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Optimal Statistical Structure Validation of Brain Tumors Using Refractive Index

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Abstract

Tumour segmentation from brain MRI is more than a decade old problem in the field of medical imaging. Till date automated brain tumour segmentation happens to be a difficult task due to the variance and complexity of tumour growth. In this paper, we present this segmentation problem for the purpose of determining the exact location of brain tumour using refractive index study on the structural analysis of both tumorous and normal tissues. Initially, as per existing survey 3 kinds of features namely, intensity-based, texture-based, and symmetry-based are extracted from the structural elements. Then reduction of this feature set is performed and similar features are clustered together. Refractive index analysis is performed on each of the clusters from the MR T2 relaxation time. Deviation from a threshold value of RI for majority of pixels in a particular cluster denotes it to be the tumorous region.

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Keywords: tumors; PCA; clustering; refractive index;

1. Introduction

A brain tumour is an abnormal growth of cells in the brain, which can be cancerous (malignant) or non-cancerous (benign). It develops as an intracranial tumour created by abnormal and uncontrolled cell division normally in the brain (neurons, glial cells, astrocytes, oligodendrocytes, ependymal cells and myelin producing Schwann cells), lymphatic tissue, blood vessels, in the cranial nerves, brain envelopes (meninges), skull, pituitary and pineal gland[1].

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It also spreads from cancerous tissues located in other organs (metastases). Brain tumours are usually located in the posterior fossa in children and in the anterior two thirds of the cerebral hemispheres in adults, although it can affect any part of the brain. Regardless of their growth rates, both the malignant and benign tumours have similar effects on the brain. In this context, MR imaging is a well-suited scanning technique to monitor and evaluate brain tumours.

Often, the process of MRI brain tumour segmentation faces an open challenge due to large variance and complexity of tumour characteristics (shape, size, location, intensity variation, etc.) in images. Image processing techniques such as fuzzy connectedness[2] and deformable model[3] have been proposed for MRI brain tumour segmentation. Most of the previously performed studies work falls into the category of pattern recognition methods[4,5,6]. The key to successful pattern recognition methods is to extract effective features. Intensity-based statistical features are the most straightforward and have been widely used. But due to the complexity of the pathology in human brain and the high quality required by surgical diagnosis, only intensity features cannot achieve acceptable results. Thus many texture features have been presented for tumour segmentation. Texture based features provide good results but they are usually associated with large dimensions and not all dimension provide useful information. Xiao Xuan and Qingmin Liao[7] had gone through such statistical analysis and developed a classifier to select the most discriminative features using Adaboost[8].

In this paper, a similar structure based statistical analysis is conducted and then applied for brain tumour segmentation. First of all, the entire image is pre-processed. Secondly, a pixel itself is not considered, rather a pixel along with its neighbouring pixels together comprising a block is considered. From each block three types of features are obtained, namely intensity-based, symmetry-based and texture-based, followed by edge based feature from the original image. Consequently Principal Component Analysis[9] is applied on the dataset followed by k-means clustering[10]. Finally as a novel step in the problem, refractive-index analysis is done on each image pixel and depending on a threshold value, the cluster having most number of pixels greater than the threshold is declared to represent the tumorous section.

2. Methodology

2.1. Pre-processing

Pre-processing is necessary because the MRI suffers from inherent artefacts. The intensity variation is enhanced and noise is reduced. 2-D adaptive Wiener filtering[11] is used for this purpose.

A Wiener Filter is a class of optimum linear filter which is applied to the image adaptively, i.e. tailoring itself to the local image variance. Where the variance is large, it performs little smoothing. Where the variance is small, it performs more smoothing. The local mean (μ) and variance (σ) are estimated in a small M×N neighbourhood around each pixel. A pixel wise Wiener filter is created using these estimates. Eq. 1 gives the filter equation.

$$b(i,j) = \mu + \frac{\sigma^2 - \upsilon^2}{\sigma^2}[a(i,j) - \mu] \tag{1}$$

Here, a(i, j) and b(i, j) are the pixel values in the original and resulting image respectively and ν is the average of all the local estimated variances (the expected noise variance).

2.2. Structure elements

The image is viewed as structure elements rather than pixels, because it is difficult to determine which tissue a pixel represents if one focus only on the pixel, but it is much easier when the structure information of the pixel's neighbourhood[12] is considered. Therefore each pixel together with a small square neighbourhood is defined as a structure element, which is called a 'block'.

2.3. Feature Extraction

2.3.1. Intensity-based features

Intensity-based features from each structure element are obtained considering all the pixels in each block. The features extracted from each block are average intensity, central pixel intensity, minimum intensity, maximum intensity, intensity range (difference between minimum and maximum intensity), median intensity, kurtosis intensity, skewness intensity, variance and standard deviation. The intensity values reflect the physical characteristics of the tissues in the MRI.

2.3.2. Symmetry-based features

A striking characteristic of normal brain MR images is the symmetry of two cerebral hemispheres. The brain image with tumor turns asymmetric because tumor usually occurs in one cerebral hemisphere and doesn't occur symmetrically in the other. The simplest way to detect the asymmetry is subtracting one hemisphere from the other pixel by pixel. However, the human brain is not exactly symmetric, and there are always some slight variances. The asymmetry map S is calculated based on the original MR image:

$$SF(i,j) = \min_{(p,q)\in(i',j')} |I(i,j) - I(p,q)| \tag{2}$$

(i', j') is the symmetric pixel of (i, j); N_h (i', j') is a small neighbourhood of pixel (i', j'), defined by Eq. 3; ζ is the radius of N_h, which is a small value selected empirically.

$$N_h(i',j') = \{(p,q) : \| (p,q) - (i',j') \| \le \zeta\} \tag{3}$$

2.3.3. Texture-based features using Gabor filter

Gabor filtering[13] is performed on the tumor image for extracting the texture features. Because Gabor wavelets[14] capture the local structure corresponding to spatial frequency (scales), spatial localization, and orientation selectivity, they are widely applied in many research areas, such as texture analysis and image segmentation. A 2D Gabor filter is a product of an elliptical Gaussian in any rotation and a complex exponential representing a sinusoidal plane wave. The sharpness of the filter is controlled through the major axis and minor axis, which is perpendicular to the wave. The filter can be defined as:

$$\varphi(x,y;f,\theta) = \frac{f^2}{\pi\gamma\eta} e^{-\left(\frac{f^2}{\gamma^2}x'^2 + \frac{f^2}{\eta^2}y'^2\right)} e^{j2\pi x'^2} \tag{4}$$

$$x' = x\cos\theta + y\sin\theta \tag{5}$$

$$y' = -x\sin\theta + y\cos\theta \tag{6}$$

Here, f is the central frequency of the sinusoidal plane wave, θ is the rotation angle of both the Gaussian major axis and the plane wave, γ is the sharpness along the major axis, and η is the sharpness along the minor axis. The sharpness values along the major axis γ and along the minor axis η are set to 1. Image texture features can be extracted by convolving the image I(x,y) with Gabor filters.

Gabor filters with u different frequencies f_i and v different orientations θ_j are selected to obtain the texture features of the tumorous area.

$$f_i = f/(\sqrt{2})^i \qquad i=0,1,2,\ldots,u\text{-}1 \tag{7}$$

$$\theta_j = j\pi/8 \qquad j=0,1,2,\ldots,v\text{-}1 \tag{8}$$

Fig 1. depicts the Gabor filter frequencies and orientations. The values of u and v in Eq. 7 and Eq. 8 are usually chosen 5 and 8. After filtering, the first and second moments in 40 different channels are computed to compose an 80-dimensional vector.

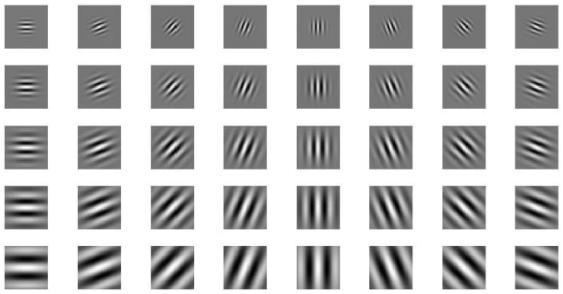

Fig. 1. Gabor Filter frequencies and orientations

2.3.4. Texture-based features using Gray Level Co-occurrence Matrix (GLCM)

The GLCM method[15] is a way of extracting second order statistical texture features. A GLCM is a matrix where the number of rows and columns is equal to the number of gray levels, G, in the image. The matrix element P(i,j|Δx,Δy) is the relative frequency with which two pixels, separated by a pixel distance (Δx,Δy), occur within a given neighbourhood, one with intensity i and the other with intensity j. One may also say that the matrix element P(i,j|d,θ) contains the second order statistical probability values for changes between gray levels i and j at a particular displacement distance d and at a particular angle (θ). Given an M × N neighbourhood of an input image containing G gray levels from 0 to G − 1, let f(m, n) be the intensity at sample m, line n of the neighbourhood. Then:

$$P(i,j \mid \Delta x, \Delta y) = W.Q(i,j \mid \Delta x, \Delta y) \tag{9}$$

$$W = \left[(M-\Delta x)(N-\Delta y)\right]^{-1} \tag{10}$$

$$Q(i,j \mid \Delta x, \Delta y) = \sum_{n=1}^{N-\Delta y} \sum_{m=1}^{M-\Delta x} A \tag{11}$$

Here, A is defined as unity if f(m, n) = i and f(m+Δx, n+Δy) = j. For all other cases, A is zero.

Because a G×G matrix must be accumulated for each sub-image/window and for each separation parameter set (d,θ), it is usually computationally necessary to restrict the (d,θ)-values to be tested to a limited number of values.

A number of texture features may be extracted from the GLCM using the following notations:

G is the number of gray levels used. μ is the mean value of P. μ_x, μ_y, σ_x and σ_y are the means and standard deviations of P_x and P_y. $P_x(i)$ is the i-th entry in the marginal-probability matrix obtained by summing the rows of P(i, j):

\

$$P_x(i) = \sum_{j=0}^{G-1} P(i,j) \tag{12}$$

$$P_y(j) = \sum_{i=0}^{G-1} P(i,j) \tag{13}$$

$$\mu_x = \sum_{i=0}^{G-1} i.P_x(i) \tag{14}$$

$$\mu_y = \sum_{j=0}^{G-1} j.P_y(j) \tag{15}$$

$$\sigma_x^{\,2} = \sum_{i=0}^{G-1} P_x(i).(i-\mu_x)^2 \tag{16}$$

$$\sigma_y^{\,2} = \sum_{j=0}^{G-1} P_y(j).(j-\mu_y)^2 \tag{17}$$

The features that are used are as follows:

- Contrast: $f_1 = \sum_{n=0}^{G-1} n^2 \{\sum_{i=1}^{G} \sum_{j=1}^{G} P(i,j)\}; \quad |i-j| = n$ (18)
- Dissimilarity: $f_2 = \sum_{n=0}^{G-1} n \left\{\sum_{i=1}^{G} \sum_{j=1}^{G} P(i,j)\right\}; \quad |i-j| = n$ (19)
- Inverse Difference Moment $f_3 = \sum_{i=0}^{G-1} \sum_{j=0}^{G-1} \frac{P(i,j)}{1+(i-j)^2}$ (20)
- Angular Second Moment: $f_4 = \sum_{i=0}^{G-1} \sum_{j=0}^{G-1} \{P(i,j)^2\}$ (21)
- Entropy: $f_5 = -\sum_{i=0}^{G-1} \sum_{j=0}^{G-1} P(i,j).\log\{P(i,j)\}$ (22)
- Correlation: $f_6 = \sum_{i=0}^{G-1} \sum_{j=0}^{G-1} \frac{i.j.P(i,j) - \mu_x.\mu_y}{\sigma_x.\sigma_y}$ (23)
- Cluster Shade: $f_7 = \sum_{i=0}^{G-1} \sum_{j=0}^{G-1} \{i + j - \mu_x - \mu_y\}^2 .P(i,j)$ (24)
- Cluster Prominence: $f_8 = \sum_{i=0}^{G-1} \sum_{j=0}^{G-1} \{i + j - \mu_x - \mu_y\}^4 .P(i,j)$ (25)

2.3.5. Edge-based features

Edge detection is a measure of sharp changes in image intensity and is an indication to discontinuities in depth and surface orientation. Canny edge detector is used for the purpose. It is a multi-stage algorithm that finds edges by looking for local maxima of the gradient of the image. The gradient is calculated using the derivative of a Gaussian filter. The method uses two thresholds, to detect strong and weak edges, and includes the weak edges in the output only if they are connected to strong edges. This method is therefore less likely than the others influenced by noise, and hence more capable to detect true weak edges.

2.4. Normalization

Normalization of the data set obtained is required to bring regularity within the data obtained from different feature sets.

ALGORITHM: *Normalization*

Let the data set X of dimension M×N be denoted as X = [X_1, X_2, X_3… X_N] such that X_i is an M×1 vector.

1. Evaluate mean centre of vector: $\overline{X} = \left(\frac{1}{M}\right) \sum_{i=1}^{N} X_i$ (26)
2. Evaluate standard deviation for each vector: $S = \left\{\left(\frac{1}{M}\right) \sum_{i=1}^{N} (X - \overline{X})^2\right\}^{1/2}$ (27)

3. Subtract the mean: $\phi_i = X_i - \bar{X}$ (28)

4. Divide by the standard deviation: $D_i = \phi_i / S$ (29)

5. Form the resultant matrix A: $A = [D_1, D_2, D_3, ..., D_N]$ (30)

2.5. Principal Component Analysis

Data dimensionality reduction is the process of reducing the number of random variables under consideration. It is an important stage in data processing to avoid the curse of dimensionality, system accuracy and reduces time and space complexity. Efficiency degrades rapidly as dimension increases. Principal component analysis (PCA) serves as an excellent tool to combat the dimensionality problem.

PCA is a statistical procedure that uses an orthogonal transformation to convert a set of observations of possibly correlated variables into a set of values of linearly uncorrelated variables called principal components. PCA is based on the following assumptions:

- The dimensionality of data can be efficiently reduced by linear transformation.
- Most information is contained in those directions where input data variance is maximum.
- The principal components are orthogonal.

PCA finds a lower-dimensional representation, while preserving the maximum amount of information from the original variables as it examines the directions that have widest variations. Key reasons for usage of Principal Component Analysis are its low noise sensitivity and reduction in data redundancy.

ALGORITHM: *PCA*

Let the data set X of dimension M×N be denoted as X = [X_1, X_2, X_3… X_N] such that each X_i is an M×1 vector. Let A be the mean centred normalized dataset.

1. Compute the co-variance: $C = \left(\frac{1}{M}\right) A^T A$ (31)
2. Evaluate eigenvectors (e) and corresponding eigenvalues (λ) of C.
3. Sort the eigenvalues in descending order and the eigenvectors accordingly.
4. Since C is symmetric, the eigenvectors form a basis, i.e., any vector X can be written as a linear combination of the eigenvectors. Thus the dimensionality reduction step includes keeping only the terms corresponding to the k largest eigenvalues. The resultant matrix is given by:
5. $$R = A.\varphi_{pca} \quad (32)$$ $$\varphi_{pca} = [e_1, e_2, ..., e_k] \quad (33)$$
6. To evaluate k, use the criterion:

$$\frac{\sum_{i=1}^{k} \lambda_i}{\sum_{i=1}^{N} \lambda_i} > \xi \text{ where } \xi = 0.9 \text{ or } 0.95 \quad (34)$$

2.6. K-Means Clustering

K-means clustering is a partitioning method that partitions the dataset into k mutually exclusive clusters. The algorithm starts with randomly selecting K number of seeds or centroids from initial data set.

ALGORITHM: *K-means clustering*

1. Calculate distance from all the selected initial centroids to all existing points inside the data set. Here, Euclidean distance has been considered. Each dataset value represents a single data point.
2. Depending upon the minimum distance criterion the clusters are formed.
3. The new centroids inside the newly formed clusters are calculated.
4. Repeat steps 1 and 2 with respect to newly generated new cluster centroids.
5. The algorithm will be continued until the convergence is reached, i.e., cluster assignments do not change.

2.7. Refractive Index Analysis

Refractive index[16] (RI) is the amount of deviation that takes place when light travels from one medium to another. Refractive index serves as a unique tool in discriminating various tissues. It is depends on water and solid components such as protein and phospholipids of brain tissue resembling hydro gel. RI of normal and pathological tissues of brain from the MR T2 relaxation time (T2 value) is used to determine relative water and solid contents of a tissue and discriminate various pathological lesions. This is based on Gladstone- Dale law of a compound like hydro gel which can predict final RI (μ) of a medium based on the RI of water content (μ_1) and solid content (μ_2) and their relative proportions as follows:

$$\mu = \mu_1.R_1 + \mu_2.R_2 \tag{35}$$

Where R_1 is the relative proportion of water present in the medium and R_2 is the relative proportion of solid present in the medium both expressed as percentage.

Eq. 35 is true for brain tissue containing water and protein/phospholipids in different percentages. It was noted that RI values of various benign and malignant tumours determined by an Abbe refractometer in the laboratory were found to be unique .They are different and depend on water and protein percentages**.** MRI is highly sensitive to water. Accurate and quantitative water and solid components like protein and phospholipids of brain lesions can be extracted in the clinical setting using T1 or T2 relaxation time.

We use T2 relaxation time for the following reasons:

- One needs to determine the water content of tissues to determine the RI of various tissues. The relaxation time in the brain is dominated by proton exchange between intracellular free and bound water and various tumour related proteins. The T2 value is strongly dependent on various protein concentrations.
- A very strong correlation between T2 and water content in brain is observed. Reduction of water content from 80% to 40% by weight decreases T2 value by a factor of 4 while T1 value by 0.66.
- T2 relaxation time changes very slightly by the strength of the magnet.

RI value (μ) of each pixel comprising the tissues can be determined by the T2 value (longitudinal relaxation time) by the following equation, where Eq. 37 gives the T2 value of a pixel:

$$\mu = 1.3338 + 4.3384\left(\frac{1}{T2}\right) \tag{36}$$

$$I = I_0 e^{-\frac{TE}{T2}} \tag{37}$$

Where: TE is the Time of echo
T2 is the transverse relaxation time
I is the pixel intensity
I_0 is the pixel intensity at TE different from image comprised of pixel intensity I

Each pixel in each cluster obtained from the dataset is analyzed against the RI value obtained. A threshold value T is determined from previous studies and if most of the pixels in a particular cluster have RI value greater than T, then the particular cluster denotes the tumorous region.

2.8. Post-processing

After the tumour has been segmented from the MRI, some artefacts are still present (which are CSF and water appearing as noise) which is needed to be removed.

ALGORITHM: *Post-processing*

1. Evaluate the area of each portion of the binary image obtained after RI analysis.
2. Retain the portion having maximum area. If more than one region has comparable area as the maximum one, retain them as well.

3. Results and Discussion

All our experiments have been performed on a computer with 1.70 GHz Intel Core-i3 processor with 2 GB system memory. All the algorithms mentioned above have been implemented using MATLAB R2013a.

In our experiment, brain MRI data is considered. The images that are considered are shown in shown in Fig. 2(a) and Fig 3(a). The same section of the brain is analysed, separately as T1 weighted and T2 weighted to study our proposed algorithm on both T1 and T2 images. Fig 2(a) shows a T1 original brain MRI. Fig 3(a) shows T2 original brain MRI. Pre-processing is done using adaptive Weiner Filter. A pixel neighbourhood of 3×3 serves as the block. Fig. 2(b) and 3(b) shows the pre-processed images. From each pre-processed image, all the features, namely- intensity-based, symmetry-based and texture-based- are extracted from the blocks and edge-based feature from the entire image. All these features together constitute the feature dataset. The dataset is normalized and following which, feature reduction is performed using Principal Component Analysis. After reduction, k-means clustering is performed on the reduced dataset. Each dataset value represents a single data point. Fig. 2(c) and Fig. 3(c) shows the respective clusters. The algorithm has been performed with 3, 4, 5, 6 and 7 clusters. On an average, both T1 and T2 images give satisfactory results up to five clusters. Four clusters yield best result for both T1 and T2 images.

For the RI analysis, two images are required of differing TE (Time of Echo) for a particular brain MRI. For T1 image, two T2 scans are required of different TE values but both in axial view. Fig. 4(a), (b) shows the chosen T2 images for both our T1 and T2 test images. Fig 4(a) is chosen as the base image with TE=20 and Fig. 4(b) as the target image with TE=94. Using Eq. 37, T2 value is calculated and Eq. 36 gives RI value of each pixel. The threshold value is chosen to be 1.38. The cluster having maximum number of pixels above the threshold limit is chosen to be the tumorous section. Fig 2(d) and 3(d) shows the chosen clusters. Fig. 2(e) and 3(e) shows the post-processed image.

4. Conclusion

In this paper, we proposed an algorithm to efficiently segment tumorous region from brain MRI scan using refractive index analysis as a validation method on statistical structure analysis. The method includes 4 steps- structural element division, feature extraction, PCA analysis and RI validation. Experimental results show the algorithm gives effective results for tumour classification in both T1 and T2 images. The effect of noise is reduced, the computational time is less and a vast number of various features that includes intensity, structural and textural features, are explored. The proposed algorithm does not give efficient result when the tumorous region is surrounded

by edema which can be seen in Fig. 3. The work can be further extended using optimal feature selection techniques applying evolutionary clustering methods to overcome this problem.

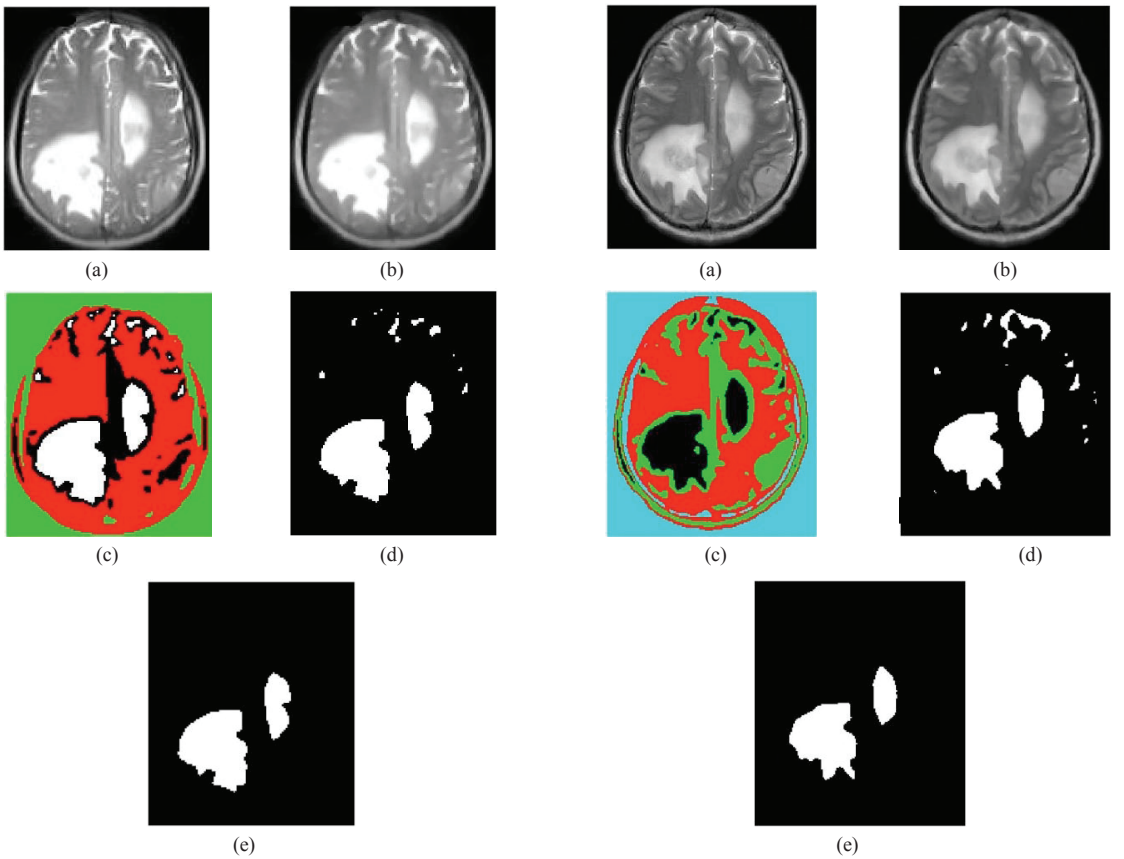

Fig 2. (a) T1 brain MRI; (b) Pre-processed MRI; (c) Clusters; (d) RI validation; (e) Post-processed Image

Fig.3. (a) T2 brain MRI; (b) Pre-processed MRI; (c) Clusters; (d) RI validation; (e) Post-processed Image

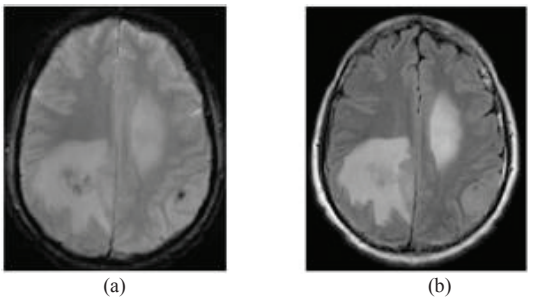

Fig.4. (a) T2 base image; (b) T2 target image

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