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Classification and Pathologic Diagnosis of Gliomas in MR Brain Images

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Abstract

Detection and classification of a brain tumour in medical images is always a challenging task, as the treatment may lead to Radiosurgery depending upon the exact shape, size, and position of a tumour. To provide a complete characterization of glioma and the degree of malignancy, classification and grading are vital. In some complicated cases, localization of the tumour, comparison of tumour tissues with adjacent regions, to make it clear for detection, and finally classification without human intervention is need of the hour. Out of the available numerous imaging techniques to detect and classify brain tumours, MRI is the most suitable non-invasive technique and has superior image quality. The edge over other techniques is its superior soft-tissue resolution and the ability to acquire different images employing contrast-enhanced agents. This research work classifies Low-Grade Glioma (LGG) and High-Grade Glioma(HGG) tumours on the basis of features obtained from extracted tumor region. The results of the classification of HGG and LGG tumours using the most prominent features are validated by five-fold cross-validation. Satisfactory and encouraging classification results are obtained using large and publicly available clinical datasets. Using the extracted features, a computer-assisted algorithm is developed that uses a machine-learning algorithm along with Gradient-Based Kernel Selection Graph Cut to provide binary classification with an accuracy of 94.6% with T1ce sequence of MRI. The proposed models can be employed to assist physicians and radiologists in the early pathological detection and classification of gliomas. The proposed framework also can be a model for validating brain tumours and their initial screening for their grading classification.

Keywords: Glioma, Accuracy, High Grade Glioma, Low Grade Glioma, MRI, Graph-Cut

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1. Introduction

One of the common tumor type caused in human CNS is called Glioma that is caused due to uncontrolled growth of glial cell. According to World Health Organization (WHO) [1] the tumors are graded on four grades based on histopathological criteria. Depending on this grading system a correlated prognosis is provided for patient treatment whilst differentiating the grade of tumor. The two classes for tumor defined by WHO are HGG and LGG. The LGG tumors are benign tumors consisting grade II and III stage of tumor and HGG are malignant tumor consisting Grade IV stage tumor. The cancer cells are absent in benign tumors with homogenous structure that are monitored via radiology. In order to completely remove these tumors patients, undergo surgery. On the other hand, malignant tumors have heterogeneous compositions and contain cancer cells. Hence, chemotherapy is the only solution for treatment for these life threatening disease. It is necessary [4] that the diagnosis of these tumor starts early for better treatment. With the significant progress in neurosciences various imaging techniques are developed for monitoring brain tumors [5]. These techniques such as Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are capable to produce better detailed pictures of brain [6].

Each MRIs create four sequences for every patient brain tumor diagnosis. These sequences are T1-weighted (T1), T2-weighted (T2), T1ce (post-contrast), and Fluid Attenuated Inversion Recovery (FLAIR) [7-8] that generate substantial tissue characterization and diagnosis. Also a better high-resolution structural information [9, 10] is displayed of the tumors at different angles. The T1ce sequence are contrast enhanced images that represent aggressive tumor. Hence, contrast enhancement sequences are primary differentiators for classifying the High-Grade Glioma(HGG) and Low-Grade Glioma (LGG) [11, 12]. The extent of malignancy in the LGGs corresponds to the development in contrast enhanced image leading to clinical deterioration. These clinical deterioration indicates tumor progression in gliomas [13, 14]. There is an uncertainty to detect the initial stage of enhancement from LGG tumors during malignant transformation. The classification [15, 16] provided by WHO aids in evaluating the glioma stage through MR Images. Development of computer-aided diagnosis system not only segments the tumor but also classifies tumor grades eventually assisting in treatment strategies.

A highly accurate automatic technique for tumor segmentation and classification is vital for following reasons: (i) clear differentiation of HGG and LGG tumors; (ii) in case of better treatment planning so that invasive approaches such as biopsy is avoided; and (iii) to provide a go-ahead of the diagnosis that is usually provided in a long term.Imaging attributes of first order such as skewness, mean, kurtosis and variance are the most instinctive features in image analysis applications that are computed using gray values of image histogram. Even though these are easiest features Lofstedt*et al.* [17] highlighted their disadvantages as they do not consider spatial interaction of image pixels. These spatial interactions forget to unregister the distribution of the grey values of image. Hence, higher-order statistics are used for registering these grey value interactions. The authors in [18] utilized GLCM texture features that calculatesprobability density function (pdf) and redundancy of similar pixel. These features were also used by Haralick*et al.* [19] focusing on the textures in the image and neighborhood grey values relationship. Other than these harlick texture features are used by authors in [20] for various MR Image applications such as detection of cancer in multiple organs (breast, brain and prostate).Other than extracting the features for just detection of tumors it has also been used for grading of tumors. For achieving this, many researchers have developed hybrid form for detecting and classifying tumors. Some of such authors are Batra*et al.* [21]for proposing hybrid technique of FCM clustering for segmentation and SVM classifier for tumor grading. In this proposed work authors extracted features by employing HAAR wavelet.

The MR images undergo intensity ambiguity due to bias field that is removed by authors by using BCFCM.For this purpose, Katti*et al.* [22] developed such system that detected and classified tumors in three classes that aremalignant,benign, and normal. The authors extracted the features employingDiscrete Cosine Transform (DCT)andDiscrete Wavelet Transform (DWT)of the tumor. Utilizing these features the segmentation is performed by the k-mean clustering method. Finally, classification is performed using Probabilistic Neural Network (PNN).Some studies [23-25] showed enormous work on improving accuracy and efficiency of diagnostic systems in brain tumor analysis. Authors in [24] presented a three stage system which involved feature extraction using

wavelets in the first stage i.e.DiscreteWavelet Transform (DWT), in the second stage Principal Component Analysis (PCA) is done for feature reduction, lastly neural networks with feed forward back propagation is employed for binary classification of brain MR image into normal and abnormal regions. Researchers in [26] developed a system with machine learning for evaluating the extent of tumor in brain MR Image. They utilized shape and texture features from the gray images that result in an ensemble classification. Another binary classification [27] of benign and malignant tumors where local and global features are extracted.

Authors proposed a algorithm that evaluates novel features predicting survival of patients through glioblastoma Multiforme. Some of the supervised classifiers used in recent studies are k-Nearest Neighbor (kNN), support vector machines (SVM) due to the higher classification accuracy obtained by them [28]. In comparison to the other artificial neural networks SVM method is preferred due to some advantages such as higher accuracy rate, direct geometric interpretation and it does not need a huge sample for avoiding overfitting [29]. Authors in [28] introduced an extension to the conventional SVM that is kernel SVM (KSVM).Li *et al*. [30] classified the different grades of the glioma by using linear SVM. The authors extracted 15 features that reflected the mass effect and were verified by the domain experts. Anitha*et al*. [31] proposed a two-tier classification by employing Self Organizing Maps (SOM) and KNN algorithms. By using the DWT the features vector is formed that is provided for the classification. KNN-TTP strategy was developed by Steenwijk [32] using the 3T Flair and T1 sequences.

To provide complete characterization of glioma and degree of malignancy in the extracted tumor regions, glioma grading (LGG and HGG) is required. In this paper, a design of MR sequence detector for effective glioma grading is proposed employing binary classification of HGG and LGG tumors from MR brain image.The complete procedure comprises segmentation and classification of the brain tumor. The segmentation is done by employing the Gradient-Based Kernel Selection Graph Cut (GBKS GC) technique [33-34] that provided accurate tumor segmentation. The tumor mask generated by this technique is used to extract the tumor region from the different sequences of the MR images. The heterogeneous regions within these sequences are employed for extracting the feature characteristics. These features provide the morphologic and texture properties of the two classes of the tumor. Authors exploit the potential features by applying the *t*-test for providing the most significant features for the classification. Further, classification is applied using SVM, k-NN, and logistic regression. The classification is done on an exclusive feature set of the different sequences resulting in the highest accuracy for the contrast enhancement T1 sequence for all the applied classifiers.

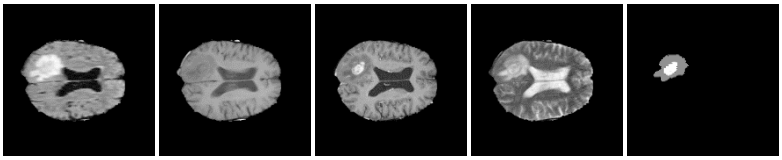
This paper contains: Section II elucidate the proposed methodology for detection and classification of different grading of brain tumor, section III provides the results and discussion that is followed by conclusion and future work.

2. Materials and Methodology

In this manuscript, tumor images of Glioblastoma (GBM) were acquired from the MICCAI BRATS challenge [35-36] standard dataset for various images of HGG and LGG as depicted in Figure 1 and Figure 2.

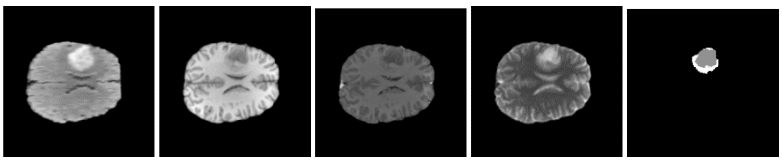
Dataset Source	MICCAI BRATS challenge [35-36]
Number of images (Total)	320
Grades present	i) HGG=210, ii) LGG=100
Sequences	I_{Flair}, I_{T1}, I_{T1ce}, I_{T2}, I_{GT}
Size	240×240
Gray level	0-6025
Resolution	90 dpi

The HGG and LGGtumor images were acquired for the simulations where all the simulations were carried in Statistica software and MATLAB 2019b software and.



(i) (ii) (iii) (iv) (v)

Fig 1. BraTS HGG dataset: (i) I_{Flair}, (ii) I_{T1}, (iii) I_{T1ce}, (iv) I_{T2}, (v) I_{GT}



(i) (ii) (iii) (iv) (v)

Fig 2. BraTS LGG dataset: (i) I_{Flair}, (ii) I_{T1}, (iii) I_{T1ce}, (iv) I_{T2}, (v) I_{GT}

The development steps of the proposed framework of Computer Aided Diagnostic (CAD) system for the binary classification of the pathologies of HGG and LGGtumors from the MR brain image is shown in Figure 3. In the pre-processing step,first step includes reduction of memory of the image by normalizing the grey-level of the in the 0-255pixelsrange. Segmentation is performed by the novel approach proposed by Dogra*et al*. [37].

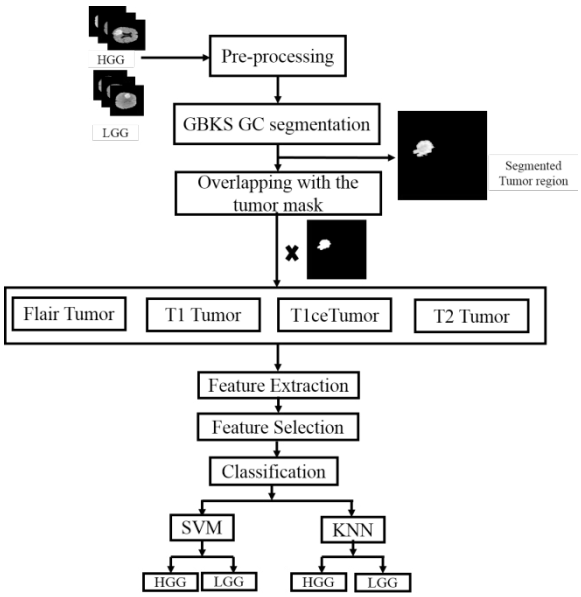


Fig. 3 Proposed methodology for the pathology diagnosis and their classification

In this technique, the graph cut segmentation method is enhanced by automatically selecting the kernel values and effectively partitioning the tumour region from the MR brain image. This method also avoids the limitation of the shrinkage problem in the graph cut. From the extracted tumour region, a binary image is formed as the tumor mask. To obtain the tumour region from all the sequences of the MR image this tumour mask is overlapped with each of the original tumour sequences. The different features were extracted [38, 39] which were selected using Statistical Analysis [40]. SVM and kNN techniques [41-43] are used for the classification of the GBM (HGG and LGG). For the analysis and classification authors have used IBM Statistical Package for Social Sciences (SPSS) Statistics. Fig 3 illustrates the steps of the process framed for design of proposed CAD for the classification of HGG and LGG from

MR brain images.

2.1 Segmentation: In this paper, the Graph cut segmentation approach is used for segmentation. In this technique, the pixels are considered as the vertices or the nodes of the graph. Each pixel is calculated to partition the pixels lying in the tumor/foreground region. Based on these penaltiesandaccording to their property, the weights evaluated in order to correctly label each image pixel. In this technique of partition is performed utilizing a cut between vertices in two groups with homogeneous pixel. The two partitions performed by the cut are known as Region of Interest (ROI)/foreground and background region. The energy function is expressed by Eq. (1) [34] that aids in performing the optimal cut when minimized.

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

L_p	Pixel label
p	Pixel value
$R_p(L_p)$	Regional term
p, q	Neighbouring pixels
N	Total pixels
λ	Positive constant term
$B_{pq}(l_p, l_q)$	Boundary term

For initialization seed points calculation is mandatory for the proposed algorithm. Dogra*et al.* [34-35] proposed Gradient-Based Kernel Selection Graph Cut (GBKS GC) novel technique for the selection of these seed points and performed the segmentation of the tumor. This technique removes the limitation of shrinkage bias in graph cut and the automatically selected seed points effectively extract the target tumor region. Hence, the segmentation in this performed using the same technique, and the results obtained for the MR images are shown in Figure 4 & Figure 5 for the HGG & LGG MR brain images respectively.

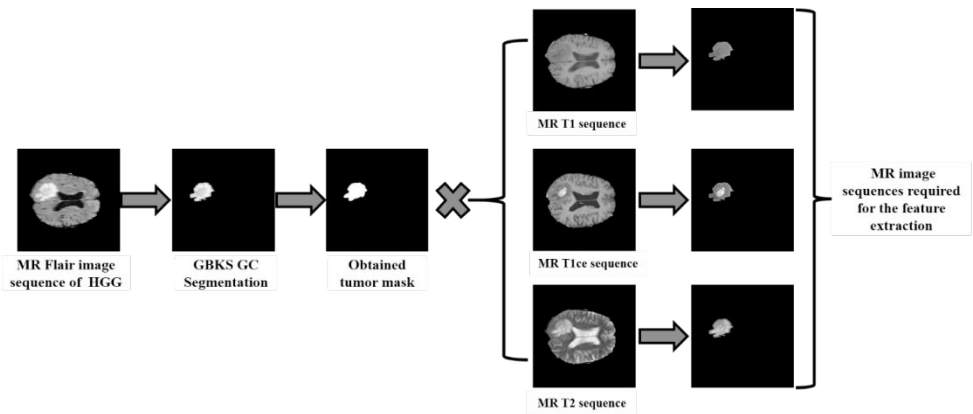


Fig 4. Segmentation of the tumor region in flair sequence of the HGG dataset. The tumor mask of the sequence is overlapped with the original images of the T1, T1ce,and T2 sequences of the MR images.

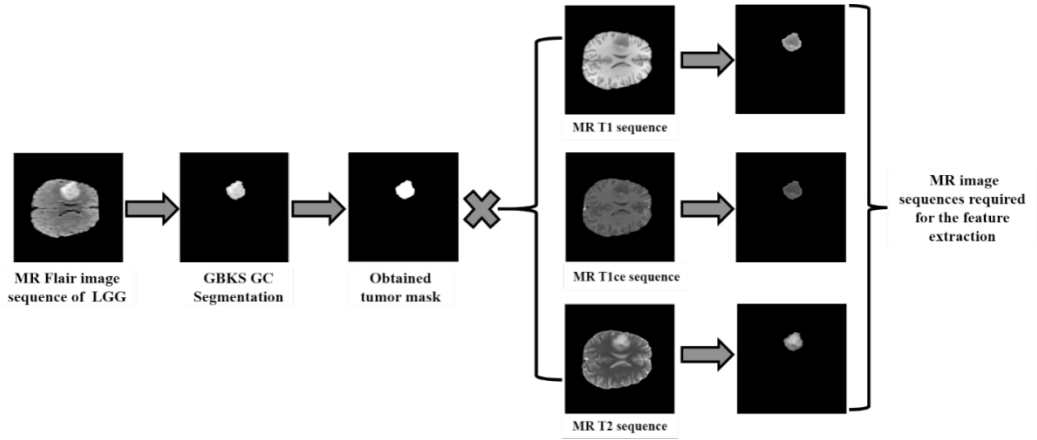


Fig 5. Segmentation of the tumor region from flair sequence of LGG dataset. The tumor mask is obtained from this sequence and overlapped with the original images of the T1, T1ce,and T2 sequences of the MR images.

Extraction of the tumor region from all the sequences present in the dataset is illustrated in Figure 4 and Figure 5. Dogra*et al*. in their proposed algorithm used the Flair sequence of the MR image for performing the segmentation as there is high contrast difference among the normal and abnormal regions of the brain. The segmented tumor region is validated with the ground truth provided in the dataset. Once the tumor region is segmented its respective tumor mask is generated in the binary from that a represents a white region that consisted of the tumor. This obtained tumor mask is overlapped with all the original sequences of the MR brain images that are: T1, T1ce, and T2. After performing this overlap, the tumor regions of the remaining sequences are obtained. All these extracted regions are subjected to feature extraction for obtaining the image texture properties.

2.2Imaging Feature Extraction: The features in general describe globally an entire region. Some other kind of features has a more local scope, often they are pixel-wise. A more interesting approach regarding textures, are Textons. By filtering an image using Gabor filters (or similar) local responses of the image to different filters, that span different frequencies, spatial orientation and extents were obtained. SIFT algorithm discard features detected too close to edges. Those features can be used for classification as well, using some kind of features embedding, similarly to Textons, in an approach that is usually referred as Bag of Words. Nowadays, especially for how concern image classification and object detection, the way to go is different. The features at the lower level of the hierarchy are generic primitive filter, while the features at the higher level encode more complex objects information's. In general, they extract features that have a kind of global scope.A total of eighteen statistical imaging features which are evaluated in this paper are tabulated in Table I[38, 40].

Table 1 **Statistical Features of** Images

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

2.3Statistical analysis for feature selection: For effectualimprovement in the accuracy of the diagnosis, only several

prominent features are selected using *t*-test [42 - 44]. In this selection,the selection is made on the basis of significance of all the imaging features. The general equation for the *t*-test is presented in Eq. (2).

$$p = \begin{cases} p \leq 0.05;\ stronglysignificant \\ 0.01 < p \leq 0.05;\ moderatelysignificant \\ p > 0.05;\ weaklysignificant \end{cases} \quad (2)$$

Where*p* is the significance value. The *p* values obtained for all the imaging features are illustrated in Figure 6..

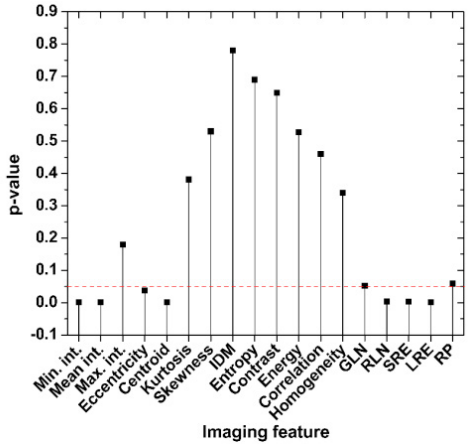


Fig6. Stem plot of p values of 18 imaging features

2.4Classification using Machine Learning Algorithm: After imaging feature reduction, classification is performed to classify the grades of the glioma from the extorted tumor region. In this paper,k-NN and SVM classifiers are used for the classification of the MR images.

3. Results and Discussion

The intricacy in the intensity distribution of the tumor region in MR images, make the complex process of grading identification of Glioma challenge for the medical research fraternity. In this manuscript, a framework for extracting the tumor region and its further classification in two broad categories of High Grade and Low Grade Gliomas has been proposed by the authors.

The proposed framework module for the segmentation includes the technique developed by Dograet al. [34-35] employing GBKS GC technique and platform employed for classification is classifiers using MATLAB 2020a. The prominent features selected on the basis of statistical analysis in the previous section and depicted in Figure 6 are usedfor the process of classification, and verified by standard performance metric: specificity, sensitivity, accuracy, and error rate, for the possible outcomes of two categories as tabulated in Table 2. The accuracy of the classification is also measured by Area UnderCurve (AUC) of ROC, larger the area, higher and better classification. All of these performances metricsare evaluated for T1, T2, Flair, and T1ce sequences, and their respective accuracies are observed.

Table 2 Possible outcomes

Actual class	Predicted class	
	HGG/0	LGG/1
HGG/0	TN	FP
LGG/1	FN	TP

3.1 Segmentation: the accurate extraction of the Glioma from the MR images is obtained by the process of segmentation, as proposed by the authors. The novel technique proposed provides an automatic segmentation

and removes the major limitation of the shrinkage problem in the conventional graph cut technique. The the mask is formedfrom the obtained extracted region from segmentation of the Flair sequence. This mask is utilized in extracting the tumour region from the rest of the sequences by multiplying it with the original images of these sequences. The highlighted region indicated in Figure 7 represents the tumour regions of all the sequences obtained from GBKS GC segmentation.

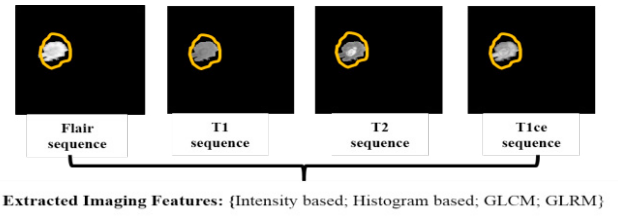


Fig 7. Extracted imaging features from Flair, T1, T2, and T1ce sequence of the extracted HGG tumor

The extracted representing features from these regions, prominent in nature and contributory are selected for the classification purpose.

3.2 Classification: The top prominent features are ascertained by performing the *t*-test, further classification by SVM and kNN classifiers are cross validated for classifying LGG and HGG tumours. The cross validation is five-fold for the accuracy purpose. The empirical investigation is performed on the different MR image sequences and all the classification protocols are investigated, to formulate the most potential sequence generatingthe highest classification accuracy for the proposed work. All the sequences comprise different intensity distributions and the same remains true from the HGG and LGG tumours. This is due to the enhancing region that is present in the LGG tumour that can only be visualized in one of the MR image sequences.

SVM classification: The performance metric evaluated to classify HGG and LGG tumouremployingSVM classifier for all the sequences are tabulated in Table 3. The SVM classifier exploits the important imaging attributes for achieving the classification.

Table 3Binary classification Performance employing SVM classifier

	SVM Classifier		
	Sensitivity	Specificity	Error rate
Flair	0.75	0.96	0.26
T1	0.53	0.78	0.30
T2	0.63	0.87	0.24
T1ce	0.96	0.98	0.07

Among all four sequences, specificity and sensitivity is calculated to obtain the highest values of classification accuracy employing SVM classifier. The metrics obtained are is 0.98 and 0.96 respectively using T1ce sequence. The error rate achieved for T1ce is 0.07which is the lowest in comparison to all the others. The evaluated results present the most efficient binary SVM classification performed on the T1ce sequence. The ROC curves are also illustrated in Figure 8 for all the sequences. The Region of Interest curve depict the true positiverate as a function of the false positive rate for diverse cut-off points. The classification module givingwider and large ROC curve depicts highestAUC, indicating highest accuracy. On analyzing the AUC for all the sequences in Figure 8, the T1ce sequence depicts the highest AUC of 0.97, whereas, the AUC for the Flair, T1 and T2 sequences are 0.67, 0.71 and 0.84 respectively.

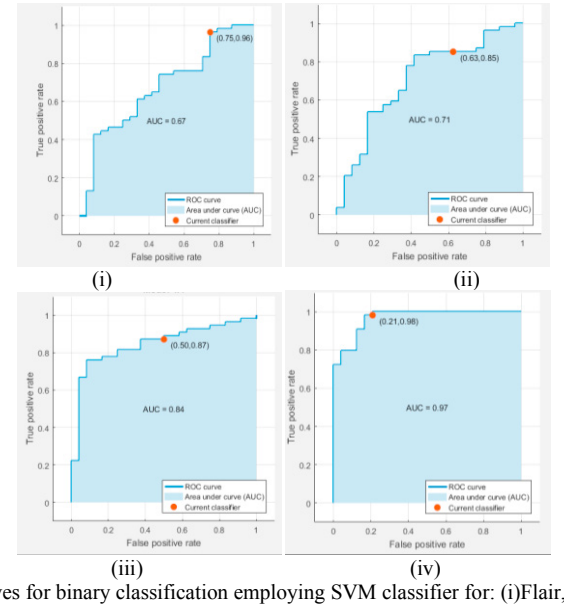


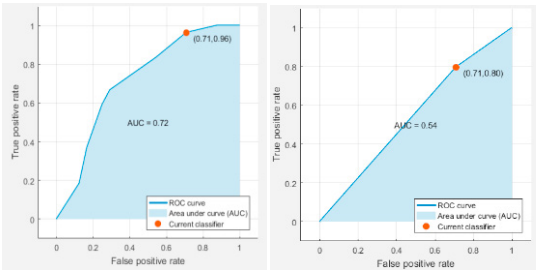
Fig 8. RoC curves for binary classification employing SVM classifier for: (i)Flair, (ii) T1, (iii) T2, and (iv) T1ce

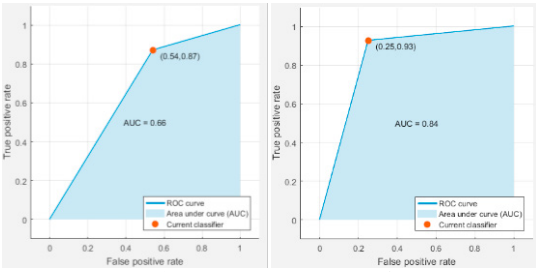
k-NN classification: The *k*-NN is used for the classification of the images in two classes, and the evaluated performance metric are tabulated in Table 4. The metrics of classification namely, specificity, sensitivity, and error rates are evaluated for all the sequences.

Table 4 Performance metric for two category classification using kNN classifier

	kNN Classifier		
	Sensitivity	Specificity	Error rate
Flair	0.77	0.96	0.24
T1	0.49	0.79	0.36
T2	0.61	0.87	0.25
T1ce	0.82	0.93	0.12

Taking into account the values obtained in Table 4, it is inferred that a maximum value for sensitivity and specificity (0.82 and 0.93 respectively) is attained for the T1ce sequence. Even the error rate achieved by the kNN classifier is lowest for the T1ce sequence is 0.12. All these values signify the best binary classification on the T1ce sequence. The ROC curve plotted for all these sequences by the kNN classifier is depicted in Figure 9.





(c) (d)

Fig 9. RoC curves for binary classification employing kNN classifier for: (i)Flair, (ii) T1, (iii) T2, and (iv) T1ce

The AUC attained by the classifier for the Flair, T1, T2, and T1ce sequences are 0.72, 0.54, 0.66, and 0.84 respectively. These values easily present that the most efficient binary classification is only provided by the T1ce sequence.

This paper presents tumor grading in two classes i.e.HGG and LGG. Better tumor analysis with accurate tumor extraction and its grading makes treatment planning become more efficient as shown through the novel method GBKSGC technique.The results of complete tumor region obtained from this method helps to obtain tumor region from all the sequences. But, it is ambiguous as to which sequence shall give the best classification results. Table 5, shows the accuracy obtained by both the classifier on all the sequences.

Table 5 Accuracy attained by SVM and kNN classifier on all sequences for tumor grading

	Accuracy	
	SVM	kNN
Flair	76.9%	75.6%
T1	71.8%	69.2%
T2	75.6%	71.9%
T1ce	**94.9%**	**91%**

It is observed that the T1ce sequence generates the maximum accuracy values of 91% and 94.9% for the kNNand SVM classifiers respectively. Hence, it is inferred that in comparison to all the sequences of the MR images the best accuracy is achieved only with the T1ce sequence. In Table 6 a comparative analysis of AUC and accuracy values is displayed of the proposed model with existing techniques on input images that are HGG and LGG tumors.

Table 6Performance comparative analysis of the proposed models with the state of the art technique for the HGG and LGGtumor in MRIs.

Proposed model	AUC under ROC	Classification Accuracy
GBKS GC+SVM	**97%**	**94.6%**
GBKS GC+kNN	84%	91%
[44]	89.6%	87.8%

From Table 6, it is analysed that our proposed model GBKS graph cut technique with SVM analysis results in 94.6% accuracy while using kNN, 91% accuracy is achieved. The evaluated values as observed from Table 6 outperform the existing technique byZacharaki*et al.* [45]. A hybrid of MRI and its perfusionis proposed in computer-assisted classification method that is for differential diagnosis. In the proposed method authors have successfully classified both classes that are HGG and LGGusingSVM method. This classification is done based on the imaging attributes that include texture and shape features extracted from tumor ROIs.

4. Conclusion

The recent technological advancement in machine learning lead to evolving of feature engineering into framework modelling. Once the tumour portion is segmented and extracted from the complex brain MR Images, it is essential to classify the malignancy of the disease to prevent invasive diagnosis and provide better patient treatment planning. This manuscript provides the exhaustive empirical analysis and comparison of recent and aptly employed machine learning algorithms for classification of brain tumours for early diagnosis purposes. After empirical formulation, it is concluded that MRI images can be used for detecting brain tumours with the help of feature engineering and machine learning algorithm. The proposed framework attains an adequate performance with the overall accuracy of 94.6 % and 91% with SVM and kNN classifiers after employing Graph cut-based kernel selection for segmentation. Results obtained using the proposed GBKS GC with the SVM model and the comparisons with state-of-the-art methods show the effectiveness of the models for brain tumour classification purposes. The work can be extended for the further classification of glioma brain tumours into different grades (Grades II, III, and IV)employing deep learning techniques.

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