Quantitative analysis of retinal layers on three-dimensional spectral-domain optical coherence tomography for pituitary adenoma

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Abstract

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Protocol

Subjects

Step 1.

The SD-OCT database of 38 patients (21 male, 17 female) with diagnosis of pituitary adenoma and 39 normal controls (19 male, 20 female) were collected between August 2015 and July 2016.The main patient exclusion criteria were: 1) presence of congenital eye disorders; 2) a history of ocular surgery; and 3) presence of any optic disc anomaly or macular disease. Healthy people with a normal ophthalmic examination were selected as the control group. This study was approved by the Institutional Review Board of the Nanjing General Hospital of Nanjing Military Command and adhered to the tenets of the Declaration of Helsinki. The informed consents were required from all subjects with verbal permissions during the process of OCT inspection.

SD-OCT examination

Step 2.

Subjects underwent SD-OCT examination by commercially available equipment Topcon DRI OCT-1 (Topcon Corporation, Tokyo, Japan) without pupil dilation. Macula was scanned using standard 6×6 mm^2 protocol, in which 3D acquisition consisted of 256 b-scan slices. The OCT image size was 512×256×992 voxels, or with the resolution of 11.72×23.44×2.3μm^3. The raw images were exported from the OCT machine in .fds format for analysis.

Retinal layers segmentation on OCT images

Step 3.

Eleven surfaces and ten layers were automatically segmented using the 3D graph-based retinal layer segmentation approach applied on the SD-OCT data, and the original images were flattened to be convenient to quantitative analysis. The macular retinal nerve fiber layer (mRNFL), ganglion cell layer (GCL) combined with inner plexiform layer (IPL)(GCIPL), and ganglion cell complex (GCC) were analyzed respectively, as well as the total retina. The segmentation results were reviewed by a retinal specialist and the images with segmentation error were excluded.

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Demarcation of the retinal quadrants

Step 4.

In view of the location deviation of scanning focus from the fovea in some OCT data, a square was centered automatically at the fovea by detecting the closest point on the central region of the interface between RNFL and GCL according to anatomical priors, with width of 5.0 mm on the en-face projection available from the 3D SD-OCT volumes, covering the macular area (about 5.0mm in diameter). To investigate the local characteristics, the square was demarcated into four quadrants: superonasal (SN), inferonasal (IN), superotemporal (ST) and inferotemporal (IT), as shown in Fig 2. Therefore, 5 measurements were made for each interested layer (i.e. SN, IN, ST, IT and global average).

Thickness measurement

Step 5.

The thickness of each interested layer was measured in metric unit micron (µm), and was obtained though multiplying the resolution (2.3µm) by the sum number of the voxels between the top and bottom interfaces of this interested layer in z-axis direction. The resulted quadrantal thickness was the average of the thicknesses in each quadrant.

Optical intensity ratio measurement

Step 6.

The raw scanned data were interpreted as 16-bit grayscale images resulting in 65,536 levels of gray, with a range from 0 to 65,535. Because raw images were used, intensity was expressed in arbitrary units (AU). The optical intensity ratio of each interested layer was obtained by normalizing the original intensity with the intensity of reference layer. Retinal pigment epithelium (RPE) or vitreous is usually used as the reference to normalize original intensity in optical characteristic measurements of OCT data, because RPE has the highest intensity and is assumed to be a uniformly scattering layer, while vitreous has the lowest intensity. In addition,outer nuclear layer (ONL) was also found possess the lowest correlation with image quality in normal eyes, should be the best choice as baseline medium. In this study, we used the RPE as the reference layer. The resulted quadrantal optical intensity ratio was the average values according to each quadrant.

Optical intensity attenuation coefficient measurement

Step 7.

The optical intensity attenuation coefficient(OIAC) in this paper was defined as shown in follows:$\mu=\log(R/\beta+1)/(2*d)$.$R$ denotes the ratio of the integrated OCT signal of interested layer over the integrated OCT signal of reference layer, d denotes the thickness of the interested layer, β is a constant. For every A-line in every volumetric scan, values for R and d were derived and the local attenuation coefficient μ were calculated according to the equation. Then the average OIAC in each quadrant of these layers was calculated. The OIAC was expressed with metric unit mm^{-1}.

Statistical analysis

Step 8.

The mean and standard deviation of thickness in each quadrant were calculated by descriptive

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statistics for mRNFL, GCIPL and GCC respectively for all subjects, as well as the total retina. The optical intensity ratio and OIAC were also obtained their means and standard deviations according to mRNFL and GCIPL respectively.

Kolmogorov-Smirnov test was used to study the normality of the data. The data were compared between the patients and the normal controls by Mann-Whitney *U*-test for non-normal variables and unpaired *t*-test for normally distributed variables. Person's correlation was used to evaluate the relationship between the mean intensity of each retinal layer and the image quality score in the determination of reference layer, and to assess the dependency between the optical intensity ratio and the thickness of mRNFL and GCIPL for patients and controls respectively. Diagnostic performances of the indices were assessed by the receiver operating characteristic (ROC) analysis. The Delong method was employed to evaluate the statistical significance of differences in the area under the ROC curves (AUC) values.

All statistical analyses were performed with the Statistical Package for Social Sciences (SPSS, version 22.0, IBM Corp. Armonk, NY) and MedCalc V.15.2 (Mariakerke, Belgium). A p value less than 0.05 was considered statistically significant.

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