# Automatic Detection and Classification of Glioma Tumors using Statistical Features

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*Abstract*: *The characterization and grading of glioma tumors, via image derived features, for diagnosis, prognosis, and treatment response has been an active research area in medical image computing. This paper presents a novel method for automatic detection and classification of glioma from conventional T2 weighted MR images. Automatic detection of the tumor was established using newly developed method called Adaptive Gray level Algebraic set Segmentation Algorithm (AGASA).Statistical Features were extracted from the detected tumor texture using first order statistics and gray level co-occurrence matrix (GLCM) based second order statistical methods. Statistical significance of the features was determined by t-test and its corresponding p-value. A decision system was developed for the grade detection of glioma using these selected features and its p-value. The detection performance of the decision system was validated using the receiver operating characteristic (ROC) curve. The diagnosis and grading of glioma using this non-invasive method can contribute promising results in medical image computing.*

*Keywords*: *Glioma; Automatic Detection*; *Texture; GLCM; t-test; p-value; Feature extraction; Classification*
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## I. Introduction

Gliomas are the most frequent primary brain tumors that originate in glial cells. Glial cells are the building-block cells of the connective, or supportive tissue in the central nervous system (CNS) [1], [2]. According to World Health Organization (WHO), gliomas are classified into four grades that reflect the degree of malignancy. Grades I and II are considered low-grade and grades III and IV are considered as high-grade. Grades I and II are the slowest-growing and least malignant, Grade III tumors are considered malignant and grow at a moderate rate. Grade IV tumors, such as Glioblastoma multiforme, are the fastest growing and the most malignant primary brain tumors [1], [3]. Classification of glioma tumors is important for clinical understanding of tumor biology, clinical response and for assessing overall prognosis with brain tumors.

Conventional MR imaging is the standard technique for diagnosis, treatment planning, and monitoring of CNS lesions, with superior sensitivity compared to alternative modalities [4]. It is routinely used for the non-invasive assessment of brain tumors, but its ability to define the tumor type and grade of gliomas is limited [5]. A biopsy and surgical resection is usually required to establish the diagnosis and subtype of a brain tumor after conventional MR imaging, but variations in tissue sampling may produce erroneous result during biopsy [6]. In this work, only conventional T2-weighted MR images are considered and this modality highlight tissues with higher concentration of water in which border definition and tumor heterogeneity are best observed [7].

Most of the segmentation technique in literature such as fuzzy c-means clustering [8], [9], Markov random fields [10], [11] level set method [12] model based techniques [13] are time consuming or complex or need human intervention. Accurate segmentation of glioma is also very important in this work because entire portion of tumor texture is considered for classification of tumor. Hence a new method for accurate detection glioma tumor is described here.

Texture features have proved useful in differentiating normal and abnormal tissues [14] in different organs using different types of imaging modalities. Texture analysis is very important in the brain tumor detection, as it is difficult to differentiate between various types of tumor tissues using shape feature alone [15]. 2D textural features have been previously employed for MRI brain tumor characterization and pattern recognition systems [16]. Classifications of primary and secondary brain tumors using first order and second order statistics from MRIs [17] have also been developed. Statistical analysis of textures from brain CT images for quantifying

tumor heterogeneity and thereby differentiate high and low grade glioma are there in literature [18]. Texture analysis using statistical quantification has proposed in literature for differentiating glioneuronal tumors as a subclass of grade III and IV malignant gliomas [19] Gray level co-occurrence (GLCM) based texture analysis is widely used in the detection of breast cancer in mammograms [20] detection of abnormal liver in CT images [21] and detection of primary and secondary tumors [17] in brain MRIs. Several approaches are developed in the literature for classification and grade detection of glioma tumors. Classification of glioma from metastatic and grading of glioma from conventional MRI and perfusion MRI, using support vector machines (SVM) [6], Artificial Neural Network (ANN) [22] and linear discriminant analysis (LDA) [23] is cited in literature. The features used for their study were tumor shape, intensity characteristics as well as rotation invariant Gabor texture features. Determination of degree of malignancy of glioma using SVM is [24], [25] also developed in the literature. The degree of malignancy was determined in their work using the features from clinical data before operation and findings from conventional T1 and T2 weighted MRI such as age, shape, gender etc.

The objective of this work is automatic detection and classification of low and high grade glioma from T2 weighted brain MRI. The framework of the method consists of detection of region of interest (ROI) using Adaptive Gray level Algebraic set Segmentation Algorithm (AGASA), feature extraction from detected tumor texture based on first order and GLCM based second order statistics, feature selection using t-test and its corresponding p-value, and classification of low and high grade glioma, based on p-values of selected features, training and performance evaluation of results using receiver operating characteristic curve (ROC).

## II.Materials and Methods

The block diagram for the entire procedure is shown in Fig.1. The steps involved were image pre-processing, detection of glioma, feature extraction process, feature selection and classification.
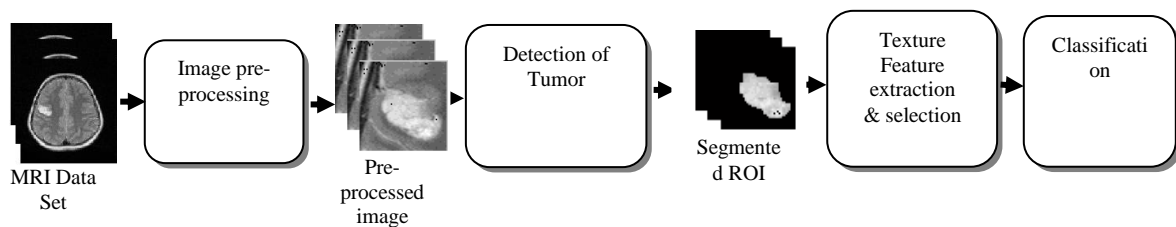


**Fig.1 Block diagram of the method**

### A. *Image Database*

The study population comprised of T2 weighted axial MRI data sets (of 135 glioma patients (87 men, 48 women; Age 18-78 years) for detection and classification. Out of this, 75 were of high grade glioma and 60 sets were of low grade.
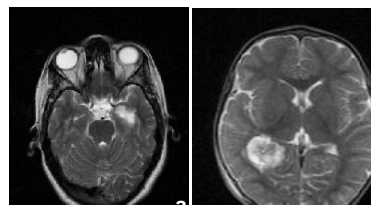


**Fig.2 Shows T2 weighted images of low grade and high grade glioma tumors**

All selected image dataset consisting of single glioma was considered for detection and classification. All patients underwent biopsy or surgical resection of the tumor with histopathological diagnosis. MR images were collected from the department of Radiology in the Sree Chitra Institute of Medical Sciences and Technology (SCIMST) and Regional Cancer Centre Trivandrum, India. The images were gray scale images and which were acquired before contrast enhancement. Fig.2 shows the examples for T2 weighted images of low and high grade tumors.

### B. Detection of Tumor

A novel method is discussed here for accurate detection of tumor tissues using Adaptive Gray level Algebraic set filtering Algorithm (AGASA). Fig.3 shows the detection of glioma. The method mainly involves repeated mathematical morphology based operations using different structuring elements [26], thresholding and masking techniques. As the first part of segmentation procedure MR Image is complimented and dilated using square shaped SE. The complemented image is subtracted from the dilated image. The subtraction of dilated image from the complemented image is done for reducing noise artefacts and partial volume effect present in the image and enhancing tumor.
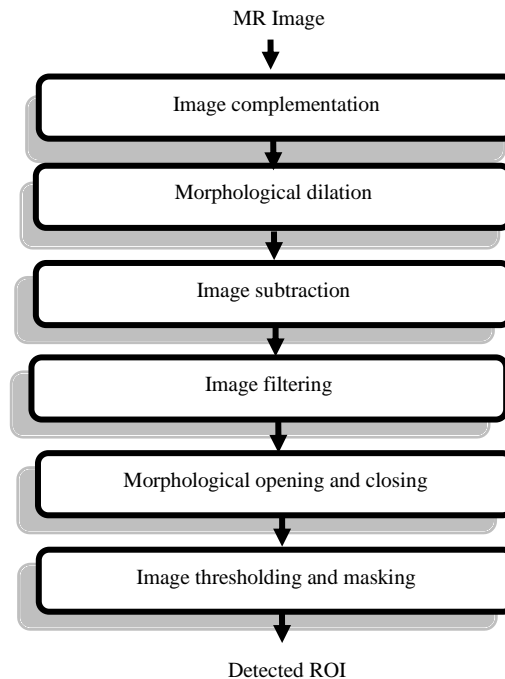
MR Image

Image complementation

Morphological dilation

Image subtraction

Image filtering

Morphological opening and closing

Image thresholding and masking

Detected ROI

**Fig.3 The flow chart for Detection of glioma**

The resulting image undergoes spatial domain filtering by correlation method for enhancing regions which are similar to the filter templates. The filtered output is again dilated with a square shaped SE. The main challenge in the tumor segmentation procedure is that usually tumor boundaries will not be clearly defined from the other regions and tumors may have heterogeneous borders and will have infiltrating nature. This boundary intrusions and protrusions are clearly visible after dilation. The main disadvantage of morphological dilation is over segmentation [27], this can be reduced to a greater extent using morphological opening operation with a disc shaped SE of suitable radius. After the opening operation, the output image undergoes closing operation. The combination of opening followed by closing or closing followed by opening can suppress noise sufficiently [27]. The tumor boundary and region of the resulting image is visually enhanced. The resultant image is thresholded by a specific threshold level to obtain the segmented ROI. The binary image thus obtained was masked with the original normalized image in order to obtain the original gray level image of the corresponding ROI. The detected tumor is validated with manual ground truth [26]

### C. Feature description

The detected tumor was considered for texture analysis. A set of textural descriptors was calculated for each ROI in the training set, using first order statistics and GLCM based second order statistics [].

#### 1) First-order statistics

For any region of interest (ROI), the mean (average Intensity) and the standard deviation (average contrast) of the gray level values in the region can be used to measure the spread of gray level values of the pixels within that region (Histogram). One class of such measures is based on statistical moments. Here statistical moments such as mean, standard deviation, entropy, kurtosis and skewness are calculated from the segmented ROI. Entropy indicates a measure of irregularity, kurtosis indicates a measure of peakedness and skewness indicates a measure of asymmetry [28]. Five descriptors were computed using first order statistics. Quantification using these first order statistical features, one can determine the given texture is coarse or fine.

*2)   Second order statistics*

GLCM is a widely used tool for analyzing statistical textural properties of different types of tissues in biomedical imaging. From the co-occurrence model, 10 Halarick descriptors are calculated in order to quantify the spatial dependence of gray level values. These descriptors are computed from the co-occurrence matrices of size [16x16], which is constructed at with an inter pixel distance of *d* = 1 and for a pixel direction θ = 0° [28]. The main texture descriptors derived from GLCM are, Correlation, Contrast, Energy, Entropy, Cluster Prominence, and Cluster Shade of gray level values and the other descriptors are relative values of these features. Contrast evaluates the amount of local intensity variations present in an image, and energy is the sum of squared elements in GLCM. It is also a measure of uniformity and angular second moment. The Correlation of a texture depicts the linear dependency of gray levels on neighboring pixels [29].

## D.  *Feature selection*

Feature selection and feature set formulation are very important, because selected features must be sufficiently discriminating and suitably adapted for the application, since they fundamentally impact the resulting quality of the detection system. Fifteen feature descriptors were extracted from the first order statistics and GLCM methods.

The t-test (test statistic) checks whether the means of two groups are statistically different or in other words it determines, the two dataset come from the same population or different population [29]. The p-value is associated with a t-test. It is the level of marginal significance within a statistical hypothesis test, representing the probability of the occurrence of a given event. The smaller the p-value, the more strongly the test rejects the null hypothesis, that is, the hypothesis being tested.  The t- test for extracted 5 first order statistical features and 7 GLCM features of low and high grade glioma are performed.  The statistical significance of each feature for the two datasets is estimated using its p-value. Using the statistically significant features a decision system is developed for classification of low and high grade glioma. This decision system does not make any assumptions about the distribution of data. The training set was used to build the decision system, while test set was used to estimate the accuracy of the system. The training and testing are based on the p-value of each feature in the feature set.

## E.  *Performance evaluation*

The accuracy and performance of detection system can be analyzed using four parameters [30], which are false positive (FP), false negative (FN), true positive (TP), and true negative (TN). For evaluating the accuracy of detection, specificity and sensitivity of detection have to be considered. Sensitivity (eqn.(1)) and specificity (eqn. (2)) are two important parameters which indicate the presence or absence of the disease.

$$Sensitivity = \frac{TP}{TP+FN} = TPR \qquad (1)$$

$$Specificity = \frac{TN}{TN+FP} = TNR \qquad (2)$$

In particular, Sensitivity is the percentage of correctly diagnosing high grade glioma and the result is also positive. Specificity indicates false positive rate (FPR). Thus, it is a measure of the probability of correctly distinguishing the absence of high grade glioma and the result is negative. The ROC analysis is done for assessing the performance. It is a graphical plot of the sensitivity against specificity for a binary classifier system at different operating points. For a perfect classifier, ROC curve will pass through upper left corner (0, 1) of the ROC space..

## III. Results and Discussion

### A.  *Detection of Tumor*

This section presents the results obtained from the automatic segmentation using spatial domain filtering techniques on T2 weighted axial MR images of 135 MR image datasets. Usually there are only four to eight slices which contain maximum gray level tumor information in a data set.
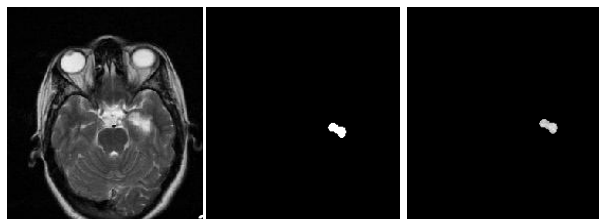


**Figure 4   Segmentation procedures from low grade glioma tumor from a T2 weighted MR image (a) original image (b) Image after thresholding (c) Segmented gray level tumor**

Fig. 4a to Fig. 4c shows the detection of images. The final output of a segmentation process is a binary image as shown in Fig. 4b. In order to retrieve the texture information, the segmented image is masked with the original image. Finally, a binary tumor mask was obtained after removing all background details using detection algorithm. This tumor mask is multiplied with the gray level image for obtaining gray level tumor. The extracted gray level tumor will be used for texture analysis.

## B. *Feature extraction and feature selection*

Table.1 portrays the ranges of values for first order statistical descriptors, such as intensity, standard deviation, entropy, kurtosis, and skewness for the two grades of glioma tumors and its respective p-values. These ranges of values determined from the statistical quantification of 135 MRI datasets of segmented ROIs (75-low grade, 60- low grade).

The t-test was performed for the first order statistical features and its statistical significance was tested for a confidence interval of 0.05 and the corresponding p-value was observed. From the Table 1, it can be observed that p-value for all the five features were $\ll 0.001$. If the p-value of two data sets are $\ll 0.001$ indicates that mean of two data sets are different or these datasets are statistically different and it is very much less than the confidence interval and the test strongly rejects the null hypothesis. This proved the effectiveness selecting these features for detection of low and high grade glioma.

**Table1. The ranges of values for first order statistical features for low and high grade glioma (training set) and its p-value**

| First order statistical features | High Grade | Low grade | P-value; |
|---|---|---|---|
| Intensity | 190-240 | 70-160 | p$\ll$0.001 |
| Std.dev. | 90-150 | 10-60 | p$\ll$0.001 |
| Kurtosis | 115-152 | 1.5-12 | p$\ll$0.001 |
| Entropy | 6.5-15 | 0.5-5.2 | p$\ll$0.001 |
| Skewness | 8-25 | 0.2-3.0 | p$\ll$0.001 |

These statistical descriptors yield characterization of high grade glioma texture as coarse texture. Usually coarse textures show heterogeneous behaviour. Entropy is a measure of randomness. Highly malignant glioma (grade IV) tumors contain heterogeneous tumors [31]. As malignancy increases heterogeneity is also increasing. Intensity, Standard Deviation, Third Moment (Skewness), Kurtosis, and Entropy are low for low grade glioma. Low grade gliomas have smooth textures when compared with high grade. This proved the effectiveness of first order statistical descriptors theoretically and these well differentiated features were selected for decision system for detection.

**Table 2. The ranges of values for second order (GLCM) statistical features for low and high grade glioma (135 patients) and its p-value**

| GLCM features | High Grade | Low grade | P-value |
|---|---|---|---|
| Auto Correlation | 40-75 | 10-30 | p$\ll$0.001 |
| Contrast | 25-55 | 5.0-16 | p$\ll$0.001 |
| Cluster prominence | 1300-1700 | 425-650 | p$\ll$0.001 |
| Cluster Shade | 100-200 | 20-80 | p$\ll$0.001 |
| Entropy | 6-15 | 0.2-1.5 | p$\ll$0.001 |
| Dissimilarity | 50-250 | 0.5-10 | p$\ll$0.001 |
| Energy | 0.2-1.5 | 3-15 | p$\ll$0.001 |

Table 2 illustrates the ranges of values for GLCM based second order statistical features and its corresponding p-values. From the Table 2, it can be noticed that, GLCM based texture descriptors for high grade glioma: dissimilarity, entropy, contrast, cluster shade, cluster prominence and auto correlation are high whereas energy is low for high grade glioma texture. These features are well enough for characterizing textural properties of a subject. Contrast, Dissimilarity, Entropy and energy are measures of non-uniformity or randomness of a texture and it is strongly correlated with texture heterogeneity [25]. From the p- values it was

observed that mean of data sets are well differentiated and the two data sets are statistically different. Hence these features were selected for classification of low and high grade glioma.

### C. Classification of low grade and high Glioma tumors and evaluation of results

Detection was done using on twelve features using selected textural descriptors. Based on p-values of the features, a decision system was developed. Statistical significance of each feature was tested according to the test rejects or accepts the null hypothesis and grade of glioma is determined. If the test is rejected decision system will detect the ROI for the decision level is true are considered as high grade or otherwise it is a low grade tumor. Out of the 135 patient image dataset, 85 data sets were used for training purposes and 50 data sets (30-high grade glioma, 20-low grade glioma) were used for test purposes. The performance of detection system was evaluated using ROC curve (Fig.5). The graph depicts the trade-off between the true-positive and false-positive rates. The sensitivity and specificity of the detection system is 99.03% and 99.53% respectively.
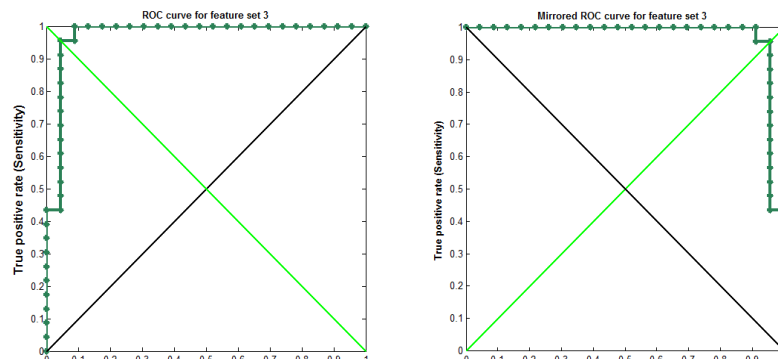


**Fig.5 shows the ROC curve for detection system Sensitivity -99.03%, specificity-99.53%, Performance of detection-Excellent test**

The method in this work showed better performance than the other existing methods [6], [18], [35]. In this work, the features selected are well discriminated between two grades and hence a decision system is sufficient for detection process. As per citations [31] tumor heterogeneity and degree of malignancy is directly related and well established using texture analysis.

### IV. Conclusion

A novel method for automatic detection and classification of low and high grade glioma from conventional MR images were presented in this paper. The axial slices of T2 weighted MRI were considered for the method. Adaptive Gray level Algebraic set Algorithm was developed for accurate detection of glioma. It is important to detect of tumor texture accurately, because entire portion is considered for further analysis and classification. Statistical texture analysis of tumor texture was done using first order and GLCM based second order statistics. Statistical significance of these features for low and high grade glioma was determined using t-test and its corresponding p-value was computed. Based on these p-values of selected features a decision system was developed for grade detection. The performance of the decision system was evaluated. The sensitivity and specificity of the detection system are 99.03% and 99.53% respectively. This method is very simple and accurate than the other existing methods. Along with the statistical features by incorporating histopathological properties, edema properties, tumor shape etc., more sophisticated and robust system could be developed for detecting all grades and sub types of glioma.

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## V. Acknowledgments