Author's response to reviews

Title: The ChromaTest, a Digital Color Contrast Sensitivity Analyzer, for Diabetic Maculopathy

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Author's response to reviews: see over
Dear Editor,

Thank you for giving us the chance to revise this manuscript once again. I hope this final draft will fulfill all the suggestions/comments from the reviewers. I personally contacted Dr. Goatman to ask for clarification of his comments to improve on this manuscript, but as you can see from the email attached below (and forwarded to Iratxe Puebla by email), he has changed his earlier comments and I have altered the manuscript accordingly. I have also changed the manuscript as requested in points 1 and 4 in the email from Iratxe Puebla including the minor revisions requested by Dr Goatman. Dr Holubkov’s comments have also been addressed with this new edition. I have indicated the specific changes made to the manuscript below.

1. The p values have been clarified as indicated by Dr. Holubkov
   a. The last paragraph of results on p.7 has been changed to read “When repeating the analysis in Table 4 for only subjects with logMar BCVA >=0.1, sensitivity to detect CSMO improves to 75% (CI: 47-91%) and specificity to 85% (CI: 67-89%) p=0.0002. Similarly, when repeating the analysis in Table 4 for only subjects with CSMO with central macular thickening, sensitivity to detect CSMO improves to 83.3% (CI: 58-96%) p<0.0001.”
   b. The text reading “χ² test: p<0.0001 comparing proportions of true positives among the test positive versus test negative subjects” has been added to the bottom of Table 4 as advised by Dr. Holubkov.

2 + 3. As stated earlier, I received correspondence from Dr. Goatman regarding these points. He has altered his stance regarding the need for comparing or changing the method in which the thresholds are derived. Unfortunately, due to the limitations of the study data, this is the only sensible way by which the data is derived. The shortfalls of this study are documented in the discussion and abstract as requested by Dr. Goatman.
   a. The comment “threshold levels were derived using the same data set for both training and testing the effectiveness since this was the first study of NPDR using the Chromatest.” has been added in the results section of the abstract.
   b. As the previous versions have indicated, the 2nd paragraph on p.10 in Discussions reads “Unfortunately, we were forced to obtain normal threshold levels through the same dataset. These levels were obtained through analysis of cases without CSMO. Therefore, the results may be biased.”

4. The VA’s have been included by changing the data for Figure 1-3 into table form (Table 1-3).

Furthermore, Dr. Goatman’s advice for minor changes have all been addressed:
Minor changes
   p.4 “The letters ARE displayed on a background…” : done
   p.5 “(figure 1)” move BEFORE full stop. : done
p.5 Include IQR for LogMAR summary statistics. The IQR is stated in paragraph 2 of results on p. 6. It reads “Interquartile range for VA NPDR and CSMO was 0.20 and 0.30, respectively.”

On behalf of all the authors, I would like thank the reviewers and editors for their time and consideration in reviewing our manuscript.

With kind regards,
Roger Wong

Email from Keith Goatman (26 July 2008):

Dear Roger,

I don't mind you contacting me at all. I'm sorry for making complicated suggestions which maybe in retrospect were unreasonable. I think there is more that could be done with the data, but that can be for another paper and this one has been delayed long enough.

I do have serious concerns about using the same data for training and testing. In a study we are currently performing the sensitivity dropped from 95% training on the test set to 15% when I trained and tested on different data. This is obviously an extreme example, but it does illustrate the care which must be taken with results generated this way.

I would be happy for the paper to be published immediately providing there is a bit in the abstract and discussion to the effect that the results are based on training using the test data, and this may have biased the results. I also think it may be a good idea to include the raw data (as you suggest) like you did in an earlier draft.

Best wishes,
Keith

Roger Wong wrote:
> Dear Dr. Goatman,
> 
> Please forgive me for contacting you directly as I am truly stuck.
> Could you help me to fulfil the revisions requested by the reviewers and editor.
> 
> I would be most grateful if you could clarify how you combined PCCT + TCCT to come up with a higher sensitivity and specificity. Also, what you mean by including the VA in the classifier. Do you mean to make the VA’s available in the data to make the point regarding colour blindess?
> (ie. Provide the data set for the readers)
> 
> Sorry again to bother you about this as the editor has given me a last chance to revise this manuscript and I do not want to make any mistakes.
Email from BMC Editor (26 July 2008)
MS: 2249073321276554
The ChromaTest, a Digital Color Contrast Sensitivity Analyzer, for Diabetic Maculopathy Roger Wong, Jaheed Khan, Temilade Adewoyin, Sobha Sivaprasad, Geoffrey B Arden and Victor Chong

Dear Mr Wong,

I am writing to you with regard to the above manuscript, which has been resubmitted to BMC Ophthalmology. I do apologise for the delay getting back to you with an editorial decision on the paper.

We approached three of the original reviewers for further advice on the last version of your manuscript and their comments are accessible in PDF format from the links below. Do let us know if you have any problems opening the files.

Referee 3:
http://www.biomedcentral.com/imedia/2096066672085418_comment.pdf
Referee 2:
http://www.biomedcentral.com/imedia/1112519586205199_comment.pdf
Referee 4:
http://www.biomedcentral.com/imedia/1250495782048759_comment.pdf

As you will see, all of the referees have raised additional concerns on the manuscript and feel that you have not paid the necessary attention to the requested revisions.

Drs Goatman and Holubkov have raised additional concerns with regard to several aspects of your statistical analyses. Please note that Dr Goatman has already assessed your manuscript three times and Dr Holubkov has seen the work twice.

You should note that it is our standard policy to allow a maximum of two rounds of revisions on manuscripts under consideration. However, given the exceptional circumstances for the review process of your paper, we are willing to allow one further revision on this submission. I must note, however, that this round of revision will be the last that we will allow. We therefore expect to received a
revised manuscript that carefully and thoroughly addresses the outstanding concerns raised by the referees.

We therefore expect you to fully address the following points in your revised manuscript and the accompanying covering letter:

1. Clarify the calculation of the p-values as requested by Dr Holubkov.
2. Clarify the thresholds for the piecewise breakdown as requested by Dr Goatman.
3. Provide a justification for your piecewise analysis vs. the approach provided by Dr Goatman, we feel that you would make a stronger case for publication if you provided a comparison of the calculations obtained using the two approaches.
4. Provide the VA information in the classifier as requested by Dr Goatman.

Please accompany your revised manuscript with a detailed covering letter providing a description of the changes made in the manuscript in response to the reviews.

Please note that, since the revisions affect the analysis of the data, and potentially, their interpretation, we will need to seek further advice on the revised paper.

Please also note that if the reviewers indicate any further shortcomings in the revised version of the manuscript we will have to decline any further consideration of the work.

Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals). It is important that your files are correctly formatted.

We look forward to receiving your revised manuscript by 25 August 2008. If you imagine that it will take longer to prepare please give us some estimate of when we can expect it.

You should upload your cover letter and revised manuscript through http://www.biomedcentral.com/manuscript/login/man.asp?txt nav=man&txt man id=2249073321276554. You will find more detailed instructions at the base of this email.

Please don't hesitate to contact me if you have any problems or questions regarding your manuscript.

With best wishes,

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