Reviewer’s report

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

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Reviewer: Francisco Javier Goñi

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STRUCTURE/FUNCTION RELATIONSHIP AND RETINAL 1 GANGLION CELLS COUNTS TO DISCRIMINATE 2 GLAUCOMATOUS DAMAGES 3 4
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Is the question posed original, important and well defined?
The research question posed by the authors should be easily identifiable and understood.
Lines 87-90 of the paper describe the aim of the study. It remains unclear for me what is the main objective of the study. It is said “to evaluate the correlation between RGC count … and structural and functional parameters… in glaucoma patients classified in three groups according to GSS2 of Brusini”. Results show i) the discriminant capacity of SAP, OCT and RGC quantity estimates, to separate different levels of damage (according to GSS2) and ii) correlations between all variables measured (Table3). These are two different questions.

Are the data sound and well controlled?
In methods, it is not specified how many examinations (SAP and OCT) were performed to obtain the data. If only one exam was performed, there is no chance to control the variability of measurements, an important parameter to correctly interpret results. RGC count may vary significantly mainly due to SAP variability. This will have an impact in the results of RGC count’s discriminant capacity to reproducibly separate levels of damage.

In line 212 it is said that differences were considered significant when the two-sided p value was < 0.05. In lines 231, 237, 240 and 251, p is related to the level 0.01 (either bigger or lower). This must be clarified. Also, Pearson’ s coefficients are showed in the text as (r >…) instead of r=…). Please clarify.

Is the interpretation (discussion and conclusion) well balanced and supported by the data?
Discussion
The discussion properly addresses the two main questions of the study. Some
argumentations are questionable nevertheless. In lines 302 to 309 it is said that results can be considered a proof of GSS2 efficacy, but they simply confirm that GSS2 separates levels of damage according only to SAP and MD-PSD values. Any other variable considered (VFI or pure structural measurements) will probably show lower discriminant performances as they are not included in the method defining the scoring system. The argument exposed in lines 271-273 is also questionable, as reasons to explain the “delay” of SAP to detect glaucoma damage are more related to the semilogarithmic conversion of differential light sensitivity, stimulus size, grid density, etc, according to studies.

The conclusions look like an extension of the discussion and can’t be easily found. They should be summarized in a short and clear way.

Are the methods appropriate and well described, and are sufficient details provided to allow others to evaluate and/or replicate the work?

Methods are well described, but some aspects, like examination quality control (in both SAP and OCT measurements) or number of examinations are lacking.

In line 122-124 it is described that a central MD was calculated (16 central points). In lines 180-183, sensitivities are considered instead. I guess sensitivities were used for RGC count algorithm estimation, but don’t find in results what central MD was used for.

What are the strengths and weaknesses of the methods?

Main strength: potential use of RGC count to potential diagnostic/classification capabilities

Main weakness: measurement variability was not considered, mainly to check for classification reproducibility.

Can the writing, organization, tables and figures be improved?

Writing is poor in my opinion. Text must be reduced, and sentences should be shorter. Some words are incorrect (ie: hypotonic, line 106; unity, line 313; actually, line 333) REVIEW

Describe properly the conclusions

Add in Discussion strengths and weaknesses of the study

Maybe one more figure (VFI vs groups) is lacking, as it measures function in a slightly different way than MD and adds significant information

Table 2 is not a table in fact. Suggest to add as part of text

Figure 1: Add (cursive) -16 central threshold sensitivity points of the visual field corresponding to GCC area.

This paper requires a revision. The clarity and/or coherence of the paper needs to be improved. Reinterpretation of results, according to methodology limitations, is recommended.