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Early Screening of Alzheimer's Disease Using Image Processing

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Abstract: Alzheimer's disease (AD) is a progressive, degenerative disorder that attacks the brain's nerve cells, or neurons, resulting in loss of memory, thinking and language skills, and behavioural changes. More than 55 illnesses are associated with the development of Alzheimer's disease. As life span is increasing, an early detection of AD emerges as possible approach to delay its consequences on patients and to increase the chance of getting potential benefits from approved medications and maintain certain good level of life. The early detection and classification of AD are important clinical support tasks for medical practitioners in customizing patient treatment programs to better manage the development and progression of these diseases. Efforts are being made to diagnose these neurodegenerative disorders in the early stages. Indeed, early diagnosis helps patients to obtain the maximum treatment benefit before significant mental decline occurs. AD has long been primarily considered a disease of gray matter. However, convergent evidence has suggested that white matter abnormalities are also important components of Alzheimer's disease. White matter abnormalities not only represent an early neuropathological event in Alzheimer's disease but may also play an important role in the pathogenesis and diagnosis of Alzheimer's disease. In this paper we present a method to separate white matter and gray matter from MRI image for finding AD at an early stage.

Keywords: Automated Segmentation, Convexhull, Relative Area, White Matter, Gray Matter, Standard Deviation, MRI of Brain.

I. INTRODUCTION

AD refers to a group of disorders caused by the gradual dysfunction and death of brain cells. This disorder can be described clinically as a syndrome that causes a decline in cognitive domain (i.e., attention, memory, executive function, visual-spatial ability, and language) [1]. Predicting AD in the early stages would be essential for improving treatment management before brain damage occurs.

Preliminary diagnosis of AD is normally by a general practitioner (GP) on the basis of clinical history of memory impairment and sometimes using established techniques such as Mini-Mental State Examination (MMSE). This usually happens after there has been a significant decline of the patient's cognitive function.

Neuro-imaging techniques could be used to diagnose and assess neurological disorders including dementias, but they require expensive specialist equipment and expert clinicians to interpret results and are clearly inappropriate as a method of detecting individual subjects with early AD within the large at-risk population.

Neuroimaging studies have found that patients with preclinical Alzheimer's disease have widespread white matter abnormalities at a stage similar to those reported in Alzheimer's disease, whereas gray matter structures were relatively intact. In addition, demyelination of the white matter is reported to occur prior to the presence of amyloid-β plaques and neurofibrillary tangles in the presymptomatic stages of Alzheimer's disease. Furthermore, in a mouse model of Alzheimer's disease, axonal disease due to impaired axonal transport was shown to precede and drive downstream production and aggregation of amyloid β peptides.

Our brain directly controls almost all movement in the body. A region of the cerebral cortex known as the motor area sends signals to the skeletal muscles to produce all voluntary movements. The basal nuclei of the cerebrum and gray matter in the brainstem help to control these movements subconsciously and prevent extraneous motions that are undesired. The cerebellum helps with the timing and coordination of these movements during complex motions. Finally, smooth muscle tissue, cardiac muscle tissue, and glands are stimulated by motor outputs of the autonomic regions of the brain.

Neurons, or nerve cells, are the cells that perform all of the communication and processing within the brain. Sensory neurons entering the brain from the peripheral nervous system deliver information about the condition of the body and its surroundings. Most of the neurons in the brain's gray matter are interneurons, which are responsible for integrating and processing information delivered to the brain by sensory neurons. Interneurons send signals to motor neurons, which carry signals to muscles and glands.

Neuroglia, or glial cells, acts as the helper cells of the brain; they support and protect the neurons. In the brain there are four types of glial cells: astrocytes, oligodendrocytes, microglia, and ependymal cells. Astrocytes protect neurons by filtering nutrients out of the blood and preventing chemicals and pathogens from leaving the capillaries of the brain. Oligodendrocytes wrap the axons of neurons in the brain to produce the insulation known as myelin. Myelinated axons transmit nerve signals much faster than unmyelinated axons, so oligodendrocytes accelerate the communication speed of the brain.

Microglia act much like white blood cells by attacking and destroying pathogens that invade the brain. Ependymal cells line the capillaries of the choroid plexuses and filter blood plasma to produce cerebrospinal fluid. The tissue of the brain can be broken down into two major classes: gray matter and white matter. Gray matter is made of mostly unmyelinated neurons, most of which are interneurons. The gray matter regions are the areas of nerve connections and processing [4-6].

White matter is made of mostly myelinated neurons that connect the regions of gray matter to each other and to the rest of the body. Myelinated neurons transmit nerve signals much faster than unmyelinated axons do. The white matter acts as the information highway of the brain to speed the connections between distant parts of the brain and body.

Deep within the cerebral white matter are several regions of gray matter that make up the basal nuclei and the limbic system. The basal nuclei, including the globus pallidus, striatum, and subthalamic nucleus, work together with the substantia nigra of the midbrain to regulate and control muscle movements. Specifically, these regions help to control muscle tone, posture, and subconscious skeletal muscle. The limbic system is another group of deep gray matter regions, including the hippocampus and amygdala, which are involved in memory, survival, and emotions. The limbic system helps the body to react to emergency and highly emotional situations with fast, almost involuntary actions [1-3].

Automated segmentation of white matter (WM) and gray matter (GM) is a very important task for detecting human emotions. This paper segmented WM and GM so that it can help to detect human emotions. The method is based on binarization, wavelet decomposition, and convex hull and produce very effective results in the context of visual inspection and as well as quantifiably.

The rest of this paper is organized as follows; in **section 2**, Brief Review of some other methods has been shortly described; in the **section 3**, procedure of proposed methods has been described; in the **section 4,** results and discussion section has been written; in the **section 5**, results and comparison are described visually as well as parametrically; the conclusion part has been describe in the **section 6;**

II. BRIEF REVIEW

There are different White matters (WM) and Gray matter (GM) extraction procedure that had been established in the past decade but research on accurate segmentation for different type of MRI of brain images and detection is still going on, but those methodologies have certain restrictions for the development of fully automated system.

Vicente Grau et. al. (2003) [1] proposed a method for accurate segmentation of GM, WM, cerebrospinal fluid (CSF) from the MRI of brain images, they proposed an improvement of watershed method and functions are based on probability calculation, normal distributions and Markov Random Field. The results show an accurate detection of the overall volumes and a clear development in recognition of the accurate location.

P. Valsasina [2] et. al. (2005) examined the progression of gray matter volume loss in 117 patients with relapsing–remitting MS, scanned monthly for a 9-month period. They studied and showed that gray matter damage is relapsing–remitting Multiple Sclerosis (MS) progress noticeably over a short period of examination, follow up the stability, and discover the different possibility of WM. P. Kochunov [3] et. al. (2006) had been proposed a methodology with diffusion tensor imaging as measure of fiber integrity in aging, dementia, and other disease processes. The resulting data is understandable in which correlations are mediated by age-dependent atrophy and also persist in the presence of age correction of various complementary imaging techniques in the assessment of brain aging.

Lucia van Eimeren (2008) [4] gives a description of white matter microstructure for the children. Individual differences in the performance in the Numerical Operation, but not the Mathematics Reasoning test correlate most strongly.

Betty M et. al. (2011) [5] proposed the procedure of gray matter volume, different tissue and edge connectivity of different tissue by the graph theory and the results describes with different situation. They show the results in intracortical matches that can be used to provide a robust statistical description of individual gray matter morphology. A artefact removal methodology briefly described by S Roy et.al.(2013) [6] which statistical and geometric approach.

M. Masroor Ahmed [7] et. al. proposed a methods to detect brain tumor, they use WM and GM extraction as a preprocessing steps, and shows all the steps for WM and GM extraction with the combines Perona and Malik anisotropic diffusion model for image enhancement and K-means clustering methodology and due to unsupervised learning it is very efficient and low error sensitive, also claim that unsupervised methods are better than that of supervised methods due to supervised methods needs some preprocessing.

III. PROPOSED WORK

Proposed work has been divided in to two stages; preprocessing stage and post processing stage. In the preprocessing step a method to remove artefact and skull elimination is described to extract gray matter and white matter as elimination of skull and artefact improve the white matter and gray matter detection. In the post-processing extraction of white and gray matter is done.

In stage one first convert input MRI image into gray image if input images are not gray image. Then binarize the image using the global thresholding method and the threshold has been selected by using the standard deviation value of the image. Threshold using standard deviation gives very effective results for MRI of brain image binarization [8-10]. The previous binarization step (binarized result) is very important for the next part of the proposed methods. It is easier to detect white and gray matter if artefact and skull portion are removed. Then complement the binarized image due to detection between the region (set as one) skull and original brain portion of the MRI of brain. Due to the different nature of MRI of brain separation of brain and skull are not easier, because some MRI images have prominent difference between skull and brain portion, and some MRI image has very difficult nature to separate between skull and brain portion.

Two dimensional wavelet decompositions [11, 12, 13] is done using 'db1' wavelet up to second level and then re- composition of the image is done using the approximate coefficient of wavelet decomposition. In this step the separation of skull and brain has been done, because loss of information means loss of pixel in between skull and brain portion i.e. separation between skull and brain are prominent, moreover due to reduction of size and removal of detailed information the white pixel of the complementary image come closure and form a complete ring. An interpolation methods and complement are used to resize the image and complete separation between brain and skull of the MRI of image. Remove all connected component except maximum area connected component because maximum area contains only brain as one pixel. As the binary image may produce wrong evaluation in the border side that's why a quick hull algorithm [14] for convex hull are computed in which the entire pixels inside the convex hull are set to 1 and outside it are set to zero. Then this binarized image multiplied pixel wise by the original MRI of brain image and gets the MRI of brain without artefact and skull. After that this image is binarized using standard deviation approach and again multiplied pixel wise with original image. Now the image contains only gray matter and white matter, gray matter relatively shaded region than white matter i.e. white matter have brighter than the gray matter. Using the previous concepts white matter has higher intensity than the gray matter. Thus calculate the total intensity and mean intensity. Mean is calculated by total intensity divided by total number of pixel without black pixel. Here total number of pixel is calculated without black pixel because black pixel contains zero intensity (main region of white and gray matter contain no zero intensity). Depending on the mean intensity, the pixel intensity above mean value selected as white matter and pixel value below or equal to the mean value selected as gray matter.

Procedure for White matter and Gray matter Extraction
Begin
Step 1: Input a gray scale image *I (x, y)*; *x* and *y* being spatial coordinates of the image. *Step 2:* B = **STATBIN**(Image I);
/* compute the binarized image*/
Step 3: **FOR** i = 0 to x **DO FOR** i = 0 to
y **DO**
IF B(i,j) =1 **THEN** set
B(i,j) ← 0
ELSE
set B(i,j) ← 1
END IF
END FOR
END FOR
/* Complement of the image has been done */
Step4: Compute two dimensional wavelet decomposition is done using 'db1' wavelet up to level two.
/* this step has been done using [c1,s1] = wavedec2(B,2,'db1') matlab function */ *Step5:* Re-composition of the image is done using the approximate coefficient of previous step.
/* this step has been done using RC = appcoef2 (c1, s1,'db1', 2) */
Step6: ***FOR*** *i = 0 to x* ***DO FOR*** *i = 0 to*
y ***DO***
IF *RC(i,j) =1* ***THEN*** *set*
RC(i,j) ← 0
ELSE
set RC(i,j) ← 1
END IF
END FOR
END FOR
/ Re-Complement of the image has been done */*
Step7: Labeling of the image RC is done using union find method and calculates area for each connected component and store in to ALLAREA.
Step8: Z = **MAX**(ALLAREA);
/* *the* maximum area of all the connected components is found out which represents the brain and the image obtained contains only the brain as 1 pixel */
Step9: A quick hull algorithms for convex hull is applied.
/* Convex hull is computed for these 1 pixel and the entire pixels inside hull set to 1
*/
Step10: GRAYIMAGE1 = I* BConvex
/* Convexed image is multiplied by original image */ Step11:
BIN2=**STATBIN**(GRAYIMAGE1);

```
Step12: GRAYIMAGE2 = BIN2*GRAYIMAGE1 /* pixel wise
        multiplication has been done */
Step13: set sum ← 0 and set count ← 0
Step14: FOR i=0 to x            DO
          FOR j=0 to y          DO
             IF GRAYIMAGE2(i,j) > 0  THEN
                  intensity ← GRAYIMAGE2(i,j)
                  sum ←sum + intensity
                  count ←count+1
             ENDIF
           ENDFOR
        ENDFOR
Step15:  average ← sum/count
Step16:  white←zeros(a111,b111)
         /* set all pixel of the white matrix zero */
Step17:  gray←zeros(a111,b111)
         /* set all pixel of the gray matrix zero */
Step18:  FOR i=0 to x  DO
            FOR j= to y         DO
               IF i6(i,j)>0  THEN
                     IF GRAYIMAGE2(i,j) >average
                        white(i,j)←1
                     ELSE gray(i,j)←1
                  END IF
              END IF
            END FOR
         END FOR
Step19: white= GRAYIMAGE2*white; Step20:
gray= GRAYIMAGE2*gray;
End
```

Procedure STATBIN (Image I)

```
/* procedure for binarize image*/ Step1: INIT =zeros(a,b); Step2: threshold =std2(I);
/* threshold selection by standard deviation of the image intesity */
Step3:  FOR I = 0 to  x   DO

            FOR j = 0  to Y            DO
               IF I(i,j)>threshold          THEN
                     Set INIT(i,j)←1

               END IF

               END FOR
            END FOR
Step 4: RETURN (image INIT)
```

Correctness of the Algorithms:

Loop invariant: At start of every iteration of loop, inner loops maximum limit width of the image and outer loop maximum limit height of the image.

Initialization: height and width are set by the height and width of the image, some initialization of matrix is set to all pixels zero, and sum, average are initialize as zero. ***Maintenance***: In each successive iteration, loop invariant moves to pixel of the image incrementing 1. Inner Loop works by moving 1, 2, 3,…, width and outer Loop works by moving 1, 2, 3,…, height depends on condition and all the function are finite in nature.

Termination: Inner loop width of the image does not exceed its height and depend upon if condition, until inner loop executes maximum width and outer loop always performs maximum height of the image.

Complexity Analysis:

Assuming that the height of the image h and width of the image w, then maximum number of iteration of loop is h*w. Thus if h = w= n then the complexity of the above program is **$O(N^2)$.** Complexity of binarization of the image also **$O(N^2)$** and maintain the above procedure. For computation of Quick hull algorithms for convexhull takes **O(NlogN)** and ordering of area takes **O(NlogN)** , thus the total time complexity is **$O(N^2)+ O(N^2)+ O(N\log N) + O(N\log N) \approx O(N^2)$.**

IV. RESULTS AND DISCUSSION

The procedure of proposed method has been described above and different output in different step using proposed methods has been shown in Figure 2 below. Figure 1(A) contains the original input image and Figure 1(B) is the binarized output in which threshold selection has been done by standard deviation of the image. This binarization method has been very effective especially for MRI of brain image and also very helpful to extract original brain (without artefact and skull) from total MRI image. Then complement of the binary image, after that two dimensional wavelet decomposition is done using 'db1' wavelet up to level two is shown in Figure 2(C) and re-composition of the image is done using the approximate coefficient. In this step, due to reduction of size and removal of detailed information the white pixel of the complementary image come closer and form a complete ring (skull). After the elimination of artefact and skull, Figure 1(D) shows the output image after artefact removal and skull elimination, thus in Figure 1(D) contains only the brain portion. As the goal of the proposed methods are extractions of white matter and gray matter, so image must contains only white and gray matter. The basic things is that relative brighter portion are white matter and shaded portion are gray matter, except that some other non shaded portion below the shaded intensity are removed by applying binarization again and binarized image is multiplied by Figure 1(D) image and the desire results have been shown in Figure 1 (E); after calculating mean value and depending on this mean value Figure 1(F) shows the binarized white matter and Figure 1(G) shows the binarized gray matter and finally Figure 1(H) shows the output contains white matter and Figure 1(I) shows the output contains gray matter. The gray matter and white matter extraction are very effective from transverse MRI of brain by proposed methods. Outputs for other type of brain MRI image are shown in comparison section. Data base are collected from BrainWeb [9] with Modality T1, Slice thickness 1mm (in-plane pixel size is always 1x1mm), Noise: (calculated relative to the brightest tissue) 3%, Intensity non-uniformity ("RF") 20 %.

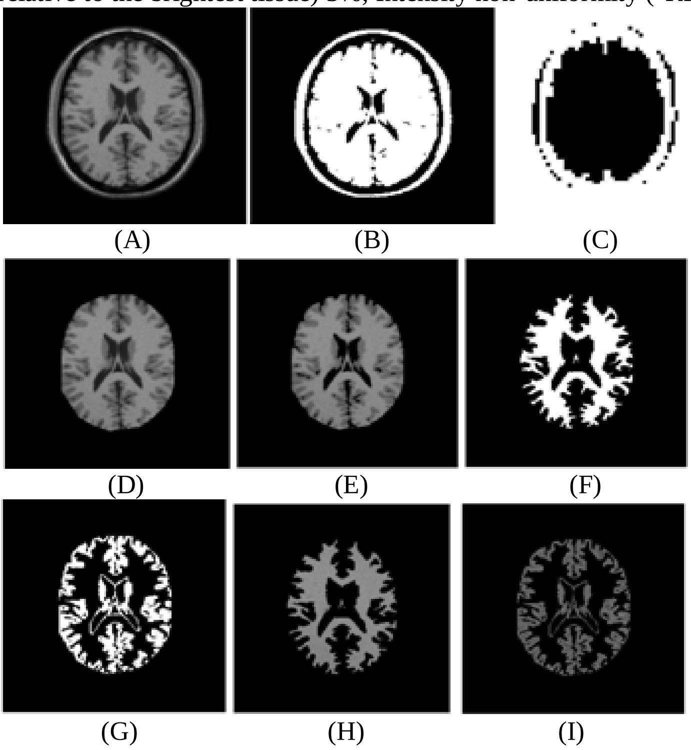

Figure 1: (A) is original image; (B) is the binarized output image; (C) is the output after complementing and using wavelet decompositions using 'db1'; (D) output image after artefact removal and skull elimination; (E) is output image contains only white matter and gray matter; (F) is the binarized white matter; (G) is the binarized gray matter; (H) is the output contains white matter; (I) is the output contains gray matter.

V. COMPARISON

The procedure and output of different steps has been described above. Proposed method produced very good results visually. In this section proposed method has been compared with some ground truth image [8] for each type transvers , sagittal , coronal MRI of brain image. It produces very good results for each type of gray matter extraction but fails for white matter extraction from sagital type of MRI of brain image. From visual inspection proposed methods produces very effective results and in visual inspection may have any biasness, that's why quantification process has been used with very low error rate. Thus proposed methods produces very effective results for MRI of brain Images.

VI. CONCLUSIONS

Here an intelligence system for gray matter and white matter extraction with and without artefact and skull region technique has been presented. The proposed methods are very useful for three different (Transvers, Sagittal, Coronal) type of images. The automated process has very low time complexity with very easy methodology. The results improve and overcome the problem of existence of skull portion with respect to other existing methodologies. The proposed methodology finally utilized to find out Alzheimer's disease from MRI of brain.

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