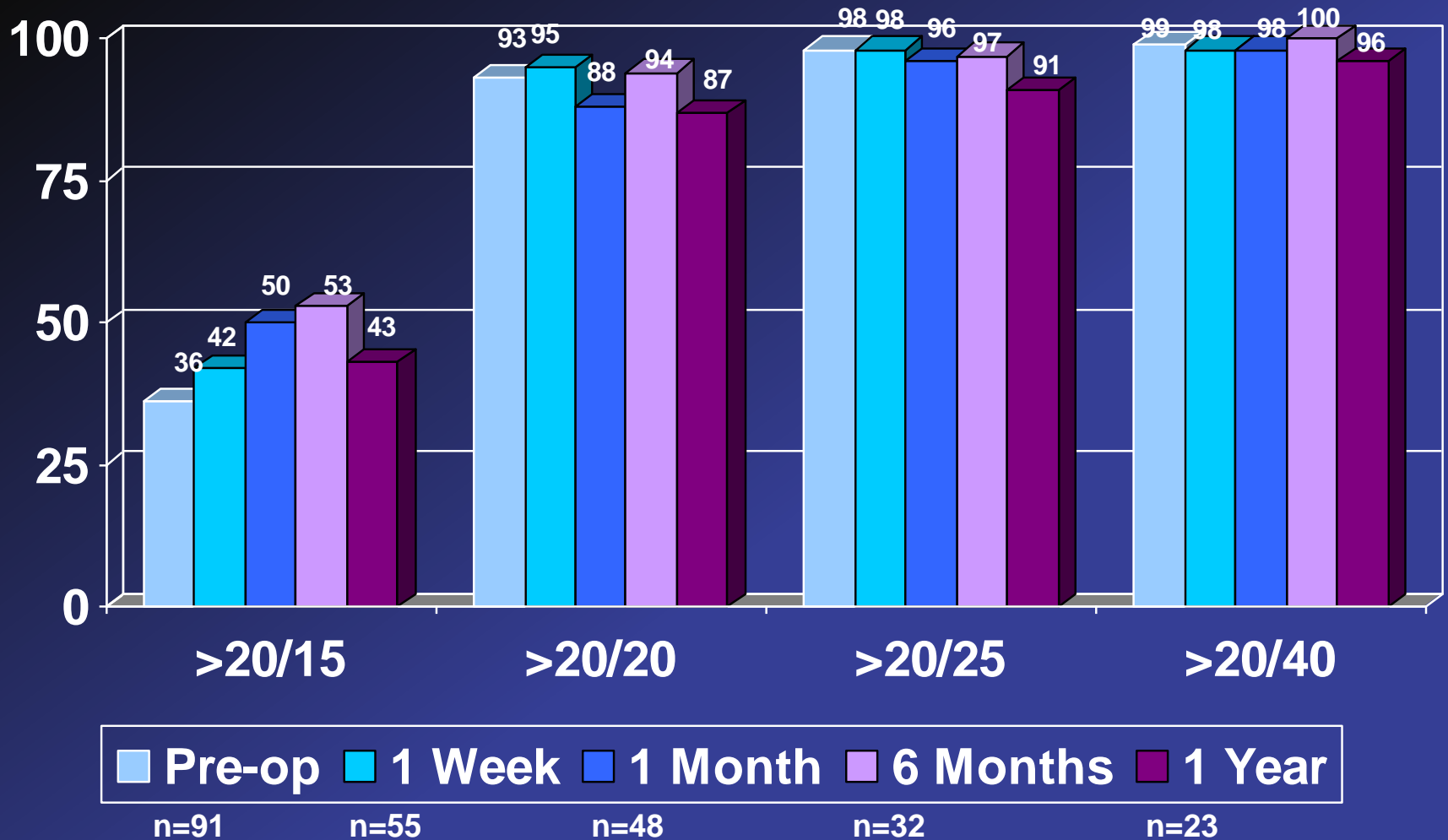
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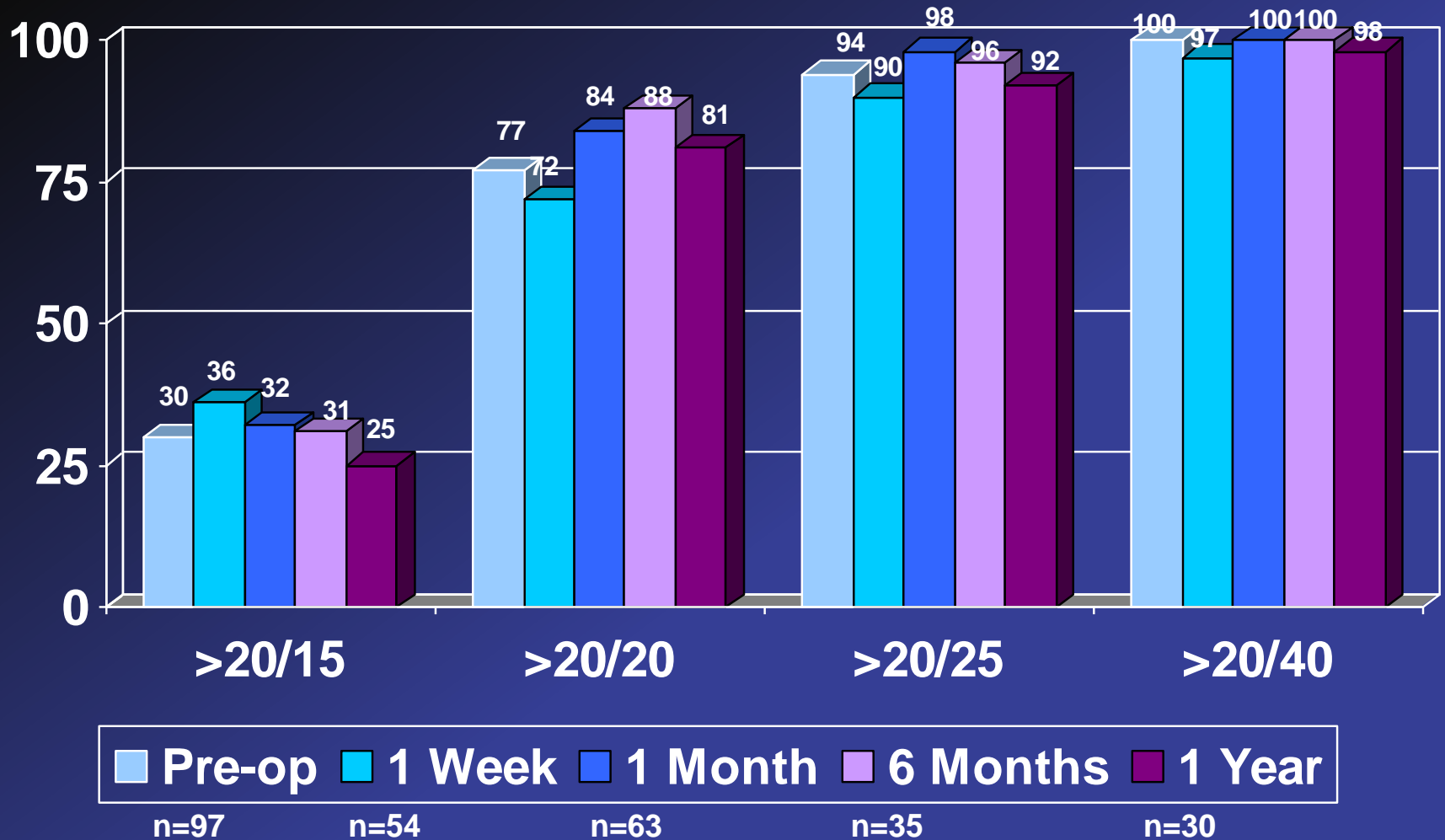
SBK Xtra BCVA (-1 to -4D SE)



SBK Xtra BCVA (-4 to -6D SE)



SBK Xtra BCVA (>-6D SE)



Thank you!