SEGMENTATION OF RETINA OCT IMAGES FOR THE EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE

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ABSTRACT

Alzheimer's disease (AD) is a common form of senile dementia. Although our understanding of the key steps underlying neurodegeneration in Alzheimer's disease (AD) is incomplete, it is clear that it begins long before symptoms are noticed by patient. Conventional clinical decision making systems are more manual in nature and ultimate conclusion in terms of exact diagnosis is remote. In this case, the employment of advanced Biomedical Engineering Technology will definitely helpful for making diagnosis. Any disease modifying treatments which are developed are most possibly to be achieving success if initiated early in the process, and this needs that we tend to develop reliable, validated and economical ways to diagnose Alzheimer's kind pathology. However, despite comprehensive searches, no single test has shown adequate sensitivity and specificity, and it is likely that a combination will be needed. There are several imaging techniques used in clinical practice for the diagnosis of Alzheimer's type pathology. There are lot of tests and neuroimaging modalities to be performed for an effective diagnosis of the disease. Prominent of them are Magnetic Resonance Imaging Scan (MRI), Positron Emission Tomography (PET), Single Photon Emission CT Scanning (SPECT), and Optical Coherence Tomography (OCT).In the recent studies made on Alzheimer's disease it is clearly investigated that are some parameter changes on the retina of the eye of the AD patients. In this research we have proposed a new scheme based on Wavelet Networks (WN) for the segmentation of OCT retinal images for the early diagnosis of AD.

KEYWORDS*: Alzheimer disease; wavelet networks; OCT; early diagnosis; biomedical technology*

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1.0 INTRODUCTION

Alzheimer's disease (AD) is a progressive deteriorating and loss function of the neurons in the human brain. It leads to loss of memory of the subject and weakens the proficiency in doing a sequence of actions regularly following (Sandeep and Sukesh, 2005; Sandeep et al., 2017). AD is the sixth-leading cause of death among various diseases and is 70% widespread in all cases of dementia (Alzheimer's Assocoation, 2012). According to another report every 71 sec, someone develops Alzheimer's disease and the rate doubles roughly every 10 years after age 65 (Alzheimer's Disease International, 2011). Some studies show that almost 36 million people are believed to be living with Alzheimer's disease and other types of dementias. This will increase to about 66 million by 2030 and nearly 115 million by 2050 (Alzheimer's Disease International, 2010). The development of AD can be placed into four stages.

The first stage is called Mild Cognitive Impairment (MCI) that does not make prominent changes in day to day living. The second and third stages of the disease are called as Mild and Moderate AD. These stages describe the distinctive nature by a rise in cognitive shortfall, and reduction in independence. The fourth stage is called Severe AD in which the affected person almost dependent on caregivers and an overall decline of personality (Frosh et al., 2010). Alzheimer's disease is one of the underlying causes of dementia, the term used to point out weakened brain functions and related symptoms like difficulty in performing routine tasks, memory loss, confusion, loss of intellectual functions and poor judgment. The above mentioned conditions are similar symptoms of below mentioned neurological disarrays. This includes Alzheimer's disease, Frontotemporal Dementia , vascular dementia, Dementia with Lewy Bodies and Parkinson's disease. AD is the most common type of dementia and is clinically evident when there is gradual loss of brain functions. The symptoms thus occurring may lead to disorientation and aphasia (difficulty in language), indicating cortical dysfunction, agnosia (impairment in recognizing object and people), apraxia (impaired motor function) and significant of all, memory impairment. As the disease develops drastically, the patients suffer disability and immobility.

The brain of such patients shows gross cortical atrophy with ventricular enlargement. The most widely known neuropathological hallmarks of AD

are senile plaques which are seen outside the neuron and neurofibrillary tangles that are seen inside the neuron. Neurofibrillary tangles are filamentous bundles in cytoplasm of the neurons displacing or encompassing nucleus. In the pyramidal cells, they appear as 'flame' while in rounder cells they appear as 'globos tangles' (Haevey et al., 2006). Senile plaques present outside the neuron, appear as spherical bodies bearing dilated and tortuous neuritic processes around an amyloid beta core which contains some abnormal proteins like amyloid beta plaques which are derived through the processing of Amyloid Precursor Protein (APP) (Haevey et al., 2006; Cummings et al., 1998). Familial causes or genetic reasons involved in disease pathology include mutations on chromosomes 21, 14 and 1. Risk factors for AD are elder age, small head size, history of head trauma, lower intelligence, and female gender (Yaari and Corey, 2007; Larson et al., 2006).

The imaging modalities tests that were established for AD are Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography and neuropsychological tests. CT scans were used to check for structural deterioration of the brain and increased ventricle size. It was noticed that at firstly cerebral atrophy was predominant in AD patients than control subject. However it was discovered later that healthy people also have cerebral atrophy. Patients with dementia may not have cerebral atrophy at least in the early stages of the disease. From these findings it was difficult to distinguish between a healthy elderly patient and a patient with dementia. So the CT scans have been deemed as clinically not as useful in the primary diagnosis of AD. After CT structural MRI was introduced to evaluate MCI (mild cognitive impairment) to AD in addition to clinical measures. Structural MRI measures the whole brain volumes, medial temporal lobe structures, and ventricular volumes. Therefore MRI can be helpful in differentiating between MCI and AD (Mayeux, 2003).

PET is an imaging modality that uses biochemical ways of getting images rather than structural information. Alzheimer's disease is one of the underlying causes of dementia. Dementia is the term used to indicate impaired brain functions and encompass symptoms like memory loss, confusion, difficulty in performing routine tasks, loss of intellectual functions and impaired judgment. PET technology includes the detection of photons which records

the levels of radioactivity beginning from given points in time and space. Positron emitting radioisotopes are used to generate the radioactivity (Harvey et al., 2003). PET scan measures different compounds in the brain especially the fluorodeoxyglucose (FDG) that can compete with glucose for metabolism and absorption in neurons. With AD the neurons intake of glucose and FDG becomes less. By projecting the regions of decreased FDG uptake, PET can help in the early diagnosis of AD, even in the absence of the gross structural damage detected by other imaging techniques such as CT or magnetic resonance imaging (Chu et al., 2010).

Some studies have been conducted to examine patients that are amyloid positive or amyloid negative, PET has been used extensively to study AD, and it is evolving into an effective tool for early diagnosis. PET is a very costly scan to perform the test for AD, it has been the most useful to provide visual images in the detection of the disease. There are some recent advances in technology that can not only detect AD, but it can possibly explain the symptoms and how the disease works. The neuropsychological tests are used to examine the specific type and level of cognitive impairment that the patient is having. Some of them that were, " Mini Mental State Examination, Trial Making Test parts A and B, Digit Symbol Substitution Test, Digit Span forward and backward, Rey Auditory Verbal Learning Test, category fluency, and the Clock Drawing task" (Larson et al., 2006). All of these tests are helpful in showing the memory recall of a patient and the realizable areas where the patient may degrade. Using the above different tests, it can be helpful to determine the types of treatment plans which are to be used. However neuropsychological tests alone are not helpful in detecting early AD, trials were often conducted combining neuropsychological tests with clinical tests and various imaging modalities. For an effective and early diagnosis of AD, a population based study is necessary and required, which gives an idea about the various tests involved in determining AD.

Recently, studies show that there are changes not only in the brain but also in the retina of Alzheimer's disease patients (Kesler et al., 2011; Frost et al., 2010, Ohno, 2011). For this purpose we have used the OCT images of retina of AD patients obtained from OCT camera for the diagnosis. The standard approach in automatic OCT image analysis consists of image acquisition, preprocessing, image segmentation, feature extraction, feature selection and classification.

Image acquisition is done by OCT camera which is shown in Figure 1 where it is a kind of imaging technique used to examine the different eye related disease.

Preprocessing is by using median filter which removes unwanted noises on the obtained OCT image of the eye. For the different steps involved in OCT image analysis of retina, segmentation is the most important stage of all. Image segmentation is defined as the process of partitioning a digital image into multiple segments. The goal of segmentation is to simplify and/or change the representation of an image into something that is more meaningful and easier to analyze.

Figure 1. OCT device and OCT image obtained on the screen

Image segmentation is mostly used to locate objects and boundaries like lines, curves etc. in images. More accurately, image segmentation is the process of assigning a label to every pixel in a digital image such that pixels with the same label share certain visual characteristics. The result of image segmentation is a set of segments that collectively cover the whole image, or a set of contours extracted from the image. Each of the pixels in a region is similar with respect to some characteristics such as such as color, intensity, or texture.

There are different ways for the segmentation of images in the artificial intelligence field. Most prominent and popular of them are fuzzy logic and artificial neural network (ANN) approaches for segmentation of medical images (Cheng et al., 1999; Jiang et al., 2010). Apart from above another promising computational intelligence method that has been widely used for various applications in different areas is wavelet network (WN). A wavelet can be called as a wave like oscillation with amplitude that begins at zero, increases, and

then decreases back to zero. A family of wavelet scan is formed from a function, called "mother wavelet," which is confined in a finite interval. "Daughter wavelets" are then formed by shifting and scaling of mother wavelet. Wavelets are mainly useful for compressing image data from a larger one. Wavelet network takes full advantage of the characteristics of denoising, back ground reduction, and recovery of the characteristic information and Neural Network capacity of universal approximation (Balabin et al., 2008; Zhang & Benveniste, 1992; Pati & Krishnaprasad, 1992; Szu et al., 1992). For this reason, it has a great ability to be used in many different applications (Zhang et al., 2005; Jemai et al., 2011). For instance, in image processing wavelet networks have overcome many of the limitations in other intelligent methods such as artificial Neural Networks. The main advantage of wavelet networks over similar architectures such as multilayer perceptrons (MLP) and networks of radial basis functions (RBF) is the possibility of optimizing the wavelet network structure by means of efficient deterministic construction algorithms (Galvao et al., 2004).

In this paper a specific wavelet network for segmentation of OCT images is employed. Wavelet networks are classified into two groups. They are adaptive wavelet networks (AWNs) and fixed-grid wavelet networks (FGWNs) (Billings and Wei, 2005). Adaptive wavelet network is continuous wavelet transform whereas FGWN is discrete wavelet transform. Due to numerous shortcomings of AWNs like for example, complex calculations, sensitivity to initial values, and the problem of measuring initial values, their application is limited (Billings and Wei, 2005).. In an FGWN, the outer parameters of the network like number of wavelets, scale, and shift parameters value are determined. The only inner parameters of the network, weights are specified by algorithms similar to the least squares. These types of networks do not need training. In AWNs, initial values of network parameters including weights of neurons, shifts, and scales of wavelets are selected randomly or using other methods. These parameters are then updated in the training stage by means of techniques such as gradient descent or back propagation (BP). Then, the optimized values of network parameters are calculated. But in an FGWN, the number of wavelets, as well as the scale and shift parameters, can be determined in advance and the only unknown parameters are the weight coefficients which are calculated through methods such as least squares. So in proposed FGWN, there is no need to specify random initial values for parameters or to use gradient descent,

BP, or other iterative methods. Normally, in training stage of an adaptive network, all the parameters change; on contrary, in FGWN only, the weights are specified during an on iterative process. Thus, it could be concluded that FGWNs do not need training procedure. A three-layer FGWN with one hidden layer is employed Specific wavelet network or OCT image segmentation. The procedure for image segmentation in this paper is as follows. At first the input data are normalized. Then, after selecting a proper mother wavelet, which is usually Sombrero because of its desirable characteristics such as convenient calculates on, adaptability to Gaussian structures, and robustness against noise (Gonzalez et al., 2006). Next a wavelet lattice is formed. Wavelet lattice is a hyper shape of shift and scale values of wavelets. The huge dimensions of this hyper shape should be decreased and effective wavelets should be selected. All of these are accomplished through two stages of screening. This paper is unique as it employs two stages of screening. This gives ground to increase the popularity of the wavelet lattice and to estimate the function in a more accurate way which is most beneficial and significant for larger scales. The author's previous works in the area of Biomedical Engineering will definitely help to develop a new proposed tool using latest biomedical methods for the solution of the early diagnosis of AD.

2.0 METHODOLOGY

2.1 Structure of Wavelet Network

The output signal of a wavelet network with one output f and inputs d as in Equation (1),

$$X = \begin{bmatrix} x_1 \\ x_2 \\ \vdots \\ x_d \end{bmatrix} \tag{1}$$

and wavelons q (wavelet neurons) in the hidden layer as in Equation (2) is given by

$$\sum_{i=1}^{n} w_i \psi_{pi,qi}(X) = \sum_{i=1}^{n} w_i 2^{-p_i d/2} \psi(2^{pi} X - qi) \tag{2}$$

where w_i, i =1, 2,..., n are weight coefficients, ψ_{pi} ,$_{qi}$ are dilated and translated versions of a mother wavelet function, ψ and pi, qi are scale and shift parameters, respectively and shown in Figure 2 (Galvao et al., 2004).

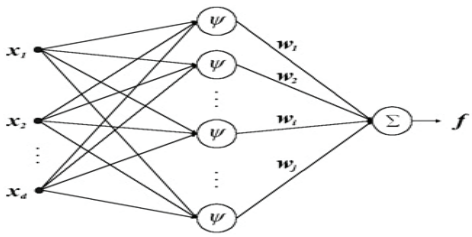

Figure 2. Three-layered WN structure with one hidden layer.

2.2 Algorithm for Building an FGWN

A major advantage of wavelet networks over other neural architectures is the availability of efficient construction algorithms for defining the network structure (Oussar and Dretfus, 2000). In FGWN, after determining the structure, the weights wi in Equation (1) can be obtained through linear estimation techniques. In this study, a constructive method is employed to build an FGWN. Suppose we have P input–output data in the form $\{x^{(k)}, f^{(k)}, k = 1, 2...P\}$ is given in Equation (3).

$$X^{(k)} = \begin{bmatrix} x_1^{(k)} \\ x_2^{(k)} \\ . \\ . \\ x_d^{(k)} \end{bmatrix} \tag{3}$$

where $X^{(k)}$ is the input d-dimensional vector and inputs matrix is the $X = [X^{(1)}...X^{(k)}...X^{(P)}]$. The output vector is shown in Equation (4).

$$f = \begin{bmatrix} f_1^{(1)} \\ . \\ . \\ f_2^{(k)} \\ . \\ . \\ f_d^{(k)} \end{bmatrix} \tag{4}$$

The FGWN structure is determined by the following algorithm.

2.2.1 Normalization

In many cases, input data of wavelet network vary within a wide range and this variability reduces the efficiency of wavelet network. Thus, this first stage is considered as the data pre processing stage in which the input data are normalized to a certain range in order to avoid data scattering. Here the values of *R, G*, and *B* matrices of each colour OCT image are mapped into [0,1] range by performing normalization process as in Equation (5) (Baron & Girau, 1998).

$$x_{n,new}^{(k)} = \frac{x_{n,old}^{(k)} - t_k}{T_k - t_k} \tag{5}$$

where $x_{n,new}^{(k)}$ is the value of each colour matrix after normalization (located in [0,1] range), and t_k and T_k are minimum and maximum values of these matrices, respectively.

2.2.2 Selecting the mother wavelet

Due to better regularities and also the ease of frame generation, wavelet frame is employed. Here *d*-dimensional Sombrero radial wavelet is used to implement WN (Zhang, 1997). It is expressed as in Equation (6).

$$\psi(x) = \eta \| x \| = (d - \| x \| \hat{} 2)\, e\hat{} \,(- \| x \| \hat{} \, 2 | 2) \tag{6}$$

2.2.3 Choose the scale and shift parameters

In this stage, minimum and maximum scale levels in the form [P_{min}, P_{max}] and shift parameter are to be employed.

2.2.4 Formation of wavelet lattice

In this step regarding a hyper shape on the wavelet parameters space that was selected in the previous stage, wavelet function is calculated for all input vectors as in Equation (7).

$$\psi_{pi.qj}(x) = 2^{-p_i d/2} \psi(2^{p_i} x - q_j) \tag{7}$$

where $i = 1,.., P_{max} - P_{min} + 1$.

In this equation $\psi_{pi.qj}(x)$ is calculated by Equation (6). The spatial figure is called wavelet lattice.

2.2.5 *Screening*

There are two types of screening in this stage.In primary screening, for every scale level selected in stage 4, I_k set is formed for each input vector. In secondary screening, the shift and scale parameters of wavelets that are selected in at least two set of the Sets in stage 5 are determined and set I is formed

2.2.6 *Formation of wavelet matrix*

Suppose that the number of selected wavelets in the last stage as L. In addition, to make the writing simpler, the couple index of (p,q) is replaced with single index of $\{m= 1,\ldots,M\}$. In this stage, $Wp\times M=[\psi 1,\ldots,\psi l,\ldots,\psi M]$ matrix is calculated for all the input vectors and for all the selected shift and scale parameters that are in set I as in Equation (8).

$$W=\begin{bmatrix}\psi_1(x^{(1)})\ldots\ldots\ldots\ldots\psi_M(x^{(1)})\\ \psi_1(x^{(2)})\ldots\ldots\ldots\ldots\psi_M(x^{(2)})\\ \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\\ \psi_1(x^{(P)})\ldots\ldots\ldots\ldots\psi_M(x^{(P)})\end{bmatrix} \tag{8}$$

The nodes with red and blue circles are the members of sets in stage 5, respectively, and the nodes with circles in both red and blue colors are the members of set I.

2.2.7 *Performing orthogonal least square (OLS) algorithm*

After two stages of screening, some of matrix members are still redundant. There as on is that only the input in formation and not the output information is taken into account for forming the wavelet matrix. A fast and efficient model structure determination approach has been implemented using the OLS algorithm. This approach has been extensively studied and widely applied in nonlinear system identification (Galvao et al., 2004). According to the OLS algorithm, to select the best subset of W, assuming that the size of this subset is known and denoted as s, the following steps should be taken .At first ,the most significant wavelets in

W is selected. Next, all other (not selected) wavelets are made orthogonal to the selected one. In the second step of the algorithm, the most significant of the remaining wavelets is again selected; then in this step, all non selected wavelets are made orthogonal with respect to the selected one, so that second selected wavelet with addition to the first one can determine the best approximation. And then, the algorithm goes on for the rest of wavelets. Since all remaining wavelets are made orthogonal to all selected ones in each step of the algorithm, the improvement of each selectable wavelet is isolated (Davanipoor et al., 2012). After employing this stage, wavelet network is constructed as in Equation (9).

$$f = \sum_{i=1}^{s} w_i \psi_i(x) \tag{9}$$

where s is the number of wavelons in the hidden layer and wi is the weight of wavelons.

After performing the OLS algorithm, W is composed of ortho normal matrix N and upper triangular matrix A. So, Equation (5) can be rewritten as in Equation (10).

$$f = QA\theta \tag{10}$$

2.2.8 Selecting the number of wavelons

Wavelons are the nodes creating the hidden layer of the wavelet network. By choosing the ideal number of wavelons, index is calculated as in Equation (11) (Zhou et al., 2008).

$$MSE = \frac{1}{P}\sum_{k=1}^{P}(\hat{f}^{(k)} - f^{(k)})^2 \tag{11}$$

Then, the number of wavelons will change until the desired error measure is achieved.

2.2.9 Calculating wavelons weight coefficient

This stage is the last stage of the algorithm. The weight of wave l on s is measured by the least-squares method. This is done as in Equation (12).

$$N^T f = A\theta \tag{12}$$

The algorithm from the previous stage is used in the present stage for segmentation of the OCT images. From images database, a number of images are randomly chosen for formation of FGWN. At first the values of *R, G*, and *B* matrices of each colour OCT image are mapped into [0, 1] range by performing normalization process. FGWN is formed with three inputs, a hidden layer, and an output. In order to form the FGWN, the values of three colour matrices are considered as network inputs. These matrices are related to the five chosen images from the selected images for segmentation. From these images, some pixels are selected randomly (ranging from 1000 to 5000 pixels for a 485×716 image). If the pixel is inside the layer, network output will be considered as 0,and if the pixel is outside the layer, the output will be considered as 1. In this way, the FGWN is formed. After that, the value of the three matrices *R, G*, and *B* for each pixel are considered as FGWN inputs, and the output of FGWN is a binary image that shows the segmented of original image as in Figure 3.

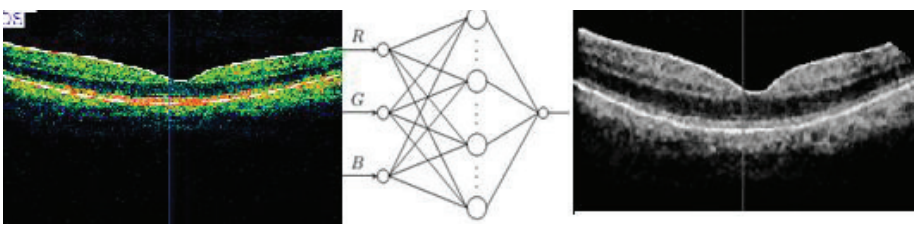

Figure 3. Presented FGWN for segmentation of OCT images

After segmentation post processing is done .Since extracting the features of retinal layer is the most essential part of diagnosing AD, extracting the exact boundary of the layer is a vital task. For this, after segmentation with an FGWN the space between two shapes is filled, extra parts are eliminated, and the noise is removed. Then, the exact boundary of the layer is extracted. This is done by appropriate morphological processes, including erosion, dilation.

3.0 RESULTS AND DISCUSSION

This database includes different OCT images of retina taken under the same environmental conditions. All of these images are 24-bit *R, G*, and *B* colour, with 485 × 716 size, and are taken from patients suspected to Alzheimer's Disease. Whether or not the patients have caught the disease is determined by MRI and is diagnosed by the opthalmologist. It is worth noting that the

database images employed in this paper were free of any noise or artifacts. In case of noisy images (images which are not of desired quality or the results of segmentation are not satisfactory), or necessity of elimination of the hairs, a pre processing stage be used (Lee et al., 1997). Among the 30 images selected for segmentation using the proposed FGWN, five images were used for building the network structure (formation of the wavelet lattice, determination of the shift and scale parameters, a calculation of the network weights), and the rest were used for testing it. In our experiments, 10–12 wavelons are enough to achieve good results. Since extracting the features of retina is the most essential part of diagnosing Alzheimer's Disease, extracting the retinal layer is a vital task. For this, after segmentation with an FGWN and according to the proposed algorithm, the space between two shapes is filled, extra parts are eliminated, and the noise is removed. Then, the exact boundary of retina layer is extracted. This is done by appropriate morphological processes, including erosion, dilation, closing and opening, and region filling. Size, shape, and kind of structuring elements were based on images dimensions and type of their objects that are selected tentatively and provisionally.

As mentioned before, segmentation is the most important and critical stage of the three stages of automatic diagnosis of retinal layer which has a very significant role in the final outcome. Because of this reason, the performance of this state should be examined by means of appropriate criteria. Here the retinal fibre layer which is the most significant feature in detecting Alzheimer's Disease is extracted by FGWN with an acceptable accuracyOur method is quite simple and considering the satisfactory results of this study, it is very applicable for detecting AD by means of the computer or robot.

4.0 CONCLUSION

In this study a new approach for the segmentation of OCT retina images based on fixed grid wavelet network (WN) has been employed. A wavelet lattice is formed. Parameters of wavelets are determined with two screening stages. Orthogonal least squares algorithm is used to calculate the network weights and to optimize the network structure using the developed algorithm, hence provides a useful tool for the analysis of OCT retina images. From the existing work we get a segmented image; in the future works the feature extraction,

feature selection and classification can be done. Feature extraction is a sub-division of improved image of improved image into constituent parts or isolation of some aspects of an image for identifying or interpreting meaningful object forms, which includes finding lines, circles or specific shapes. Later from the extracted features, best of the feature can be selected and used for classification and detection of Alzheimer's Disease.

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