Author’s response to reviews

Title: Comparison of outcomes after topography-modified refraction versus wavefront-optimized versus manifest topography-guided LASIK

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Author’s response to reviews:

Responses to the reviewers’ and the editor’s comments

We deeply appreciate the editor and reviewers for their thoughtful, constructive comments that have provided us with valuable opportunities to improve our work. We have revised the manuscript to address the issues raised by the reviewers and the editor.

Editor Comments:

It is important that your manuscript gives a clear and complete account of your study, and BMC supports reporting initiatives that contribute to this. Please ensure that your manuscript adheres to the appropriate STROBE guideline for your methodology, and include a completed checklist with your revision as a supplementary file. You can see more information here: https://www.biomedcentral.com/getpublished/writing-resources/reporting-guidelines

- We confirmed that our manuscript adhered to the STROBE guidelines for our methodology. We also included a completed checklist with our revision as a supplementary file.

BMC Ophthalmology operates a policy of open peer review, which means that you will be able to see the names of the reviewers who provided the reports via the online peer review system. We encourage you to also view the reports there, via the action links on the left-hand side of the page, to see the names of the reviewers.
We confirmed the names of the reviewers and their reports via the online peer review system. We appreciate their time and consideration.

Reviewer reports:

William R. Barlow, MD (Reviewer 1):
Interesting paper. The discussion was concise and appears to have been cleaned up nicely as was requested after first review. I have no concerns about the revised draft.
-&gt; We appreciate this favorable comment.

Kyong Jin Cho (Reviewer 2):
The authors showed that TMR-LASIK overcorrected astigmatism and showed higher residual postoperative astigmatism compared with WFO- and conventional TG-LASIK.
The major strength of this paper is that they firstly identified overcorrection of astigmatism after TMR ablation by conducting vector analysis of astigmatic change.
It seems to be well designed and analyzed.
-&gt; Thank you for this favorable comment.

Miguel Ángel Teus (Reviewer 3):
The authors should be congratulated for this interesting research.
-&gt; We appreciate this friendly comment.

I have the following comments/queries.

#1. The authors select only one eye per patient (which is correct), but do not state the criteria used to select one of the eyes when both eyes were eligible (i.e. fulfilled the inclusion/exclusion criteria). Please do in the methods section.

-&gt; Thank you for this constructive comment. As we already described in the Methods section, we only included the right eye of each patient in order to avoid possible inter-eye correlations. We rephrased our statement as follows in the revised manuscript (page 5).
Methods: Patients who underwent TMR-LASIK (85 patients), WFO-LASIK (70 patients), or manifest TG-LASIK (40 patients) were enrolled, and only the right eye of each patient was analyzed in this study to avoid possible inter-eye correlations.

#2. I do not see any reason to use the 0.75D as a limit to assess the predictability of the refractive correction, as the authors do in the current paper. Please use the more conventional 0.5D and 1D as cutoffs.

-&gt; We do not fully agree with this point. Given that the cut-off point of -0.75D is widely accepted as clinically-significant nearsightedness and has been used to assess the predictability of the refractive correction (Spada L and Giovannetti F, Clinical Ophthalmology, 2019; D’arcy F at al., Acta Ophthalmologica, 2012), we believe that our analysis was appropriate. Nevertheless, following the reviewer’s suggestion, we have additionally analyzed our data using 0.5D and 1D as cutoffs. We rephrased the following sentence (page 8) and Table 4 in the revised manuscript as follows.

Results: The percentages of eyes having MRSE within ± 0.5 D and ± 1.0 D of emmetropia measured at three months were 70.0% and 88.5% of eyes in the WFO group, 72.5% and 92.5% of eyes in the manifest TG group, and 68.2% and 91.7% of eyes in the TMR group (P = .888 and .724, respectively; Figs. 1b, 2b, and 3b).

Table 4:

<table>
<thead>
<tr>
<th>Parameter (Mean ± SD)</th>
<th>Subgroup 1 (CA &lt; RA)</th>
<th>Subgroup 2 (CA &gt; RA)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative 3 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSE (% of D within ± 0.5)</td>
<td>68.8</td>
<td>68.1</td>
<td>.999</td>
</tr>
<tr>
<td>MRSE (% of D within ± 1.0)</td>
<td>93.8</td>
<td>91.3</td>
<td>.999</td>
</tr>
</tbody>
</table>

Nauman Hashmani, MBBS (Reviewer 4):

#1 (Introduction-1). I’m not sure if conventional TG-LASIK is the appropriate term. I would label it Manifest TG LASIK as the current recommendation even out of Alcon are not of Manifest TG LASIK. If anything, the conventional TG LASIK would be the "modified TMR" Alcon introduced.
We appreciate this constructive comment. Following the reviewer’s suggestion, we replaced ‘conventional TG-LASIK’ with ‘manifest TG-LASIK’ throughout our manuscript and rephrased our statements as follows in the revised manuscript (pages 2 and 4).

Abstract: To compare the outcomes of myopia and myopic astigmatism corrected with topography-modified refraction laser in situ keratomileusis (TMR-LASIK), wavefront-optimized (WFO) LASIK, and topography-guided (TG) LASIK with a correction target based on the manifest refraction (manifest TG-LASIK).

Background: In his study, a topographic adjustment was applied relative to the amount and axis of astigmatism, and TMR-LASIK showed better visual and refractive outcomes compared with TG-LASIK with a correction target based on the manifest refraction (manifest TG-LASIK) [6].

#2 (Introduction-2). The FDA study was NOT the first study of the Contoura Platform. However, the FDA platform was the first to study this platform on virgin eyes. The second sentence in your introduction requires alteration. I am unsure what the author is trying to communicate in that second sentence. It needs reworking.

-&gt; Thank you for this critical comment. We modified that sentence in response to the reviewer’s comment in the revised text (page 4) as follows.

Background: Customized refractive surgery based on corneal topography has been widely used to correct myopia, astigmatism, and higher-order aberrations (HOAs). It has also shown satisfactory surgical outcomes and common post-laser in situ keratomileusis (LASIK) symptoms including light sensitivity, glare, and halos [1, 2].

#3 (Methods-1). There is no mention in the methods whether these are virgin eyes undergoing primary procedures or do these include eyes that been previously operated on.

-&gt; Thanks for this comment. We rephrased our statement as follows in the revised manuscript (page 5).

Methods: We included virgin eyes of patients with preoperative refractive error between -0.50 and -7.50 diopters (D) of spherical myopia and between 0.00 and 3.00 D of astigmatism and distance visual acuity correctable to 0.1 logMAR or better.

#4 (Methods-2). You mention this is a retrospective study yet you also mention the surgical protocol was randomly determined? If there was randomization taking place would this not be a prospective study? Additionally, how did this randomization take place?

-&gt; We appreciate this constructive comment. There was a misdescription of the sentence in the original manuscript. Originally, we intended to mention that the surgical protocol used for each patient was selected according to the surgeon’s subjective determination on a case-by-case
basis. We rephrased the text in the revised manuscript as follows (page 5). We apologize for any confusion or inconvenience that this misdescription may have caused.

Methods: The surgical protocol used for each patient was selected according to the surgeon’s subjective determination on a case-by-case basis.

#5 (Methods-3). You mention that you did corneal topography and corneal wavefront analysis at all follow-ups. Are these not the same test? Topography simply gives you higher order aberrations as a derivation of curvature and it is not a true wavefront analysis. I would remove this point.

-&gt; Thank you for this thoughtful comment. Following the reviewer’s suggestion, we modified our statement as follows in the revised manuscript (pages 5 and 6).

Methods: Preoperative examinations included manifest refraction, cycloplegic refraction with Mydrin-P (Santen, Osaka, Japan; tropicamide 0.5% and phenylephrine HCl 0.5%), and corneal topography assessment utilizing the WaveLight® Topolyzer VarioTM (Alcon, Fort Worth, TX, USA).

#6 (Results-1). It is interesting to note that despite superior results in the "conventional" group, the TMR group has more eyes. Is there any reason for this?

-&gt; We appreciate this constructive comment, which is related with comment #4 (Methods-2). Because our data were retrospectively analyzed and the ‘conventional’ TG-LASIK and TMR-LASIK groups produced comparable visual outcomes and predictability of the refractive correction, it was difficult to conclude which surgical method was superior during the time period in which surgical procedures were done. Thus, we assume that the difference in the number of patients among groups is inherent to the retrospective nature of this study as the surgical protocol used for each patient was selected according to the surgeon’s subjective determination on a case-by-case basis. We wish the reviewer could consider this limitation as we already mentioned in the final paragraph of the Discussion section (page 14).

#7 (Discussion-1). The 3rd paragraph of the discussion is largely a restatement of the results. A discussion provides further insights into the results by way of comparison with different studies and a chance for the author to present his own viewpoints. Please refrain from repeating the results.

-&gt; We agree with this comment. Following the reviewer’s suggestion, we refrain from repeating the results. We rephrased our statements as follows in the revised manuscript (pages 12 and 13).

Discussion: Our results showed that the predictability of the refractive correction and visual outcomes did not differ significantly among WFO-, manifest TG-, and TMR-LASIK, similar
with those of previous contralateral-eye comparisons of WFO-LASIK with manifest TG- or TMR-LASIK [4-6]. However, in this study, the mean value of postoperative RA was higher in TMR-LASIK, and TMR-LASIK showed a significantly-skewed distribution of postoperative RA toward higher astigmatic values than WFO- and manifest TG-LASIK. On the other hand, a previous comparison between WFO- and TMR-LASIK reported conflicting results with respect to RA [6]. When we performed vector analysis of astigmatic change to evaluate the reason for the difference in postoperative RA between our result and that of the previous study [6], TMR-LASIK significantly overcorrected astigmatism more than WFO- or manifest TG-LASIK, and the astigmatism values in the eyes of the TMR group with larger CA than RA were significantly more overcorrected compared with eyes having smaller CA than RA. In addition, the preoperative magnitude difference between CA and RA with ME showed a significant relationship, implying that astigmatism in eyes having larger CA than RA has a higher potential to be overcorrected than that of eyes having smaller CA than RA. Since Kanellopoulos [6] did not perform a vector analysis of astigmatic change, and no information on the magnitude difference between preoperative CA and RA was provided, the reason for the difference in distribution of postoperative residual astigmatism between the two studies needs to be further investigated. Meanwhile, although the current treatment guideline of ContouraTM Vision recommends that the correction target of a cylinder be based on the midpoint between CA and RA in eyes having a larger CA than RA, no convincing evidence has been released to support this recommendation. Considering our results showing astigmatic overcorrection of eyes having a larger preoperative CA than RA in TMR-LASIK, the midpoint correction target could be speculated to also overcorrect astigmatism although the degree of overcorrection would be smaller than that of TMR-LASIK.

#8 (Discussion-2). The author points out that astigmatic overcorrection occurs in eyes with CA &gt; RA. It would be beneficial if the author would point out why they think this is.

-&gt; Thank you for this constructive comment. We focused on the effect of magnitude difference between preoperative CA and RA in TMR-LASIK group because postoperative cylinder in the TMR group was significantly higher than that in other groups and the subsequent vector analysis of astigmatic change identified that there was a significantly larger amount of astigmatic overcorrection in the TMR group compared to other groups. Considering that the correction target in TMR-LASIK is based on the corneal topographic astigmatism value, we hypothesized that eyes with a larger preoperative CA than RA in TMR-LASIK have a potential for overcorrection of astigmatism. Indeed, when we performed a subgroup analysis of the TMR group according to the magnitude difference between preoperative CA and RA, eyes having CA &gt; RA showed significantly greater ME than eyes having CA &lt; RA. In addition, preoperative magnitude difference between CA and RA was significantly associated with ME when we performed a multivariable-adjusted linear regression analysis. We included and rephrased the following sentences into the revised manuscript as follows (page 10).

Results: In addition to the fact that the correction target in TMR-LASIK is based on the corneal topographic astigmatism value, the aforementioned vector analysis finding of astigmatic overcorrection in the TMR group led us to investigate whether a certain relationship exists between the overcorrection of astigmatism and the magnitude of difference between preoperative
CA and RA. To gain insight into this question, we divided the TMR group into two subgroups: Subgroup 1 having CA < RA (n = 16) and Subgroup 2 having CA ≥ RA (n = 69).

#9. Overall, I feel this a strong study with a proper analysis in topography guided eyes given that the above concerns are addressed.

-&gt; We carefully addressed the issues raised by the reviewer point-by-point. We hope that the reviewer agrees and that it is satisfactory.

#10. Additionally, I feel this manuscript would benefit for English editing services.

-&gt; Following the reviewer’s suggestion, our manuscript was reviewed by someone who is fluent in English.

I would recommend this study for publication as it does confirm what the Wallerstein study initially suspected. I would like to congratulate the authors.

-&gt; We appreciate this favorable comment.