Glioma Classification of MR Brain Tumor Employing Machine Learning

Jyotsna Dogra, Shruti Jain, Meenakshi Sood

Abstract: ***The remarkable performance achieved by machine learning for glioma classification has gained immense attention in the medical domain. The accurate knowledge of the glioma grading provides better treatment planning and diagnosis. In this research work a hybrid approach is proposed that integrates the Glioma segmentation and binary classification of the High and Low Grade Glioma. The proposed framework consists of several steps including targeted tumor segmentation, feature extraction, feature selection and classification using machine learning techniques (Support Vector Machine (SVM) and k-Nearest Neighbor (kNN)). An accurate segmentation of the targeted tumor region is obtained by applying the fuzzy clustering technique and the first order and second order statistical features are extracted from the complete imaging feature set. The most prominent features are selected using the t-test that are provided for performing the classification using SVM and kNN classifiers. The proposed hybrid framework was applied on a population of 300 MR brain tumor images diagnosed as 200 HGG tumors and 100 LGG tumors. The binary SVM and kNN classification, accuracy and performance metric is assessed by 10-fold cross validation. An accuracy of 94.9% and 91% is obtained for SVM and kNN classifiers respectively.***

Index Terms**: Machine learning, classification, glioma, Magnetic Resonance Imaging (MRI), Accuracy.**

I. INTRODUCTION

Gliomas are the most common tumor type of central nervous system caused due to the abnormal growth of the glial cells. World Health Organization (WHO) [1] has provided a grading system (I-IV) for classifying the tumor type on the basis of the histopathological criteria. This grading provides a correlated prognosis for the treatment of the patient [2] and differentiation between the low grade tumor and high grade tumor. The low grade tumors belonging to grade II and III are benign and the high grade tumors belonging to grade IV are malignant [3]. The benign brain tumors do not contain any cancer cells comprising a homogenous structure and are radiologically monitored. These tumors undergo surgery for complete removal of the infected part and do not persist again. The malignant brain tumors contain cancer cells that have heterogeneous composition. These are often life threatening
and are treated through chemotherapy. The diagnosis [4] of these tumor in an appropriate time is a vital part in planning the treatments of the patient. Neurosciences have significantly progressed by employing various imaging tools for the monitoring of brain [5]. To produce detailed pictures of the brain [6] imaging technologies are utilized such as magnetic resonance imaging (MRI) and computed tomography (CT).

The detection of MRI tumor size and location is widely done by the MR imaging techniques that plays an important role in diagnosis and surgical planning [7-8]. The wide use MRI is due to the its advantages such as there are no harmful radiation and it is a non-invasive technique [9]. The different sequences used in MRI provide substantial tissue characterization, diagnosis and thorough monitoring of gliomas. These sequences are T1, T2, T1ce and Flair that generate the high resolution structural information [10] of the tumors. The malignant evolution in the LGGs correspond to the development of contrast enhancement that leads to clinical deterioration. These are the common indicator of malignancy of the tumor progression in gliomas [11]. The initial stage of enhancement in a low-grade lesion during the process of malignant transformation is uncertain.

The glioma classification of the MR images is required for providing an assistance in imaging evaluation. The computer aided diagnosis system provide this facility of classification that has a crucial role in the procedures regarding treatment strategies. The accuracy of the developed automatic techniques for classification are applicable for (i) distinction between the HGG and LGG; (ii) avoid any invasive approach such as biopsy in case of any ambiguity; and (iii) to provide a go ahead of the diagnosis that are usually provided in a long term.

The 2D MRI image is a matrix of pixel that characterizes the associated intensity, texture and spatial features. It is essential to extract the features for measuring and assessing the tissue heterogeneity and structural patterns that reveal the internal organization of brain tissues [12]. The feature extraction is a mathematical statistical procedure that extracts the quantitative parameter of resolution changes, abnormalities that are not visible to the naked eye [13]. Different information [14] is retrieved through the quantified features such as texture, symmetry etc. The texture features represent the distribution of the magnetic field that reflects the internal structure [15]. Authors in [16] employed textural features from the t1 contrast enhancement sequence for differentiating the metastatic and primary tumors using probabilistic neural network.

The most instinctive and easiest features computed for image analysis applications are the first order statistics consisting mean, variance, kurtosis and skewness. These features are based on the gray level values of the histogram of the image. Lofstedt *et al.* [17] has described the limitation of

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these features due to the inconsideration of the spatial interaction of the pixels. Any changes in the spatial distribution of the image intensity values are not registered. This pixel interaction is considered in the texture analysis that use higher order statistics. The GLCM texture features [18] are based on the probability density function and the frequency of occurrence of all the similar pixels are taken into account. Haralick *et al.* [19] also quantified the texture features using GLCM matrix that quantified the neighborhood pixel's relation. Some researchers [20-21] have applied the harlick texture features to the various application such as MR images for detecting breast cancer, brain cancer and prostate cancer. In the recent time these feature extraction aid in the classification in various applications.

Some of the hybrid form of segmentation and classification is previously done by many researchers. Batra *et al.* [22] proposed FCM clustering with SVM classifier for segmenting and classifying the tumor on the basis of feature extracted using HAAR wavelet transform. The authors also provided bias field correction using BCFCM. Katti *et al.* [23] developed an algorithm for tumor detection and classified the tumor in three classes of cancer, non-cancerous and normal. The features are evaluated by the authors by means of DCT and DWT. Segmentation is done using k-mean clustering method with respect to the features obtained.

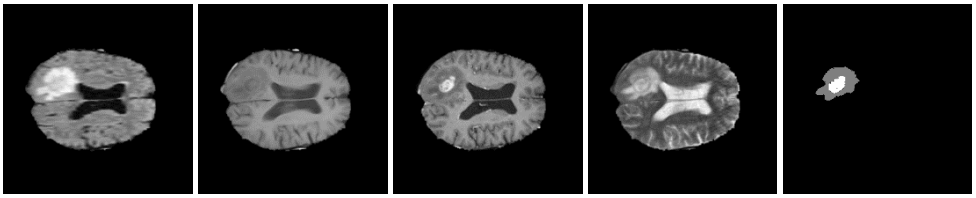
Some researchers [24-26] have shown studies regarding the improvement in accuracy of the CAD systems. El-Dahshan *et al.* [24] presented a three stages system: (i) feature extraction using discrete wavelet transform, (ii) applying PCA for feature reduction, and (iii) classification using feed forward backpropagation among normal and abnormal inputs. Authors in [25] provided ensemble classification of the segmented brain tumors as benign and malignant. Zacharaki *et al.* [26] proposed texture and shape features for the machine learning algorithms to identify and evaluate the malignancy of the brain tumors. Hseih *et al.* [27] extracted the global and local features by proposing a computer diagnosis system for predicting in two classes of malignant and benign tumor. Authors in [28-29] proposed a model with novel features for predicting the survival in glioblastoma Multiforme.

In this paper fuzzy clustering is used to obtain the seed values given to the graph cut technique that provide the accurate tumor region. These segmented images are classified using the binary classifier SVM and kNN methods of machine learning.

The structure of the rest of this paper is organized as follows: Section II consist of the materials used for the experiment, Section III gives a detail explanation for the methodology proposed for classification. The results and discussion for the experiment performed is given in Section IV and Section V respectively.

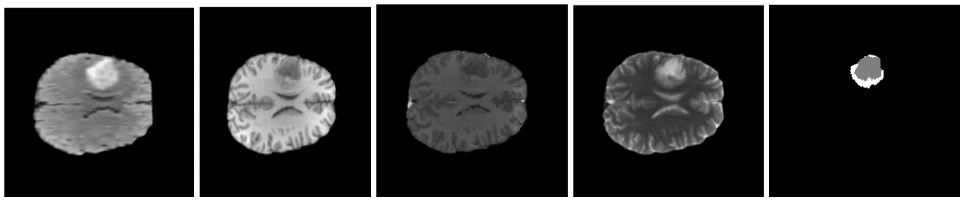
II. MATERIALS

From the standard dataset of the MICCAI BRATS challenge [30-32] 320 images (both HGG and LGG) MR brain images were obtained These images of HGG and LGG contain all the multimodal sequences that were acquired from various scanners at 3T: T1-weighted, T2-weighted, T1ce (post contrast) and Fluid Attenuated Inversion Recovery (FLAIR). All the MR images were segmented by one to four raters and were then approved and revised by expert neuroradiologist a providing the ground truths. These images have following attributes: size 240×240; gray levels: 0-255 and resolution: 96 dpi. The tumor images acquired are of Glioblastoma (GBM/HGG) and LGG.



(a) (b) (c) (d) (e)

Fig 1. BraTS HGG dataset: (a) I_{Flair}, (b) I_{T1}, (c) I_{T1ce}, (d) I_{T2}, (e) I_{GT}



(a) (b) (c) (d) (e)

Fig 2. BraTS LGG dataset: (a) I_{Flair}, (b) I_{T1}, (c) I_{T1ce}, (d) I_{T2}, (e) I_{GT}

III. METHODOLOGY

The process steps of proposed Computer Aided Diagnostic (CAD) system for the binary classification of the High Grade Dataset containing Glioma (HGG and LGG) tumors are illustrated in Figure 3. The steps involved in this methodology are: pre-processing, segmentation, overlapping, feature extraction, feature selection and classification. In the first step the pre-processing is done to reduce the memory space of the image by scaling the gray-level of the pixels in the range 0-255. Then, the segmentation is done by hybrid

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technique proposed by Dogra *et al.* [33] that integrates fuzzy clustering for the knowledge of initial seed points and further performs the segmentation using graph cut. From the extracted tumor region first order and second order statistical imaging features are evaluated. The most appropriate and prominent features are selected by using IBM Statistical Package for Social Sciences (SPSS) Statistics. These features help in the classification of the glioma regions. The classification if performed by applying two machine learning techniques: Support Vector Machine (SVM) and k-Nearest Neighbor (KNN). The classification is performed on extracted of the features set obtained from al the sequences of the MR images. Finally, the input feature set is classified in high grade glioma (HGG) and the low grade glioma (LGG) tumor classes.

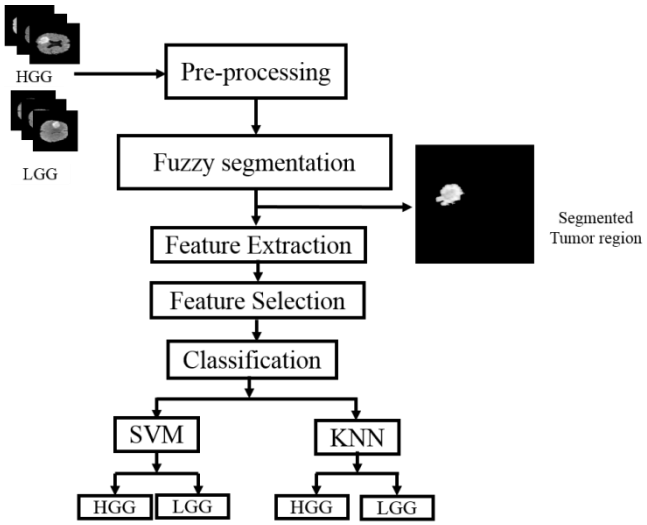

Figure 3 Proposed methodology for classification of the HGG and LGG tumor.

A. Segmentation

In Graph cut segmentation approach image is interpreted as graph where the pixels are the nodes or the vertices of the graph. To identify the pixel intensity lying in the tumor region regional penalty of each pixel is calculated. Based on these penalties the weights are assigned and the correct labels are assigned to each pixel according to their property. The MAP-MRF framework [34] is formulated for the label assignment. In graph cut segmentation, cut refers to the partitioning of the vertices in two groups representing the regional characteristics. These partitions are referred as object region or ROI and background region. The best cut is obtained by minimizing the energy function given as follows [35]:

$$E(L) = \lambda \sum_{p \in P} R_p(l_p) + \sum_{\{p,q\} \in N} B_{pq}(l_p, l_q) \qquad (1)$$

L_p is the labels of the pixels p in the image for which the penalty is calculated by the regional term $R_p(L_p)$. Pixels p, q belong to the neighboring pixels N, λ is a positive constant term and provide a relative contribution. Regional term in the energy equation reaches to a minimum value if the labelling is correctly done. The second term is the boundary term which tends to give minimum value when two neighboring pixels p, q is different. Large value of the boundary term signifies similarity of the neighboring pixels. Seed points calculated by the proposed algorithm [33] are used for the initialization. These points are provided to the graph cut technique to perform the tumor extraction as depicted in Figure 4. In the Figure 4 (a) and Figure 4 (c) the original HGG and LGG images are shown that are the input images. The proposed technique by Dogra *et al.* 33] is applied on these images and the extraction of the tumor region is performed as shown in Figure 4 (b) and Figure 4 (d).

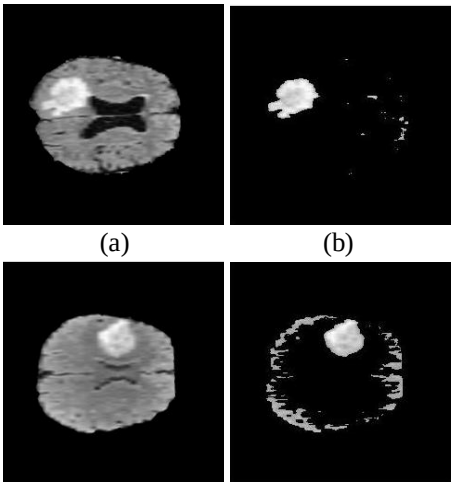

Fig. 4 (a) Original HGG image, (b) Segmented image using Fuzzy+Graph Cut, (c) Original LGG image and (d) Segmented image using Fuzzy+Graph Cut.

B. Imaging Feature Extraction

Various high level information of tumor region such as texture, shape, contrast and color are an essential requirement for the classification. Among these features the texture analysis is the most important feature that gives a human visual perception. Feature extraction provides higher level imaging features of an image regarding shape, contrast, texture and color. From these features the prominent features are selected that improve the effectiveness of the diagnostic system. This task becomes problematic due to the complex and diverse tissue structure of the brain. A total of 18 first order and second order statistical imaging features are computed. The features such as mean intensity, eccentricity and centroid of the pixel intensity values provide the measure of central tendency. Kurtosis, skewness and Inverse Difference Moment (IDM) are the histogram shape based features of the image.

The gray level distribution in an image is evaluated from the first-order statistic features. Second-order statistics features do this where pixels are considered in pairs.

Table 1 Imaging features

First Order Statistical Features		Second Order Statistical Features	
Intensity based	**Histogram based**	**GLCM**	**GLRM**
Minimum intensity	Kurtosis	Contrast	Gray-level non-uniformity (GLN)
Maximum intensity	Skewness	Energy	Run length non-uniformity (RLN)
Mean intensity	Inverse Difference Moment (IDM)	Correlation	Short run Emphasis (SRE)
Eccentricity	Entropy	Homogeneity	Long Run Emphasis (LRE)
Centroid			Run Percentage (RP)

The second order statistical features calculated are the Gray Level Co-occurrence Matrix (GLCM) and Grey-Level Run-Length Matrix (GLRM) features. The complete set of imaging features extracted in this paper are listed in Table 1.

C. Statistical analysis for feature selection:

Only some of the prominent features are selected for effectively improving the accuracy of the diagnosis. This selection is performed using t-test. In this selection the significance of all the imaging features is observed and the selection is made respectively. The general equation for the t-test is presented in equation 2.

$$p = \begin{cases} p > 0.05;\ weakly\ significant \\ 0.01 < p \leq 0.05;\ moderately\ significant \\ p \leq 0.05;\ strongly\ significant \end{cases} \quad (2)$$

where p is the significance value. All the values below 0.05 represent significant difference between HGG and LGG ($p<0.05$) and are the strongly significant features, and the values above 0.05 represents otherwise (termed as weakly significant) ($p>0.05$). The dash line represents the critical value where p equals to 0.05 and is responsible for the feature selection.

D. Classification

After imaging feature reduction these are submitted to the classification procedure for determining the glioma grade from the extracted tumor region. The binary classification of the total population of MR images is performed by using SVM and kNN classifiers.

i. Support Vector Machine (SVM)

SVM is the most effective linear classifier with good mathematical intuition that was given by V. N. Vapnik in 1933 [9749108, 33]. It is a supervised learning technique based on the finding of the decision surface. This decision surface is formed by the support vectors that are the closest and the equidistant points to this plane. A graphical understanding of the SVM is shown in Figure 7 where (x, y) are the feature attributes. The distance of a point (x_i, y_j) from the decision boundary is defined as the function margin as given in
equation 3.

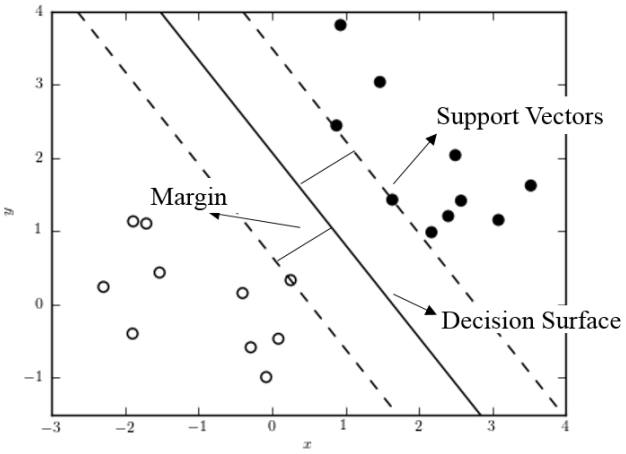

Fig 5. Graphical presentation of SVM technique

The distance of a point (x_i, y_j) from the decision boundary is defined as the function margin as given in equation 3.

$$\gamma^i = y_i(w^T x_i + b) \quad (3)$$

where, w^T are the hyperplane parameter that are normal to the surface of the decision boundary, x_i is the point that is mapped to the higher dimensional space and b is the constant. If the point is further away from the surface, we have higher confidence in the classification of the point. So, larger functional margin means more confidence in predicting the class of that point.

ii. k-Nearest Neighbor (kNN)

Another supervised technique used particularly for the classification purpose is kNN. The main idea for this method is that it has similar output for similar training samples. For the input population nearest value is identified that is able to assign classes to all the samples. Consider $X_i = \{x_1, x_2, \ldots, x_{iN}\}$ and $X_j = \{x_1, x_2, \ldots, x_{jN}\}$ the sample population, thus to measure the similarity between them the distance is calculated as given.

$$Dist(X_i, X_j) = \sqrt{\sum_{m=1}^{N} (x_{im} - x_{jm})^2} \quad (4)$$

In the Eq. 4 Euclidean distance is described that evaluates similarity among two pixel points. Hence, the pixels obtain the class to which some of them commonly resemble.

iii. Performance Metric

The accuracy and error rate of the classification outcomes are verified by evaluating the performance metric. These metrics describe the efficiency of the classification that are based on the following terms for the possible outcomes.

True Positive (TP) is the HGG class predicted in the presence of the LGG class of the glioma.

True Negative (TN) is the LGG class predicted in the absence of the HGG class of glioma.

False Positive (FP) is prediction of HGG class in the absence of LGG class.

False Negative (FN) is prediction of LGG class in the absence of HGG class.

The performance metric used are: sensitivity, specificity, accuracy and error rate. Sensitivity represents the probability of predicting actual HGG class. Specificity value defines prediction of LGG class. Accuracy is the amount of correctly prediction made by the total number of predictions made. The error rate (ERR) is the amount of predicted class that have been incorrectly classified by a decision model. The overall classification is also provided by the Area Under the Curve (AUC) that represents better classification if the area under the curve is more. All of these performance metric is evaluated for Flair sequences and accuracy are observed.

IV. RESULTS

Glioma grading identification from the MR images is a complex process due to the intricate intensity distribution in the tumor region. In this paper have developed a technique for extracting the tumor region and classifying these regions of all the sequences in the HGG and LGG classes. The proposed approach for the segmentation is performed by fuzzy technique developed by Dogra *et al.* [33] and the classification performed on Matlab. All the imaging features selected from Figure 6 are employed in the process of classification. The obtained results are verified by evaluating the performance metric.

A. Segmentation

The segmentation performed in the proposed method provides the accurate extraction of the Glioma from the MR images. The technique proposed by Dogra *et al.* [33] provides segmentation and provides the most efficient seed points for the graph cut method for initialization and accurate segmentation. The segmentation is performed on the Flair sequence and from the obtained extracted region the imaging features are extracted.

The results obtained are depicted in Figure 6 for the HGG and LGG images. The Figure 6 (a), (b), (c) and (d) show few HGG segmented images with clear visibility of the tumor region from the Figure 6 (e), (f), (g) and (h) are the LGG segmented images. The result images contain complete population of the segmented HGG and LGG segmented images that are classified using machine learning scheme.

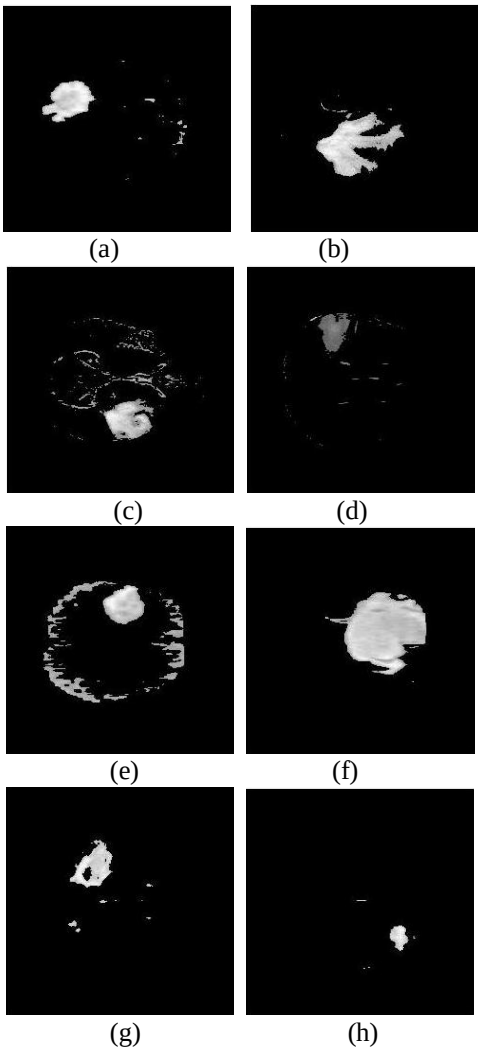

Fig 6. (a), (b), (c) and (d) Extracted imaging features from extracted HGG images; (e), (f), (g) and (h) LGG images

B. Classification

A 10-fold cross validation of classifying HGG and LGG tumors by applying two different classification methods (SVM and kNN) using the top prominent features obtained from the t-test. All these classification is performed on the different MR image sequences and investigate the highest accuracy for the proposed work.

i. SVM classification:

The results present in Table 2 show the performance metric evaluated for the binary classification of HGG and LGG tumor by applying SVM classifier for all the sequences. The SVM classifier utilizes the prominent imaging features for performing the classification. The highest values attained for sensitivity and specificity on applying SVM classifier is 0.82 and 0.96 respectively for the Flair sequence with accuracy attained for flair is 89.9%. The ROC depict the true positive rate as a function of the false positive rate for diverse cut-off points. Best classification has a ROC curve with highest area under the curve (AUC). On analyzing the AUC Flair sequence obtains a values of 0.92.

ii. kNN classification:

The kNN is the next classifier used for performing the binary classification and the evaluated performance metric are presented in Table 2. The sensitivity, specificity and error rate are calculated for all the sequences. On observing the values in the table it is inferred that sensitivity and specificity values attained are 0.78 and 0.96 respectively and the accuracy achieved by the kNN classifier is 86.5%. The ROC curve for the kNN classifier attains 0.86 value for the Flair segmented images.

Table 2 Performance metric for binary classification using SVM and kNN classifier

Classifier	Sensitivity	Specificity	Accuracy
SVM	0.82	0.96	89.9%
kNN	0.78	0.96	86.5%

V. DISCUSSIONS

This paper presents a binary classification of the high grade glioma and low grade glioma tumors from the MR images. This classification solely depends on the features extracted from the segmented tumor regions. Hence, the accurate segmentation of the tumor region is critically important that is achieved in the proposed model by applying fuzzy segmentation [33]. After the segmentation is performed the extracted tumor regions form the flair sequences are present. In the prosed model SVM and kNN classifiers are employed for performing the binary classification.

The Table 3 illustrates the comparison of AUC and accuracy values of the proposed models with the existing technique applied for the HGG and LGG tumor classification. It is depicted form the attained values that our proposed models outperform the existing technique. Zacharaki *et al.* [36] proposed a computer assisted classification method combining conventional MRI and perfusion MRI for differential diagnosis. Authors have provided the high grade and low grade glioma binary classification using SVM method and the extracted features include texture and the shape feature from the target regions.

Table 3 Comparative analysis of the proposed models with the existing technique for the high grade and low grade glioma tumor in MR images.

Proposed model	AUC	Accuracy
Fuzzy GC+SVM	0.92	89.9%
Fuzzy GC+kNN	0.86	86.5%
[36]	0.89	87.8%

VI. Conclusion

In this paper the authors have provided an efficient modification to the conventional graph cut technique. This is done by developing an automatic selection of the initial seed points through fuzzy clustering that provide the most efficient extraction of tumor. Further, a binary classification is done using machine learning on the MR extracted brain images between the HGG and LGG classes. The highest accuracy value of 89.9% is obtained the SVM classifier. The proposed work shows a significant improvement in the accuracy value that implies the proposed methodology is better than the existing.

The accuracy value is obtained for the Flair sequence and in the future the proposed method will be applied on all the sequences of the MR images in order to increase the accuracy.

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