Author’s response to reviews

Title: Comparison of glaucoma diagnostic ability of ganglion cell-inner plexiform layer according to the range around the fovea

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Version: 1 Date: 03 Oct 2019

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Date: September. 30, 2019

Dear Editor

Attached please find the revised manuscript entitled “Comparison of glaucoma diagnostic ability of ganglion cell-inner plexiform layer according to the range around the fovea”. A point-by-point response to each of reviewers’ comments follows. The authors wish to thank the Editorial Board for their thoughtful consideration and recommendations, and hope that this revised manuscript now meets your requirements for publication.

Reviewer #1:

I think that this work has some interesting points that are worth to be shared with the community. The main one is that the diagnostic value of assessing ganglion cell-IP layer thickness is increased if we use a smaller zone than that is now currently used (the circular ETDRS macular grid). Nevertheless there are some flaws.

First of all the definition of glaucoma: "Gluacoma was defined as the following criteria: asymmetric cup-to-disc ratio ≥ 0.2, vertical cup-to-disc ratio > 0.7, neural rim thinning, localized notching, disc hemorrhage and RNFL defects with corresponding glaucomatous visual field (VF) defects" Structural effects are quite detailed but what is exactly a "corresponding" defect? Patients with VF defects not corresponding to structural damage were excluded? If the diagnosis of glaucoma was made almost exclusively based upon structural damage it is quite obvious that correlation with a new structural test will be high. It would be more interesting to know if GCIPL measurements were highly correlated with a diagnosis made upon "functional (VF) defects". Nothing is said on the relationship between GCIPL analysis and the visual field. Visual field data are given only to confirm that Global parameters (MD; PSD and VFI) were different between normal and glaucoma eyes.

Answer) I agreed your comments. Corresponding glaucomatous visual field defects demonstrated the visual field defect on the corresponding position at the optic nerve head change based on the structure-function relationship using Garway-Heath map. As your comments, I added the specific explanation about functional damage in the present study. Unfortunately, we did not analyze the diagnostic ability of the GCIPL according to the location of visual field loss.
One important consideration is that the diagnostic sensitivity of GCIPL measure in this work seems to be higher in the smaller scan zone, that corresponds to about 6-8° of visual field. So it would have been really interesting to compare the GCIPL data and the 24-2 and 10-2 visual field analysis. In the discussion at line 236 the Authors state: "Furthermore, because the GCIPL parameters in zone 1 were based on a 4 × 4 mm² area centered on the fovea, this area also exhibited a strong relationship with visual field defects within 6 degrees of the fovea" but it is not clear if this statement is an opinion of the Authors and Whence they derived it, as no data about correlations with visual field are given.

Answer) This sentence was the opinion of the authors. Although we did not evaluate the relationship between GCIPL and visual field defect, the previous studies written by the last paragraph demonstrated the GCIPL within 7.2 degrees of the retina had shown the greater relationship with functional loss than those outside 7.2 degrees. Then, we expect the GCIPL parameters in zone 1 based on a 4 × 4 mm² area centered on the fovea might be a strong relationship with visual field defects within 6 degrees of the fovea.

For preventing misinterpretation of this sentence, we move this sentence to the previous paragraph, and change to the following sentence.

“Since the GCIPL parameters in zone 1 based on a 4 × 4 mm² area around fovea might be a stronger relationship with visual field defects within 6 degrees of the fovea, the further study will be needed for evaluating the structure – function relationship.”

One more problem is that the scan is not centered on the fovea and therefore especially in some eyes (tilted discs) there may be a wide variation in the measure in superior and inferior sections. The Authors correctly state that in the discussion but I think that a stronger underlining of this point should be done.

Answer) We fully agreed your comments. So, as your comments, we tried minimizing the variation of the scan not to be equally centered on the fovea. We added the following sentences in the limitation section.

“For minimizing the variation of the fovea in the scan, we compared the parameters in the superior and inferior areas between each zone 2 and conventional ETDRS area, then the data in the present study showed the reliable correlation and agreements between two area.”

What is the usefulness of a wide scan (9x12 mm) if the best results are yielded by a 4x4 analysis? perhaps it would be better to use a smaller scan well centered on the fovea. A wide scan may be useful to acquire in the same scan the macula and the peripapillary area to analyse both ganglion cells and RNFL, but nothing is said about nerve fibre layer in this paper.

Answer) Since the purpose of the present study was to compare the glaucoma diagnostic ability of GCIPL parameters according to the area around fovea using wide-angle SS-OCT, we did not mention the RNFL parameters. As your comments, we added the average RNFL thickness in table 1.

I don't completely understand why the Authors choose to limit to three and six squares the analysis per sector and didn't use the complete square (4x4 and 6x6) with 4 and 9 squares per sector instead of 3 and 6 and perhaps some motivations may be useful.

Answer) When setting up the area around fovea, we tried to define the zone as close as the circular area. Then, we expect that zone 1 and zone 2 was similar to circular 4 x 4 mm and 6 x 6 mm area. In the text is said that both groups didn't differ for sex, age, Axial length, spherical equivalent and CCT but in table 1 there is no information about sex and CCT.

Answer) As your comments, we added the data about sex and CCT in table 1.

In the "Materials and Methods" section is described that repeated measures were obtained to assess intraobserver agreement, but in the results and in the discussion there is nothing in this regard: the Authors should expose the data and discuss it or eliminate this section in Materials and Methods.

Answer) We mentioned the result of intraobserver agreement as ICC (intraclass correlation coefficients) in Result sections. Figures 2 and 3 are quite useless as they state that in all cases there is a good agreement between the
two scan patterns in more than 93% of cases. Moreover it is stated in the text that the small differences were not correlated to any parameters so I think this 2 figures may be eliminated using a table if the Authors think it is not enough to describe the results in the text.

Answer) As your comments, the result of Bland-Altman scatterplot was explained as the table 4 and 5 in Result section, instead of Figure 2 and 3.

There are some imperfections in the english translation: frequently were is used instead of was and retina instead of macula- At line 161 is written: "three groups" when there are only two.

Answer) As your comments, the manuscript has been re-edited by professional Springer Nature Author system, which was linked to the online site of “BMC ophthalmology”.

At line 225 i think that the meaning as that when GCIPL is reduced the diagnostic ability of its measurement is increased, the english phrasing is confusing as one could understand that it is more useful to measure it where it is naturally thinner i.e. more far away from the foveal center.

Answer) I fully agreed with reviewer’s comments. We revised this confused sentence as the following sentence.

“the diagnostic ability of GCIPL parameter would increase as its measurements get closer to the fovea.”

Reviewer #2:
This is an interesting paper aiming to compare the glaucoma diagnostic ability of the ganglion cell-inner plexiform layer (GCIPL) thickness depending on the range around the fovea using wide-angle Swept-Source OCT (SS-OCT). There some limitations of the study noticed already by the authors in the discussion section.

Answer) As your comments, the present study had some limitations, and we mentioned these limitations in the manuscripts.

It would very important to apply this methodology to hypertensive or preperimetric glaucoma cases in order to evaluate the results of GCIPL thickness and specifically the zone 1 as well as in normal tension glaucoma cases.

Answer) Unfortunately, the present study did not include hypertensive or preperimetric glaucoma cases. The preent study included the glaucoma patients with glaucomatous optic neuropathy corresponding with visual field defect on the basis of the criteria applied to the study.