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Peripapillary choroidal thickness in glaucoma measured with optical coherence tomography

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ABSTRACT

As choroidal changes have been suggested in glaucoma, we examined peripapillary choroidal thickness (CT) in patients with and without primary open-angle glaucoma (POAG) using spectral-domain optical coherence tomography (SD-OCT). We collected measurements retrospectively on 70 eyes of 70 patients consecutively undergoing SD-OCT. POAG ($n = 31$) and suspect eyes ($n = 39$) had two reliable and repeatable Humphrey 24-2 visual fields with glaucoma hemifield test outside or within normal limits, respectively. A 360-degree peripapillary scan was performed using the standard protocol for retinal nerve fiber layer (RNFL) assessment. Using provided software, two independent masked investigators manually segmented CT as the area of visible choroidal vasculature. Agreement between investigators was determined using Lin's concordance correlation coefficient (CCC). A single masked observer determined clock hours of parapapillary atrophy (PPA) and the presence of ßPPA for each optic nerve quadrant. Correlation between RNFL and CT was assessed; two-sample *t*-tests were used to determine differences in RNFL and CT between POAG and suspect eyes; and linear regression was used to model changes in RNFL and CT. We found that independent measurements of CT by two observers were highly correlated (Lin's CCC for global CT; $\rho_c = 0.93$, $p < 0.001$). RNFL and CT measurements were not significantly correlated for any peripapillary location ($|r| \leq 0.15$, $p \geq 0.22$). Global CT (ß = −1.94, 95% confidence interval [CI] −2.76, −1.13) but not RNFL thickness (ß = −0.18, 95% CI −0.58, 0.22) decreased significantly with age. Compared to suspect eyes, eyes with POAG had significantly thinner RNFL measurements at all locations ($p \leq 0.005$) but CT measurements did not differ between groups for any location ($p \geq 0.13$). Adjusting for glaucoma status and age, total (ß = 3.15 95% CI −0.24, 6.53) and ß clock hours of PPA (ß = 1.33, 95% CI −1.72, 4.38) were not significantly associated with global CT; the spatial distribution of PPA was not associated with underlying CT, though PPA was graded subjectively and may have been subject to spatial mismatch with a singular peripapillary eccentricity on SD-OCT. We conclude that eyes with POAG did not demonstrate reduced CT nor was there a correlation between RNFL and CT maps. This study does not support the use of CT assessment in glaucoma diagnosis or management.

1. Introduction

While glaucoma is a leading cause of blindness worldwide, its pathogenesis is still not fully understood (Quigley, 1996). Currently, glaucomatous optic neuropathy (GON) can be detected by stereoscopic examination of the optic nerve, optic nerve photography and/or computerized imaging technologies. Known features of GON include atrophy of the retinal nerve fiber layer (RNFL), focal or diffuse narrowing of the neuroretinal rim, optic disc splinter hemorrhage and parapapillary atrophy (PPA) (Townsend et al., 2009; Harper and Reeves, 2000; Theodossiades and Murdoch, 2001).

Some investigators have suggested that peripapillary choroidal atrophy may be present in GON and that clinical evaluation of choroidal thickness (CT) may be a useful tool in its clinical detection (Spaide, 2009; Yin et al., 1997). In a histopathological study of normal eyes and eyes with primary open-angle glaucoma (POAG) or optic atrophy, Yin et al. (1997) found that POAG eyes had the thinnest choroid both globally and in the peripapillary region. More recently, Spaide et al. (2008) used spectral-domain optical coherence tomography (SD-OCT) to measure CT. They have reported CT in normal eyes, (Margolis and Spaide, 2009) high myopia (Fujiwara et al., 2009) and central serous chorioretinopathy (Imamura et al., 2009). Spaide (2009) have suggested that choroidal thinning may

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also be a feature of glaucoma and that areas containing PPA may correspond to the areas of greatest choroidal atrophy in glaucoma patients. However, this hypothesis was based on data from only 5 glaucoma patients and without conducting a study or specific quantitative analysis to examine CT in glaucoma.

We undertook the present study to determine if CT values measured by SD-OCT collected during routine glaucoma assessment could provide a reliable assessment of CT. We sought to determine whether different observers could measure CT reliably and to determine if previously reported age–CT relationships could be replicated in order to validate this CT measurement technique. Finally, we investigated whether CT values differ between the eyes of patients with POAG and those of glaucoma suspects with normal visual fields.

2. Materials and methods

This retrospective cross-sectional study was approved by the Institutional Review Board at Weill Cornell Medical College and New York Presbyterian Hospital and adhered to all tenets of the Declaration of Helsinki. Patients under 18 years of age or with a history of visually significant cataract or corneal disease (visual acuity <20/40), inflammatory eye disease, exfoliation or pigment dispersion syndrome, ocular trauma, or non-glaucomatous optic neuropathy or visual field loss were excluded.

Included patients had documented bilateral open angles with at least two reliable (fixation loss <33%; false-positive rate <33%; false-negative rate <33%) and repeatable 24-2 SITA-standard automatic perimetric examinations with the Humphrey Field Analyzer II (Carl Zeiss Meditec, Dublin, CA). Each included patient had undergone optic nerve digital stereophotography of acceptable or excellent quality with a Topcon TRC 50EX Retinal Camera (Topcon Co., Tokyo, Japan) within 12 months of inclusion. POAG eyes had two reliable and repeatable visual fields with the glaucoma hemifield test outside of normal limits and pattern standard deviation cluster criteria ($P < 5\%$) corresponding with documented neuroretinal rim narrowing or notching on stereophotographs. All POAG patients were on intraocular pressure (IOP) lowering therapy at the time of SD-OCT. Glaucoma suspects were typically referred due to family history or physiologic cupping; eyes in this cohort had all IOP measurements <21 mm Hg, two normal perimetric exams with the glaucoma hemifield test within normal limits and intact neuroretinal rims documented with stereophotography, regardless of cup-to-disc ratio.

Consecutive patients undergoing SD-OCT (Heidelberg Spectralis® HRA+OCT; Heidelberg Engineering, Heidelberg, Germany) who met inclusion criteria were retrospectively enrolled in the present study. Indications for OCT included existing GON in one or both eyes or suspected glaucoma including enlarged or asymmetric cup-to-disc ratio. A 360-degree 3.4 mm diameter peripapillary circle scan was performed using standard protocol for RNFL assessment (Leung et al., 2010). Using the provided Heidelberg Eye Explorer software (version 1.5.12.0; Heidelberg Engineering), a reader masked to clinical patient data manually delineated CT as the area of visible choroidal vasculature between the outer retinal pigment epithelial border and the inner scleral wall (Fig. 1). In order to determine interobserver agreement for our technique, CT was manually segmented by a second independent and masked reader for the first 17 eyes enrolled in the study.

For each included eye, optic nerve stereophotography was evaluated using a stereoscopic viewing lens by a reviewer masked to all patient data. The presence and extent of both alpha and ßPPA was recorded in clock hours, and the presence or absence of ßPPA in the nasal, inferior, superior and temporal quadrants was noted.

Lin's concordance correlation coefficient (CCC) (Lin, 1989) was used to assess interrater agreement for CT measurements made by two masked independent investigators. Correlation of RNFL and CT measurements was assessed for each peripapillary location using Pearson correlation. The chi-squared test was used to compare categorical patient variables, and two-sample *t*-tests were used to

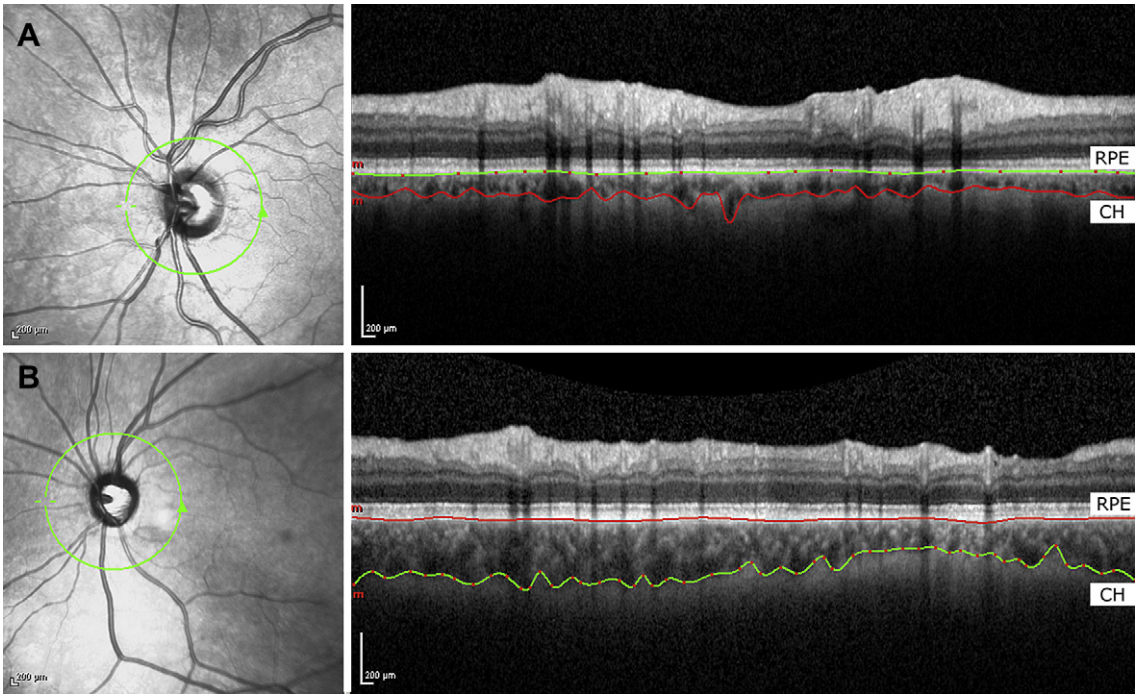

Fig. 1. Images from 360-degree peripapillary SD-OCT scans. Examples of images depicting choroidal thickness and demonstrating manual delineation of choroidal vasculature lying between the outer border of the retinal pigment epithelium (RPE) and the posterior choroidal vessels (CH). A: Patient with thin choroid. B: Patient with thick choroid. SD-OCT: spectral-domain optical coherence tomography, POAG: primary open-angle glaucoma.