Accelerated versus Standard Corneal Collagen Cross-linking in Pediatric Keratoconus Patients: 24 Months Follow-up Results

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Pediatric Keratoconus

- Negative prognostic factor
- 27.8% of patients are at an advanced stage at the time of diagnosis*
- Aggressive progression if left untreated, 88%**
- Waiting for confirmation of progression is not essential
- Corneal collagen cross-linking (CXL) should be performed as soon as a diagnosis of keratoconus has been made

*Léoni-Mesplié S, Mortemousque B, Touboul D, et al. Scalability and severity of keratoconus in children. Am J Ophthalmol 2012; 154: 56-62.

**Chatzis N, Hafezi F. Progression of keratoconus and efficacy of pediatric [corrected] corneal collagen cross-linking in children and adolescents. J Refract Surg 2012; 28: 753-758.

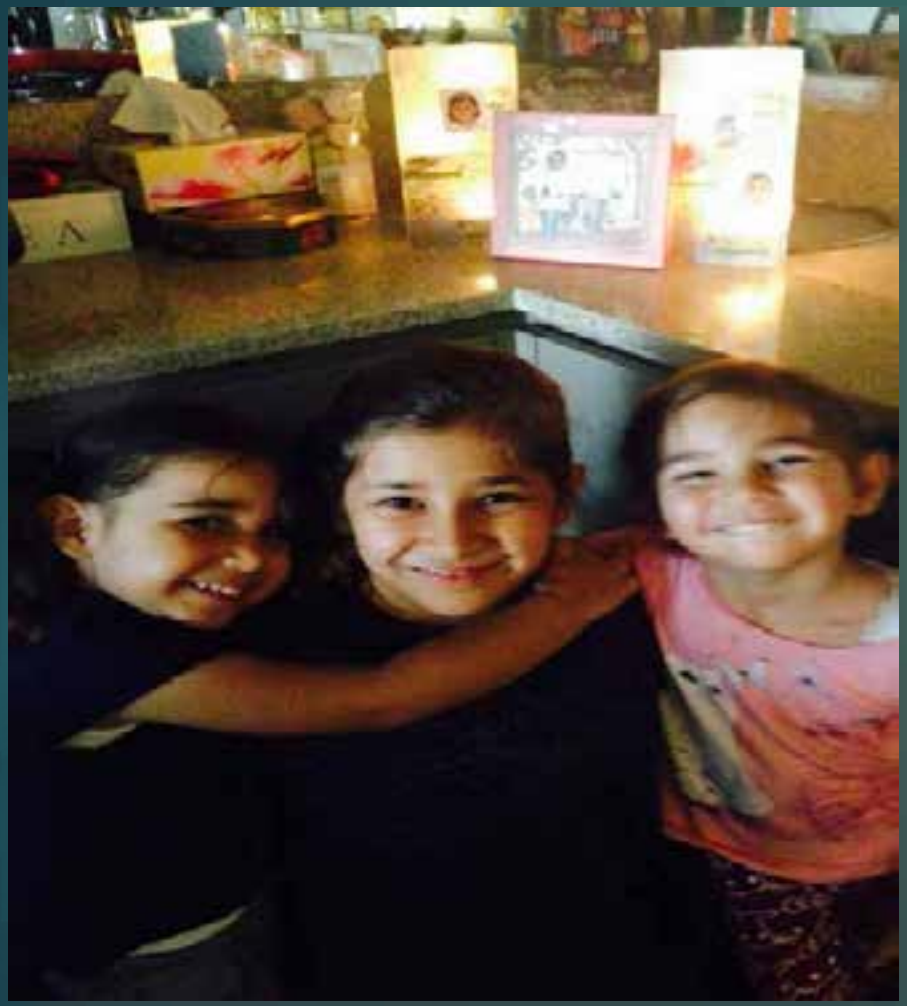
Pediatric Keratoconus-CXL

- Dresden protocol (Standard)
  - 30 minutes riboflavin, 30 minutes UVA (3mW/cm^2)
  - 5.4J/cm^2 total dose
  - Long surgical time
- Accelerated (ACC-CXL)
  - introduced in recent years
  - higher irradiance to shorten treatment duration

Accelerated-CXL

- Bunsen–Roscoe laws of reciprocity
  - *All photochemical reaction processes depend only on the total absorbed energy that is determined by radiant intensity and exposure time*
- Greater UVA irradiance intensity with lower total exposure time when compared to standard protocol
- Constant radiant exposure of 5.4 J/cm^2

Accelerated-CXL



Purpose

- To compare the 24-month clinical and topographical results of accelerated (9 mW/cm^2 for 10 minutes) and standard (3 mW/cm^2 for 30 minutes) CXL treatments in pediatric keratoconus patients.

Methods

- Retrospective
- Keratoconus Center, Ankara Ataturk Training and Research Hospital
- Consecutive keratoconus patients <18 y.o.
- Follow-up: 24 months

Methods

Exclusion criteria

- >18 years old
- Corneal thickness < 400 µm
- Presence of any central or paracentral corneal scar
- History of herpetic keratitis, active ophthalmic inflammation or infection prior to CXL
- Follow-up < 24 months

CXL procedures

- Topical or general anesthesia
- The corneal epithelium was removed mechanically, 8.5 mm zone after loosening the corneal epithelium with 20% alcohol solution
- 0.1% riboflavin in 20% dextran T500 solution (Meran, Istanbul)

Methods

Treatment Parameters of the Standard and Accelerated CXL Procedures

	Intensity (mW/ cm^2)	Treatment Time (min)	Dose (J/cm^2)
Standard CXL	3	30	5.4
Accelerated CXL	9	10	5.4

Methods

- Main Outcome Measures (Pre-CXL, 6, 12, and 24 months after CXL
- Uncorrected (UCVA) and best corrected visual acuity (BCVA)
- Spherical equivalent (SE), topographical cylinder (topoCYL)
- K1, K2, and maximum K (Kmax)
- Thinnest corneal pachymetry (ThCT)
- Slit-lamp examination
- Progression (Increase in Kmax≥1D 24 months after CXL)
- Sirius 3D rotating Scheimpflug camera and topography system (CSO, Italy)

Results

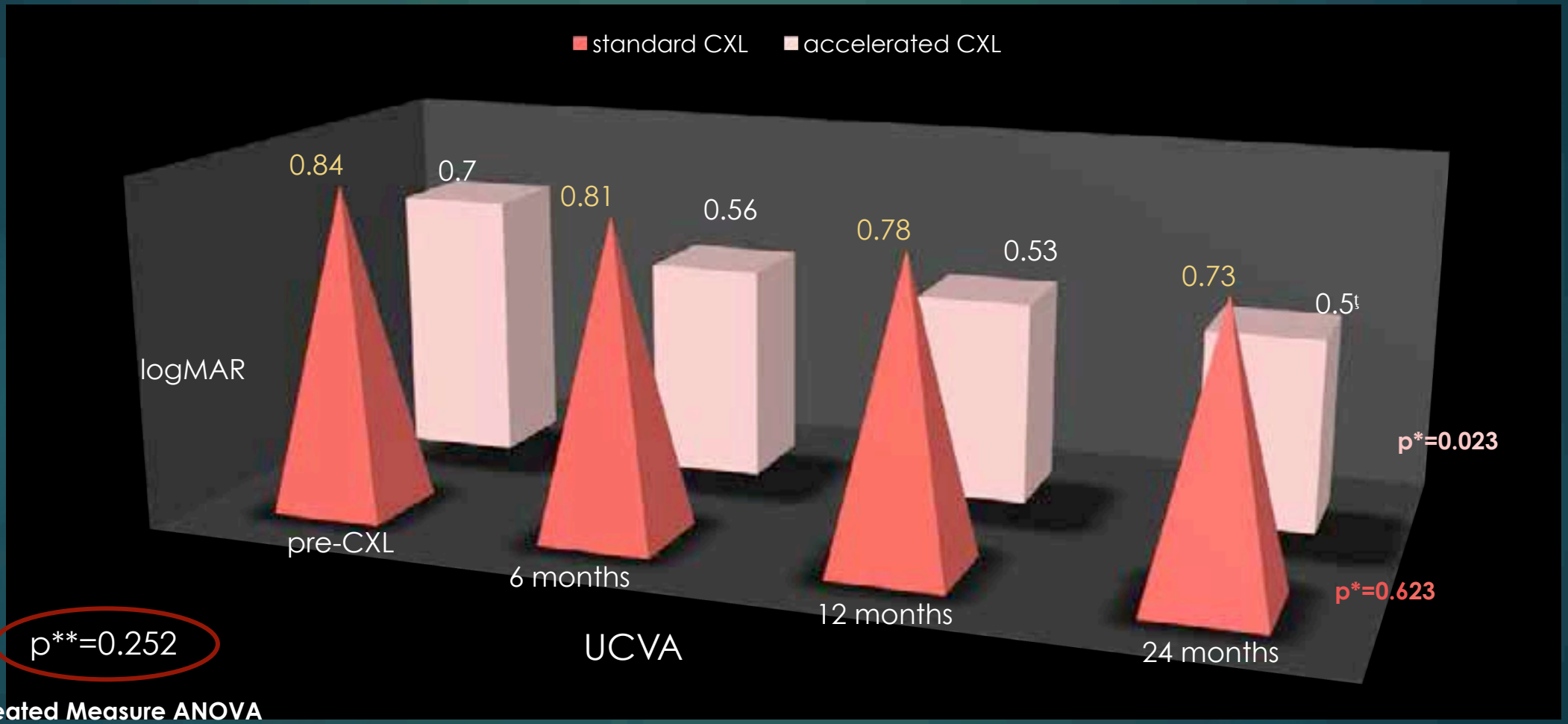
#	Standard CXL	Accelerated CXL
Patients	29	35
Eyes	38	49

Results

Baseline Demographic, Clinical and Topographic Parameters

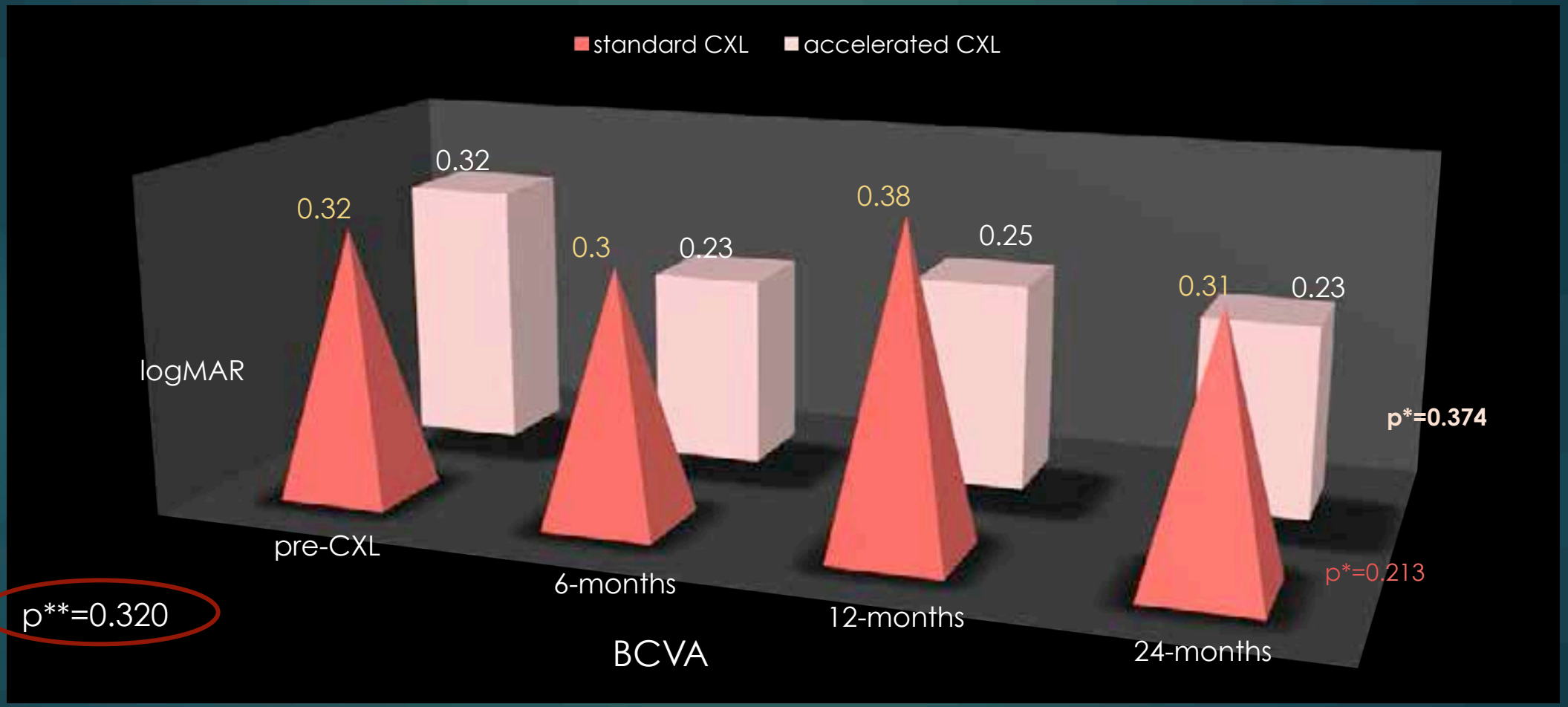
	Standard CXL	Accelerated CXL	p
Age (years)	15 (11-17)	14.9 (10-18)	0.896
Sex (M:F)	8:21	10:25	0.519
UCVA (logMAR)	0.84±0.46	0.70±0.46	0.185
BCVA (logMAR)	0.32±0.21	0.32±0.32	0.921
SE (D)	-4.0±2.44	-3.84±2.33	0.783
Topo-CYL (D)	-4.17±1.56	-3.4±1.64	0.098
K1 (D)	46.96±3.61	46.42±3.41	0.482
K2 (D)	51.15±4.11	49.80±3.96	0.131
Kmax (D)	58.74±4.04	56.71±5.53	0.062
ThCT (µm)	438±5	448±5	0.318

Changes in Mean UCVA between pre-CXL and 24 months post-CXL



Repeated Measure ANOVA
0.011, difference between pre-CXL and 24 months post-CXL, Repeated Measure ANOVA, Post Hoc test
value was obtained by comparing the changes in the UCVA from pre-CXL to 24 months post-CXL between the two
ups, Independent Samples T Test

Changes in Mean BCVA between pre-CXL and 24 months post-CXL



p* Repeated Measure ANOVA

p** value was obtained by comparing the changes in the BCVA from pre-CXL to 24 months post-CXL between the two groups, Independent Samp Test

Accelerated CXL

- UCVA: 63.3% eyes, stable or improved
- BCVA: 69.2% eyes, stable or improved
- No loss of ≥ 3 Snellen lines

Standard CXL

- UCVA: 73.3% eyes, stable or improved
- BCVA: 73.5% eyes, stable or improved
- No loss of ≥ 3 Snellen lines

Changes in Spherical Equivalent between pre-CXL and 24 months post-C

	pre-CXL	6 months	12 months	24 months	p*
Standard CXL	-4.0±2.44	-3.73±2.16	-4.01±2.72	-3.50±1.96	0.466
Accelerated CXL	-3.84±2.33	-3.89±2.72	-3.39±2.3	-3.56±2.05	0.054

p**=0.968

p* Repeated Measure ANOVA

p**value was obtained by comparing the changes in the SE from pre-CXL to 24 months post-CXL between the two groups, Independent Samples T Test

Changes in Topo-CYL value between pre-CXL and 24 months post-CXL

	pre-CXL	6 months	12 months	24 months	p*
Standard CXL	-4.17±1.56	-4.36±1.66	-4.23±1.64	-4.15±1.56	0.136
Accelerated CXL	-3.40±1.64	-3.51±1.80	-3.42±1.91	-3.34±1.82	0.754

p**=0.853

p* Repeated Measure ANOVA

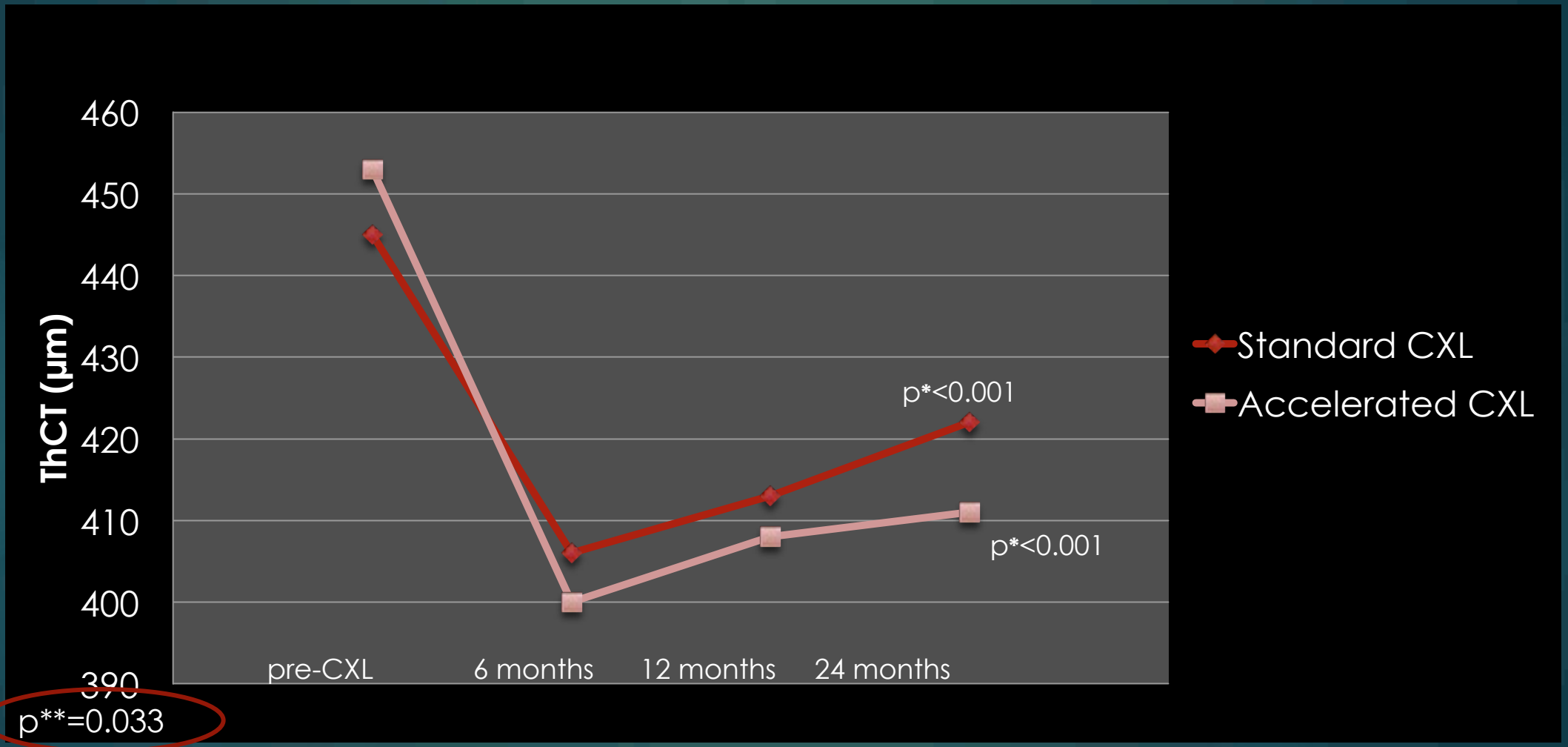
pvalue was obtained by comparing the changes in the SE from pre-CXL to 24 months post-CXL between the two groups, Independent Samples T Test**

Changes in K values between pre-CXL and 24 months post-CXL

K1	pre-CXL	6 months	12 months	24 months	p*	
Standard CXL	46.96±3.61	46.65±3.35	45.40±7.96	46.19±3.12	0.067	p**=0.5
Accelerated CXL	46.42±3.41	46.17±3.47	45.86±3.54ŧ	45.78±3.50ŧŧ	<0.001	
K2						
Standard CXL	51.15±4.11	51.33±3.80	51.06±3.54	50.89±3.40	0.064	p**=0.3
Accelerated CXL	49.80±3.96	49.38±4.23	49.36±4.16&	49.21±3.99&&	0.001	
Kmax						
Standard CXL	58.74±4.04	58.7±4.28	58.12±4.06	58.11±4.12	0.075	p**=0.4
Accelerated CXL	56.71±5.53	55.99±5.59	55.58±5.55£	55.69±6.37	0.001	

Repeated Measure ANOVA
p=0.001, difference between pre-CXL and 12 months post-CXL; ŧŧ p<0.001, difference between pre-CXL and 24 months post-CXL; & p=0.006, differe
tween pre-CXL and 12 months post-CXL, && p=0.001 difference between pre-CXL and 24 months post-CXL; £ p=0.001 difference between pre-CX
months post-CXL, Repeated Measure ANOVA, Post Hoc test
* value was obtained by comparing the data from pre-CXL to 24 months post-CXL between the two groups, Independent Samples T Test

Changes in ThCT between pre-CXL and 24 months post-CXL



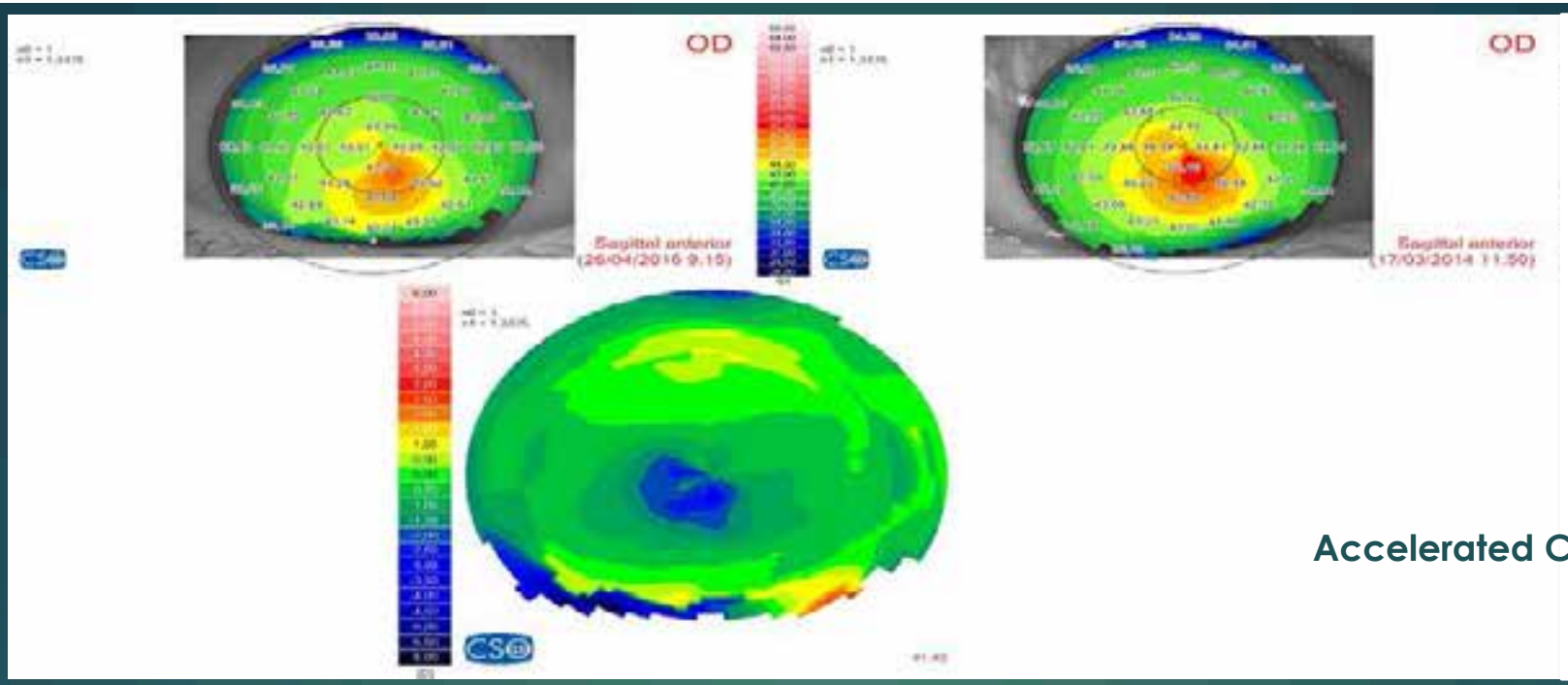
p* , Repeated Measure ANOVA

p value was obtained by comparing the changes in the thCT from pre-CXL to 24 months after CXL between the two groups, Independent Samp**
T test.

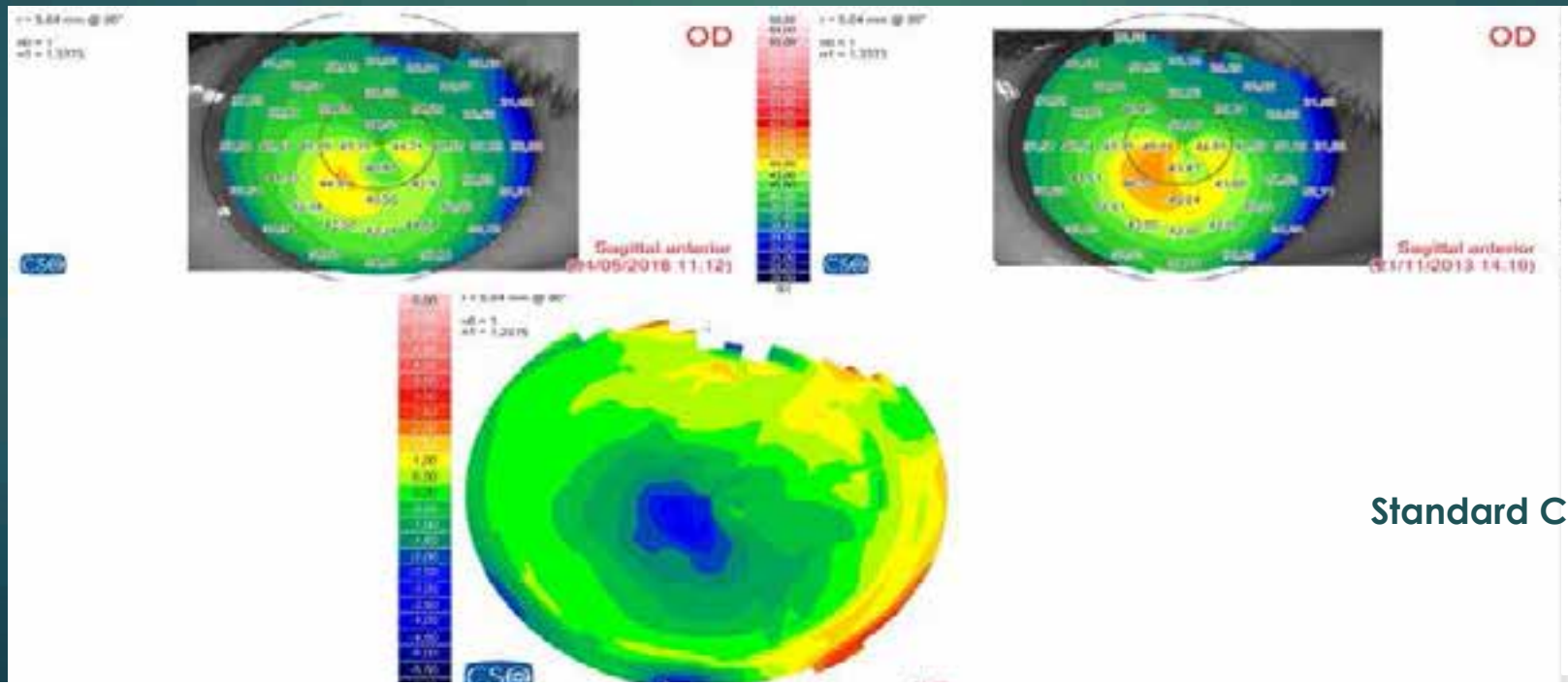
Changes in Visual and Topographical Parameters between pre-CXL an 24 months post-CXL

	Standard CXL	Accelerated CXL	p*
UCVA (logMAR)	-0.08±0.5	-0.20±0.39	0.252
BCVA (logMAR)	0.002±0.39	-0.07±0.32	0.320
SE (D)	0.44±1.65	0.46±1.44	0.968
Topo-CYL (D)	0.01±0.8	0.05±1.01	0.853
K1(D)	-0.49±1.05	-0.63±0.73	0.514
K2 (D)	-0.22±2.13	-0.59±0.97	0.358
Kmax (D)	-0.61±1.91	-1.01±3.27	0.482
ThCT (µm)	-24±36	-41±29	**0.033**

*Independent Sample t Test



Accelerated CXL



Standard CXL

Progression (*Increase of Kmax≥1D two years after CXL treatment*)

Standard CXL	13.1% (5/38)	
Accelerated CXL	16.3% (8/49)	p*=0.754

*Chi-square test

- No complications were observed in standard CXL
- No complications were observed in accelerated CXL

Discussion

24 month

- Shetty et al. Accelerated corneal collagen cross-linking in pediatric patients: two year follow-up results. Biomed Res Int. 2014;2014:894095.

24 month

- Ozgurhan et al. Accelerated corneal cross-linking in pediatric patients with keratoconus: 24-month outcomes. J Refract Surg. 2014;30(12): 843-49.

12 month

- McAnena et al. Corneal collagen crosslinking in children. J AAPOS. 2015;19:228-32 .

6 month

- Ulusoy et al. Accelerated corneal crosslinking for treatment of progressive keratoconus in pediatric patients. Eur J Ophthalmol. 2016

Discussion

- All these studies revealed that accelerated CXL is an effective and safe procedure for the management of keratoconus in pediatric patients
- Visual acuity and keratometric values are improved or remained stable
- No comparison with the standard CXL (no control group)

Discussion

- Our study; Visual acuity, topographical values, and progression rate did not show statistically significant difference between standard and accelerated CXL 24 months after treatment
- The corneal thickness was thinner in eyes treated with accelerated CXL 24 months after treatment
- Progression rate was 13.1% in the standard and 16.3% in the accelerated group

Conclusion

- Our 24-months results of accelerated and standard CXL revealed that the efficacy and safety of accelerated CXL are the same as standard CXL in pediatric keratoconus patients

Conclusion

- Accelerated CXL appears to stop the progression of keratoconus in pediatric patients during the 24 months period after the procedure
- Further studies with longer follow-up periods and larger sample sizes are needed to validate our findings

Thank you…

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