On Bloodvessel Branching Analysis for the Detection of Alzheimer's Disease

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Abstract

Alzheimer's Disease (AD) is increasingly prevalent in modern society and methods for its diagnosis are only just starting to emerge. Given images of brain tissue, we show how Alzheimer's disease can be detected from the branching structures of blood vessels. This is achieved by a new approach which counts the branching points and derives measures which are suited to the analysis of small branching structures. The measures are formulated to be rotation, scale and position invariant and are deployed in tandem with more standard measures. Analysis on a database comprised of brain tissue samples from subjects who are normal, with Alzheimer's and age matched normal has shown capability to classify correctly images of brain tissue from subjects afflicted with Alzheimer's disease.

1 Introduction

Alzheimer's Disease (AD) is the commonest form of dementia, affecting nearly a million people in the UK and with no effective treatment. Diagnosis is difficult, as many neurodegenerative conditions present similar characteristics [1]. Amyloid beta (Aβ) is a normal product of metabolism, cleaved from an amyloid precursor protein (APP). Young brains are equipped with different mechanisms to break down and eliminate Aβ, but with ageing and on the background of different genotypes the elimination of Aβ fails, leading to its accumulation and to AD [2]. The accumulation of Aβ in the walls of blood vessels of the brain reflects a failure of its elimination along the walls of blood vessels.

In recent years, researchers have tried to detect AD by processing images of the human brain. Most have used MRI and CT scans to detect the abnormalities. For example, shape changes were detected in the corpus callosum in AD [3]. In addition, texture was evaluated to discriminate a brain with AD from one without [4], while a new method was introduced to measure the thickness of the human cerebral cortex by considering the white and the grey matter. However although the methods using computer vision have been demonstrated some detection capability, little attention has been given to detecting the abnormalities of specific components in the brain that are affected by amyloid beta, such as the blood vessels. The concept of the early onset detection of AD has yet to receive much

research attention. Naturally, any approach that can detect AD at the onset or early in its progression could be invaluable in medical planning.

Blood vessels have previously been analysed in diagnosis of diabetes, hypertension and atherosclerosis [5] supporting their potential use for Alzheimer's Disease diagnosis. The previous importance of the blood vessels suggests detecting abnormalities of the blood vessels is important in human condition analysis, and coupled with observations concerning Aβ drainage suggests that analysis of the branching structure might give an indication of the presence of AD. There is a general computer vision aspect in branching in that natural patterns such as sea fans, water flow in the rivers and trees show structural similarity suggesting automated analysis is appropriate there as well.

The detection of a blood vessel's pattern can use many established features such as density and tortuosity for Alzheimer's disease detection [6]. In this study, we describe the blood vessel's overall structure of by their density, by a new invariant measure of branching structure, and by their tortuosity. Our aim is to detect the signs of AD at an early stage by focusing on the objects that have been most affected by this disease.

Current approaches to analysing branching structures in medical images currently concentrate on ductal trees [7] and vascular structures [8]. These are largely large scale analyses of topology whereas blood vessels in segments of brain tissue are considerably smaller. Further, there is no analysis of this sort directed towards the detection of Alzheimer's disease.

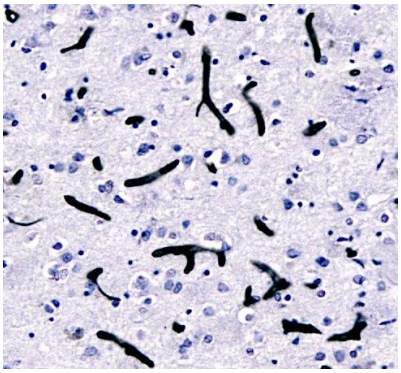


Figure 1: Example Image of Brain Tissue

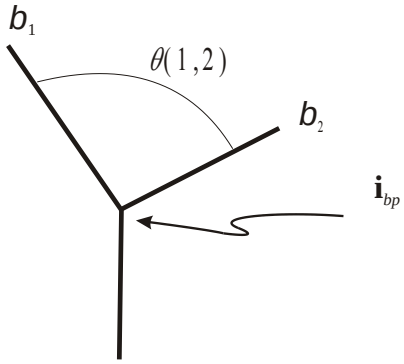


Figure 2: Branching Structure

In this paper, we propose a new analysis of the branching structure, with a measure which is invariant to rotation, scale and translation. This measure together with density and tortuosity are analysed on a database of images of brain tissue derived from young people, old people with Alzheimer's disease and age-matched old people without Alzheimer's disease to show that these new measures have detection capability.

2 Materials and Methods

2.1 Brain Images

We have used images of human tissue from the Brain Tissue Resource in Newcastle derived using a Nikon Eclipse E600 microscope fitted with a digital camera Nikon Coolpix 950 at fixed ×10 magnification, Fig. 1. We have five samples of tissue from; young, older

age-matched control and older Alzheimer's subjects. This dataset appears small compared with large scale image analysis datasets, and the purpose here is proof-of-concept and this size suffices for that purpose.

2.2 Density

The density is defined as the number of branches in the image which is determined by detecting the points at which branching occurs. Images are first thresholded using Otsu's technique and then thinned to provide a skeleton. A potential branching point $I(V)$, is calculated for each point V, of the skeleton where the $N_i(V)$ are the neighbours i of the analysed point, V. Should there be more than two neighbours V is classified as a branching point $\boldsymbol{i}_{bp}$, Eqs. 1 &2.

$$I(V) = \frac{1}{2}\left(\sum_{i=1}^{8} |N_i(V) - N_{i+1}(V)|\right) \tag{1}$$

$$\boldsymbol{i}_{bp} = I(V) > 2 \tag{2}$$

After obtaining the branching points $\boldsymbol{i}_{bp} = (x_{bp}, y_{bp})$, the branching points are then excluded when counting the number of branches, giving the density D. The vessels I_{vessel} are determined via 8-way connectivity and counted excluding the branching points as

$$D = \sum \left(I_{vessel} \cup \overline{I_{bp}}\right) \tag{3}$$

2.3 Description of the Branching Structure

The detected branching points allow for the new analysis of the branching structure. Essentially we have segments of blood vessels which are at different inclinations to the branching points. For a branching point bp with N branches each of length $L(n)$ the branching structure, as shown in Fig. 2, can be described by a composite measure which is derived from the branch length and relative inclination of the vessels. The average vector product of pairs of branches and the angle between them, gives the measure B which is invariant to rotation, translation and scale (size).

$$B = \sum_{i=1,N,j=1,N} L(i) \times L(j) \times \cos(\theta(i,j)) / N \quad i \neq j \tag{4}$$

As this equation appears to favour smaller angles, a version not using the cosine was also deployed, though this was found to have lower performance.

2.4 Other measures

We also described vessel structure using a standard measure of tortuosity τ

$$\tau = c / L \tag{5}$$

where c is the total length of the curve and L is the length of a straight line connecting the curve end points. This measure suffices for the analysis here though could be extended [9]. Here the tortuosity is averaged over all detected branches in an image.

3 Results

Figure 3 shows the results of correct classification rate achieved by using the function shown in eq. 4, and classified using the *k* nearest neighbour rule across the whole dataset and compared to version that used the pure angle (without the cosine function). Clearly, using the averaged dot product improves the correct classification rate.

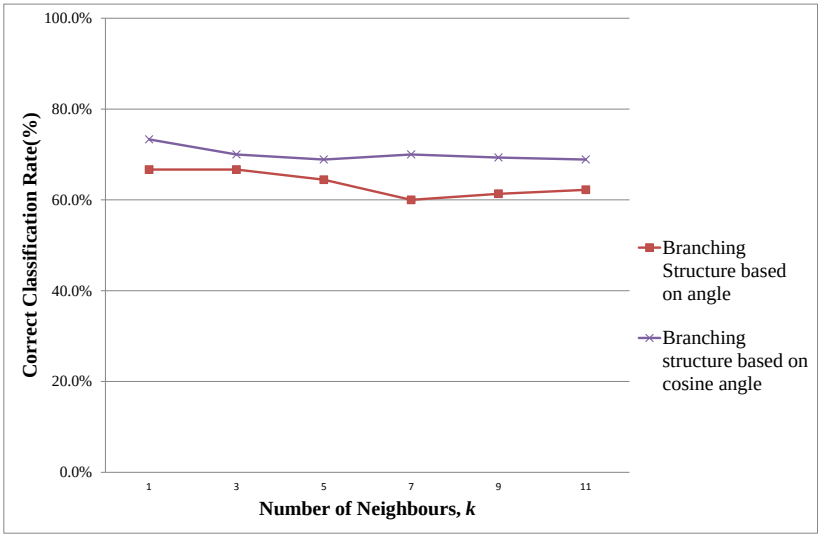
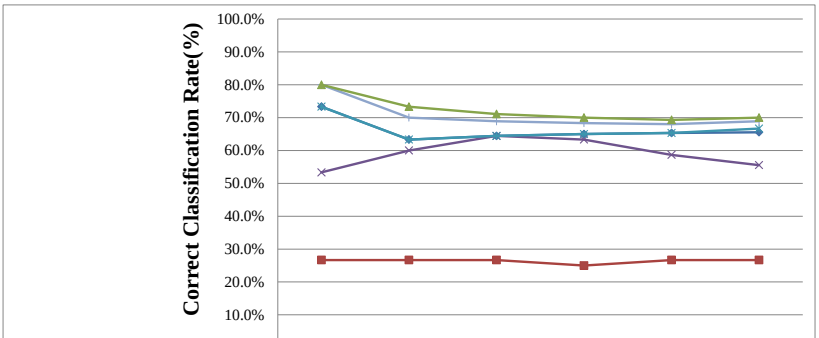


Figure 3: Correct classification rate using alternative branching measures.

Next, Figure 4 shows the Correct Classification Rate for the images when divided into three groups; young, old-matched control and old with Alzheimer's disease. Here, samples are classified by correct classification is achieved when an image from a sample without Alzheimer's disease is correctly classified as not having the disease. Correct classification also occurs when a sample from an older subject with Alzheimer's disease is correctly classified as that. The horizontal axis is the value of *k* used within the *k*-NN rule.

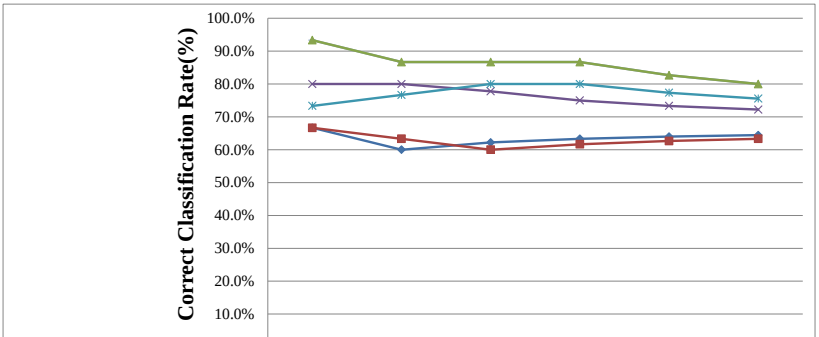
In Fig. 4 the features used are the density *D*, the tortuosity τ or the branching measure *B* or combinations thereof, combined as a feature vector for use with the *k*-NN rule. By this analysis, each measure contributes to successful discrimination of subjects with Alzheimer's disease, suggesting that image based analysis of brain tissue samples could prove a suitable avenue for research, as predicted by physical analysis and the postulated effects of Aβ.



Number of neighbours, *k*	1	3	5	7	9	11
Density	73.3%	63.3%	64.4%	65.0%	65.3%	65.6%
Basic Tortuosity	26.7%	26.7%	26.7%	25.0%	26.7%	26.7%
Branching	53.3%	60.0%	64.4%	63.3%	58.7%	55.6%
Basic Tortuousity + Density	73.3%	63.3%	64.4%	65.0%	65.3%	66.7%
Branching + Density	80.0%	70.0%	68.9%	68.3%	68.0%	68.9%
All features	80.0%	73.3%	71.1%	70.0%	69.3%	70.0%

Figure 4: Correct classification rate and for each feature combinations versus the number of nearest neighbours *k*

Next, in Figure 5 we combine the young datasets with the control dataset to perform the discrimination of the brain tissue with AD from normal brain tissue. This provides ten images from young and age-matched control subjects, together with five samples from subjects with Alzheimer's Disease.



Number of neighbours, *k*	1	3	5	7	9	11
Density	66.7%	60.0%	62.2%	63.3%	64.0%	64.4%
Basic Tortuosity	66.7%	63.3%	60.0%	61.7%	62.7%	63.3%
Branching	80.0%	80.0%	77.8%	75.0%	73.3%	72.2%
Basic Tortuosity + Density	73.3%	76.7%	80.0%	80.0%	77.3%	75.6%
Branching+Density	93.3%	86.7%	86.7%	86.7%	82.7%	80.0%
All features	93.3%	86.7%	86.7%	86.7%	82.7%	80.0%

Figure 5: Correct classification rate overall and for each feature combinations versus the number of *k* using 2 groups

Clearly in this figure, the CCR for branching structure shows capability to differentiate the AD from other normal brain. By combining the density with branching structure, we can see some enrichment of CCR suggesting the continuity of this combination for this research.

4 Conclusions

Studies suggest that the drainage of the protein Aβ is consistent with presence of Alzheimer's disease and this suggests that image based analysis of blood vessel structure might indicate the presence of Alzheimer's disease. Here we have deployed the standard measures of density and tortuosity for this analysis and have developed a new technique which is suited to analysis of the small branching structures to be found in these images. The new measure is formulated to have requisite invariant properties for this analysis.

In general, our initial result shows that the branching structure has become a major contributor to discriminate AD from a normal brain. In addition, a basic measure of tortuosity has shown some contribution to correct classification and has motivated us to increase the performance of the classification by finding a better way to analyse tortuosity.

Note that so far the study is in vitro and this study is sufficiently encouraging for translation to in vivo 3D MRI image analysis.

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