Author's response to reviews

Title: Reproducibility of Corneal Graft Thickness measurements with COLGATE in patients who have undergone DSAEK (Descemet Stripping Automated Endothelial Keratoplasty)

Authors:

Melissa H.Y. Wong (melwhy@singnet.com.sg)
Annabel Chew (annabel_chew@yahoo.com.sg)
Hla M Htoon (hla.myint.htoon@seri.com.sg)
Beng H Lee (benghai@i2r.a-star.edu.sg)
Jun Cheng (jcheng@i2r.a-star.edu.sg)
Jiang Liu (jliu@i2r.a-star.edu.sg)
Donald T Tan (donald.tan.t.h@snec.com.sg)
Jodhbir S Mehta (jodmehta@gmail.com)

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Second Revision of Manuscript 1919134325636301 - Reproducibility of Corneal Graft Thickness measurements with COLGATE in patients who have undergone DSAEK (Descemet Stripping Automated Endothelial Keratoplasty)

We would like to thank the editor and reviewers’ kind comments. We have made the following changes as shown below. With regards to your question about our ethics committee, we have also added in our manuscript that our study had the approval of the hospital’s Ethics Committee (Singhealth Institutional Review Board) and was conducted according to the tenets of the Declaration of Helsinki.

We look forward to your response.

Yours sincerely,

Dr Melissa Wong,
Assoc Prof Jodhbir S Mehta

Singapore National Eye Centre,
11 Third Hospital Avenue,
Singapore 168751
Fax: (65) 6226 3395
Reply to reviewer 1 comments:

Thank you. We have incorporated the corrections as indicated in your pdf file into the paper.

In addition, below are specific replies to your questions:

1) In this retrospective study, 50 high resolution cornea OCT images of 23 patients who had undergone DSAEK in either eye were obtained from a common data base. How and why were they selected?

Reply: Thank you. We have elaborated on the paragraph. Please see pg 7 lines 127-131 “In this retrospective study, 50 high resolution cornea OCT images of 23 patients who had undergone DSAEK in either eye were obtained from a common data base. The data base encompasses all anterior segment OCT images which are kept in the hard disk drive of the OCT machine These 50 images were selected as they had the best quality images with both cross-sectional ends of the DSEK graft seen.”

2) More than one horizontal scan was performed but the best quality scan was selected for measurements. By whom?

Reply: Thank you. We have changed the sentence to “More than one horizontal scan was performed but the best quality scan was selected by the technician performing the scan.” Pg 7 lines 152-153

3) The images are first filtered and converted to a binary image through the Canny edge detector (what is it?)

Reply: The images are first filtered and converted to a binary image through the Canny edge detector which uses an algorithm to detect a range of edges in an image. Pg 8 lines 159-161. We have also referenced it to reference number 7. Canny, J., A Computational Approach To Edge Detection, IEEE Trans. Pattern Analysis and Machine Intelligence, 8(6):679–698, 1986
4) **Two ophthalmologists (MW, AC) independently performed the image analysis of high resolution cornea images from the Visante OCT machine.** *(Did they use the other instruments as well for testing?)*

Reply: Thank you. No other instruments were used. The scans were selected and downloaded from the Visante OCT machine and stored on a desktop before using the COLGATE program on these images.

We have rephrased the sentence to make it clearer. Please refer to page 9 lines 1781-82. “Two ophthalmologists (MW, AC) independently performed the image analysis using the COLGATE program on the same set of 50 high resolution cornea images selected and downloaded from the Visante OCT machine. The two individuals were taught how to use the software but it was the first time using it on the 50 ASOCT images.”

5) **The two individuals were taught how to use the software, but it was the first time using the software on the 50 ASOCT images. What does this mean?**

Reply: It means that MW and AC were trained in the usage of the COLGATE program but it was the first time they were using it on ASOCT images.

The sentence “The two individuals were taught how to use the software but it was the first time using it on the 50 ASOCT images” was included in response to another reviewer’s comment.

6) **Each ophthalmologist then manually readjusted the corner points as well as points on the anterior and posterior margins of the graft to create a best fit curve for the graft. Show a figure**

Reply: Thank you. Please see line 183 pg 9. “They used the COLGATE program to obtain the best fit curve over the entire graft. (Figure 2A)”

7) **Bland-Altman analysis was performed to analyze inter and intra observer as well as between automated and semi-automated agreement using MedCal Version 9.6.4.0. (Source?)**
8) *This relationship* (between calculations made by observer 1 and observer 2 for the two sets) *were reflected in the linear correlation values* (*r*=0.913 for the first set and *r*=0.969 for the second set) *and these were found to be statistically significant* (*p* <0.xx?).

Reply: We sincerely apologise for the typo error. We have changed it to “This relationship (between calculations made by observer 1 and observer 2 for the two sets) was reflected in the linear correlation values (*r*=0.913 for the first set and *r*=0.969 for the second set) and there was no statistical significance in the calculations made between the two observers for each set of readings. Pg 11 lines 222-226

9) The Optovue system also utilizes similar caliber software in a similar manner with similar potential errors of measurement. Corneal graft thickness is a surrogate marker for the physiological ‘well-being’ of the donor corneal allograft as a thin graft implies a healthy endothelium (one can have a thick graft and good cell density and good vision as well) and clear cornea free of corneal edema. (*This does not seem to make sense because DSAEK graft thickness is determined by the technique of creating the graft and not the cell density. It would probably read better: The postop DSAEK total corneal thickness...*)

Reply: Thank you for your suggestion. We have rephrased the sentence to “The Optovue system also utilizes similar caliber software in a similar manner with similar potential errors of measurement. The post op DSAEK total graft thickness is a surrogate marker for the physiological ‘well-being’ of the donor corneal allograft as a thin graft implies a healthy endothelium and clear cornea free of corneal edema.” Please see pg 15 lines 324-329
10) **Hence knowing the post operative graft thickness will allow the surgeon to better visually rehabilitate the patient. (This statement does not make sense. If the surgeon finds one pattern or another and has a certain refractive error postop, what can they do at that point?)**

Reply: Thank you. Knowing the refractive error allows the surgeon to discuss possible future graft refractive procedure options with the patient.

We have elaborated on the sentence. Please refer to pg 16 lines 338-340. “Hence knowing the post operative graft thickness will allow the surgeon to better visually rehabilitate the patient with future graft refractive procedures.”

11) **Its use can be extended to evaluating penetrating keratoplasty grafts, as anterior and deep anterior lamellar grafts as well as Laser assisted in situ-Keratomileusis (LASIK) flaps. (If current OCT images cannot define the LASIK flap interface more than a few weeks postop, how can the software be useful?)**

Reply: Thank you. We have omitted the option of LASIK in the sentence. Please refer to pg 16 lines 342-343. “There are other uses of this software. Its use can be extended to evaluating penetrating keratoplasty grafts, as well as anterior and deep anterior lamellar grafts.”

12) **The inbuilt automatic boundary detector can also be extrapolated to evaluate iris profile as well as measurements of the trabecular iris surface area (TISA) in glaucoma patients. REF?**

Reply: Thank you. We have referenced TISA to reference number 17 on page 20.