



Multilevel Lacunarity Analysis Based Quantitative Parameter Sets for Gliomas Grade Classification

Manu Gupta ^{a,*}, Sravan K. Vittapu ^b, Sakshi Gupta ^c

^a Department of Electronics and Communication Engineering, Sreenidhi Institute of Science and Technology, Hyderabad, India

^b Department of Electronics and Communication Engineering, Nalla Narasimha Reddy Education Society's Group of Institutions- Integrated Campus, Hyderabad, India

^c Health Department, Panipat, Haryana, India

* Corresponding Author Email: manugupta5416@gmail.com

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Abstract: In this study, a multilevel lacunarity analysis based quantitative parameter set is proposed for gliomas grade classification. The proposed feature set extracts multiscale texture information from segmented T2-weighted magnetic resonance images and characterize spatial heterogeneity of gliomas through lacunarity analysis. The lacunarity features are computed from multiple binary images generated using adaptive Otsu's thresholding method. Lacunarity features at two spatial scales ($r=2$ and $r=4$) are computed from three threshold levels. A feature set of six multilevel features is constructed for glioma discrimination. Statistical analysis using student t-test demonstrated that multilevel lacunarity based texture features are significantly distinct between high grade (HG) and low grade (LG) glioma patients ($p<0.05$). The Cohen's d effect size values ranged from 1.252 to 1.706 confirming the strong discriminative capability of the proposed lacunarity-based features. Gliomas grade classification was accomplished with support vector machines (SVM), k-Nearest Neighbor (k-NN), linear discriminant analysis (LDA), Naive Bayes, subspace discriminant ensemble and decision tree classifiers. The results obtained shows that Naïve Bayes classifier perform better in comparison to other classifiers by providing accuracy of 92.0 ± 4.4 %, sensitivity of 90.0 ± 4.0 % and specificity of 95.0 ± 5.6 % for grade classification of Glioma patients. Our results suggest that the multilevel lacunarity based texture features identified in this study can discriminate LG and HG gliomas and can assist radiologists in classification of gliomas.

Keywords: Gliomas, Magnetic Resonance Imaging (MRI), Texture, Multilevel Lacunarity, Classifiers, Grade Classification.

1. Introduction

Brain tumors result from uncontrollable cell growth within the brain and may affect normal brain function, leading to neurological effects [1]. Brain tumor accounts for one of the key reasons for increase in death rate in both children and in adults. Gliomas are one of the most prevalent primary brain tumors [2]. World health organization has categorized them based on histological features such as growth patterns etc. to categorize into different grades. Low grade (LG) tumors are usually noncancerous, whereas high grade (HG) tumors are cancerous in nature [3].

Magnetic resonance imaging (MRI) remains the gold standard imaging technique for the detection and evaluation of brain tumors [4]. However, this qualitative method can often result in operator bias as well as consume more time. The current gold standard for tumor grading is biopsy, which is an invasive process. There is

need to identify some quantitative parameters which can support the radiologist in diagnosing tumors with reliable accuracy.

Cellularity, neovascularity and necrosis are some of the important biological features which are related with the malignancy in tumors and patient prognosis [5]. Variations in intra-tumoral features lead to texture heterogeneity among gliomas. A high rate of textural heterogeneity indicates higher malignancy in tumor regions [6]. Therefore texture heterogeneity is an important characteristic that needs to be considered clinically for grade identification in tumors and treatment planning [7].

Recently, numerous methods have been developed to utilize texture features for early classification of brain tumors. The literature review has been summarized in Table 1 [8-15]. The survey carried out indicates that texture analysis of brain MRI images could prove useful in distinguishing brain tumors.

Existing approach have a few limitations such as that they used multimodal MRI images for feature extraction which make these methods computationally expensive and most methods lack multiscale structural heterogeneity modeling of tumor, leading to performance saturation and limited interpretability.

Lacunarity is a measure which quantifies the texture roughness in an image in terms of gap distribution and is utilized in various studies to quantify spatial heterogeneity or homogeneity of studied textures [16, 17]. Gomides *et al.* [18] used lacunarity as tool for studying complexity of image texture in satellite images of urban areas. Lacunarity analysis helps quantify the complexity of texture patterns in terms of the arrangement and distribution of different urban elements. Liu *et al.* [19] has used lacunarity to measure

the necrotic patterns in glioblastomas. Necrosis is an important feature of brain tumor, glioblastoma, and exhibit structural and spatial complexity. In the study by Bhattacharjee *et al.* [20] effect of scale on texture analysis is investigated. The findings suggest that lacunarity provides a measure of nonhomogeneity and spatial distribution in intensity for region of interest.

In present study, multi-level lacunarity based texture analysis is performed to characterize spatial heterogeneity and classify LG and HG gliomas in tumor segmented T2-weighted MRI images. These images are advantageous for brain tumor detection because they provide better contrast for tumorous tissues as compared to any other conventional MRI image types [10].

Table 1. Literature Survey

S.No	Paper	MRI sequence Used	Features Used	Segmentation Technique	Classification Process	Reported Task
1	Gore <i>et al.</i> [8]	T1-weighted, T2-weighted and FLAIR	Local Binary Pattern (LBP) and Local Ternary Pattern (LTP) based histogram features	segmented data using ground truth	Random Forest classifier	Phenotyping high-grade glioma
2	Alves <i>et al.</i> [9]	T1-weighted images, T1-weighted with contrast medium images, and T2-weighted images	Gray level co-occurrence matrix (GLCM), Gray level run length matrix (GLRLM) and Wavelet transform	segmented data from radiologist	Support vector machine (SVM), Random Forest, k-nearest neighbors (kNN) classifier	Differentiate brain tumors from inflammatory lesions
3	M Gupta and S Gupta [10]	T2-Weighted MRI	Zernike Moment Descriptors	Segmentation using active contouring	SVM, Naive Bayes, and bagged trees classifiers	Glioma grade classification
4	Kumar <i>et al.</i> [11]	T2-Weighted MRI	Local first-order texture features and global shape features	Segmentation performed manually using TexRad tool	Random Forest classifier	Glioma grade classification
5	Alis <i>et al.</i> [12]	T2 Weighted – FLAIR and T1 Weighted MRI	Histogram parameters and high-order texture features	Segmented manually	Artificial Neural Network classifier	Glioma grade classification
6	Yu <i>et al.</i> [13]	Clinical MRI	Histogram features (first and second order), GLCM and run length matrix features	Segmented manually	Random forest, SVM, and back propagation neural network classifier	Tumor and healthy classification
7	Khan <i>et al.</i> [14]	T2-Weighted MRI	LBP, Entropy, GLCM, standard deviation and margin fluctuation	Convolution Neural network	statistical analysis using Fisher's exact test	Low grade glioma analysis
8	Zhou <i>et al.</i> [15]	T1-weighted images, T1-weighted with contrast medium images, and T2-weighted images	GLCM, Run length matrix, gray-level size zone matrix and histogram parameters	Segmented manually	Radiomics Method	Glioma grade classification

Gray scale-segmented tumor images were then decomposed into multiple binary images using the two stage decomposition process proposed here, using statistical analysis. Extracted features were evaluated for their ability to differentiate LG from HG gliomas. Finally, the tumorous brain MRI images are classified as low or high grade using various supervised classifiers, with extracted multi-level lacunarity feature set as input. It is demonstrated that the proposed feature set measured over T2-weighted MRI images of glioma patients works efficiently and can estimate grade of gliomas with higher accuracy.

This paper is organized as follows: Section 2 provides details regarding the image dataset used and the methodology followed for texture pattern analysis of gliomas in this work. Section 3 gives information about various performance metrics, calculated to estimate the performance of proposed method. Section 4 gives results and discussion on proposed study. Section 5 concludes this work.

2. Methodology

The proposed study aims at texture analysis of brain MRI images of glioma patients using multi-level lacunarity process so as to perform glioma grade classification. The Figure 1 describes the complete workflow followed in the proposed method. The framework is developed using T2-weighted MRI images

and segmented tumor regions obtained from ground truth. First, the input MRI T2-weighted brain images are loaded. These images were obtained from the BRATS 2012 dataset [21], which provided skull-stripped images with ground truth. From dataset 50 patients, comprising 29 HG and 21 LG cases, are used. For each patient, 60 axial slices over brain volume were analysed, resulting in approximately 3000 axial MRI slices in total. As the current study focused on texture analysis of the tumor region, T2-weighted MRI images are preferred, as they provide sufficient contrast to capture intensity variations [10]. Moreover, use of a single modality reduces computational complexity of the model.

The MRI images are pre-processed so as to reduce the bias field effect using FAST (FMRIB's Automated Segmentation Tool) algorithm available in FSL (FMRIB Software Library) tool [22]. FAST applies Hidden Markov Random Field and Expectation Maximization techniques for intensity correction [22]. The pre-processing helps to reduce intensity inhomogeneity in images. The pre-processed MRI images are then decomposed into a stack of axial slices. Next, the tumor region is separated from the MRI slices and multi-level lacunarity process is performed on them. Finally, statistical analysis of extracted feature set and tumor classification as LG or HG is performed. In the subsequent sections, further details for each step is provided.

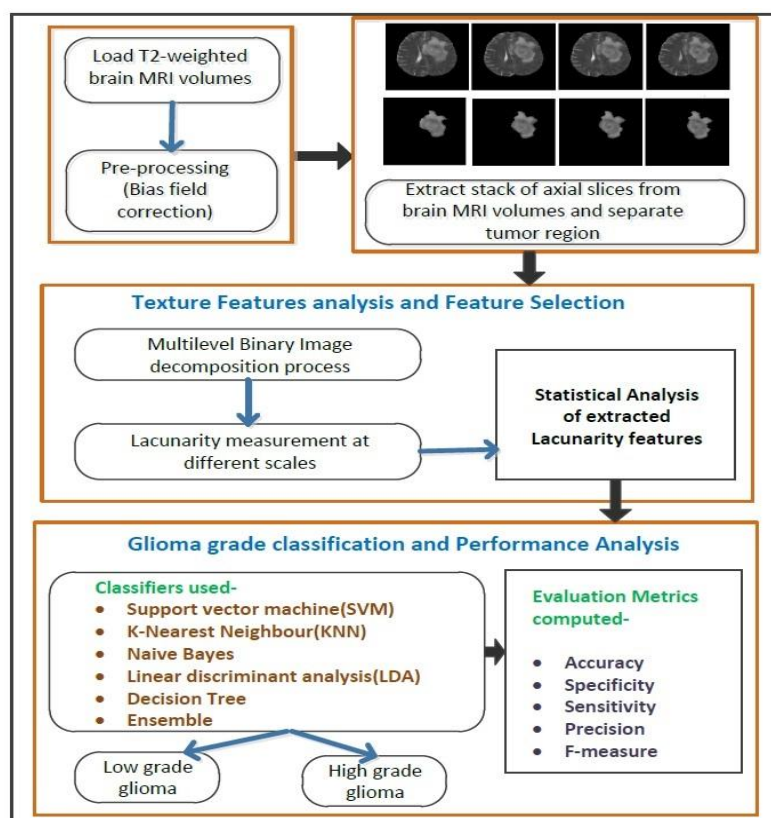


Figure 1. Methodology followed for proposed method.

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2.1 Texture Analysis using Multilevel Lacunarity

Texture analysis is one of the main objectives in biological image processing using computer vision and pattern recognition techniques, since texture represents one of the primary visual attributes present within an image. In study by Varghese *et al.* [7] the importance of heterogeneity in analyzing tumor aggressiveness is described. Texture analysis gives valuable information regarding spatial organization and structural arrangements within images that represent variations within tumors, reflecting their variations. Therefore, texture analysis has become widely utilized as part of radiotherapy treatment planning to characterized intratumor heterogeneity and predict clinical outcome [6].

Lacunarity is one of the key methods used to characterize image texture appearance. It computes the structural gaps and inhomogeneity in an image thereby measuring its texture roughness [18]. In proposed work, an effective method to characterize the texture patterns in MRI images of glioma patients using a novel multilevel lacunarity based feature set is proposed. In order to perform texture feature extraction process, a stack of axial slices from preprocessed T2-weighted MRI images

is extracted. Tumor region is separated in this stack of T2-weighted MRI slices by multiplying it with the corresponding tumor mask stack from ground truth images, given in the database. As, the ground truth images in database contains binary masks of tumor region, multiplying it with T2-weighted image generates their corresponding gray scale images. This multiplication process results in a stack of tumor segmented grayscale T2-weighted MRI axial slices. Next, the slices having tumor are separated from this axial image stack and are used for further processing. Figure 2(a, b) and Figure 3(a, b) displays the T2-weighted MRI image and the corresponding tumor separated region (in an axial slice) for a typical LG and HG glioma patient respectively.

The texture information is extracted from glioma MRI images axial stack using multilevel lacunarity process which is performed using following two operations:

- (i) Each of the axial slices of tumor segmented gray scale T2-weighted images are separated into multiple binary images using two stage binary decomposition method.
- (ii) Lacunarity value is computed for every multilevel binary image using different scales.

2.1.1 Binary Image Decomposition Process

The successive thresholding operations were applied on slices of tumor separated grayscale T2-weighted MRI images to decompose them into multiple binary image using recursive Otsu thresholding algorithm. The threshold values are computed so as to minimize the intra class variance or maximize the between class variance. The between class variance is computed as follows:

$$\sigma_B^2(t) = \frac{[\mu_T \omega(t) - \mu(t)]^2}{\omega(t)(1-\omega(t))} \quad (1)$$

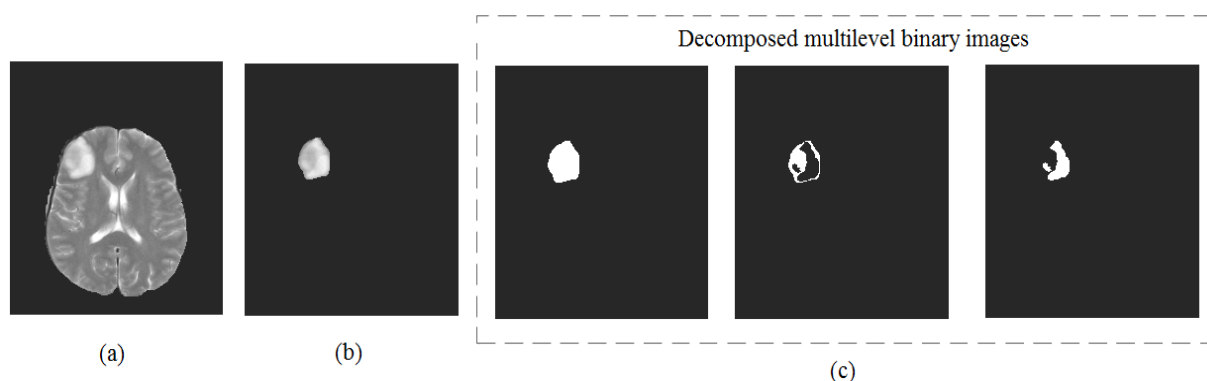


Figure 2. (a) T2-weighted image, (b) the corresponding tumor separated region, and (c) the decomposed binary images for one of the axial slices from LG glioma case.

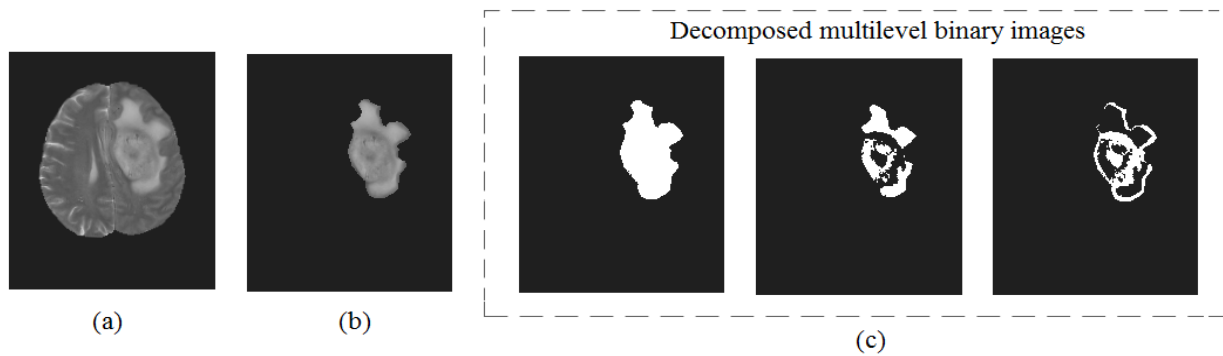


Figure 3. (a) T2-weighted image, (b) the corresponding tumor separated region, and (c) the decomposed binary images for one of the axial slices from HG glioma case.

Where, μ_T represents global mean intensity, $\omega(t)$ refers to cumulative probabilities of gray levels till threshold t , $\mu(t)$ refers corresponding cumulative mean intensity. The optimal threshold is obtained from equation (2) by maximizing the between-class variance:

$$t^* = \arg \max_t \sigma_B^2(t) \quad (2)$$

In the proposed method, number of thresholds n_t is fixed as $n_t=3$, generating three adaptive threshold values $T = \{t_1, t_2, t_3\}$. These values are vary for each tumor image and are determined from gray level intensity distribution of image.

The obtained threshold values were applied to generate binary images for tumor separated grayscale T2-weighted MRI images ($I(x, y)$) using following equations (3) and (4).

$$I_{s1}(x, y) = \begin{cases} 1 & \text{if } I(x, y) \geq Ti \\ 0 & \text{otherwise} \end{cases} \quad (3)$$

$$I_{s2}(x, y) = \begin{cases} 1 & \text{if } Ti < I(x, y) < Ti + 1 \\ 0 & \text{otherwise} \end{cases} \quad (4)$$

where, $Ti \in \{T\}$. Using $n_t=3$, five binary images are generated for each T2-weighted grayscale tumorous image, out of which only three images are found to be different while remaining two doesn't provide any additional information. Hence, for further analysis only three binary images (I_{B1} , I_{B2} and I_{B3}) are used for lacunarity feature extraction. Figure 2 (c) and Figure 3(c) display the decomposed binary images for a typical LG and HG glioma patients respectively.

2.1.2 Lacunarity Based Feature Generation

Lacunarity measures the spatial distribution of image pattern describing its texture. It analyses the gap size distribution in images to distinguish their spatial patterns at different scales [18]. The wider the gap size distribution range, the higher the lacunarity in that image. Lacunarity parameter is dependent on scale values and it reflects the degree of inhomogeneity in an image. Lacunarity has been used previously to describe the texture patterns in various applications like morphology

of urban areas [18], analysis of computed tomography images [22] etc.

In this study, lacunarity is measured for the multiple binary images obtained in the previous step by applying gliding-box algorithm at different scales. For measurement, binary image was split up into square windows of variable length. The window of particular length ($r \times r$) is then glided across the image and at each position, within the window, the number of points (s) with intensity zero (black pixels) are counted. This produces a distribution (r, s) for different window sizes. The first moment $Z(1)$ and second moment $Z(2)$ are now computed from these values of r and s . The lacunarity values at a scale r is computed as given below [18]:

$$\Lambda(r) = \frac{Z(2)}{Z(1)^2} \quad (5)$$

Lacunarity parameter is calculated based on various values for window size (r). It is a dimensionless parameter calculated as the ratio of the variance to square of the mean. Lacunarity value varies with a change in the value of window size (r), so it is a scale-dependent parameter. It measures the roughness of texture pattern and quantifies how space is filled. In general, the heterogeneity of spatial structure decreases with increase in window size [16, 23].

Hence in this study we have considered window size of only 2 and 4 for lacunarity computation of three binary images (I_{B1} , I_{B2} and I_{B3}) obtained from two stage binary decomposition method in the previous step. This generates in total multilevel lacunarity based feature set of size 6 for each of the axial slice in a stack of tumor separated grayscale T2-weighted MRI images. To take into consideration the texture variation in all the axial slices for each glioma case, a mean score is computed over the complete stack, for each parameter in the extracted feature set. Let this mean feature set be defined as ($L2_{B1}$, $L4_{B1}$, $L2_{B2}$, $L4_{B2}$, $L2_{B3}$, $L4_{B3}$) where subscript defines the binary image and its prefix define the lacunarity scale, which are further used for glioma classification.

2.2 Classification using Machine Learning Methods

The multilevel lacunarity based feature set computed in the previous step is given as input to classifiers to perform glioma grade classification. The classification algorithms employed include Support Vector Machines (SVM), k-Nearest Neighbour (k-NN), linear Discriminant Analysis (LDA), Naive Bayes, Subspace Discriminant Ensemble Classifier, and Decision Tree classifiers. To mitigate overfitting and selection bias during classification, the data was split into training and testing sets using K-fold Cross Validation.

SVM classification systems create an optimal hyperplane to divide the dataset into two distinct classes. These systems utilize nonlinear mapping functions, known as kernels, to project the training data from input space to a higher-dimensional space, generating hyperplanes for binary classification [24]. K-NN classifiers assign a class to a data point based on the majority vote of its neighbours [25]. In this method, a test sample is categorized according to the most prevalent class among its K nearest neighbours from the training set. LDA seeks features that, when combined linearly, provide optimal separation between two different classes.

Naive Bayes method is a probabilistic approach to classification. In this method, the relationships between features sets and classes are expressed as probabilities[26].The class for testing sample set is decided on the basis of its probability for given features Subspace Discriminant Ensemble classifier is a classification method that combines multiple base classifiers, each trained on a subspace of the dataset. A fine-grained decision tree classifier is also implemented in proposed model for classification tasks. It works recursively to build its tree by applying split conditions at every node in order to divide training records into subsets with similar class labels, with an ultimate aim to identify attributes and split conditions which minimize class label mixing resulting in nearly pure subsets [27].

3. Evaluation Metrics

In this section, the performance metrics utilized to quantitatively assess proposed glioma grade classification techniques will be described and

explained. Confusion matrix will be determined from output from classifier as shown in Table 2 when calculating these metrics. The evaluation metrics computed for proposed method are:

$$Accuracy = \frac{TP+TN}{TP+TN+FP+FN} \times 100 \quad (6)$$

$$Specificity = \frac{TN}{(TN+FP)} \times 100 \quad (7)$$

$$Sensitivity = \frac{TP}{(TP+FN)} \times 100 \quad (8)$$

$$Precision = \frac{TP}{(TP+FP)} \quad (9)$$

$$F-Measure = 2 * \frac{Precision * Recall}{(Precision+Recall)} \quad (10)$$

where, Recall= $\frac{TP}{(TP+FN)}$, TP stands for true positive, FP for false positive, FN for false negative and TN stands true negative. Positive represent HG gliomas while negative stand for LG gliomas, in this study.

4. Results and Discussion

In this section the effectiveness of multilevel lacunarity-based feature set extracted in this work to quantify texture heterogeneity of gliomas is assessed.

4.1 Evaluation of Multilevel Lacunarity Based Feature Set To Characterize Texture Difference in LG and HG Glioma Images

The statistical analysis of feature set generated using multilevel lacunarity process i.e. (L2_{B1}, L4_{B1}, L2_{B2}, L4_{B2}, L2_{B3}, L4_{B3}) is conducted to assess their ability to distinguish LG gliomas from HG gliomas effectively. The Kolmogorov-Smirnov (KS) test is performed to measure the normality of multiple lacunarity parameters being extracted. The result from KS test shows that all the features are normally distributed. In next step, two sample student's t-test for unequal variance is carried out. In proposed study, t-test is performed within 95% of certainty, giving degree of significance (α) as 0.05.

Table 2. Confusion Matrix

PREDICTED BY CLASSIFIER	ACTUAL CONDITION		
		Positive cases	Negative cases
	Positive cases	TP	FP
	Negative cases	FN	TN

Table 3. Average and standard deviation of multilevel lacunarity based texture feature set for HG and LG glioma groups, corresponding p values from t-test with significant level of 0.05 and Cohen's Effect Size values

Multilevel Lacunarity Based feature set	High-grade glioma Mean SD		Low-grade glioma Mean SD		p-value	Mean difference for HG and LG glioma groups	Cohen's d Effect Size values
F1=L2 _{B1}	1.0401	0.0204	1.0181	0.0065	0.0000041	0.0221	1.7
F2=L4 _{B1}	1.0391	0.0202	1.0175	0.0064	0.0000046	0.0217	1.682
F3=L2 _{B2}	1.0202	0.0079	1.0109	0.0038	0.0000018	0.0093	1.706
F4=L4 _{B2}	1.0188	0.0076	1.0102	0.0037	0.0000039	0.0086	1.686
F5=L2 _{B3}	1.0157	0.0144	1.0054	0.0047	0.0009117	0.0103	1.324
F6=L4 _{B3}	1.0139	0.0132	1.0046	0.0041	0.0011238	0.0093	1.252

The variation in mean and Standard Deviation (SD) of extracted feature set for LG and HG gliomas is also examined. In addition, the Cohen's d effect size values are also computed to measure the difference between HG and LG gliomas.

Table 3 summarizes the results obtained for the same. As analyzed from results in Table 3, the mean values for multilevel lacunarity based features are much greater for HG gliomas as compared to LG gliomas. Higher lacunarity values for multiple binary images from HG gliomas signify larger variation in gap size distribution in these images. This observation reflects the higher texture heterogeneity present in MRI images of HG in comparison to LG gliomas. The increased heterogeneity in HG gliomas might be because of their higher malignancy as compared to LG gliomas. Lacunarity parameter varies with variation in the spatial structure of pixel intensity distribution and scale (window size) considered for its computation. It is observed from Table 3 that for the same binary image, lacunarity value decreases as window size is increased. This indicates that the spatial structure homogeneity increases as window size increases. This is the reason that we have considered only smaller window sizes for lacunarity computation in this study ($r=2$ and 4). Also as the window size increases the computation time for feature extraction will also increase. The mean values for HG and LG glioma groups at different scales and mean difference in these groups is also measured and summarized in Table 3. As observed the mean difference between HG and LG glioma groups is lower for window size of 4 as compared to window size of 2 for all the three binary image set. This also supports that the measurement of texture heterogeneity in images by lacunarity can be discriminated much better using lower window size as compared to higher ones. The Cohen's d values ranges between 1.252 to 1.706 reflecting large effect sizes. The results obtained reflects that the six multilevel lacunarity based features computed in this study- L2_{B1}, L4_{B1}, L2_{B2}, L4_{B2}, L2_{B3}, L4_{B3}, gave significantly different ($p<0.05$) values for LG and HG

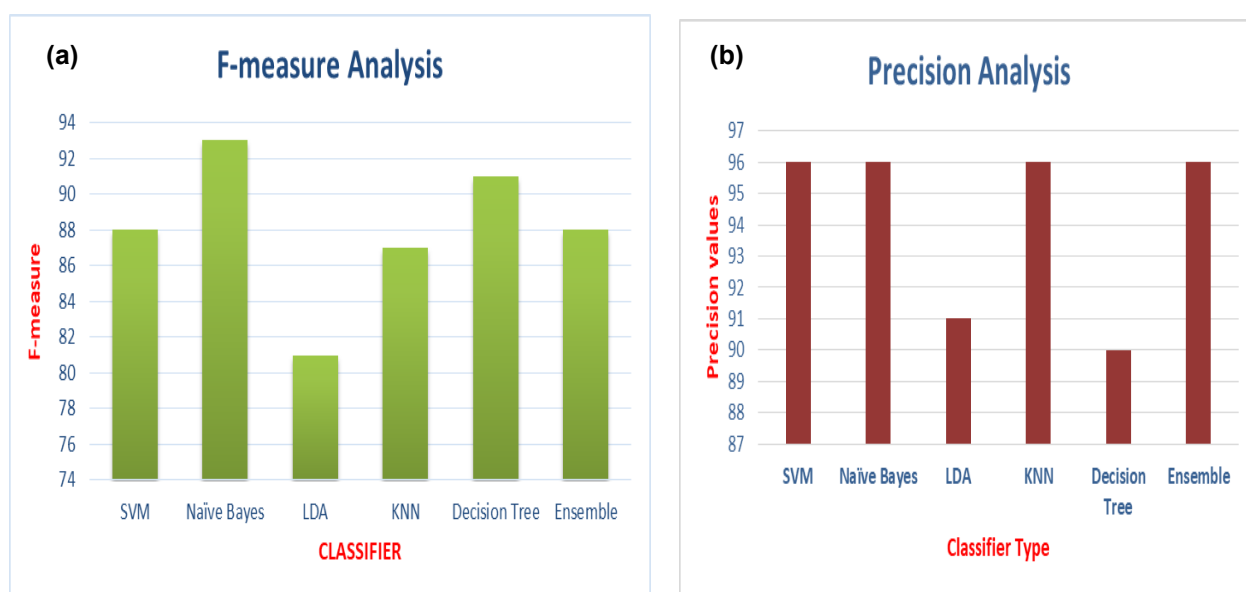
glioma patients. These findings shows that extracted multilevel lacunarity features posses strong discriminatory capability and can be further utilized for glioma grade classification. The proposed feature set successfully captures the texture pattern difference between different glioma grades and reflect the heterogeneity of their spatial structures.

4.2 Glioma grade Classification

The extracted multilevel lacunarity based features set: (L2_{B1}, L4_{B1}, L2_{B2}, L4_{B2}, L2_{B3}, L4_{B3}), is fed into various classifiers, including SVM (RBF kernel), KNN, LDA, Naive Bayes, Decision tree, and Ensemble classifiers. The aim is to determine which classifier best distinguishes between LG and HG gliomas. A K-fold ($k=5$) cross-validation approach is employed to partition the data from fifty glioma patients, comprising the extracted features and output class, into training and testing sets. The data of fifty glioma cases comprise of 29 HG cases and 21 LG cases. The K-fold method splits the entire input dataset into five distinct subsets. During each iteration one subset is used for testing and the remaining four sets are used for training, rotating the testing set each time. This process is repeated five times to ensure that every data point is included in both the testing and training datasets at least once, thus ensuring quality and reliability. The performance metrics are calculated by computing average results obtained across five folds. The classifier's performance is assessed using the evaluation metrics outlined in Section 3, with the results averaged across all five trials. By averaging performance metrics over multiple iterations, K-fold cross validation offers a more reliable estimate of generalization performance while reducing potential biases from single testing sets. Table 4 presents mean $\pm$ standard deviation values obtained for the accuracy, sensitivity, and specificity parameters from different classifiers using multilevel lacunarity-based features as input with five-fold cross validation method.

Table 4. Performance analysis of proposed method with fold-wise variability across 5 folds

S. No	Classifier	Accuracy (in %)	Sensitivity (in %)	Specificity (in %)
1	SVM	88.00±4.6	83.00±5.2	95.00±6.5
2	Naive Bayes	92.00±4.4	90.00±4.0	95.00±5.6
3	LDA	80.00±6.2	72.00±8.5	90.00±5.8
4	KNN(K=5)	86.00±5.4	79.00±6.8	95.00±6.0
5	Decision Tree	90.00±5.1	93.00±7.4	86.00±5.2
6	Ensemble	88.00±6.8	82.00±6.0	95.00±6.0

**Figure 4.** Comparative analysis of (a) F-Measure and (b) Precision values for different classifiers with extracted feature set as input.

It is found that the glioma grade classification accuracy attained from Naïve Bayes classifier is higher ($92.0 \pm 4.4\%$) in comparison to that achieved from other classifiers considered in this study. Additionally, the values of sensitivity ($90.0 \pm 4.0\%$) and specificity ($95.0 \pm 5.6\%$) are also high reflecting stable behaviour of Naïve Bayes Classifier. The comparative analysis of F-measure and precision values for different classifiers is illustrated in Figure 4. It is learned that precision value of 96% is attained for SVM, Naïve Bayes, KNN and Ensemble classifier, however Naive Bayes classifier offers highest F-measure value of 93% for glioma classification. Through performance analysis, it is observed that Naive Bayes classifier achieves better results and outperforms SVM, K-NN, LDA, Decision tree and Ensemble classifiers for glioma grading with extracted feature set.

The Naïve Bayes classifier may have achieved superior performance due to the low-dimensional nature of the proposed feature space. Since the six multiscale lacunarity features capture complementary aspects of

texture heterogeneity with limited redundancy, the probabilistic assumptions of the Naïve Bayes classifier are reasonably satisfied, which results in stable classification performance.

4.3 Comparison with other Methods

The performance of the proposed multilevel lacunarity-based feature set extracted in this study to measure texture heterogeneity in gliomas and their classification is compared with other works from the literature [8, 10, 11]. Local binary and ternary patterns-based histogram features were used by Gore *et al.* [8] for gliomas classification. The authors in [10] computed Zernike moment descriptors for glioma classification. Kumar *et al.* [11] used a set of significantly different local first-order texture features and global shape features for tumor classification. Alis *et al.* [12] used histogram parameters and high order texture features in their study. Table 5 summarizes the performance comparison of the previous method and proposed work for glioma grade classification.

Table 5. Performance comparison of proposed method with existing works

Authors	MRI sequence Used	Features Used	Classifier	Accuracy Obtained (%)
Gore <i>et al.</i> [8]	Multimodal MRI (64 patients)	Local Binary Pattern and Local Ternary Pattern based histogram features	Random Forest	84.62
M Gupta and S Gupta [10]	T2-Weighted MRI (50 patients)	Zernike Moment Descriptors	Naïve Bayes	90
Kumar <i>et al.</i> [11]	T2-Weighted MRI (83 patients)	Local first-order texture features and global shape features	Random Forest	83
Alis <i>et al.</i> [12]	T2 Weighted –FLAIR and T1 Weighted MRI (40 patients))	Histogram parameters and high-order texture features	Artificial Neural Network	88.3
Proposed	T2-Weighted MRI (50 patients)	Multilevel Lacunarity	Naïve Bayes	92

It is observed that the proposed method using a multilevel lacunarity-based feature set effectively captures the texture heterogeneity associated with glioma grade while maintaining a lower dimensionality as compared to other texture feature sets from the literature.

4.4 Discussion and Biological Interpretations

Our findings reflect a significant difference in extracted lacunarity measures at multiple scales for HG and LG gliomas. This shows their capability to differentiate spatial distribution of texture roughness in low and high glioma grades efficiently. Higher lacunarity values for HG gliomas at multiple scales reveal that they are more heterogeneous with a wider range of gap size distribution in its images as compared to LG gliomas. The intra-tumoral variations in cellularity, necrosis and vascular growth processes are the main reasons for heterogeneity in gliomas [28]. These comprise some of the main parameters considered to identify tumor grade histopathologically. Necrosis which represents the decaying cells, forms the area of the non-enhanced region within the cell are is found as strongest prognostic factors to determine survival rates in glioblastoma [29]. Liu *et al.* [19] has shown that necrotic patterns vary significantly for different gliomas grades. As high grade tumors grow faster, the number of active cells involved in them are more as compared to that present in low grade tumors. Hence, more blood vessels are formed to support the growth of high grade tumors [30, 31]. This variation of blood vessels growth in high grade and low grade gliomas may result in a change in contrast or intensity distribution in them.

A set of lacunarity features computed at different scales ($r=2$ and $r=4$) from multiple binary images of different glioma grades in proposed study assess the structural variations in them. Furthermore, they offer insights into texture roughness by measuring gap size

distribution differences for high grade images against those for lower grades gliomas images. Additionally the analysis conducted shows that proposed multilevel lacunarity-based feature set measures texture heterogeneity in gliomas with higher accuracy. Statistical study and classification results demonstrate that multilevel lacunarity-based features provide an effective means for differentiating high grade from low grade gliomas. However, the proposed study has certain limitations. The analysis was performed on a public dataset and has to be studied on clinical dataset for validation. In addition, it lacks evaluation on deep learning based feature extraction frameworks which will be included in future works.

5. Conclusion

In this study, a novel multilevel lacunarity approach is proposed for measuring texture heterogeneity among different grades of glioma using segmented glioma regions in T2-weighted MRI images. Adaptive thresholding using recursive Otsu process is employed to generate multiple binary images from T2 weighted MRI images. Subsequent lacunarity feature set calculations at different scales were extracted from these binary images to characterize the texture pattern. The results from multilevel lacunarity analysis indicates that low grade gliomas presents lower lacunarity at multiple scales in comparison to high grade gliomas. This reflects that texture in T2- weighted MRI images of LG glioma images are more homogeneous as compared to HG gliomas. Statistical analysis demonstrates significant difference between LG and HG gliomas. Furthermore, the classification results demonstrate that proposed feature set distinguishes between different glioma grades effectively using conventional machine learning methods. Naïve Bayes classifier achieve highest classification accuracy of $92.00 \pm 4.4\%$. The findings from this study establish that multilevel lacunarity features can effectively measure texture

heterogeneity in LG and HG gliomas in segmented T2-weighted MRI images. In future work, longitudinal study on glioma patients' needs to be performed to access the efficacy of extracted feature set in detecting growth of tumors. Also, the further study to measure the morphological variations with increasing tumor malignancy is required.

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Authors Contribution Statement

Manu Gupta: Methodology, Conceptualization, Investigation, Writing - Original Draft, Writing - Review & Editing. Sravan K. Vittapu: Investigation, Writing - Review & Editing. Sakshi Gupta: Methodology, Formal Analysis, Writing - Review & Editing. All the authors have

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Data Availability

The data supporting the findings of this study can be obtained from the corresponding author upon reasonable request.

Has this article screened for similarity?

Yes

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