Reviewer's report

Title: Structure/function relationship and retinal ganglion cells counts to discriminate glaucomatous damages

Version: 6  Date: 24 July 2015

Reviewer: Enrico Martini

Reviewer's report:

Major compulsory revisions
1) The declared aim of the study is to assess the correlation between the estimated RGC count and structural and functional parameters in different stages of the disease. In the paper there is only a general correlation between many parameters but always regarding the entire study group and not the different stages. The only measure regarding the 3 different groups is the mean of RGC count (peripapillary and macular) and some OCT parameter (avg RNFL, avg GCC, temporal RNFL are reported in fig.2-6) and the significance of difference between groups (but no correlation) Some more data are cited in the text (lines 234-243) but there is no complete data presentation (I think a table with all different mean measures in the 3 group could be useful).

As I mentioned the correlation is calculated only in the entire group and it is not surprising that most all parameters show good correlation as the cell count estimate is calculated using OCT and visual field parameters.

You should add the correlation in the different groups or change the declared aim of the study.

2) In the methods section you diffusely explain Global loss volume and Focal loss volume (OCT parameters), in the table 1 there are data about correlation of these 2 parameters and the other OCT, visual field and RGC count parameters but in the text there is no comment on this.

If you feel that these data do not add any significant contribution you should eliminate them, otherwise I feel that you should comment on it.

3) Some statements are contradictory: I think that if you use and accept GSS that is based entirely on visual field as your reference standard you cannot assume that perimetry is not able to discriminate early damage from normal (lines 232-234): your data show that VFI is not sensitive enough in early cases while PSD and MD can do it, and it is not surprising considering that GSS is based exactly on MD and PSD.

4) In table 1 you should add the significance of difference between groups for all parameters. This would be very useful in the judgement about the performance of different tests and different parameters in discriminating between the different stages.

Minor essential revisions
1) In the DISCUSSION section the last sentence (lines 328-330) is quite obscure how "glaucoma characteristics of each individual patient " could affect the estimate of RGC count. You should explain better or else eliminate this sentence.

2) In table 2 in the SAP derived formula there is in the final formula a "gl" that is not cited or explained in the legenda. The "m" and "b" values how can be obtained? The linear function that is cited how is calculated? I think that some explanation is due in addition to the citation of the original work.

3) In the line 104 is cited BCVA > 0.5: is it an inclusion criterion? If it is, it should be clearly stated.

4) In statistical analysis description at line 206 is written "three treatment groups". I think it refers to 3 groups of severity and it should be corrected.

5) In the "Methods" section it would be advisable to better explain which are the parameters whose correlations are explored, otherwise the table 3 is the only point where you can find every data and most of them are highly significant, so it is difficult to extract any sense.

6) I think that it is obvious that any global index will be poorly sensitive in differentiating between normal and early disease and will be more sensitive in established and advanced disease. Perhaps it would be interesting to investigate whether focal damage index is more sensitive in these cases.

DISCRETIONARY REVISIONS

I feel that some of the results are explained by your subgroup classification: probably if you put GSS stages 1, 2 and 3 together the differences between groups in the VF and OCT parameters will be more significant.

There is also as you correctly cited an imbalance between groups with most of cases in the very early disease and this may affect correlation results

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests