Author's response to reviews

Title: The effect of incorrect scanning distance on boundary detection errors and macular thickness measurements by spectral domain optical coherence tomography: a cross sectional study

Authors:

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Version: 2 Date: 1 October 2014

Author's response to reviews: see over
September 29, 2014

Ms. Elaine Patricia Cruz
Journal Editorial Office
BioMed Central

Re: MS: 1441872960132412

Dear Ms. Cruz,

Thank you for reviewing our submitted manuscript. We have now revised it to answer the reviewers’ comments. For your further consideration, we have submitted electronically the revised manuscript as MSWord file. For easier review, the current additions to the text are shown in blue color.

We appreciate the review that our paper has received. In what follows we itemize each comment and refer to the place in the new manuscript that has been changed in response. We hope that our revised manuscript will now meet the standards of BMC Ophthalmology.

Truly yours,

Gabor Mark Somfai, Ph.D.
Visiting Assistant Professor
McKnight Vision Research Center
Bascom Palmer Eye Institute
University of Miami Miller School of Medicine
Reviewer: Igor Kozak

Reviewer's report:

Major Revisions:

1. As the authors mention in the Discussion, the instrument they use probably has a compensatory software to smooth out signal from slightly different scanning distances. Again, it would be helpful to know if other instruments do the same and to what extent. We are grateful to Dr. Kozak for his valuable comment. Almost all OCT devices smooth out the effects of antero-posterior movement along the z-axis but unfortunately we found no description about it in the user manual of our RTVue-100 device as it is commonly proprietary information and thus the company does not disclose it. We believe this did not have any effect on our measurements; instead, the lateral smoothing may have hidden the effects of boundary detection errors. We elaborated this latter in the manuscript making our point clearer. Unfortunately, there is similarly very little information available about the algorithms used in the software of various OCT devices; therefore, we did not discuss it in the manuscript.

2. How many eyes did the authors scan to find out that 2.5 cm is the ideal measuring distance? Were any reproducibility studies done determine that? Were then images taken exactly at 2.5 cm from the cornea or at the crisp fundus image? We thank the reviewer for this important question. We completed the Methods section with the discussion of this issue. The examination distance was stated empirically by the measurement of the distance of the instrument from where the fundus was visible in the entire fundus image window (see Fig. 3C) for the first five eyes. We found it to be approximately 2.5 cm from the surface of the center of the cornea which is why we used it as the optimal distance of imaging. We did not perform any reproducibility studies to confirm this as precise positioning was only required for the bad scan settings. We note that focus was set automatically during the procedure, therefore the sharpness of the fundus image was not a criterion.

Minor Revisions:

1. In Results, the mean numbers of signal strength index (SSI) for optimal and suboptimal scanning distance are statistically different but yet fairly close. I wonder what is the SSI in exemplary image in Figure 3 but assume that it should be more that mean difference in the presented results. The SSI values of the images used for Figure 3 was 66.8 for the suboptimal and 72.4 for the optimal distance settings. We included this information in all figure legends. The purpose of this figure was to visualize the most frequent error types and differences we found between the two scanning sessions.

2. In Discussion, page 8, line 170, the citation does not match the reference
number, please correct. For the latest review of imaging artifacts on OCT, please review Chhablani J et al. Saudi J Ophthalmol. 2014 Apr;28(2):81-7. We thank the reviewer for noting this. We corrected the number of the reference above. For the review of latest studies of imaging artifacts on OCT we read the mentioned publication and we used it as a reference in line 180, page 8 in our manuscript.

3. Please mention manufacturer of RTVue.
We mentioned the manufacturer of RTVue in lines 78-79 on page 4.

Reviewer's report

Reviewer: Gabor G Deak

Reviewer's report:

Varga et al. present data about segmentation errors on SD-OCT images caused by improper acquisition distance. This is generally an interesting topic, the study was well designed, and the manuscript is well written. However there are some concerns:

Minor Essential Revisions

1) Why did you do the examinations without pupillary dilatation? Generally OCT machines do better when the images are captured in mydriasis, and in the clinical practice probably 95% of the images are done in mydriasis. It would be nice if you could include some data imaged in mydriasis, or if not than at least discuss this point in the discussions section.

We agree with the reviewer as based on our clinical practice SD-OCT machines indeed do better quality images in mydriasis. However, a previous study (Massa, G. C., et al. Eye 24.9 (2010): 1498-1502.) showed that in case of SD-OCT, pupil dilation did not have a significant influence on the measurement of thickness of the retinal nerve fiber layer. Besides this, the latest SD-OCT models do not require pupil dilation. We pointed out the importance of the fact of non-mydriatic imaging in the Discussion, also mentioning this as a potential shortcoming of the study. We also highlighted that our initial motivation for non-mydriatic imaging was the aim to reproduce the real-life settings of a screening situation where an operator with basic training captures images in non-mydriatic circumstances.

2) In this study only the RTvue OCT was used. Either the patients should be scanned with different SD-OCTs as well, or it should be stated in the discussions section, and throughout the paper, that these results imply only to this specific instruments, and that other OCT systems may produce different results.

We thank Dr. Deák for his very valuable comment. Indeed we agree that our results may not be generalized for other devices and therefore we completed the Discussion section with this statement as a shortcoming of our research. To relate our results to
other research performed earlier we mentioned those studies that involved RTVue OCT and compared its error type and rate to other devices.

3) It should be stated in the results section, that the correlation between RBDEs and SSI was low/moderate (as shown in Table 3)
We made this correction in line 154 of the Results section.

Discretionary Revisions

1) The heading of table 1 may be misleading "Retinal boundary detection error scores obtained with optimal and suboptimal scan distance settings and their correlation with the SSI values.", since the p-values in this table seem to be calculated on the optimal/suboptimal BRD difference, and the p-values of the RBD/SSI correlations are in table 2.
We corrected the heading of Table 2 accordingly.

Reviewer's report

Reviewer: Andrea Giani

Reviewer's report:

Varga & Tatrai and co-Authors present a study in which they evaluated the influence of scan distance of OCT on retinal thickness measurements (RTM) and errors in retinal boundaries detection (RBDE). They found no effect on RTM, while in healthy and DME patients this factor influenced RBDEs. In AMD patients OCT distance did not show any effect. Again, in healthy and DME patients there was a negative linear correlation of RBDEs and quality scan, while no such correlation was found in AMD.
Because RTM is so important in clinical trials and daily practice, trying to find possible confounding factors is undoubtedly useful. However, this study shows some relevant flaws that need to be carefully addressed by the Authors.

Major Compulsory Revisions:

1. The most important lack in the paper is that data about RTM is missing. This is only briefly cited in the abstract and in the results section, but the actual numbers are not provided, no statistical description or tests are shown. Since this is the most important objective of the study (and the most relevant from a clinical point of view), it is important for the reader to see this data, even if negative. I suggest inserting a table, and describing what kind of analysis was executed.
We thank Dr. Giani for this extremely important comment. We agree that the most important message of our manuscript is that optimal distance settings are mandatory in order to obtain reliable retinal thickness measurement (RTM) results by SD-OCT. Therefore, we completed our manuscript with Table 5 containing the data of the RTMs per ETDRS regions in all study groups for both scanning distance settings.
2. The Authors analyzed 600 scans, and this is a really appreciable job. However, the score for RBDEs is subjective, and it was executed by only one operator. Moreover, it is not reported if this operator was blinded for the protocol used, which is very important to avoid any possible bias. In Figure 3B a white arrow indicates an error in the nasal periphery of the scan, and the same in the temporal periphery of Figure 4A and Figure 4B: to me these errors are really minimal, and I wonder if a second independent operator would mark these as errors or not. Because all the results of the study are based on this subjective scoring, it would be important to have at least a second analysis to confirm the reproducibility of the results.

We thank the reviewer for this reflection. We added statements related to these questions both in the Methods and Discussion sections of the manuscript. Indeed, the scoring of the retinal boundary detection errors was performed by only one operator. However, the grading protocol was strict, detailed and it was based on the scoring method of an acclaimed and well-referred study by Sadda et al. (Sadda, SR., et al. Ophthalmology 113.2 (2006): 285-293.) which minimizes the personal component of the grading process. Also, Sadda et al. were using only one grader in their study, similarly to our work. Based on this we would not expect a second analysis to have different accuracy.

Regarding the second remark, the operator was not blinded for the protocol, but was blinded for the study groups and scanning distance settings of the images in the course of the error scoring. To make this clear to the readers we also highlighted this fact in the revised manuscript.

We also agree with the remark that the peripheral errors of the mentioned scans are seemingly small. However, the distance from the predicted segmentation line is considerable, qualifying for an error mark in our protocol which is why we marked them in the figures.

3. The conclusions of the Authors on their data from line 236, page 10, are not completely convincing,

a. especially when they affirm that “the proprietary algorithms used to obtain the regional retinal thickness measurements could certainly smooth out small differences between the scan distance settings”. First, this is a hypothesis and for that reason the word “certainly” has to be removed. Second, the algorithm is of extreme importance in identifying retinal boundary, but once this is done it has no impact on RTM. Maybe the Authors refer to the interpolation process, if so they should better explain.

We thank the reviewer for noting this. We agree that our statement is a hypothesis and therefore we removed the word “certainty” from the text. Also, we corrected the quoted paragraph to be more precise regarding the smoothing effect on RTMs.

b. Consequent to the previous, at page 10, line 240 the Author postulate that OCT distance may influence reliability in following up thickness change, but they have no data to affirm that, and, since no influence was found in RTM I’m not really sure if this is the case.
We agree with the reviewer that our research did not assess the impact of boundary detection errors on the follow up of thickness changes. Instead, our findings raise the possibility that OCT scans with more boundary detection errors could influence the measurement and follow-up of retinal thickness changes. These measurements are playing an important role in the therapeutic decisions of patients with DME or AMD and this underlines the importance of central measurement errors. We revised the Discussion section of the manuscript addressing this question in depth.

c. In the Conclusions section the sentence from line 255 to line 259 is too long and confusing. Moreover, based on their data, I'm not really sure if I can agree with their last sentence: “optimal distance settings are mandatory in order to obtain reliable results by SD-OCT.” While this is obviously desirable from a technical point of view, it seems that their paper fails to show a clinically relevant impact of this factor.

We agree with this remark and are grateful for the suggestion to focus the basic message of our research clinically oriented. In order to make it more clear and less confusing we rewrote the conclusion section.

Minor Essential Revisions:

1. Cancel “probably” at page 3, line 62
   This correction was made.

2. Add a reference at page 4, line 70
   We added two references here.

3. The statistical analysis is not complete. While using the Wilcoxon test is not wrong, it is not sufficient and should be added a more sophisticated tests for concordance, like ICC followed by direct comparison of confidence intervals.
   We thank the reviewer for this very valuable comment. We completed our statistical analysis accordingly by the calculation of ICC for the SSI values, RBDE scores and regional retinal thickness values of the two scanning settings. We added this in the Methods sections and included additional tables 4 and 6 showing these results.

4. Page 7, line 153, “markedly higher” implies some sort of analysis, which is not reported.
   The expression “markedly higher” was used to underline the noticeable difference of the AMD group from the others. We deleted it from the text.

   The word “proliferation” was used to describe the study group in the mentioned article. Schneider et al. used this expression for the fibrovascular proliferative tissue formation, and therefore we changed “proliferation” to this term in order to make it clearer.

6. The entire paragraph from page 9 line 216 to page 10 line 228 is confusing and needs to be rewritten.
We thank the reviewer for this observation. The mentioned paragraph was completely revised.

7. MM5 protocol is explained in Figure 2 and its legend, but should be also reported in the Methods section. We thank the reviewer for noticing this. We included the explanation of the MM5 protocol in the Methods section accordingly.

8. In Figure 8A there is no arrow for the central error. We made this change, now an arrow shows the central error also.

9. In Table 1 RBDE acronym has to be defined. The RBDE acronym was changed to its definition, retinal boundary detection error.

10. In Table 3 third column, a p-value cannot be 0.000, it is a statistical nonsense: if the number is very low please indicate <0.001. The corresponding correction was made.