**Australian Journal of Basic and Applied Sciences**, 8(4) Special 2014, Pages: 325-331

AENSI Journals

**Australian Journal of Basic and Applied Sciences**

ISSN:1991-8178

Journal home page: www.ajbasweb.com

# 3D Effect of Treatment on Optical Coherence Tomography (OCT) Image Using 3D Disease Generating Model

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**ARTICLE INFO**

***Article history:***
*Received 20 November 2013*
*Received in revised form 24 January 2014*
*Accepted 29 January 2014*
*Available online 5 April 2014*

***Key words:***
*inner limiting membrane; retinal pigment epithelium; optical coherence tomography; active net., temporal subtraction technique*

**ABSTRACT**

Optical coherence tomography (OCT) images is important for assisting ophthalmologists in clinical decision making in terms of both diagnosis and treatment. 3D-OCT consists of 128 2D-OCT images representing crosssectional structure. OCT has proven clinically useful for diagnosing a variety of retinal diseases. Some ophthalmologists desire the automatic measurement of a retinal thickness and its quantitative evaluation. Previously, the automatic measurement methods of the retinal thickness have been reported for retinal OCT images. However, the methods extracted the retinal border lines intermittently for OCT images, but they cannot measure the effect of treatment for an abnormal area automatically. And it's difficult in evaluating the effectiveness of laser treatment or medication. In this paper, we propose a new three dimensional (3D) disease generating model to display the effect of treatment. To extract the change of the abnormal area, we applied the automatic measurement method of a retinal thickness in OCT image, which is the dynamic contour model ("One Directional Active Net (ODAN)") proposed by our research group to extract two retinal border lines, which are Inner Limiting Membrane (ILM) and Retinal Pigment Epithelium (RPE). The proposed generating model generates the border line of disease based on ILM, and employs the temporal subtraction technique to detect the effect of treatment. We confirmed the usefulness of the proposed model using the generated disease OCT images from normal retinal OCT images. We are considering that the proposed method is useful as the visual evaluation for the effect of treatment for retinal disease.



**To Cite This Article:** N.A.H. Nguyen, S.Tsuruoka, H. Takase, H. Kawanaka, H. Matsubara, H.Yagami, F. Okuyama, 3D Effect of Treatment on Optical Coherence Tomography (OCT) Image Using 3D Disease Generating Model. ***Aust. J. Basic & Appl. Sci.,*** *8(4): 325-331, 2014*

## INTRODUCTION

In ophthalmology, Optical Coherence Tomography (OCT) is employed to obtain the tomographic images of retina non-contactly and noninvasively. In a retina diagnosis using OCT, eye-grounds are irradiated with near infrared (NIR) (820nm) LED light. Incident waves reflect on boundaries where the density of retina tissue changes and interference waves are generated by the incident and reflected waves. OCT devices observe the interference waves, as a result. The tomography image shown in Fig.1, 2 and 3 is generated by the difference among these waves (N. Tanno, T. Ichikawa and A. Saeki, 1990; Tsubota, 1995; Wolfgang Drexler and James G. Fujimoto, 2008).

The generated OCT image can show the status of macular area and discus nervi optici as an image, and the needs of retina diagnosis using OCT images have been growing (S. Kishi, 2006; U. Schmidt-Erfurth, R. A.Leitgeb, and S. Michels *et al* 2005).

There are many retinal diseases such as glaucoma, age-related macular degeneration and so on, and most of these retinal diseases cause vision loss. Their pathogenic mechanisms are not well understood and the quantitative evaluation of the disease condition is important in the treatment of these diseases.

Currently the method that calculates the thickness be-tween Inner Limiting Membrane (ILM) and Retinal Pigment Epithelium (RPE) (S. Ohno, and S. Kinoshita 1981) is mainly employed to evaluate quantitatively the condition of retinal diseases, the development of the extraction method for ILM and RPE has been required as a practical application. And in medical ophthalmology, it's difficult in evaluating the effectiveness of laser treatment or medication because the current analysis of the OCT apparatus cannot measure the effect of

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treatment for abnormal area (treated area) automatically. Moreover, there is a clinical database problem on OCT image that we didn't store the pair of the pre-treated OCT images and the post-treated OCT images now.

In this paper, we propose a new disease generating model based on normal OCT image for three dimensional (3D) display to create assumption data of pre-treated OCT image (Fig. 4) and display the effect of treatment on 3D Optical Coherence Tomography Images to estimate and show the change explicitly in the volume of the abnormal area by using OCT images. By applying a method of extraction ILM and RPE that proposed by Namakwa *et al* (A. Yamakawa, D. Kodama, S. Tsuruoka, H. Kawanaka, H. Takase, F. Okuyama, and H. Matsubara, 2010) and we can extract the treated area by using temporal subtraction technique.

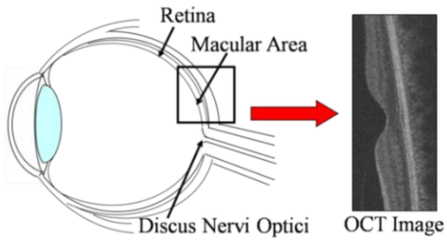


**Fig. 1:** Example of tomographic image of retina by OCT

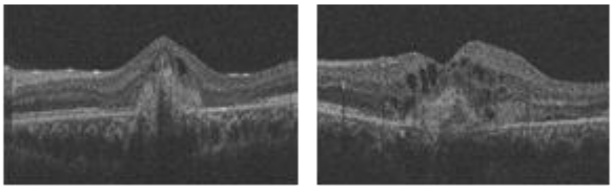

**Fig.2:** Examples of retinal OCT image with disease

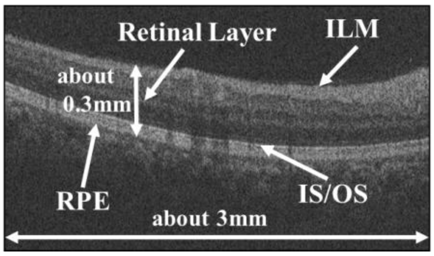


**Fig. 3:** Inner limiting membrane and retinal pigment epithelium

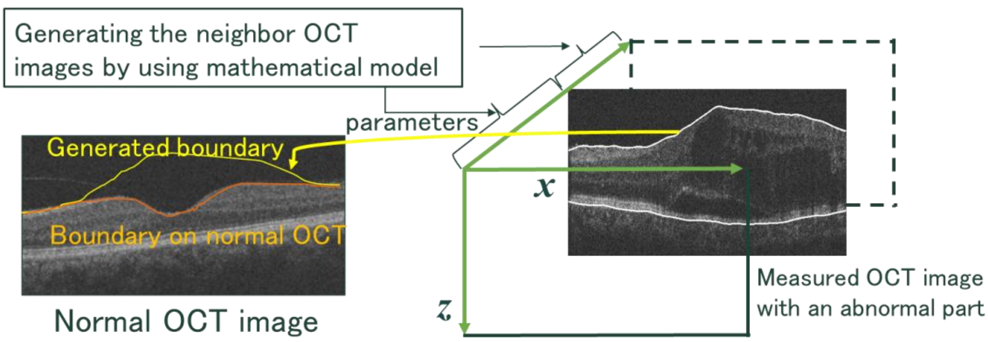


**Fig. 4:** New disease generating model of the boundary based on Normal OCT image

In this paper, OCT images of normal retina and retinal disease (diabetic macular edema disease) are used as the experimental materials. These OCT images are digitized to a pixel size of 20μm (horizontal) × 6μm (depth), a 16-bit grey scale and resolution of 512 × 480 pixels. The size of interesting area is about 0.3mm × 3mm.

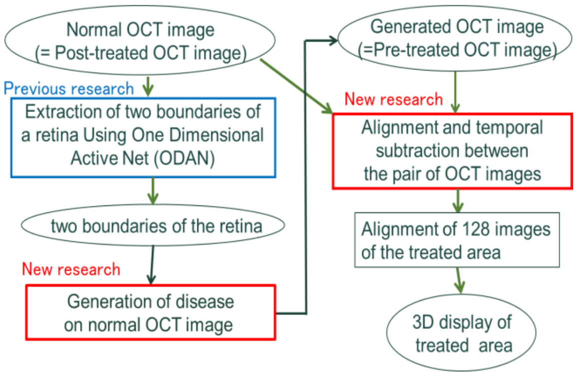


**Fig. 5:** Process flow of research

Fig.5 shows the process flow of our research. At the first, we extract boundaries of retina by using One Directional Active Net (ODAN) proposed by A. Yamakawa (A. Yamakawa, D. Kodama, S. Tsuruoka, H. Kawanaka, H. Takase, F. Okuyama, and H. Matsubara, 2010). Then, we generate a disease OCT image from normal OCT image to create pre-treated OCT image. Finally we extract the treated area by using temporal subtraction technique. Obtained treated area will be reconstructed in 3D by software "Image J" provided by National Institute of Health (NIH).

In this paper, $x$ axis means horizontal direction, $y$ axis does superposition direction, slice number, and $z$ does depth.

## MATERIALS AND METHODS

I.EXTRACXTRACTION OF TWO BOUNDARIES OF RETINA USING ONE DIMENSIONAL ACTIVE NET (ODAN)

### *A. Setting the initial position of ODAN:*

In the proposed method, one of the important processes is the automatic extraction method of border line using "One Directional Active Net (ODAN)", which is a modified dynamic contour model (Active Net K. Sakaue, and K. Yamamoto, 1991). ODAN is based on the energy minimization theory. The repetitive operation in ODAN processes until the most outside nodes of the active net converges the border line of the object.

On ODAN, to reduce a processing time, we confine the object of processing to the neighborhood of retina. To set the initial position of ODAN along the neighborhood of the retina, we extract the neighborhood of ILM and IS/OS (upper layer of RPE) using edge enhancement techniques. Two reasons of employing the boundary of IS/OS are (1) IS/OS exist parallel to RPE, and (2) IS/OS can be extracted a certain level of boundary by edge enhancement.

At first, we applied smoothing process for 20 times separately to noise reduction. This process can remove noises in edge enhancement. In the next step, we applied edge enhancement by the first derivative filter. After the edge enhancement, we normalized intensity in 65535 values (16 bits). After this, we applied Otsu's binarization method by a discriminant analysis. Extracted ILM and IS/OS image is scanned from tops and bottoms, and finds two points that change white pixel from black one. We set the top nodes and the bottom nodes of ODAN from the two detected points with a margin. This processes in a transverse direction, and the extracted initial net. ODAN transforms the position of every node to minimize the total energy of every node. The number of nodes of ODAN is 660 (= height 12 × width 55). But sometimes this process would miss the position of edges in retinal diseases. To avoid this edge missing problem, we set the initial position of ODAN manually.

### *B. Extraction of ILM and RPE by ODAN:*

ODAN represents the behavior of dynamic contour model based on mechanics equation as energy, and it extracts the object from image by finding stability state with energy minimization. Conformity characteristics energy of net and image is one of energy function in ODAN. The power reducing this energy corresponds with the power drawing net to characteristic region in an image. It is possible to extract the selected region by defining energy function that represents remarkably characteristics of region hoping to extract for conformity characteristics energy of image.

In an OCT image, the intensity of a pixel in retinal layer is generally higher than the surrounding tissue because the NIR laser beams strongly reflect at the retinal border lines (ILM and RPE) and the strength of interference waves become high.

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In this paper, the conformity characteristics energy of image is defined as the follow equation, because ILM and RPE can be extracted properly by the regional average and the degree in separation of intensity in the conformity characteristics energy of image

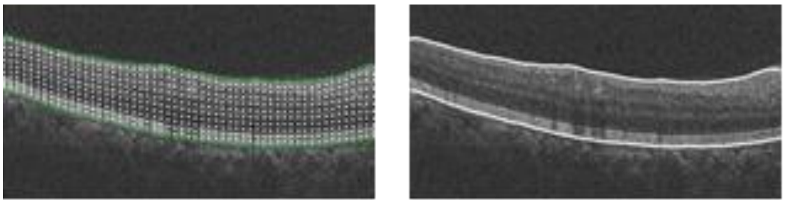
$$E_{image}(p,q) = \omega_1 I_{nf}(p,q) + \omega_2 D_{nf}(p,q) \tag{1}$$

$I_{nf}(p,q)$ :Average of intensity in neighborhood region at a node point $(p,q)$
$D_{nf}(p,q)$:Degree in separation of intensity in neighborhood region at a node point $(p,q)$
$\omega_1,\omega_2$ :Weight (on the inside nodes: $\omega1 < 0$, $\omega2 > 0$;
on the most outside nodes: $\omega1 > 0$, $\omega2 < 0$)

For each node points, the method sets the neighborhood region (13×13 pixels). The method calculates the average and the degree in separation of intensity in the neighborhood region. If the average and the degree in separation of intensity are the smaller, then the value of conformity characteristics energy of image is the smaller. On the inner retinal layers in OCT image, the average of intensity is high and the degree in separation is small. Therefore we gave weight (ω1 is negative weight and ω2 is positive weight) on the inside nodes of ODAN to lead to inner retinal layer. Also on the most outside nodes of ODAN were gave weight (ω1 is positive weight and ω2 is negative weight) to lead to boundary of the retinal layer. By defining conformity characteristics energy of image as equation (1), ODAN transforms to surround the retinal layer. ODAN can detect the retinal border lines (ILM and RPE).

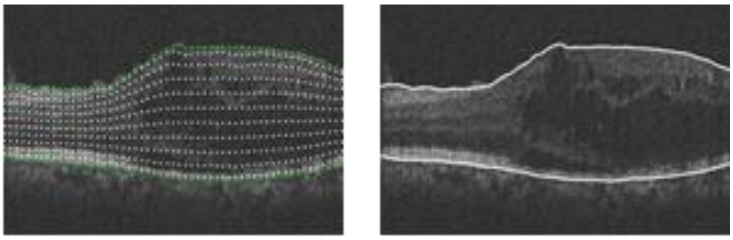
### *C. Extracted Results:*

Fig.6 shows an experimental result by ODAN of normal retina. And Fig.7 shows an experimental result by ODAN of abnormal retina. It shows the extracted result that the retinal border lines (ILM and RPE) can be extracted by ODAN. This result shows that ODAN can resolve the intermitted problem of the border lines. Processing time is about 10 seconds per one OCT image.



(a) Active Net on OCT image (b) Extracted border lines

**Fig. 6:** Final position of Active Net and the extracted border lines (normal retina)



(a) Active Net on OCT image (b) Extracted border lines

**Fig. 7:** Final position of Active Net and the extracted border lines (abnormal retina)

## *II. Extraction Of Treated Area On 3d Oct Image*

### *A. Disease generating model:*

We don't have the pair OCT image of pre-treatment and post-treatment OCT Image currently on the same patient. To evaluate visually the display of the effect of treatment on OCT image, we generate the abnormal area artificially from the original binary OCT image. We explain the proposed disease generating model.

We use the binary normal OCT image extracted border lines. Disease generating model employs in the following piecewise quadratic function for position $x_i$ in equation (2).

$$\Delta Z(x_i) = \begin{cases} \max(0, a_1(x_i - x_0)^2 + b\ ) & if\ x_i < x_0 \\ \max(0, a_2(x_1 - x_0)^2 + b\ ) & if\ x_i > x_0 \end{cases} \tag{2}$$

where $a_1<0$, $a_2<0$, $b>0$

The artificial abnormal area is given by equation (3). The image including artificial abnormal area ($\tilde{Z}(x_i)$) is considered as before treatment image, and the original image ($Z(x_i)$) is considered as after treatment image.

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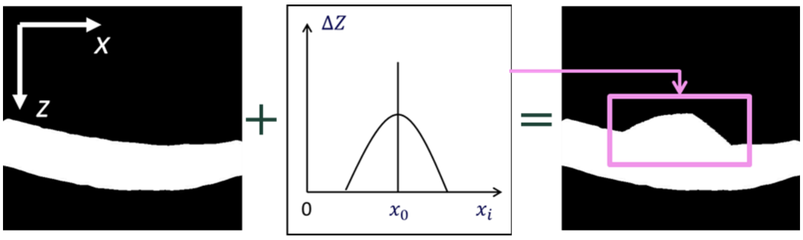
$$\tilde{Z}(x_i) = Z(x_i) - \Delta Z(x_i) \tag{3}$$

where
$Z(x_i)$: depth position of ILM
$\Delta Z(x_i)$: piecewise quadratic function (eq.(2))




(a) $Z(x_i)$ (b) $\triangle Z(x_i)$ (c) $\tilde{Z}(x_i)$

**Fig. 8:** Disease generation model on binary OCT image

***B. Extraction of Treated Area by Subtraction Using the pre-treated and the post-treated OCT images:***

Temporal Subtraction is the subtraction of two or more digitized OCT images that were acquired at different times. The subtraction process eliminates a static region in the image, and it extracts the changed part using the subtraction for each pixel between the pre-treated image and the post-treated image by equation (4). We regard the disease generated image by eq. (3) as the pre-treatment image, and the input normal image as the post-treatment image.

$$d(i, j) = f(i, j) - g(i, j) \tag{4}$$

where $d(i, j)$: subtraction image
$f(i, j)$: pre-treated image
$g(i, j)$: post-treated image

***3. Experimental Results:***

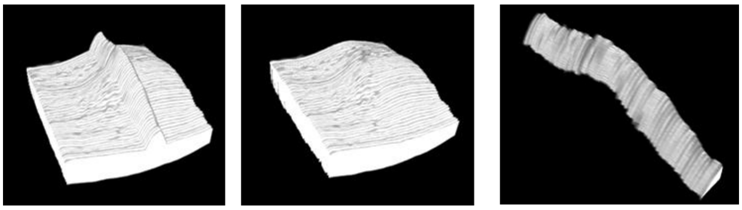
We applied the proposed method to the generated images (OCT images with 128 slices in each set). Fig.9 and Fig.10 shows the 2D extracted binary OCT images of retinal OCT image with the artificial abnormal area which were generated with different parameters. And Fig.11 and Fig.12 shows the experimental results in 3D reconstruction images of retinal OCT image of two samples. The 3D display was reconstructed from 128 slices of OCT images using "ImageJ" by US National Institute of Health (NIH).

(a) Pre-treatment (b) Post-treatment (c) Effect of treatment

**Fig. 9:** 2D extracted binary OCT image (sample A)

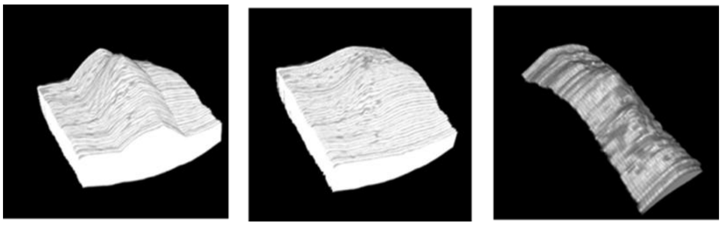
(a) Pre-treatment (b) Post-treatment (c) Effect of treatment

**Fig. 10:** 2D extracted binary OCT image (sample B)



(a) Pre-treatment (b) Post-treatment (c) Effect of treatment

**Fig. 11:** 3D display of the effect of treatment (sample A)



(a) Pre-treatment (b) Post-treatment (c) Effect of treatment

**Fig. 12:** 3D display of the effect of treatment (sample B)

***Discussion:***

With 3D display, it's easy to valuating the effectiveness of laser treatment or medication for the medical doctor and the patient to understand the effect of the treatment. The proposed system is useful for informed consent for the treatment.

As the remaining problem of the proposed model, the generating model is determined by trial and error now. We are considering the automatic determination of the coefficient of this disease generating model from the OCT image with an abnormal area. To improve the extraction of boundaries, we should introduce the new criteria for ODAN. For the realistic situation, the alignment between pre-treated image and post-treated image is the important problem.For the main text, use the Times or Times Roman 10 point typeface. Text should be single-spaced and justified. Indent the first line of each paragraph by 0.2" to the right.

***Conclusion and Future Works:***

In this paper, we proposed a disease generating model for three dimensional (3D) display of the effect of treatment method based on Temporal Subtraction Technique on 3D Optical Coherence Tomography Images. The system can show the change explicitly in the volume of the abnormal area by applying automatic extraction method "One Directional Active Net (ODAN)". The results of the experiment for normal and disease OCT image suggest that our method can extract the treated area on two retinal border lines (ILM and RPE). The proposed method will become useful in medical ophthalmology as this system will provide easily the display of the effect of treatment to patients.

However, because current ODAN just can extract two retinal border lines (ILM and RPE), so the proposed method just work with the diseases that the retinal thickness was changed, and not working with the changes of internal disease. In the future, we will have to develop a new method based on ODAN to extract the other lines in retina in order to show the change of the internal disease and we will confirm the usefulness of this method using many more experimental materials.When numbering equations, enclose numbers in parentheses and place flush with the right-hand margin of the column.

## ACKNOWLEDGMENT

This work is supported by JSPS KAKENHI (Grant-in-Aid for Scientific research (C) (23500555) from 2011 to 2013.

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