Application of Image Processing in Automatic Description for Optical Coherence Tomography and Measurement of Choroidal Thickness

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Abstract

Purposes

Currently, many eye diseases have been found to be associated with changes in choroidal thickness. The purpose of our study was to develop an efficient and fully automated method to quantify choroidal thickness using spectral-domain optical coherence tomography (SD-OCT), as it is widely available.

Methods

The patients in this study underwent an SD-OCT scan. Choroidal thickness was both manually and automatically measured from the posterior edge of the retinal pigment epithelium (RPE) to the outer border of the choroid at the fovea. The performance of the automatic method was evaluated by comparing the results to those obtained using the manual measurements.

Results

A total of 23 eyes from 23 healthy adults were scanned using SD-OCT. The mean macular choroidal thickness by automatic and manual measurements were 164.34±52.72 and 182.50±74.98 μm, respectively.

Conclusions

This study presented an efficient method to detect the boundaries of the choroid to measure choroidal thickness. This fully automated method can be effectively applied by ophthalmologists on clinically-available SD-OCT devices for choroid evaluation. (Cheng Ching Medical Journal 2019; 15(4): 23-32)

Keywords : Choroidal thickness, Optical coherence tomography, OCT, Automation

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Introduction

Choroid is a vascular layer in the eye lying between the retina and the sclera. The choroid provides oxygen and nourishment to the outer layers of the retina[1]. A variety of eye diseases including polypoidal choroidal vasculopathy (PCV), central serous chorioretinopathy (CSCR), age-related macular degeneration (AMD), and diabetic retinopathy have been found to be associated with changes in the thickness of the choroid[2]. Therefore, it is important to accurately measure the thickness of this vascular layer to understand these eye diseases.

An increasing number of investigators have studied the choroidal thickness in healthy eyes and eyes with various pathologies[2,3]. Optical coherence tomography (OCT) is a medical image technique that uses light to capture micrometer-resolution images from optical scattering media in a stable, quick, and noninvasive way[4]. Ordinarily, choroidal thickness is measured manually by measuring the length from the outer boundary of Bruch membrane to the inner border sclera[2]. It is not always easy to get a clear choroidal image by OCT, because light is scattered by pigment of retinal pigment epithelium (RPE), which makes strength of reflexed signal of SD-OCT depth-dependent. There are some ways to make it easier to measure choroidal thickness. One of them is the swept source optical coherence tomography (SS-OCT) and one is enhanced depth imaging (EDI)[3]. Choroidal thickness is now used clinically to assist diagnosis and monitor treatment response in some chorioretinal diseases.

Since measuring the choroidal thickness by manual segmentation is time consuming and the accuracy of manual choroidal thickness measurement varies from one doctor to another, it is definitely useful to develop reliable and objective automated methods to measure the choroidal thickness. In the past studies, there were some automated OCT image segmentation procedures for measuring choroidal thickness[2-6]. However, artifacts of images and weak signal from the deep retina and choroid in OCT often make it so difficult to measure accurate choroidal thickness in OCT. (Figure 1) The purpose of this study was to develop an efficient and fully automated method for quantification of choroidal thickness in clinically ubiquitous SD-OCT images.

Methods

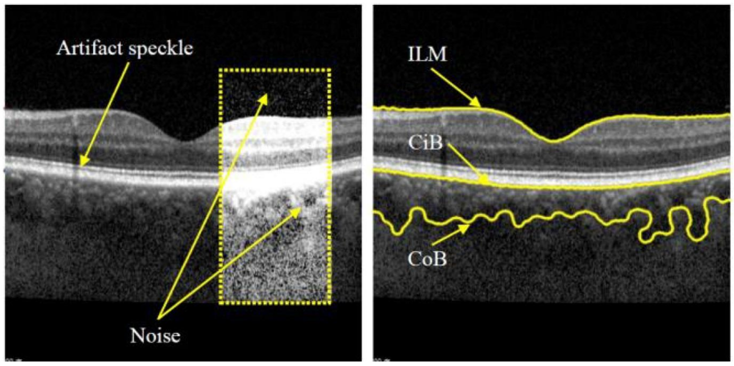
This study was approved by the Institutional Review Board of Taichung Veterans General Hospital. The research adhered to the Declaration of Helsinki.

Data Acquisition

This study utilized the OCT image database from 23 patients at the Department of Ophthalmology of Taichung Veterans General Hospital. The database included only one OCT image sequence from each patient. All patients underwent Spectralis SD-OCT scan (Heidelberg Engineering Inc., Heidelberg, Germany). The scan protocol composed 6×6 mm area which was determined by 25 scans. Each scan was separated by 24μm. The quality of the scan was assessed by the operator. Scans with low signal strength or severe motion artifacts were repeated until adequate quality was achieved. Mydriatic agents would be used if necessary. Each monochrome OCT imaging was quantized into eight bits with 256 gray levels.

Each OCT image sequence contained 25 two-dimension (2D) scans, the spatial resolution of each scan was 1008×596 pixels. For discarding redundant image contents, this study cropped every 2D scan into a 480×480 image slice. Figure 2 illustrates the relationship between an original 2D scan and the extracted image slice.

We recorded OCT parameters including central



(a) (b)

Figure 1. (a) an original OCT image with a contrast enhanced area and (b) location of the three desired layers

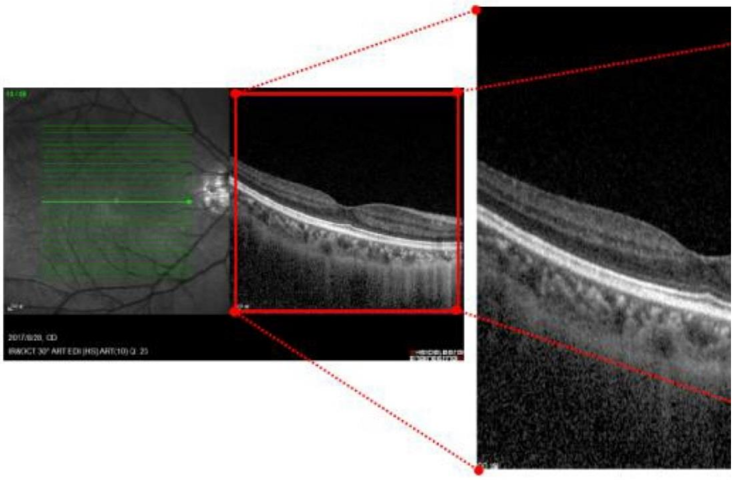


Figure 2. Image slice was cropped from an original 2D scan

choroidal thickness, the peak, the thinnest and the average choroidal thickness. Central choroidal thickness was defined as the thickness at the central point of fovea using the built-in function of SD-OCT. Peak height was defined as the greatest perpendicular height of the choroidal thickness which was measured from the RPE line to the outer segment of the choroid. The choroidal thickness as measured by the manual segmentation and the proposed method were recorded.

Flowchart of the Proposed Method

Figure 3 presents a flowchart of the proposed method. The proposed segmentation method showed in the flow chart is composed of three main parts which are ILM detection, CiB detection and CoB detection.

Image Pre-processing

Generally, OCT images contain considerable noises, speckles and vessel shadows that make segmentation difficult. Pre-processing is a significant issue before the segmentation. The effective pre-processing method for contouring should aim to reduce noises and preserve the useful information, such as edge and boundary of the layers. This study began with calculating the structure tensor and smoothing it with a traditional denoising filter, i.e. Gaussian low-pass filter. This filter is a 2D convolution operator used to blur images and remove details and noises. In this concept, it is similar to the mean filter, but it uses a different kernel that represents the shape of a Gaussian (bell-shaped) hump. However, Gaussian low-pass filter blurs the sharp boundary of anatomical structures constantly.

The anisotropic diffusion method that based on a partial differential equation is very practical not only in image denoising but also in preserving the important boundary information[7]. A sophisticated filter that performed the modified curvature diffusion equation (MCDE) has been shown more aggressive than anisotropic diffusion at enhancing and preserving edges for low-contrast image. The MCDE denoising method modified the anisotropic diffusion equation

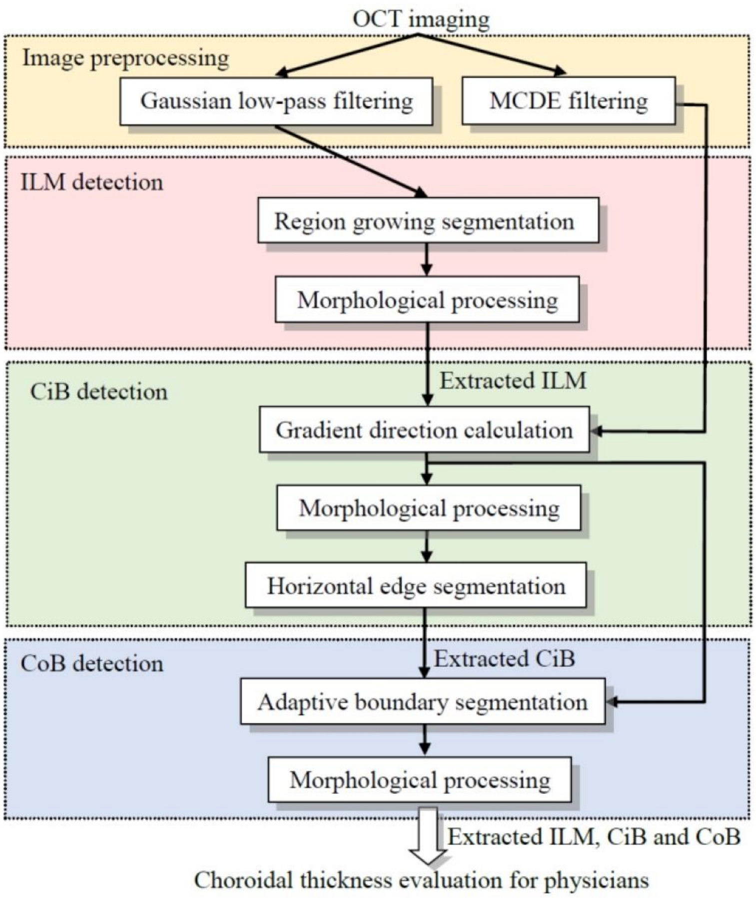


Figure 3. Flowchart of the proposed method

and utilized a variable conductance to enhance the contrast of image edges. The MCDE method is particularly effective for both good noise attenuation and faithful detail preservation.

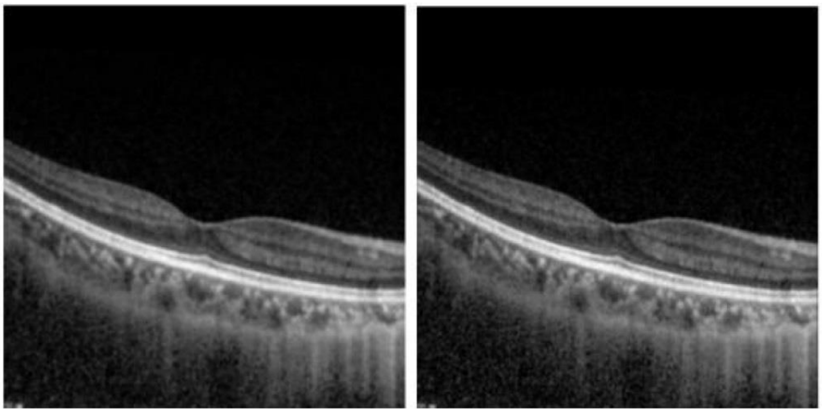
Because the three desired layers comprise distinct image characteristics, the proposed method performed the Gaussian low-pass filtering as primary pre-processing operator for ILM detection. The pre-processed image by using the MCDE method was utilized to extract CiB and CoB. Figure 4 shows results of pre-processing of the cropped OCT image slice in Figure 2.

Internal Limiting Membrane (ILM) Detection

The proposed method performed the region growing method, a practical region-based image segmentation algorithm, to locate the retina area and find the ILM. This approach is also classified as a pixel-based image segmentation method since it involves the selection of initial seed points. Region growing method examines neighbouring pixels of initial seed points and determines whether the pixel neighbours should be added to the desired region. The proposed method selected a seed point outside the retina area automatedally to extract the connected region by using the region growing method. Then binary morphological operators closing and fill-hole was utilized to polish the obtained region. Boundary of the polished region was identified as the extracted ILM. Figure 5 shows the result of ILM detection.

Choroidal inner boundary (CiB) detection

The CiB is under ILM and apparent in OCT imaging. The proposed method utilized the extracted ILM to discard the area above ILM and then performed gradient direction calculation to the pre-processed image by using the MCDE method. An image gradient is a directional change in the intensity or color in an image. Mathematically, the gradient of a two-variable function (here the image intensity function) at each image point is a 2D vector with the components given by the derivatives in the horizontal and vertical



(a) (b)

Figure 4. Result of image pre-processing: (a) Gaussian low-pass filtering and (b) MCDE filtering

(a) (b)

Figure 5. Result of ILM detection: (a) connected region outside the retina area and (b) extracted ILM

directions. At each image point, the gradient vector points in the direction of largest possible intensity increase and the length of the gradient vector corresponds to the rate of change in that direction.

The proposed method utilized the gradient direction image as input to determine horizontal massive edges, as shown in Figure 6(a). An automated thresholding algorithm was used to generate the binary edge image (Figure 6(b)). Morphological operators, i.e. dilation, closing and fill-hole, were utilized to exclude undesired edges and located the region under the CiB. Boundary of the obtained region was identified as the extracted CiB. Figure 6(d) shows the result of CiB detection.

Choroidal outer boundary (CoB) detection

The proposed method first discarded the area above the extracted CiB and then performed the MCDE pre-processed image to identify CoB. As the same as CiB detection procedure, the gradient direction calculation was performed to generate edge image (Figures 7(a)-(b)). The morphological operators were utilized to exclude undesired edges and located the region under the CoB (Figure 7(c)). Boundary of the obtained region was identified as the extracted CoB (Figure 7(d)).

However, the CoB is the most difficult to be identified in the three desired layers. That is because the light of the OCT becomes weaker when going through the retina and OCT imaging is easy to have noise in this region between choroid and sclera. If the extracted CoB was unsatisfied (Figure 8(a)), the proposed method performed the region-based segmentation to locate CoB adaptively. The adaptive thresholding method which binarizes image using local first-order statistics as adaptive threshold was used to identify vessel areas of choroid, as shown in Figure 8(b). After eliminating region above extracted CiB, morphological operators closing and fill-hole was utilized to connect and smooth vessel areas (Figure 8(c)). Boundary of the obtained region was identified as the extracted CoB (Figure 8(d)).

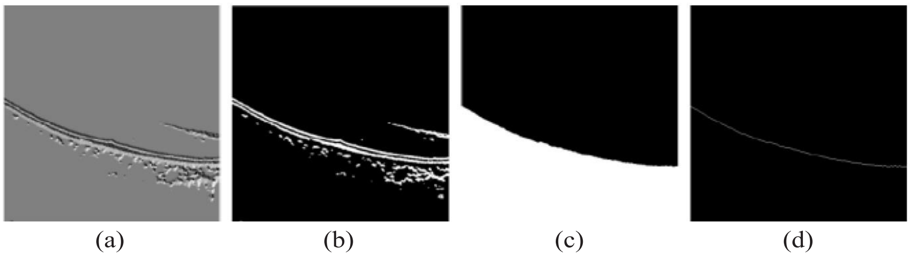


Figure 6. Result of CiB detection: (a) gradient direction image, (b) binary edge image, (c) region under the CiB and (d) extracted CiB

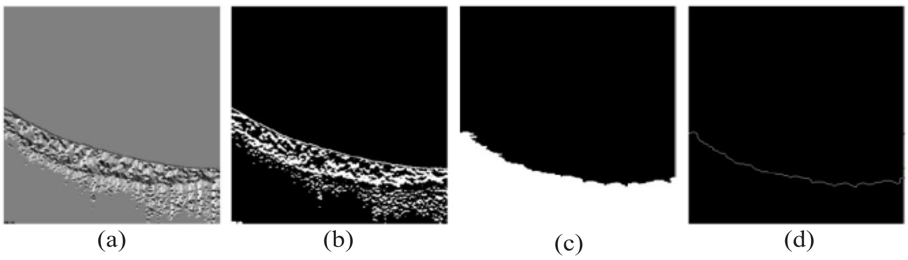


Figure 7. Result of CoB detection: (a) gradient direction image, (b) binary edge image, (c) region under the CoB and (d) extracted CoB

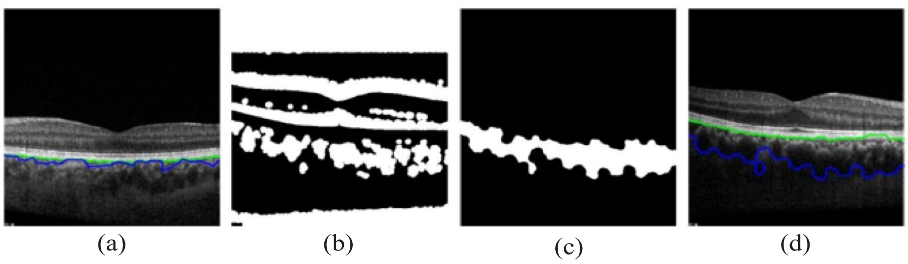


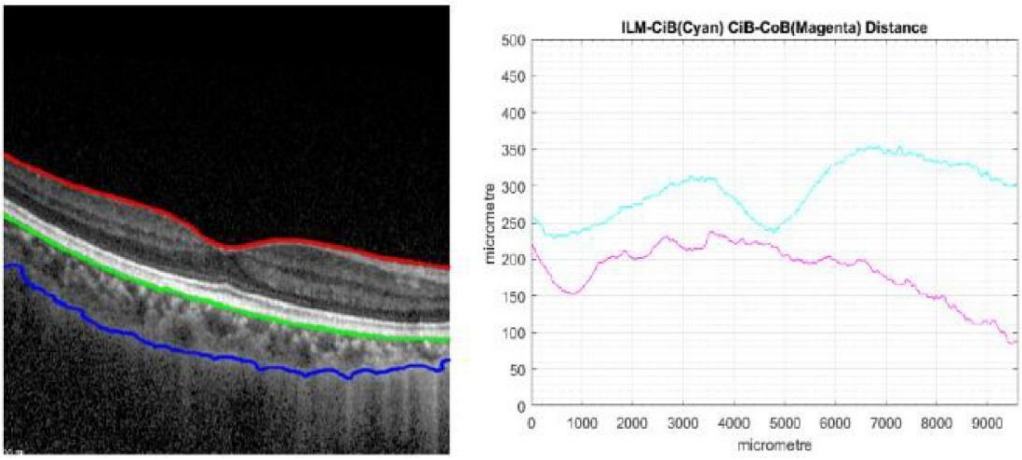
Figure 8. Adaptive CoB segmentation (extracted CiB (green) and CoB (blue)): (a) unsatisfied CoB, (b) binarized image, (c) vessel areas and (d) extracted CoB

Results

This study experimented 23 healthy adults with manually sketched OCT contours to test the accuracy of the proposed method. In this work, the image pre-processing method was first performed to reduce noise and preserve detailed information. The proposed method used the Gaussian low-pass filter of size 5×5 with standard deviation 2.0. The MCDE method set the conduction coefficient kappa as 70 experimentally. Image segmentation procedures always employed region growing method with the threshold as 0.5 to extract boundaries of desired layers. Figure 9(a) demonstrates the final result of the cropped OCT image slice in Figure 2 by using the proposed method.

In an image coordinate plane, the distance between two points is usually given by the Euclidean distance (2-norm distance). The distance from a point to a line is the shortest distance from a fixed point to any point on a fixed line in Euclidean geometry. This study evaluated two thicknesses between the three layers by the Euclidean distance. The thickness between ILM and CiB was obtained to identify the central slice. The distance between CiB and CoB was estimated as choroidal thickness. Figure 9(b) illustrates the evaluated thickness (μm) of the cropped OCT image slice in Figure 2.

Figure 10 shows the results applying the proposed segmentation method on various cases. Average execution time of each case was less than 5.0 seconds. These simulations were made on a single CPU Intel Xeon E3-1225 3.3 GHz personal computer with Microsoft Windows 10 operating system and the



(a) (b)

Figure 9. (a) Segmentation result (extracted ILM (red), CiB (green) and CoB (blue)) and (b) evaluated thickness between ILM, CiB and CoB

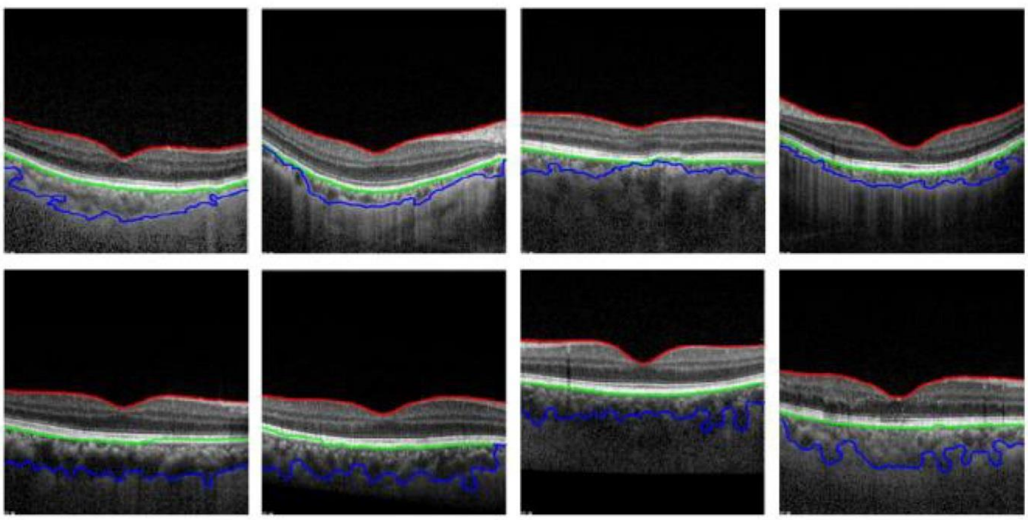


Figure 10. Final segmentation results (extracted ILM (red), CiB (green) and CoB (blue))

program development environment was MATLAB (R2016b) software (The MathWorks, Inc., Natick, MA). Figure 11 compares the results applying the proposed segmentation method and manual segmentation, showing that automated segmentation could delineate the vascular layer more precisely.

Mean macular horizontal CT was 164.34±52.72μm by automated segmentation; and 182.50±74.98μm by manual segmentation.

Discussion

In this paper, we proposed a novel technique for automated choroid layer segmentation in SD-OCT images. The pre-processing of the proposed method applied an MCDE filter to reduce the noises but preserved the boundaries in the OCT imaging. An adaptive segmentation method was used to generate the desired boundaries by the selected slice within the OCT scans and then the region based segmentation automatedally produced precise delineation of the ILM, CiB and CoB. In our study, the results of automated choroid segmentation were similar with those of manual segmentation.

In the present study, we used Spectralis SD-OCT to scan a 6×6 mm area which was determined by 25 scans. The mean macular CT was found to be 164.34±52.72μm by automated segmentation; and 182.50±74.98μm by manual segmentation. These results demonstrate that the proposed method can accurately segment the choroid of SD-OCT images.

The choroidal thickness measured by our method is generally thinner than that by the manual segmentation. The reason is that the proposed measures were taken from the posterior edge of the RPE to the precise outer aspect of the choroidal vessels, and manual segmentation includes partial outer border of choroidal stroma.

Ruiz-Medrano et al.[8] who used SS-OCT and Flores-Moreno et al.[9] who used SD-OCT provide data about mean macular choroidal thickness. Ruiz-Medrano had a result of 301.89μm in adults. Flores-Moreno had a result of 257μm in healthy patients. Masaya Hirata found it to be 191.5μm with SS-OCT manually[10]. These previous results are slightly different from ours probably due to differences in age distribution, races, and scanning protocol. Another possible reason is that the measures were taken from the posterior edge of the RPE to the outer aspect of the choroidal vessels, rather than the outer border of choroidal stroma.

Traditionally, the thickness of the choroid has been evaluated using several different approaches, including simple measurement at a few points, or using a radial or raster scan protocol. Some studies used the Early Treatment Diabetic Retinopathy Study (ETDRS) grid to construct a choroidal thickness map, and averaged the thicknesses of all measurement points within each of nine areas based on the ETDRS grid to obtain mean sectorial choroidal thickness. However, measurement of a few sampling points tends to be influenced by focal thickening or thinning of the choroid or, more often, by irregularity of the inner chorioscleral border[11]. In this study, we presented an efficient method for detecting the boundaries of choroid and estimating the choroidal thickness. We accurately defined the posterior vessel border to obtain vascular choroid thickness and measured the choroidal thickness at every single pixel, rather than at a few sampling points. An automated measurement of the choroidal thickness that can measure any pixel on the scan performed in the present study was superior to previous studies analysing the averaged choroidal thickness in the ETDRS grid, which may miss focal choroidal thinning.

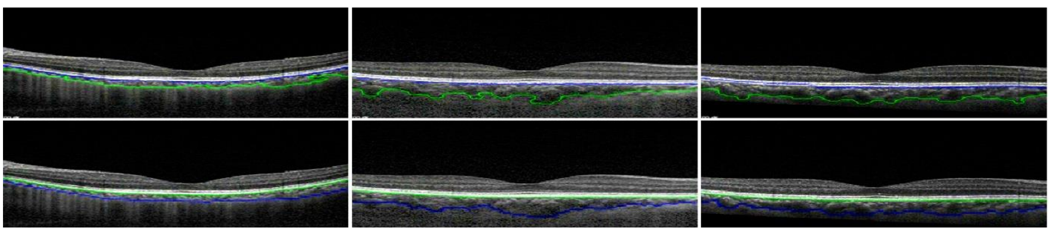


Figure 11. The results applying the automated segmentation method and manual segmentation: automated segmentation (upper row) (CiB (blue) and CoB (green)) and manual segmentation (lower row) (CiB (green) and CoB (blue))

Many diseases associates with changes in the choroidal vascular layer. Mehreen Adhi et al. used SD-OCT to evaluate the morphology and vascular layers of the choroid in Stargardt disease and reported focal choroidal thinning in 21 of 41 eyes (51%), and attenuation of large choroidal vessel layer in 8 of 41 eyes (20%) with Stargardt disease[12]. Daniela Ferrara et al. found that patients progressing with advanced AMD tended to have irregularities of the choroidal vessels and choriocapillaris attenuation progressed with AMD severity[13]. According to histology, choroidal stroma is the extravascular tissue containing collagen and elastic fibers, fibroblasts, nonvascular smooth muscle cells, and numerous large melanocytes that are juxtaposed to the blood vessels[1]. Measuring to the posterior vessel border seems reasonable because the choroidal thickness is usually measured as a marker for choroidal vascular perfusion. Sumru Ona et al. reported that choroidal stroma-to-choroidal vessel lumen ratio was significantly higher in patients with active Behçet uveitis, and no significant differences in subfoveal choroidal thickness was found between patients and control subjects[14]. On the other hand, some diseases are associated with pachychoroid. Lee WK et al. reported that dilated Haller vessels (pachyvessels) were identified under the site of neovascular ingrowth in 94% of patients with PCV and a significantly lower choriocapillaris/Sattler layer to total thickness ratio in the pachyvessel zone[15]. We believed that measuring total choroidal thickness including the suprachoroid layer may underestimate the extent of choroid thinning. Therefore it is important to accurately map the thickness of this vascular layer to understand the natural processes and development the eye as well as to potentially detect and monitor eye diseases. In the present study, we measured the choroidal thickness by precisely delineating the margin of choroidal vessels rather than the choroidal stromal layer. Thus, we could detect the pathology of choroidal vascular thinning or thickening with high sensitivity.

The main limitation of this study is that only healthy adult volunteers were included in this study. We did not apply the proposed method on pathological eyes. Further studies to apply this method on a larger number of patients are warranted. However, our results obtained by an automated measurement of choroidal thickness were with high reproducibility and were consistent with manual measurement of the choroid.

The automated assessment of the choroidal thickness is not only time-saving but also objective. With the automated segmentation of choroidal outer border provided by the SD-OCT, we were able to analyze the choroidal vascular thickness precisely.

In summary, this article presented an efficient method for detecting the boundaries of choroid and estimating the choroidal thickness, with high-speed scanning, high sensitivity and high reproducibility. Firstly, the proposed method utilizes image smoothing operators with regional characteristic as pre-processing procedure to reduce noise in the OCT images. Then the similarity of the gray-level is performed to divide the retina region. The boundary of choroid is obtained by measuring the gradient of pixel with morphological operators in the OCT imaging. The results from computer simulation reveal that the method always identified choroidal boundary accurately. Such a method provides robust and fast automated sketching for evaluating the value of choroidal thickness on OCT imaging.

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應用影像處理於視網膜光學斷層掃描下自動描繪及測量脈絡膜厚度

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摘要

目的

目前發現許多的眼科疾病與患者的脈絡膜厚度變化有關。本篇研究的目的在介紹一個自動且有效率的方法，這方法可應用於此項眼科正確且方便的脈絡膜檢查方式-視網膜光學斷層掃描檢查中脈絡膜厚度數據的量測。

方法

所有的患者都是接受頻域式光學同調斷層檢查（SD-OCT）。脈絡膜厚度分別使用手繪及自動化量測，本研究測量黃斑部中央窩從視網膜色素上皮細胞層的外邊界到脈絡膜層的外邊界的厚度。 再將自動化量測的結果與手繪測量的結果進行比較。

結果

總共23個正常眼睛的頻域式光學同調斷層檢查影像被納入此研究。使用自動化方式測量出的平均脈絡膜厚度爲164.34±52.72μm，使用手繪方式測量出的平均脈絡膜厚度爲182.50±74.98μm。

結論

本篇研究提出一個高效率的方法來幫助醫師偵測脈絡膜的內外邊界，再藉此進一步地量測脈絡膜厚度。這個完全自動化的方式可以有效地應用在臨床頻域式光學同調斷層檢查影像，幫助眼科醫師評估脈絡膜。（澄清醫護管理雜誌 2019；15（4）：23-32）

關鍵詞：脈絡膜厚度、視網膜光學斷層掃描、光學同調斷層掃描、自動化

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