Author's response to reviews

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

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Author's response to reviews: see over
I think this article should be taken into account because it is an original research never published on a scientific journal. The main topic is the structure/function relationship of the optic nerve in glaucoma: in particular, the moderate relationship between visual field test and optical coherence tomography (OCT) measures is not always able to discriminate patients at various stages of glaucomatous disease. This is why in this article it is proposed a new approach to the patient based on the number of retinal ganglion cells empirically calculated. We used a mathematical algorithm previously developed by Medeiros et al. to estimate circumpapillary retinal ganglion cells number by using visual field and OCT datas; nevertheless, unlike Medeiros, we also calculated the ganglion cells number in the macular region using the ganglion cells complex thickness measured by OCT. After that, we noticed that circumpapillary and macular retinal ganglion cells number could discriminate absence of disease, early and advanced glaucoma. This could be useful in those cases in which diagnosis of glaucoma is not sure and in particular as a method for a follow-up of patients.

RESPONSE TO EDITOR’S COMMENT  [“To my understanding, the authors use a formula that incorporates OCT and VF measures to predict total RGC numbers, and then show that these numbers vary over disease severity (which are defined by these same measures) and OCT measures (which are part of the formula for determining RGC numbers)]

Actually, glaucoma patients evaluation is based on the Visual Field and Spectral Domain OCT examinations. These tests are performed separately and their results are used by the ophthalmologist for glaucoma diagnosis and therapeutic choice. Several studies in the past demonstrated that correlation between functional and structural parameters is just moderate. Moreover, glaucoma specialists also take into account other data (age, life expectancy, severity of disease, compliance to therapy, neuropathy progression rate, risk factor, eccentricity, defect position in the visual field, etc.) that are left to a personal and subjective evaluation. Clinical reasoning is based on the combination of all these parameters (included Visual Field and OCT data): they join in a medical process that gives to the ophthalmologist the possibility to decide how treat the disease. Having said this, we must remember that glaucoma is an optic neuropathy with progressive retinal ganglion cells loss: for this reason we can’t absolutely leave out the RGCs number from our clinical reasoning. Unfortunately, a direct estimate of this number is not possible (it requires a retinal biopsy), so that we must be satisfied with an indirect evaluation. Medeiros’s formulas to estimate retinal ganglion cells number represent not only an interesting combination of functional and structural parameters, but also a method to take into account all other data (eccentricity, age, differential light sensitivity, axonal density, etc.) in an objective way: just a number to summarize a wide and partially personal clinical reasoning. Retinal ganglion cells number reflects the severity of disease (based also on PSD value, not included in Medeiros formulas) and well correlate with functional parameters themselves (PSD and VFI). At the same time RGCs number has a good correlation with sectorial thicknesses obtained with OCT: a better correlation with a specific sector could have indicated the region from which retinal ganglion cell loss starts, but we are not able to demonstrate it with our results.