Astigmatism Treatment Bias in a Topography-Guided vs Wavefront-Optimized LASIK Meta-analysis

We read with interest the meta-analysis by Cheng et al, "Topography-Guided [TCAT] Versus Wavefront-Optimized [WFO] LASIK for Myopia With and Without Astigmatism: A Meta-analysis."[1] The authors included seven randomized controlled trials of TCAT-LASIK versus WFO-LASIK. However, they did not account for the differing astigmatism laser programming protocols between the TCAT and WFO groups. The astigmatism magnitude and axis inputs, which are programmed by the surgeon on the excimer laser planning software, varied among the seven studies.

The subjective clinical manifest refraction remains the gold standard treatment target for LASIK. The effectiveness and predictability of this long-standing approach using WFO and TCAT has been widely published.[2] Some TCAT surgeons advocate modifying the Manifest protocol to target the anterior corneal astigmatism (ACA) magnitude and axis in eyes with primary LASIK, such as with Topography-Modified Refraction (TMR)[3] or Layer Yolked Reduction of Astigmatism (LYRA).[4] Those protocols ignore posterior corneal, ocular, and cortical astigmatism, leading to inferior astigmatism treatment accuracy in several studies.[5-8]

The 2019 article by Zhang and Chen[9] included in the meta-analysis by Cheng et al is a TCAT study using the TMR treatment protocol. This study design[9] failed to investigate only one independent variable. The two software programs being compared had differing modalities of treatment, with the TCAT group targeting plano ACA, ignoring subjective refractive astigmatism (RA), and the WFO group targeting plano RA. Therefore, the superior astigmatism accuracy in the RA-treated WFO group and inferior accuracy in the ACA-treated TCAT group was anticipated.[9] It further confirmed that TCAT outcomes based on treating the ACA are inferior to TCAT treatment targeting the manifest RA.[5,6,8] The conclusion of Zhang and Chen that TCAT was not as accurate in astigmatism correction was invalid because of the study design. These scientific concerns were highlighted in a previous correspondence.[10]

The study by Zhang and Chen contributed nearly half of all data in the meta-analysis of Cheng et al, disproportionately representing the analyzed groups. The final pooled relative risk calculations are therefore biased, and the scientific validity of this otherwise well-conducted meta-analysis comes into question. Because the calculated relative risk depends on both the software used and astigmatism treatment target, the meta-analysis cannot conclude on TCAT versus WFO because these two groups also had different astigmatism treatment modalities (ACA vs RA target treatment). Future comparative studies and meta-analyses should control for TCAT treatment protocols and nomogram accuracy. Network meta-analyses would also be appropriate in this area. We appreciate the authors' work in bringing attention to this important topic.

REFERENCES

1. Cheng S-M, Tu R-X, Li X, et al. Topography-guided versus wavefront-optimized LASIK for myopia with and without astigmatism: a meta-analysis. *J Refract Surg.* 2021;37(10):707-714. doi:10.3928/1081597X-20210709-01

2. Wallerstein A, Gauvin M, Ruyu Qi S, Cohen M. Large axis difference between topographic anterior corneal astigmatism and manifest refractive astigmatism: can topography-guided LASIK target the manifest axis? *J Refract Surg.* 2021;37(10):662-673. doi:10.3928/1081597X-20210712-05

3. Kanellopoulos AJ. Topography-modified refraction (TMR): adjustment of treated cylinder amount and axis to the topography versus standard clinical refraction in myopic topography-guided LASIK. *Clin Ophthalmol.* 2016;10:2213-2221. doi:10.2147/OPTH.S122345

4. Motwani M. The use of WaveLight® Contoura to create a uniform cornea: the LYRA Protocol. Part 3: the results of 50 treated eyes. *Clin Ophthalmol.* 2017;11:915-921. doi:10.2147/OPTH.S133841

5. Wallerstein A, Gauvin M, Qi SR, Bashour M, Cohen M. Primary topography-guided LASIK: treating manifest refractive astigmatism versus topography-measured anterior corneal astigmatism. *J Refract Surg.* 2019;35(1):15-23. doi:10.3928/1081597X-20181113-01

6. Kim J, Choi SH, Lim DH, Yoon GJ, Chung TY. Comparison of outcomes after topography-modified refraction versus wavefront-optimized versus manifest topography-guided LASIK. *BMC Ophthalmol.* 2020;20(1):192. doi:10.1186/s12886-020-01459-0

7. Trinh L, Bouheraoua N, Roman S, Auclin F, Labbe A, Baudouin C. Excimer laser programming of refractive astigmatism vs. anterior corneal astigmatism in the case of ocular residual astigmatism (ORA). *J Fr Ophtalmol.* 2021;44(2):189-195. doi:10.1016/j.jfo.2020.04.059

8. Aboalazayem F, Hosny M, Zaazou C, Anis M. Primary topography-guided LASIK: a comparative study comparing treating the manifest versus the topographic astigmatism. *Clin Ophthalmol.* 2020;14:4145-4153. doi:10.2147/OPTH.S282248

9. Zhang Y, Chen Y. A randomized comparative study of topography-guided versus wavefront-optimized FS-LASIK for correcting myopia and myopic astigmatism. *J Refract Surg.* 2019;35(9):575-582. doi:10.3928/1081597X-20190819-01

10. Wallerstein A, Gauvin M, Cohen M. Topography-guided ablation targeting the anterior corneal astigmatism yields inferior outcomes vs targeting the manifest refractive astigmatism. *J Refract Surg.* 2019;35(12):815. doi:10.3928/1081597X-20191030-01

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TABLE 1
Results With and Without the 2019 Zhang & Chen Article

Index	Analysis 1	Analysis 2	Conclusion
UDVA ≧ 20/20	[RR = 1.01, 95% CI (0.97 to 1.06), *P* = .64]	[RR = 1.02, 95% CI (0.95 to 1.09), *P* = .58]	Same
UDVA ≧ 20/16	[RR = 0.96, 95% CI (0.80, 1.16), *P* = .69]	[RR = 0.99, 95% CI (0.82 to 1.20), *P* = .91]	Same
PMSE ≤ 0.50 D	[RR = 1.06, 95% CI (1.02 to 1.11), *P* = .003]	[RR = 1.07, 95% CI (1.00 to 1.13), *P* = .04]	Same
Ablation depth	[WMD = -6.84, 95% CI (-29.47 to 15.79), *P* = .55]	[WMD = -6.84, 95% CI (-29.47 to 15.79), *P* = .55]	Same
Surgically induced HOAs	[WMD = -0.11, 95% CI (-0.15 to -0.06), *P* < .00001]	[WMD = -0.09, 95% CI (-0.16 to -0.02), *P* = .01]	Same
Surgically induced SA	[WMD = -0.04, 95% CI (-0.05 to -0.03), *P* < .00001]	[WMD = -0.04, 95% CI (-0.05 to 0.03), *P* < .00001]	Same
Surgically induced coma	[WMD = -0.15, 95% CI (-0.28 to -0.01], *P* = .03].	[WMD = -0.20, 95% CI (-0.40 to -0.00), *P* = .049]	Same
Surgically induced trefoil	[RR = 0.01, 95% CI (-0.00 to 0.02], *P* = .08].	[RR = 0.01, 95% CI (-0.00 to 0.02), *P* = .08]	Same

Analysis 1 = analysis without excluding the 2019 Zhang & Chen article; Analysis 2 = analysis excluding the 2019 Zhang & Chen article; UDVA = uncorrected distance visual acuity; RR = relative risk; PMSE = postoperative manifest spherical equivalent; D = diopters; WMD = weighted mean difference; HOA = higher order aberrations; SA = spherical aberrations

Reply

It is my pleasure to hear from Drs. Wallerstein and Gauvin regarding our article published in the October 2021 issue of the *Journal of Refractive Surgery*.[1] They pointed out the 2019 article by Zhang and Chen[2] used TCAT-LASIK with Topography-Modified Refraction (TMR, targeting the anterior corneal astigmatism [ACA] in the study), whereas the other six studies included in the meta-analysis used TCAT-LASIK targeting the subjective clinical manifest refraction.

We acknowledge this limitation of our meta-analysis, which has not been mentioned and discussed in our study.[1] Nevertheless, we re-conducted the analysis of all endpionts in our study by excluding the 2019 article by Zhang and Chen and found that all of the conclusions remained unchanged (**Table 1**).

As suggested by Wallerstein and Gauvin, comparative studies or meta-analyses should control for TCAT treatment protocols and nomogram accuracy. This would be a valuable recommendation for future research in the field of refractive surgery. Many thanks to Drs. Wallerstein and Gauvin for their comments.

We noticed that much work has been done recently by Drs. Wallerstein and Gauvin to advocate TCAT-LASIK targeting the subjective clinical manifest refraction rather than targeting ACA magnitude and axis in eyes with small or large preoperative axis discrepancy between refractive astigmatism and topography-measured ACA.[3-5] They have committed a lot of their time to providing high-quality clinical evidence in favor of TCAT-LASIK targeting subjective clinical manifest refraction rather than targeting ACA magnitude and axis for the sake of patients. Their contribution to this research field is acknowledged and deeply appreciated. We also appreciate the contribution of Alpins, who first described treatment of patients with combined topography and refraction parameters.[6-8]

REFERENCES

1. Cheng SM, Tu RX, Li X, et al. Topography-guided versus wavefront-optimized LASIK for myopia with and without astigmatism: a meta-analysis. *J Refract Surg.* 2021;37(10):707-714. doi:10.3928/1081597X-20210709-01

2. Zhang Y, Chen Y. A randomized comparative study of topography-guided versus wavefront-optimized FS-LASIK for correcting myopia and myopic astigmatism. *J Refract Surg.* 2019;35(9):575-582. doi:10.3928/1081597X-20190819-01

3. Wallerstein A, Gauvin M, Qi SR, Cohen M. Effect of the vectorial difference between manifest refractive astigmatism and anterior corneal astigmatism on topography-guided LASIK outcomes. *J Refract Surg.* 2020;36(7):449-458. doi:10.3928/1081597X-20200609-01

4. Wallerstein A, Gauvin M, Ruyu Qi S, Cohen M. Large axis difference between topographic anterior corneal astigmatism and manifest refractive astigmatism: can topography-guided LASIK target the manifest axis? *J Refract Surg.* 2021;37(10):662-673. doi:10.3928/1081597X-20210712-05

5. Wallerstein A, Gauvin M, Qi SR, Bashour M, Cohen M. Primary topography-guided LASIK: Treating manifest refractive astigmatism versus topography-measured anterior corneal astigmatism. *J Refract Surg.* 2019;35(1):15-23. doi:10.3928/1081597X-20181113-01

6. Alpins N, Stamatelatos G. Customized photoastigmatic refractive keratectomy using combined topographic and refractive data for myopia and astigmatism in eyes with forme fruste and mild keratoconus. *J Cataract Refract Surg.* 2007;33(4):591-602. doi:10.1016/j.jcrs.2006.12.014

7. Alpins N, Stamatelatos G. Clinical outcomes of laser in situ keratomileusis using combined topography and refractive wavefront treatments for myopic astigmatism. *J Cataract Refract Surg.* 2008;34(8):1250-9. doi:10.1016/j.jcrs.2008.03.028

8. Alpins NA. New method of targeting vectors to treat astigmatism. *J Cataract Refract Surg.* 1997;23(1):65-75. doi:10.1016/s0886-3350(97)80153-8

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