

Fuzzy Qualitative Reasoning Model for Astrocytoma Brain Tumor Grade Diagnosis

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Abstract

Background: Magnetic Resonance Imaging (MRI) is the most prominently used image acquisition method for brain tumor diagnosis, treatment and research. **Objective:** In this paper, a fuzzy qualitative reasoning model for diagnosing the grade of Astrocytoma brain tumor using various subtypes of MR images (T1, T1c+, T2, Flair) is explained with its implementation details. **Methods:** The fuzzy model is implemented in 5 stages namely preprocessing, segmentation, feature extraction, feature selection and building a Fuzzy Inference System (FIS) for diagnosis. In preprocessing, anisotropic filtering is used to remove noise and artifacts whereas the edge information and smoothness are retained. Then the tumor region is segmented by applying active contour method. From the segmented tumor region, textural and shape features are extracted and stored along with the clinical parameters like age, gender and mass effect of the patient for feature selection. The features are analyzed in different dimensions like image, patient, patient with subtype, to determine the sensitive feature subset and its range that discriminates the grade of the tumor. Based on this outcome a Mamdani based fuzzy qualitative reasoning model is built with optimal rule set for tumor grade diagnosis. **Findings:** The constructed fuzzy model is validated using real data set of MR images and clinical report of patients. The grade of tumor identified is same as that specified in the patient's report and hence the model provides better accuracy. **Novelty:** The novelty of this research work are: subtypes of MR images with analysis in different dimensions, identification of optimal rule set (minimum number of rules without ambiguity), recognition of irregular shape tumor, suitable model for any knowledge based diagnosis.

Keywords: Active Contour Method, Anisotropic Filtering, Astrocytoma Brain Tumor, Fuzzy Qualitative Reasoning Model, Magnetic Resonance Images, Optimal Rule Set, Textural and Shape Features

1. Introduction

Medical imaging techniques are rapidly developing in the recent age due to the technological growth and requirement. The popularly used imaging techniques for brain related disease analysis are Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and Single Photon Emission

Computed Tomography (SPECT). In these modalities, SPECT and PET are used widely in blood flow analysis of brain. CT images are suitable for identifying the structural region of the brain tumor whereas MRI provides soft tissue discrimination of brain tumor and edema because of its ability to generate scans in the axial, sagittal, coronal or oblique planes with different subtypes. In MRI, the subtypes T1, T2 and T1c+ provides boundary region,

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tissue growth, contrast region respectively for tumor analysis¹.

Stefan Bauer (2013) conducted a survey of MRI based medical image analysis for brain tumor studies that are elaborative in nature, and show the importance of MRI in brain tumor analysis². In reality the MR images cannot be acquired without noise³. Therefore, it is essential to remove the noise before processing like segmentation for Region of Interest (ROI) identification, feature extraction, feature selection and classification/understanding for diagnosis⁴.

Automated diagnosis of brain tumor has been practiced over the past decade since brain tumor occurs in people of all ages, but statistically, it is found to be more frequent in children and the aged. Brain tumor diagnosis in its early stage is very essential, since aggressive grade IV tumor reduces the average life expectancy. The fact that the number of cancer affected people has increased substantially over the years (from 1970 to 2012) is evident from the statistics of Brain tumor research⁵. The routine clinical practice currently followed lacks periodical assessment of the tumor grade with respect to area/volume during the pre-operative and post-operative stages, and often suffers from inconsistent expert opinion. Hence recent research has focused on automated Computer Aided Disease Diagnosis (CADD) system for brain tumor recognition.

Most of the research work on CADD for brain tumor recognition focuses on distinguishing tumor images from non tumor images or multiple tumor type with non tumor images, using classification techniques such as Artificial Neural Networks (ANN), Support Vector Machine (SVM) and other classifiers are listed⁶. However, the classification technique requires more training samples and does not offer scope for adding new knowledge to the existing one. The classifier performs better only when the testing samples are similar to that of training samples. In the cited research works, traditional feature extraction techniques have been applied and there is no prominent focus on retrieving the features that indicate the grade of a tumor. To overcome these drawbacks, reasoning based understanding techniques have emerged in recent years to incorporate image information, clinical

information and expertise knowledge in analysis and recognition.

The machine learning techniques can be called understanding techniques when they have knowledge base and rules which require human knowledge (expert) for classification. The various understanding methods are: ontology-based approach, case based reasoning, graph grammar and fuzzy based reasoning. Ontology based approach requires predefined domain knowledge in building ontology, therefore it is difficult to use it for medical images⁷. Graph grammar is suitable only for structured medical images like x-ray images⁸. Case based reasoning fails to identify the cases, which is not in the background knowledge base. From these discussions, we conclude that fuzzy based reasoning is suitable for medical images since it resolves the uncertainty in nature^{9,10}.

The research papers which contributes to fuzzy reasoning in various disease diagnosis are: the generic medical fuzzy expert system for diagnosis of cardiac diseases designed¹¹, heart disease diagnosis¹², fuzzy cognitive map model for grading urinary bladder tumors discussed¹³ and a Web-Based Decision Support System (WBDSS) using Fuzzy Logic (FL) for the diagnosis of typhoid fever¹⁴. Fazel et al (2013) used a type-II approximate reasoning method of fuzzy in recognizing the tumor grade in brain MRI in image level (slice) for single subtype images with more than one rule for each grade. In our work, we extended the analysis to all subtypes of MR images in different dimensions like patient-wise and patient-wise with subtype, and derived a optimal rule set using fuzzy qualitative reasoning model.

This research work has taken up Astrocytoma and attempts a solution. Because it is the most common type of glial tumor that appears in various parts of the CNS, including the cerebellum, the cerebrum, the central areas of the brain, the brainstem, and the spinal cord, it is usually malignant, and statistically 30% of tumor patients are diagnosed with this type. There are four grades in Astrocytoma as per the report of WHO: Grade I (Pilocytic Astrocytoma), Grade II (Diffuse Astrocytoma), Grade III (Anaplastic Astrocytoma) and Grade IV (Glioblastoma

Multiforme)^{15,16}. The classification and grade of an individual tumor helps to predict the likely behavior of that tumor and the findings will be useful to the radiologist and physicians as a precision tool for decision making process¹⁷.

In this research work, a fuzzy qualitative reasoning model has been proposed to identify the grade of Astrocytoma brain tumor in MR images by considering all subtypes of MRI and clinical information. In this model, the extracted image features and clinical data are analysed in different dimensions like image-wise, patient-wise and patient-wise with subtype for the selection of relevant features and its sensitive range to derive optimal set of fuzzy rules for grade discrimination.

This paper spans across the following sections: Section 2, explains the proposed fuzzy model for Astrocytoma brain tumor grade diagnosis, Section 3 describes about the experimental results and performance analysis. Conclusion and future directions are stated at the end.

2. Proposed Fuzzy Model

The proposed fuzzy model for the diagnosis of Astrocytoma brain tumor grade has been implemented in five stages as shown in Figure 1. Initially, preprocessing is done using Anisotropic filtering to remove the noise and artifacts of the MRI brain images. Active contour segmentation is performed to identify the region of interest (ROI), from which textural and shape features are extracted. Then the extracted features and data from clinical report were analyzed for the dimensions like image, patient and patient with subtype using SQL to select the apt feature subset. The analysis was also used to identify the range for membership function creation of FIS and in defining the optimal set of rules for building a FIS.

2.1 Preprocessing - Anisotropic Filtering

The Anisotropic filtering method, applies the law of diffusion on pixel intensities for smoothening the texture of an image. A threshold function controls the diffusion at the edges in the image thereby preserving them. This is an interesting characteristic of the filter which

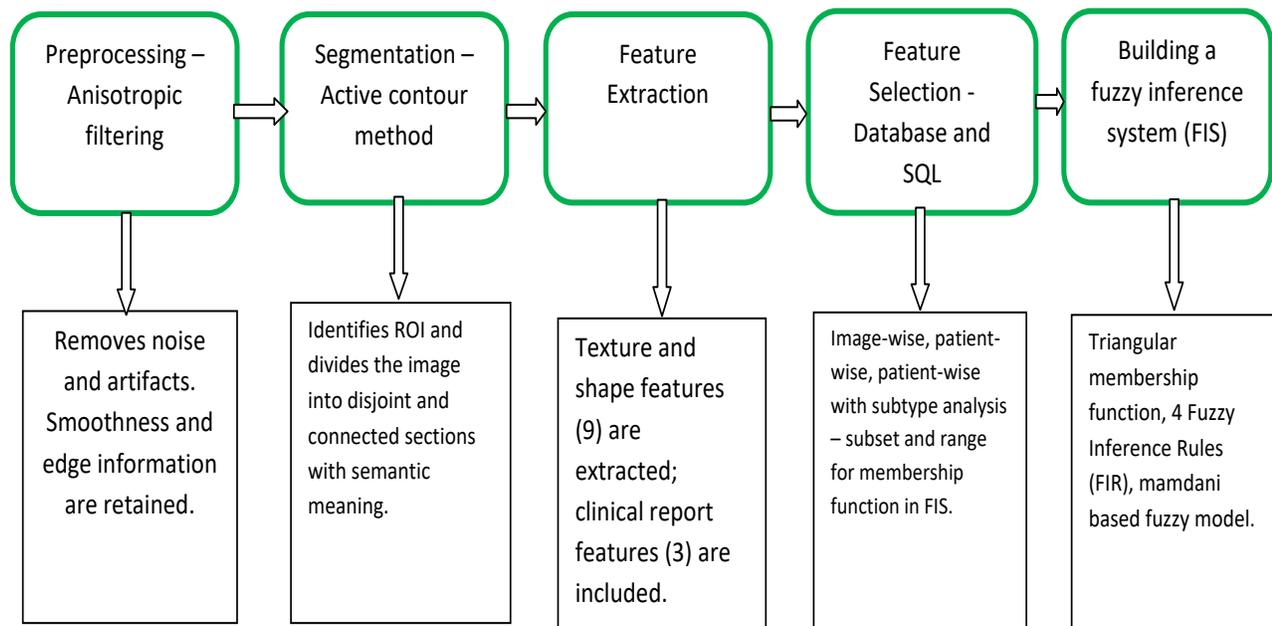


Figure 1. Stages in building a fuzzy model.

removes the noise rather than smoothing the edges in the image. The Neumann boundary condition specified in¹⁸ is used in this work for pre-processing of MRI brain tumor images and its corresponding algorithm is given below.

Algorithm

Input – an image I

Output – denoised image $D(s)$

Model used – Neumann boundary condition

Let $u(x,y,t)$ represent an image field of I with coordinates (x, y) at time t while D is the diffusion coefficient. The diffusion flux ϕ is defined as given in Equation 1.

$$\phi = -D\nabla u. \quad (1)$$

$$\partial u / \partial t = -\nabla \cdot \phi. \quad (2)$$

Putting (1) and (2) together, the diffusion equation is

$$\partial u / \partial t = \nabla \cdot (D\nabla u), \quad (3)$$

where “ \cdot ” represents the inner product of two vectors. When D is a constant, the diffusion process is isotropic.

If D is a function of the directional parameters, the diffusion process becomes anisotropic. Jitendra Malik et al., suggested two well-known diffusion coefficients as given in Equation 4 and Equation 5.

$$D(s) = 1/(1+(s/k))^2 \quad (4)$$

$$D(s) = \exp[-(s/k)^2] \quad (5)$$

where $s = |\nabla u|$ of an image, k is the coefficient of diffusion strength.

2.2 Segmentation - Active Contour method

Segmentation is the process of partitioning a medical

image into multiple segments/objects (sets of pixels). For segmenting the tumor region, Chan-Vese model¹⁹ of active contour is used along with region based local statistics computation from Thi-Thao²⁰. This model is best suited for the extraction of irregular shape that cannot be achieved in classical segmentation i.e. thresholding or gradient based methods²¹.

Algorithm

Input parameters

I – an input image

ϕ_0 – an initial level set created through mask

max – number of iterations for which curve evolves

rad – radius of the local region

alpha – smoothness term over which curve evolves

Output – segmented tumor region

Model used – Chan vese model

create the initial mask and set as ϕ_0

initialize $\phi = \phi_0$

repeat

compute the narrow band or window bound and set as wbx

calculate the window for local statistics

for $i = 1$ *to* $\text{size}(wbx)$

%update level set function using chan vese model

% local means μ_1 and μ_2 of image intensity inside and outside the curve C are defined

% $W_k(x)$ is the local window with size 30 X 30 in experiments

% Ω is the entire image domain

% I is the image, x is a pixel

if the point is local interior then
 calculate the interior mean

$$\mu_1(x) = \text{mean} (I \in (\{x \in \Omega \mid \varphi(x) < 0\} \cap W_k(x)))$$

 else
 calculate the exterior mean

$$\mu_2(x) = \text{mean} (I \in (\{x \in \Omega \mid \varphi(x) > 0\} \cap W_k(x)))$$

 end
 end
 compute the gradient descent
 maintain the CFL condition
 reinitialize φ to the signed distance function to its zero contour
 until max or convergence point
 return the segmented tumor region mask from φ

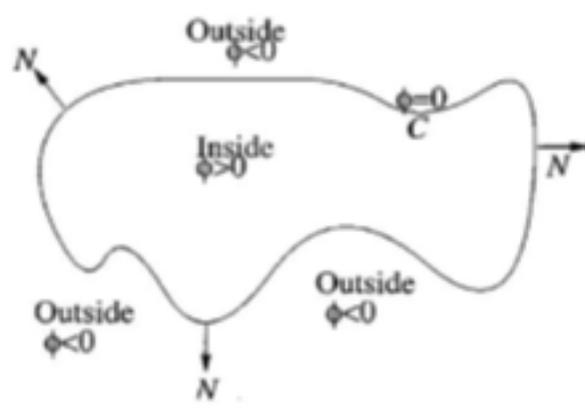


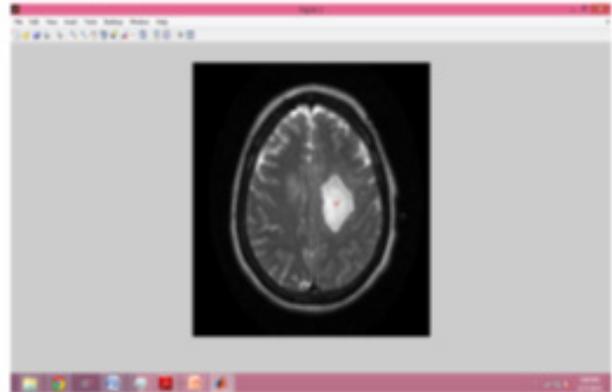
Figure 2. Contour representing a signed distance function.

Working

In the input image, mask is created using the region of interest selection tool in MATLAB (imellipse) for tumor segmentation. This mask serves as the initial curve (initial level set function) for the algorithm and then evolves in the neighborhood to obtain the final segmented region based on the properties of the pixel intensities in the image. The local region statistics must be computed for each of the points along the evolving curve as shown in Figure 2.

2.3 Feature Extraction - Textural and Shape based Features

From the segmented tumor region, values of nine features such as circularity, area, perimeter, elongation ratio, compactness, major axis length, minor axis length, centroid and mean intensity are extracted²². The segmented region with label is shown in Figure 3.



R – Segmented boundary region (shown in white)

$R(x)$ – Pixels of region R

R_I – inside the region R

Figure 3. Segmented tumor region with label.

Area

Area is the count of number of pixels in the segmented region as defined in Equation (6).

$$A = p_1 + p_2 + \dots + p_n \quad (6)$$

where

$$p_1, p_2, \dots, p_n \in R_I$$

Perimeter

It is the distance around the boundary of the segmented region. It is computed as the distance between each adjoining pair of pixels around the border of the region as given in Equation (7).

$$P = \sum_{i=1}^{m-1} d(i, i+1) \quad (7)$$

where m is size of R , $d(i, i + 1)$ is the distance between the adjacent pixels of the boundary region R .

Circularity

Circularity, specifies whether the tumor is circular or not. If circularity value approaches 1, the shape is nearer to circular. It is computed as defined in Equation (8).

$$C = \frac{4 * \pi * A}{P^2} \tag{8}$$

In the above formula, A denotes area and P denotes perimeter.

Elongation Ratio

It is the ratio of longest axis to the shortest axis in the segmented region as given in Equation (9).

$$ER = \frac{AC}{BD} \text{ of } R \tag{9}$$

Compactness

The compactness measure of a shape, sometimes called as shape factor, is a numerical quantity representing the degree to which a shape is compact. It is computed as mentioned in Equation (10).

$$C_p = \frac{P^2}{A} \tag{10}$$

where P is the perimeter and A is the area.

Centroid

The center of the segmented region is computed from the major and the minor axis intersection point of the region. It is represented as ‘O’ in Figure 3.

Mean Intensity

The mean intensity is computed by summing the pixel intensity of the region and dividing it by the area as given in Equation (11).

$$MI = \sum_{i=1}^n P_i | n \in R \tag{11}$$

where n is the number of pixels in R and is the i^{th} pixel intensity.

In addition to these nine features, three more features (age, gender, mass effect) are included from the clinical report.

2.4 Feature Selection and Sensitive Range Identification for Grade using Database and SQL

The nine features extracted from the segmented tumor region and the additional three features from the clinical report are parsed into separate tables and stored in a database for analysis. The analysis is carried out for selecting the feature subset with its range for discriminating each grade of Astrocytoma brain tumor. It also helps in identifying the range for membership function and the rules required to construct the fuzzy system.

The features are grouped in three aspects for analysis. They are:

- i. Analysis of features for each image (image-wise)
- ii. Analysis by taking average of all features for all images of a given patient (patient-wise)
- iii. Analysis by taking average of all features for each subtype of MRI images separately for a given patient (patient-wise with subtype).

2.5 Fuzzy Qualitative Reasoning Approach

The fuzzy qualitative reasoning approach is one of the methods in fuzzy based approximate reasoning. Based on the analysis performed using SQL, a FIS is implemented in three stages as shown in the following Algorithm.

Algorithm

Input - IP - Input parameters (features)

OP – Output parameter (grade)

range – set of value to define grade

Output- Fuzzy Inference System with optimal rules

Model used – Mamdani qualitative reasoning model

```

begin FzzyInferenceSystem
    set Type='mamdani'
    Version=2.0
    NumInputs=7
    NumOutputs=1
    NumRules=4
    AndMethod='min'
    OrMethod='max'
    ImpMethod='min'
    AggMethod='max'
    DefuzzMethod='centroid'
begin MembershipFunctinCreation
    for i = 1 to IP
        for j = 1 to OP
            define the range and create the member-
            ship function
        end
    end
begin Fzzy Inference Rules
    for k = 1 to OP
        select the appropriate membership function and
        create the fuzzy rules
    end
end

```

The created FIS is validated with test samples for the linguistic values defined in Table 1.

3. Experiments and Results

3.1 Dataset

The data set consists of various sub types of MR brain images (T1, T1c+, T2, PD, FLAIR) for the four grades of

Table 1. Fuzzy linguistic value for the grades

Grade	Fuzzy linguistic value
I	0 – 1
II	1.1 - 2.0
III	2.1 – 3.0
IV	3.1 – 4.0

Table 2. MRI brain tumor images of Astrocytoma for training and testing

Grade type	No. of patients images for training	No. of patients images for testing
Grade I	20	6
Grade II	18	4
Grade III	17	3
Grade IV	25	7
Total images	80	20

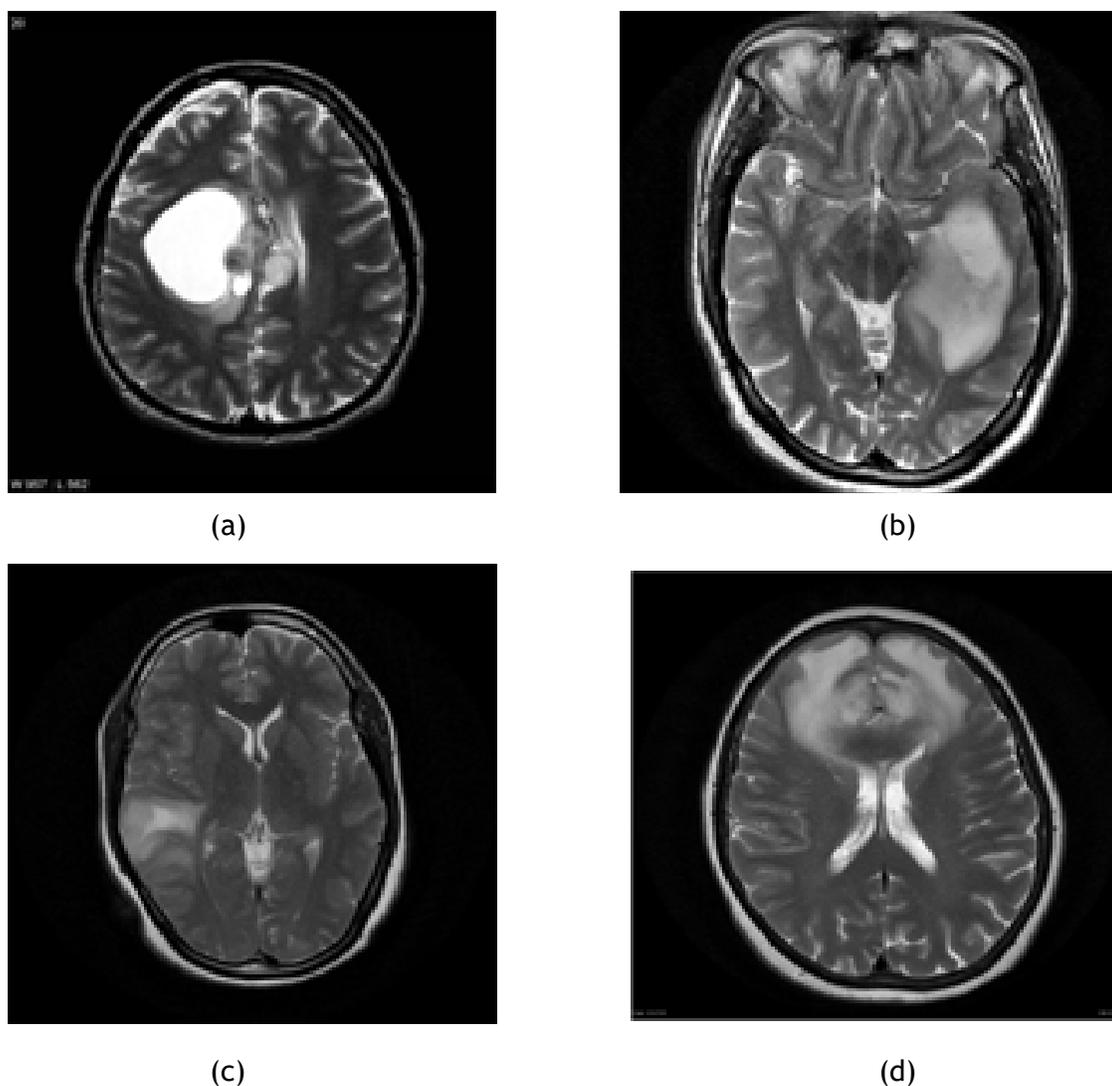


Figure 4. (a) Grade1 – Patient1 (b) Grade2 – Patient1 (c) Grade3 – Patient3 (d) Grade4 – Patient6.

Astrocytoma tumor. The images are collected from different sources such as Harvard medical school, Bharat scans and Radiopaedia²³⁻²⁵ and have been divided into training set and test set respectively as given in Table 2. The training set has images of 80 patients with different grades (grade I-20, grade II-18, grade III-17, grade IV-25) and the test set has images of 20 patients with six in grade I, four in grade II, three in grade III and seven in grade IV respectively. The sample image of each grade from the training set for sub type T2 of MRI is given in Figure 4.

3.2 Experimental Steps and Analysis

The brain images are pre-processed using anisotropic filtering method to remove the noise and artifacts from the image and as well the edge information is preserved. For visualization, the T2 MRI image of grade I Astrocytoma before and after pre-processing is shown in Figure 5.

The tumor region is segmented from the pre-processed image using active contour method and the resultant image obtained during each stage of segmentation is shown in Figure 6.

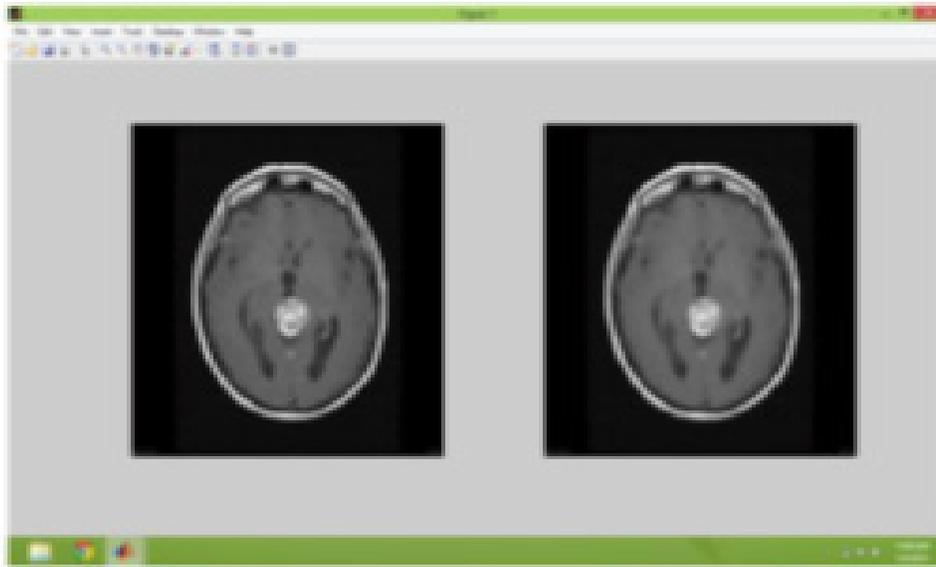
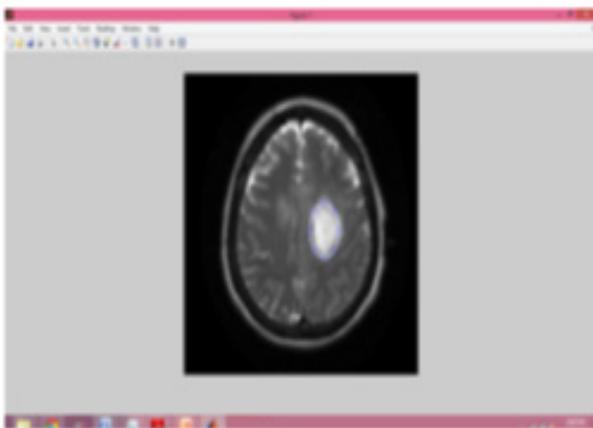


Figure 5. Pre-Processed T2 MRI image of grade I Astrocytoma.

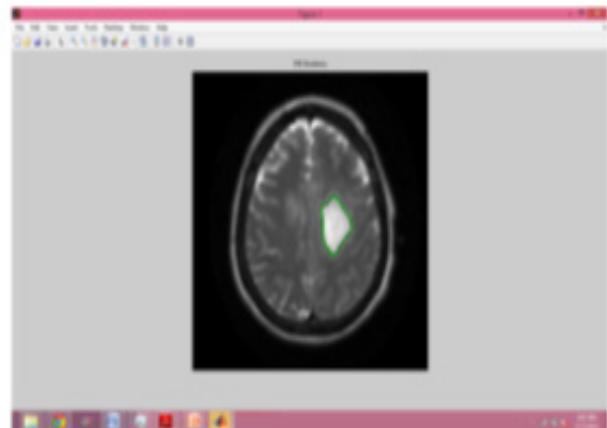
The textural and shape based image features are extracted from the segmented tumor region. With the extracted nine features, clinical report features such as age, gender and mass effect of the tumor are also included for next level of analysis.

The features are stored in a database, and analysis is performed using SQL queries in different dimensions like image-wise, patient-wise, patient-wise with subtype

for feature selection and also the appropriate range for membership function in discrimination of tumor grade is calculated and given in Table 3. From the analysis made, we inferred that patient-wise feature values with 6 image features (perimeter, area, circularity, elongation ratio, compactness, mean intensity), and 1 clinical feature (age) is adequate in grade discrimination of Astrocytoma brain tumor. In Table 3, the min and max value of each selected



(a)



(b)

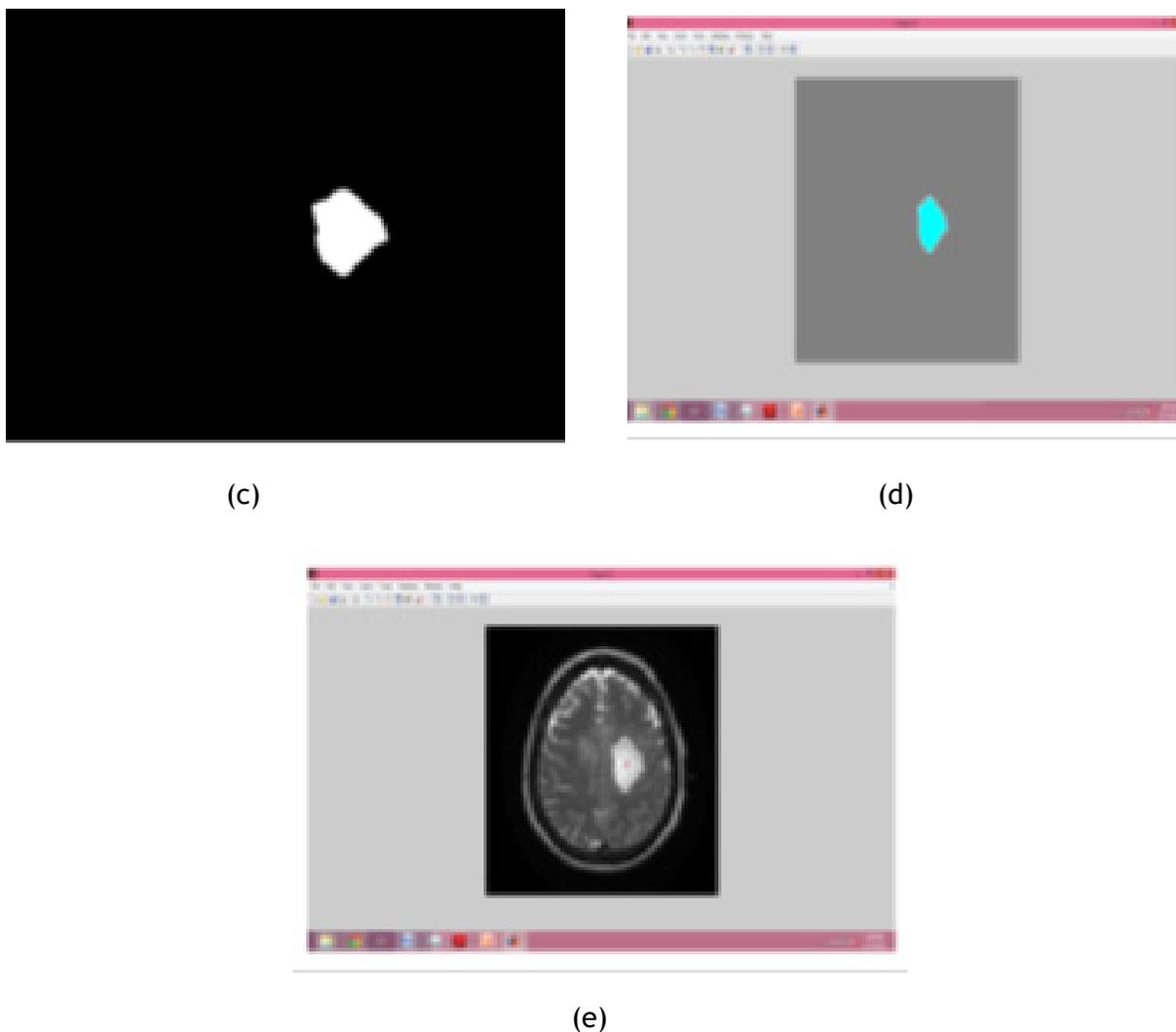


Figure 6. (a) Region of Interest(ROI) marked by user in the form of ellipse for T2 MRI image of grade I Astrocytoma (b) Segmented region after 100 iterations (c) Segmented region (d) Plot of boundary points of the tumor region (e) Centroid of the tumor region.

feature is tabulated and these values are used in the definition of membership function for each feature (parameter) in specific grade while building a FIS model.

Using membership function, Fuzzy Inference Rules (FIR) are constructed as specified below with the help of fuzzy tool box available in MATLAB. The constructed rule set is given below:

Rule 1: If (perimeter is g1) and (age is g1) and (area is g1) and (circularity is g1) and (er is g1) and (comp is g1) and (mi is g1) then (output is g1)

Rule 2: If (perimeter is g2) and (age is g2) and (area is g2) and (circularity is g2) and (er is g2) and (comp is g2) and (mi is g2) then (output is g2)

Rule 3: If (perimeter is g3) and (age is g3) and (area is g3) and (circularity is g3) and (er is g3) and (comp is g3) and (mi is g3) then (output is g3)

Rule 4: If (perimeter is g4) and (age is g4) and (area is g4) and (circularity is g4) and (er is g4) and (comp is g4) and (mi is g4) then (output is g4)

Table 3. Minimum and maximum values of each parameter (feature) in MF creation

Grade / Min/Max	Grade I		Grade II		Grade III		Grade IV	
	Min	Max	Min	Max	Min	Max	Min	Max
Age	12	40	14	35	40	45	35	80
Perimeter	293.4	551.6	440.0	647.7	299.0	433.9	164.2	703.7
Area	3412.1	14850.8	7774.3	13775.4	3245	10528	1223	15069
Circularity	0.35	0.62	0.40	0.67	0.44	0.69	0.30	0.74
Elongation Ratio (er)	1.3	2.28	1.2	1.61	1.2	1.92	1.20	2.85
Compactness (comp)	21.31	40.5	19.2	34.5	18.63	32.97	17.38	50.3
Mean Intensity (mi)	82.55	115.79	81.16	98.8	95.89	141.23	57.89	177.36

The procedure for constructing fuzzy inference system (FIS) with sample snapshots is given in Appendix A. The constructed fuzzy model is validated using the real data set collected from Bharat Scans (2015) for 20 patients. The derived linguistic fuzzy values of the test set samples matches with the actual grade specified in the clinical report, since the derived values are in the range of defined fuzzy values of each grade. Approximately,

for 2/3 of patients, the actual linguistic fuzzy value is the maximum limit of the defined fuzzy value. For remaining patients (1/3), the calculated linguistic fuzzy value is in the range of it. The developed fuzzy model gives 100% accuracy, since it recognizes the tumor grades of all 20 patients as in clinical report. Also, the obtained linguistic fuzzy value of first four patients is given in Table 4 for sample purpose out of 20 patients.

Table 4. Linguistic fuzzy value for the test set with expected and actual grade

Patient	Grade specified in clinical report	Linguistic fuzzy value	Grade predicted from FIS	Defined linguistic value
Patient 1	II	2	II	1.0 – 2.0
Patient 2	I	0.537	I	0.0 – 1.0
Patient 3	IV	3.57	IV	3.0 – 4.0
Patient 4	I	0.725	I	0.0 – 1.0

From Table 4, for Patient 1, the actual linguistic fuzzy value is the maximum limit of the defined fuzzy value. For Patient 2, 3 and 4, the calculated linguistic fuzzy value is in the range of it. It is possible to incorporate more rules when new cases arise in evaluation and the system can be validated for more patients also.

4. Conclusion and Future Directions

A fuzzy model has been developed to identify the grade and the area of Astrocytoma brain tumor in MRI brain images acquired with different subtypes. This model has been implemented in five stages namely pre-processing, segmentation, feature extraction, feature selection and qualitative reasoning approach. The contribution lies in stage 4 and stage 5. In stage 4, using SQL, the features are analyzed image-wise, patient-wise and patient-wise with subtype (T1, T1c+, T2, PD, FLAIR etc.) to determine the feature subset and its range that discriminates the grade of the tumor. The analysis carried out is further used for defining the membership function and deriving the rules. In stage 5, a FIS is built using mamdani method with minimum number of rules (optimal set) without disjunctions and ambiguity. The proposed model was validated using real test images of 20 patients' MR scans and it has been observed that, the derived fuzzy linguistic values are in the range of defined fuzzy values of specific grade. From this we inferred that the grade of the tumor identified matches exactly with the grade specified in the patient report. This model has given 100% accuracy for four patients' MR scans of different grades and also the knowledge base of fuzzy rules can be updated for any new cases to retain the system as a diagnostic tool for grade discrimination.

In segmentation, selecting the initial contour (ellipse shape) is done manually but it can be automated to avoid human interruption. The developed system is open for analyzing the images with tumor at multiple locations and small lesions. The sample space considered constitutes only MRI images of Astrocytoma Brain tumor but it is significant to note that the same approach can

be extended to several other types of tumors also. The parameters used for the analysis are image based features and limited clinical features, thus allowing for the extension of the system to categorize tumor based on various modalities of images like PET, SPECT, CT and fused images.

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