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Original Article

Automated classification of childhood brain tumours based on texture feature

Daisy Das[1], Lipi B. Mahanta[1*], Shabnam Ahmed[2], Basanta Kr. Baishya[3], and Inamul Haque[3]

[1] *Central Computational and Numerical Sciences Division, Institute of Advanced Study in Science and Technology, Guwahati, 781035 India*

[2] *Department of Pathology, Guwahati Neurological Research Centre, Sixmile, Guwahati, 781006 India*

[3] *Department of Neurosurgery, Gauhati Medical College, Guwahati, 781032 India*

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Abstract

We propose a framework for automated classification between normal and abnormal biopsy samples of childhood brain tumour with emphasis on childhood medulloblastoma, a most common childhood brain tumour, using texture features. Texture is a measure to analyze the variation of intensity of surface of an image and the connection of pixels satisfying a repeated grey level property. The feature set consisted of a total of 172 features belonging to five texture features, GLCM, GRLN, HOG, Tamura and LBP. The performance of each feature set was evaluated both individually and in group, using six different classifiers, Linear Discriminant, Quadratic Discriminant, Logistic Regression, Support Vector Machine and K-Nearest Neighbour algorithms. Here, feature of tamura, global low order histogram and local second order GLCM outperforms the local texture measure of LBP and GRLN. Using 80 normal and malignant images of 10x magnification we obtained an optimal accuracy of 100% by combining all five textural features.

Keywords: CNS tumours, medulloblastoma, biopsy, classification, texture feature

1. Introduction

Tumours are clumps of cells that grow from normal to abnormal due to various reasons. Not all tumours are cancerous. Some tumours are benign or non-cancerous. Benign tumours represent half of all primary brain tumours. Their cells look relatively normal, grow slowly, and do not spread (metastasize) to other sites in the body or invade brain tissue. For our purpose of study we have chosen childhood medulloblastoma; as medulloblastoma is the primary brain tumour in children (Furataet *al*., 1998). Medulloblastoma is defined as a densely cellular, midline cerebella tumour that arises over the roof of the fourth ventricle. To analyze the difference between normal and abnormal tissue samples we have made a study on the histopathological images of normal and malignant tissue samples. Microscopic view at the tissue level has sheets-like arrangement of closely packed cells, with large dark size nuclei. This classic pattern is mostly prevalent. With correct diagnosis an improved 2- and 5-yr survival rate has been reported for childhood medulloblastoma (Davis, Freels, Grutsch, Barlas, & Brem, 1998). According to (Polednak & Flannery, 1995) it constitutes approximately 20% of all childhood primary nervous system tumours. Although the diagnosis of medulloblastoma tumours using molecular biology is a newly emerging concept, its application in under-developed and developing countries is applicable only in the research phase. Its use as an

*Corresponding author
Email address: lipimahanta@yahoo.co.in, lbmahanta@iasst.gov.in

alternative to histopathology analysis will take time and that too only occasionally. This is because there is a severe lack of trained pathologists in these regions and hence the patient: pathologist ratio is highly skewed. Moreover, the cost involvement is another factor why histopathology analysis is here to stay. Further, it has been established that the prognosis is mainly associated with the histology of the malignancy (Furata *et al*., 1998). This implies that automated tools supporting histopathology analysis are vital to screen out the malignant patients so that trained pathologists may concentrate on them without having to deal with all the patients. The diagnosis of the histopathological slides is affected by individual pathologist experience and skills. Computer-added diagnostic tools have been used for decades to provide better diagnosis in medical and clinical analysis.

In cell-morphology-based methods the cells are the regions of interest where the various shape, size and structural features are studied for classification into different subgroups. However, it cannot depict the scanner-level information of the tissue type which is an important aspect of any tissue level diagnosis. Even diagnosis by a pathologist is done under two categories, i.e. cell level and tissue level. A pathologist inspects a large number of slides under microscope every day belonging to patients of myriad diseases. Clearly the features or characteristics of each of these slides are diverse too. The entire course of treatment is based on the diagnosis of the pathologist, making it so profound. Over the years, texture-based analysis has been used to build computer aided systems for diagnosis purpose for medical images. Textural feature includes the arrangement and distribution of cells at the tissue level and also the internal structure of the cells at cell level. For medical histological image analysis texture features are very useful since they give the complete picture of cell distribution for any tissue type. Most of the studies (Deshpande, Rajurkar, & Manthalkar, 2013; Kather *et al*., 2016; Li *et al*., 2014; Naik & Patel, 2014; Patel & Gamit, 2016) on medical images have used with commonly available datasets for different types of cancer (of different domains) like Fine Needle Aspiration Cytology (FNAC) for breast (cytological), papsmear for cervix (cytological), Magnetic resonance imaging (MRI) of brain etc (radiological), Computed tomography (CT) of lungs etc (radiological), biopsy of Oral areas etc, (histopathological). But for normal tissue vs. medulloblastoma no complete work is available, primarily due to the non-availability of public histological datasets. The architectural property of normal and abnormal is significantly distinguishable. Therefore, in this paper we present a texture-based classification framework for normal and malignant tissue classification. We used texture-based computer features to study the region of interest and classify the specimens as normal or abnormal tissue.

2. Challenges and Motivation

The main difficulty to perform such study is availability of data, particularly in the region where the study was conducted. Childhood brain tumour it is highly sensitive as it is related to small infants and children. Most of the patients are diagnosed outside the region for treatment. The availability of data here is very low in / the case of childhood medulloblastoma and even lower in the case of normal samples, as in no case we can obtain normal samples from normal patients. The scarcity of benchmark data for such instances makes it difficult to compare our results. Since it is a commonly occurring abnormality and the survival of patients can be achieved with high accuracy, the study of its characteristics with the help of computer-added diagnosis is all the more essential.

3. Work Summary

The work is divided into four phases. Phase 1 is Data Base Generation. Phase 2 deals with Pre-processing. Pre-processing is done by colour channeling and CLAHE for image enhancement. In phase 3 we extracted five different textural features comprising of a 172-feature set. The final phase 4 is classification of the textural features. We studied the comparison analysis of the individual set and combination of all feature sets with six different classifiers. The final output of classes differentiates between normal and abnormal tissue samples. Figure 1 presents the block diagram of our work.

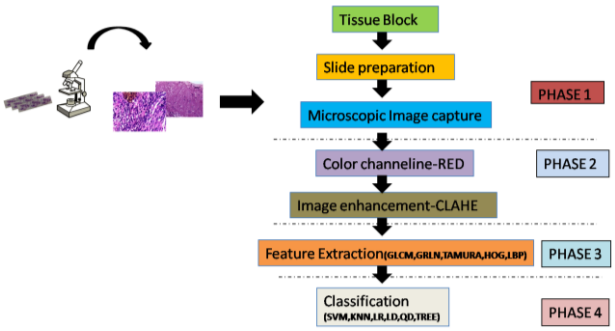


Figure 1. The block diagram

4. Material and Methods

4.1 Ethical statement

All experiments were performed by the guidelines of institutional ethics board (Registration number ECR/248/Indt/AS/2015 of Rule 122DD, Drugs and Cosmetics Rule, 1945 of India) of the Institute of Advanced Study in Science and Technology, Guwahati. Patient consent were taken in the format of Guwahati Medical College (GMCH), from where the samples were obtained, as part of their regulations.

4.2 Data generation and characteristics

The tissue blocks were obtained from GMCH, Guwahati. GMCH is the foremost Public Sector Super-specialty Hospital in the region catering to the general public and treating all diseases. The blocks that were doubted to be of childhood medulloblastoma were handed by Department of Neurosurgery, GMCH, to us. Simultaneously these blocks were analysed in the GMCH pathology laboratory for validation of medulloblastoma. The Hematoxylin and Eosin (H&E) staining of the slides taken by us was done at Ayursundra Healthcare Pvt. Limited. Ayursundra Healthcare Pvt. Ltd is one of the biggest private health care centres of the region with a strong pathology unit. After staining the slides were observed at another premier hospital, namely Guwahati neurological research centre (GNRC), Dispur, by the chief pathologist of the GNRC labo-

ratory. After the slide examination was confirmed to be of childhood medulloblastoma from both sources, we proceeded with image acquisition.

The H&E staining is used to mark the nuclei with blue and cytoplasm with pink. After the staining is done we can study the slide feature under the microscope. The images were acquired under expert supervision at GNRC. The normal tissue of brain is very difficult to obtain as brain is the vital part of a being and we cannot scrap any unnecessary tissue from it. So, we extracted the normal part from the abnormal tissue sample if any normal region was present beside it in the slide. We used 80 images each for both normal and abnormal tissue of resolution 512 X 384 of 10x magnification. The images contained both lightly stained and dark stained samples referring to the usual variation in histological samples. We have kept the number of images equal since it give a better and impartial classification accuracy without any bias for the groups classified. The abnormal tissue samples had a scanty cytoplasm with highly packed irregular cells whereas the normal sample contains undisturbed cytoplasm and much lower number of cells which had smooth edges and rounded shape under the microscope (Graham & Lantos, 2015). Figure 2 depicts a view of some of the images collected.

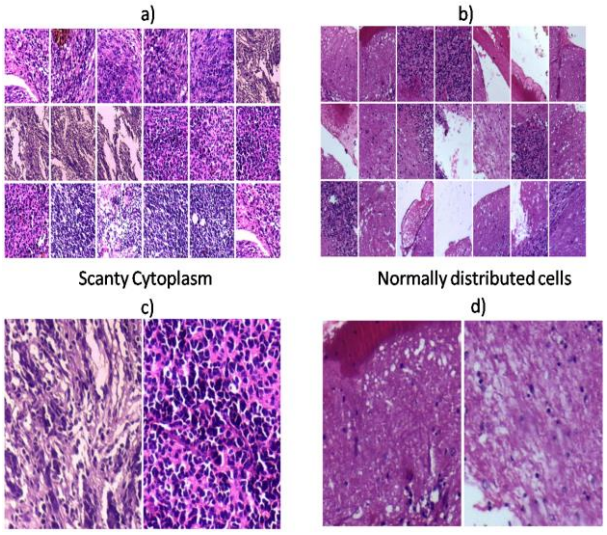


Figure 2. A view of some of the images collected

4.3 Pre-processing of the data samples

The pre-processing was performed in two phases. In phase 1 we choose an appropriate color channel for our study and in second phase image enhancement was performed to have uniform color distribution.

1) Phase 1: Choosing an appropriate channel for the work is important as not every color channel reveals the information that is required to be extracted. Color channeling entails extracting different color channels from existing RGB image to find meaningful observation. We have done all the available standard color channeling of the images and found the red channel suitable for our use as it distinctly differentiate the nucleus from cytoplasm.

2) Phase 2: To study texture-based features we needed to convert our image to a grey scale image and then perform an enhancement method so as to minimize the error of uneven staining. We have used different available enhancement methods for our study and found the contrast limited adaptive histogram equalization (CLAHE) (Zuiderveld, 1994) appropriate, as it leverages the color difference among images from different slides and highlights any local information of the image. Histogram equalization deals with normalizing the intensity of the image over the entire range of the image which results in neglect of minor difference in an image if the occurrence of the particular grey level is extremely small (Min, Lim, Kim, & Lee, 2013). Therefore an adaptive method to defend this drawback is by using CLAHE. Contrast limited adaptive histogram equalization process the whole image in blocks subdividing the whole image into smaller blocks to gain local information of the entire image. Since the architecture of tissue samples may contain some useful information in lesser quantity, CLAHE is an appropriate choice to have uniform intensity distribution.

4.4 Feature extraction

Five different textual features were studied. We studied both first order and second order characteristics of the images and considered these 5 texture features for our work which includes grey level co-occurrence matrix (GLCM), grey level run length matrix (GRLN), Histogram based features i.e. Histogram of oriented gradient (HOG), Tamura's feature and local binary pattern features (LBP). The features were studied based on the grey level intensity values of the images.

1) GLCM*:* It defines the spatial relationship among the pixels as to how often a pair of pixel appear in the image. It describes the probability of going from pixel *i* to *j* in a certain direction. We applied the well know texture feature GLCM in all four directions (0,45,90,135) and extracted the features of pixel identity pairs in terms of Autocorrelation, Contrast, Correlation, Cluster Prominence, Cluster Shade, Dissimilarity, Energy, Entropy, Homogeneity, Maximum probability, Sum of squares, Variance, Sum average, Sum variance, Sum entropy, Difference variance, Difference entropy, Information measure of correlation1, Information measure of correlation2, Inverse difference, Inverse difference normalized, Inverse difference moment normalized.

2) GRLN: Secondly we used GRLN feature extraction. GLCM (Tang, 1998) gives the occurrence of pixel pairs in a particular direction whereas GRLN gives the connected length of a particular pixel in a definite direction (Singh, 2016). We quantized the image into 16 grey levels so as to ease the computational complexity and have faster performance. The features that were extracted using GRLN were short run emphasis (sre), long run emphasis (lre), grey level non-uniformity (gln), run percentage (rp), run length non-uniformity (rln), low grey level run emphasis (lgre) and high grey level run emphasis (hgre).

3) Tamura Texture Feature: Introduced in 1978 the Tamura feature (Tamura, Hideyuki, Mori, & Yamawaki, 1978) has

six texture features, viz. coarseness, contrast, directionality, line-likeness, regularity and roughness. Experimental results show that the first three are more significant than the rest [20]. Therefore, we extracted Coarseness, Contrast and Directionality from Tamura-based features.

4) HOG: The third feature was Histogram features. This method evaluates well normalized local histogram in small grids to characterize local object appearance and shape. We obtained the first order histogram features for the pixel distribution in terms of Mean, Variance, Skewness, Kurtosis, Energy, and Entropy.

5) LBP: The fourth feature was the Local Binary Pattern. Ojala, Pietikainen, and Maenpaa (2002) introduced this feature set of rotation invariant texture pattern on local binary pattern in 1987. The LBP features encode local texture information and can be used for many tasks in-cluding classification, detection, and recognition. For every pixel of image a binary code is produced by thresholding the region with the value of the central pixel. A histogram is created based on the different pattern of this binary value.

4.5 Classification

Classification is a challenging task in microscopy biopsy images. We evaluated six standard classifiers using Matlab 2016b to check the performance of all the individual texture feature set and also to check performance for combination of the feature sets. We evaluated the feature sets performance on different model classifiers, viz. Statistical Methods, Machine learning, Clustering and Rule Based. For statistical measure we used Logistic regression, Linear discriminant and Quadratic discriminant. KNN and SVM were used as clustering and machine learning classifiers while decision tree was employed as a rule-based classifier.

The six classifiers used for evaluation were

1) Tree-based classification: Tree rule-based classifier is used to train the model using Gini diversity index with maximum splits per node limited to two.

2) Logistic Regression: Logistic Regression (LR) fits a data model that is linear in model coefficients. Linear regression depicts the relation between a response and one or more independent and dependent variable.

3) Linear Discriminant: For Linear Discriminant Analysis (LD), it computes the sample mean of each class. Then it computes the sample covariance by first subtracting the sample mean of each class from the observations of that class, and taking the empirical covariance matrix of the result.

4) Quadratic Discriminant: Quadratic Discriminant Analysis (QD), it computes the sample mean of each class. Then it computes the sample covariances by first subtracting the sample mean of each class from the observations of that class, and taking the empirical covariance matrix of each class.

5) Support Vector Machine: We used the Support Vector Machine (SVM) for two class classification. We compared the SVM with kernel function quadratic, cubic, Gaussian and linear. Before training the data samples were normalized to have equal mean and variance.

6) K-Nearest Neighbour: K-nearest Neighbour (KNN) classifies the object based on the distance measure between new sample and classes. We performed the experiments using k=10 neighbours and Euclidian distance. Before training the data samples were normalized to have equal mean and variance.

4.6 Preparing of training and testing data

5-fold cross validation was used which the data set was divided into 5 subsets, and the holdout method is repeated 5 times. 95% of the data were used as training samples and 5% as testing samples. In each iteration one of 5 subset was used as test set and 4 sets were used as training set. The advantage of this method is that every data point at some point gets to be in a test set and training set exactly once. The results obtained were based on the averages of 5 iterations.

4.7 Implementation

The experiments were implemented in Matlab® (R 2016b, Mathworks, Natick, MA, USA) and All-in–one HP pc (2.70 GHz, Intel Core i5, 4 GB Ram). In addition, built-in Matlab function, customized routines and a portion of available source code by (Rajamanickam, 2010; Sdhir, 2016; Uppuluri, 2008; Wei, 2007) were used.

5. Results and Discussion

We have evaluated the classification accuracy of individual classifiers on the individual texture features and also obtained their accuracy based on combining the feature sets. The accuracy of the samples was calculated as:

Accuracy = {(True positive + True negative)/Number of samples}*100

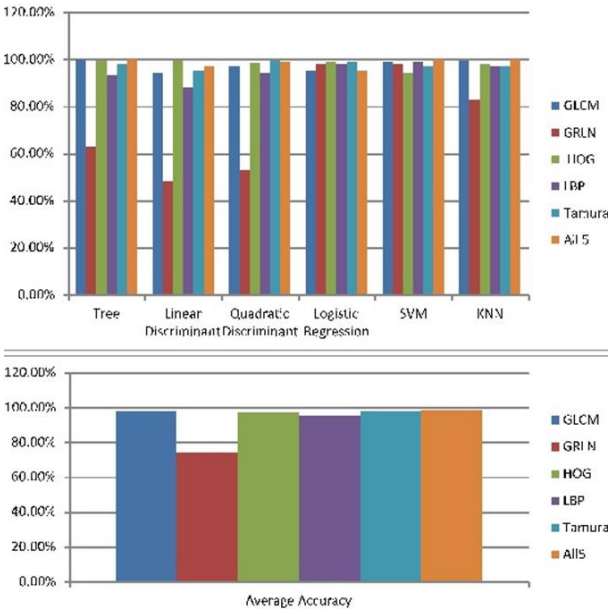
The performance evaluation tables (Table 1) are shown below. Figure 3 gives a graphical representation of the performance analysis of the methods.

5.1 Performance analysis of individual features

We performed the classification experiment with single textual descriptor to estimate the classification rate of individual texture features. The individual texture features were evaluated using six different classifiers. For GLCM, SVM, tree and KNN gave the highest accuracy of more than 99% while for GRLN we got an accuracy of 98% using logistic regression and SVM. The HOG and LBP feature gave us an accuracy of 99% using Linear discriminant and SVM respectively. The Tamura features gave an accuracy of 99.1% using logistic regression. For all five classifiers SVM and Logistic regression outshined the other classifiers in terms of accuracy for most feature sets. The minimum classification accuracy was given by Linear discriminant amounting to 48% in case of GRLN. Stu-

Table 1. Performance evaluation of classifiers

Classifiers	Accuracy				
	GLCM	GRLN	HOG	LBP	Tamura
Tree	99.75%	63%	99.3%	93.5%	98%
LD	94.4%	48%	99.4%	88%	95.4%
QD	97.2%	52.8%	98.6%	94.4%	99.5%
LR	95.4%	98%	99.1%	98%	99.1%
SVM	99.1%	98.1%	94.4%	99.1%	97.2%
KNN	99.6%	83%	98%	97.2%	97.2%
Average Accuracy:	97.5%	73.8%	97.1%	95%	97.7%
GLCM+GRLN+HOG+LBP+Tamura (All 5)					
Tree	100%				
LD	97.2%				
QD	99.1%				
LR	95.4%				
SVM	100%				
KNN	100%				
Average Accuracy:	98.6%				



GLM: Gray level co-occurrence matrix; GRIN: Gray level run length matrix; HOG: histogram of oriented gradient; LBP: Local Binary Pattern; SVM: Support Vector Machine; KNN: K-Nearest Neighbour

Figure 3. A graphical representation of the performance analysis of the methods

dying the average accuracy for the feature sets GRLN has the minimum accuracy of 73.8% and HOG,GLCM and Tamura features have maximum of 97%.The performance of the feature set based on average accuracy can be represented as GRLN <LBP<HOG<GLCM<Tamura.

5.2 Performance analysis of combined feature set

After accessing individual feature performance we thought of combining the feature set and testing the accuracy. On combination of all the texture features it gave us an optimum and maximum accuracy of 95%-100% using the classifiers. The three classifiers, Tree, SVM, and KNN, improved the accuracy to 100% in case of feature set from all five features. Out of six classifier the combination of texture gave 100% accuracy for 4 classifiers. Therefore, we can conclude that combination of features gives more accurate classification than individual feature sets. With an average accuracy of 98.6% combination of all the feature set outperforms the individual feature sets. We can state the accuracy measure as GRLN< LBP<HOG<GLCM<Tamura<all 5.

Figure 4 describes confusion matrix and the area under the Receiver Operational characteristics (ROC) curve. The area denotes the accuracy of the classifier. The AUC lies between 0 and 1 i.e.0<AUC<1. In our experiment the AUC is a perfect 1. The greatest area under the AUC better the diagnostic test. To the left is the confusion matrix which shows number of true class and predicted class value. From the matrix we can see that both the classes are correctly classified without any misclassification between true class and predicted class.

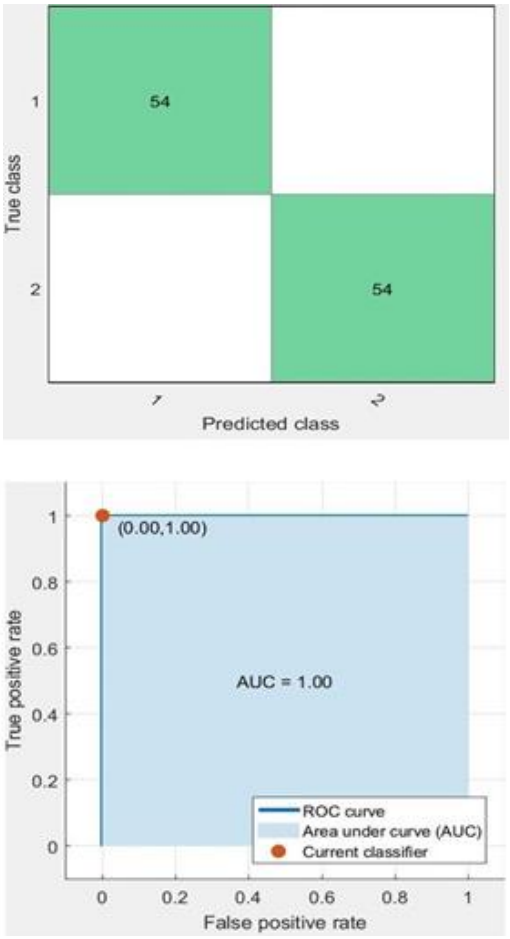


Figure 4. Confusion matrix and the area under the Receiver Operational characteristics (ROC) curve.

5.3 Correlation analysis

Since combining the features gave us a higher accuracy we performed a correlation analysis using Statistical Package for Social Sciences (SPSS) for inspection of the features of the combined set. We have done a correlation analysis for all 5 feature set comprising of 171 features, using Pearson's correlation coefficient (Figure 5). The color map shows that there is little correlation among individual feature sets however a few high correlation exist between individual features subsets. This shows that the feature set defines different aspects of texture and that combining the feature set is indeed a useful measure.

The study investigates the use of texture to differentiate between normal and abnormal brain tissue samples. We found that perception like feature of Tamura, global low order histogram and local second order feature GLCM outperforms the local texture measure of LBP and GRLN. Also that combination of the feature set produced an effective outcome.

Theoretically there are many texture features available to define texture primitives of an image. The first order histogram features define the spatial distribution of the intensity of the pixel spread in the whole image in the presence or absence of outliers or other properties that reflect the overall structure of the image. The local feature descriptor of GLCM, GRLN and LBP are the second order statics that describe the joint variability of grey levels in pair of groups of pixels. They are one of the commonly used texture descriptors of image analysis. The features that can explain the human-like visual perception are the Tamura features, which give information relating to visual description of the image surface.

The pathologist observes the histological slides and classifies them mentally based on visual perception. The experience of the pathologist is a vital factor in that case. Our proposed method can automate the task. Digital classification can be useful to decide the extent of architectural imbalance with respect to normal tissue samples. It can also be used to define the grade of the tissue samples. In addition to this technical study the work could also be used to study the biological hypotheses of normal and abnormal samples.

The 100% accuracy obtained might be because of the distinguishable difference in the arrangement of cells of the malignant and normal tissue samples. It might also happen due to the similarity property of the tissue samples in the region or might be due to lesser number of sample cases. In future we will continue our work and perform test with samples from other regions as well. If consistent performance is achieved on repetition then it can be accepted to be strongly efficient. However, we cannot deny the fact that 100% accuracy has been achieved by other researchers (Hiremath, Iranna, & Pujari, 20 07; Rahman, Mahanta, & Chakraborty, 2017) for their work in the past. Moreover, our work is open to other researchers as well who can contribute to it in the long run.

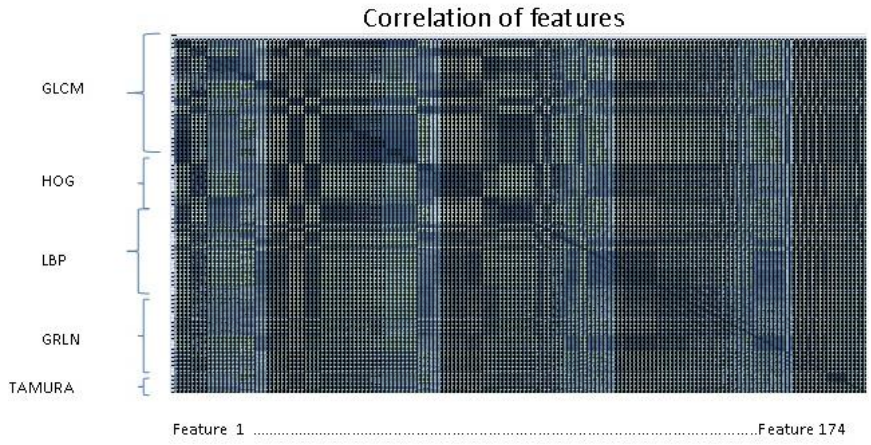


Figure 5. A correlation analysis for all 5 feature set comprising of 171 features, using Pearson's correlation coefficient

6. Conclusions

This paper presents a computer-aided diagnosis for abnormal and normal tissue samples by using texture-based features. We used 80 normal and malignant images of 10x magnification. The experiment carried out showed 100% accuracy with the all-5-feature set compared to individual feature sets and it increased the classifier average accuracy to 98.6%. Computer-aided system can lead to better diagnosis as childhood brain lesion are very critical in nature.

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