

## **Author's response to reviews**

**Title:** Correlation of Anterior Segment Optical Coherence Tomography measurements with graft trephine diameter following Descemet stripping automated endothelial keratoplasty

### **Authors:**

Gavin S Tan ([dr\\_gavintan@yahoo.com.sg](mailto:dr_gavintan@yahoo.com.sg))  
Mingguang He ([Mingguang\\_he@yahoo.com](mailto:Mingguang_he@yahoo.com))  
Donald T Tan ([donald.tan.t.h@sneec.com.sg](mailto:donald.tan.t.h@sneec.com.sg))  
Jodhbir S Mehta ([jodmehta@gmail.com](mailto:jodmehta@gmail.com))

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**Author's response to reviews:** see over

Dear Editor,

We thank you for reviewing our manuscript titled “CORRELATION OF ANTERIOR SEGMENT OPTICAL COHERENCE TOMOGRAPHY MEASUREMENTS WITH GRAFT TREPHINE DIAMETER FOLLOWING DESCOMET STRIPPING AUTOMATED ENDOTHELIAL KERATOPLASTY”.

We have made the amendments as suggested by the reviewers, and our detailed responses to the comments made by the reviewers are included below.

Thank You

Best Regards

Gavin S Tan  
Mingguang He  
Donald T Tan  
Jodbhir S Mehta

### **Reply to reviewers' comments**

#### Reviewer 1

1. The manuscript should state whether the ZAP software is commercially available and if it is, the authors should disclose a financial interest. If it is freeware, the authors should provide the site where it can be downloaded.

*The software is proprietary non-commercially available software, which can be requested free from the authors. This has been noted in the methods.*

2. In the Abstract Conclusions, it is not clear why there is a higher chance of undersizing the EK graft in eyes with larger PCAL based on what has been reported in the Abstract. It would be better to say "This software may help surgeons determine the optimal DSAEK graft size based on preoperative ASOCT measurements of the recipient.

*The abstract has been amended as suggested.*

3. Please report how the mean graft thickness in Table 1 was measured.

*The mean graft thickness was measured intraoperatively with ultrasound pachymetry. This has been detailed in the methods.*

4. In Results, it would be preferable to report R-squared throughout instead of switching from Rho to R-squared. R-squared is more intuitive because it represents the % of the total variance that is explained.

*R-squared value is derived during linear regression or correlation using Pearson's correlation coefficient. Since graft trephine diameter is not normally distributed, a non-parametric test (Spearman's) was used to assess the bivariate correlation and therefore Spearman's Rho was reported.*

5. In the model for posterior graft arc length, please specify "recipient" age, sex, etc.

*This has been specified.*

6. How do you explain that model? What does it mean? Why does it matter? Throwing in 4 extra variables did not increase the R-squared value that much over what it was with just trephine diameter. Simply adding in one more variable, recipient corneal curvature, would seem to provide a much better and more intuitive model.

*We repeated the models including recipient corneal curvature. Using backward selection of variables we found the most stable model with the highest adjusted R-square was the model which included the variables, trephine diameter, cornea posterior curvature and AC width. This suggested that the in-situ graft arc length measured on AS-OCT is dependent on trephine diameter, cornea posterior curvature and AC width. These can be measured pre-operatively and used to estimate the in-situ graft arc length.*

7. Figure 5 can be deleted in the interest of space as it was clear from Methods that the surgeon tended to select graft size based on recipient HWTW.

*Figure 5 has been removed from the manuscript.*

8. In Table 2 the numbers are reported with too many significant figures. The ASOCT measurements are not accurate to 4 or 5 significant figures. In fact the Bland Altman plots suggest the measurements are accurate to about 0.1mm.

*The measurements have been amended to report 2 decimal places.*

9. In Table 3, all the Ratios should be deleted in the interest of space. It is not intuitive what a correlation with a Ratio means and it is not explained in the text. Putting in too much information can obscure the main points you are trying to make.

*The ratios have been removed.*

10. Discussion, page 8: instead of saying "we are undersizing" in line 18, it would be better to say "the analysis showed we could have used larger grafts in eyes with larger posterior corneal arc lengths". You need to start out the paragraph by providing the rationale for why you think some grafts were undersized. For example, you could say something like: "Most of the grafts in this series were performed in eyes with pseudophakic bullous keratopathy where larger grafts with

greater replacement of functional cornea endothelial cells were desirable."

*The paragraph has been amended to explain the advantage of larger grafts in our patients and the statement about undersizing has been amended to suggest that larger grafts could have been used.*

11. The paragraph starting in the middle of page 8 and continuing through page 9 should be rewritten to tighten it up and eliminate redundancy. For example, it says there is no published information as to the optimal graft size in 2 places.

*The discussion has been revised and shortened.*

12. Page 9, line 14, it is important to explain that reference 26 was all Fuchs' dystrophy eyes, in which the central endothelium is dysfunctional but the peripheral endothelium is healthy so larger graft sizes are not needed. Those cases differ from your cases, in which most have dysfunctional peripheral endothelium.

*This has been noted in the discussion. “, this study only included patients with Fuch’s endothelial dystrophy where the endothelial dysfunction is mainly in the central cornea and larger grafts may provide less of an advantage.”*

13. Page 9, lines 15 and 16 mention slower subsequent cell loss with DSAEK vs. PK, but do not explain how that may relate to graft size. This should be explained.

*We have included a statement on the larger graft used during DSAEK which would implant greater number of endothelial cells.*

14. Page 9, line 24, hyperopic shift is also related to the thickness gradient between the center and periphery of the graft. This should be added.

*The statement on hyperopic shift and the thickness gradient between the center and periphery of the graft has been added.*

15. Figure 7 and the first 6 lines on page 10 should be deleted in the interest of space and maintaining focus. You didn't need the software to tell you that the surgeon used larger grafts over time - you already knew that he did. This extraneous information distracts from your main points.

*As suggested we have removed this figure and the statement on the figure.*

16. Minor Revision: Tables 2 and 3 need to specify the units of measurement and provide the definitions of all abbreviations.

*Units have been added and abbreviations removed.*

Reviewer 2 comments

1. Figure legends are missing.

*The legends are included in the manuscript.*

2. Figure 2: Y axis is to read as “ number of eyes”

*Figure 2 has been amended.*

3. Figure 3: give complete ASOCT parameters in all Y axis for all graphs.  
Is X axis parameter mentioned in all graphs correct? “ mean “ seems to be irrelevant here.

This depicts repeatability of study parameters in 30 eyes as mentioned in text. But there seems to be only 20 plot points in all the four graphs!!

*Complete Y axis labels have been added.*

*The Band Altman plots have been relabel. It compares the difference between 2 measurements with the mean of the 2 measurements.*

*The repeatability study was done on 20 eyes not 30 eyes. This has been amended in the manuscript.*

4. Figure 5: is x axis to read as “posterior corneal arc length”?

*Figure 5 has been omitted on suggestion of reviewer 1.*

5. Table 2: to elaborate all ASOCT graft parameters in full or elaborate abbreviations at table footnote

*The parameters have been listed in full.*

6. Page 1

title The manuscript is elaborates the correlation of the ASOCT measurement of DSAEK grafts (in-vivo graft measurements) with the trephine diameter. The title does not seem to imply the same

*The title has been amended to “CORRELATION OF ANTERIOR SEGMENT OPTICAL COHERENCE TOMOGRAPHY MEASUREMENTS WITH GRAFT TREPHINE DIAMETER FOLLOWING DESCOMET STRIPPING AUTOMATED ENDOTHELIAL KERATOPLASTY”*

7. line 2-3 The second aim is not properly stated

*This has been amended.*

8. Lines 6 - 9 Not clear if this is a prospective or retrospective study. Methods needs to be rewritten clearly

*It has been added that this is a retrospectively evaluated interventional case series.*

9. Line 17 “in a retrospective review of our clinical cases...” does not seem appropriate here

*This statement has been removed.*

10. Line 22 should this read “ intra-operative graft trephine diameter”...?

*This statement has been amended to state “intraoperative graft trephine diameter”.*

11. Page 3 Line 8 Replace “1” with “one”

*This has been amended.*

12. Line 11 Wrong citation of reference 14

*The references have been amended.*

13. Line 16 Wrong citation of reference 16  
Reference 15 is not cited in the manuscript

*The references have been amended.*

14. Line 16 Is “guestimated” an accepted term?

*This has been replaced with “estimated”.*

15. Reference 12 – 13 quoted out of sequence in the manuscript

*The references have been amended*

16. Page 5

Line 5-6 Is citation of reference 18, 19 relevant here?

*References 18 and 19 describe the use of ZAP software to measure ASOCT images.*

17. Lines 5, 10, 21 To read as figure 1a, 1b, 1c respectively

*The labels have been amended.*

18. Page 6

Line 11 To mention number of female patients as well.

*The number of female patients have been included in the text.*

19. Line 12 Mention of numbers of eyes done by sheets glide insertion technique here and in line 13 on page 4 are not corroborating. It is

probably due to the exclusion of the eyes with poor quality ASOCT pictures. This needs to be clarified clearly

*The statement has been amended to “The Sheets Glide insertion technique was used in 93 patients (85.3%) with acceptable ASOCT images.”*

20. Line 12 “pre-op” - words to be written in full . this error exists throughout the manuscript and in the figures as well and needs to be Addressed

*Use of “pre-op” has been replaced with “pre-operative” throughout the manuscript.*

21. Line 17 Inference drawn before stating the results. Sentence needs to be revised

*The sentence has been revised to state results first.*

22. Line 19 – 21 Mention significance of high intraclass co-efficient amongst all parameters

*We have added a statement that explains that the high ICC “which suggests a high level of agreement between repeated measurements.”*

23. Line 22 Rephrase line

*Statement has been rephrased to “There coefficient of variation amongst all the graft parameters were small (1.24 to 3.71%).”*

24. Line 23 Please clarify if the Band Altman plots depict mean difference between readings..

*This has been clarified to state “The Band Altman plots demonstrate that the mean difference between repeated measures are small and the limits of agreement are within an acceptable range.”*

25. Page 7

Line 1 Repetition of data depicted in table 3

*The statement has been shortened to state “Bivariate correlation showed that graft trephine diameter correlated with graft anterior arc length, graft anterior cord length, graft posterior arc length and graft posterior cord length(all  $p < 0.001$ ).”*

26. Lines 2, 3 Is “cornea arc length” to read as “posterior cornea arc length”. Please correct this in the entire manuscript

*Yes. We have corrected this in the entire manuscript.*

27. Line 5 “invivo graft trephine diameter” - is this to read as “ intraoperative graft diameter” ?

*It should read as “intraoperative graft trephine diameter. We have standardized the*

*use of this term throughout the manuscript.*

28. Line 9 “Analysis” to be inserted after “multivariate liner regression”

*Analysis has been added to the statement.*

29. Line 12 Mention models elaborated in table

*The statement has been amended to state “Models were analysed using all the parameters significant on bivariate correlation together with age and sex. After performing forward and backward selection multivariate models, we found the model using cornea posterior curvature, AC width and trephine diameter had the greatest adjusted R2 (0.697) for determining posterior graft arc length.*

30. Lines 15 -20 To be rewritten. Not clear

*The statement has been rephrased to “However, we noted that in our series, eyes with larger posterior cornea arc length, the ratio of graft posterior arc length to posterior cornea arc length was less than eyes with smaller posterior cornea arc length.”*

31. Line 27 Insert “measurements” after ‘graft’

*“Measurements” has been added to the statement.”*

32. Page 8

Line 18 Larger recipients to read as “ recipients with larger sized eyes / corneal diameter” ? clarify

*This has been amended to “which showed we could have used larger grafts in eyes with larger posterior corneal arc lengths.”*

33. Line 24 Is ‘guess-timation’ an appropriate term.

*This term has been removed from the manuscript.*

34. Page 9

Line 10 Is this to read as ‘graft posterior arc length / posterior corneal arc length’ here?

Line 13 Sentence to continue after line 12?

*The sentence has been rephrased to “There is no published information as to the optimal graft size for endothelial keratoplasty and hence also the optimal ratio of graft posterior arc length to posterior cornea arc length, although has been suggested that a larger graft with the same endothelial cell density would provide a greater total number of functioning endothelial cells to the recipient and may support greater long term endothelial cell survival.”*

35. Page 10

Line 3-6 Not clear. To be rewritten

*The paragraph has been removed as suggested by the other reviewer, as it doesn't add any value to the discussion.*

36. Line 11 To be more describe more clearly, the multiple regression analysis

*The statement has been amended to state "Our multiple regression analysis showed that, a model using posterior cornea arc length and AC width measured on ASOCT would allow us to reasonably estimate The graft arc length based on the trephine diameter chosen."*

37. Line 28 'newer' to read as Newer" ? ( next sentence.?)

*The term has been replaced with " the next generation of Fourier domain ASOCT scanners".*

38. Line 29 Rephrase line 7

*The statement has been rephrased to state "In summary we have successfully validated the repeatability of the ZAP software measurements of ASOCT images from patients who have undergone DSAEK surgery. We have also shown that the graft arc length parameters calculated from the software correlate well with the intraoperative graft trephine diameter."*