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Research Article

ROLE OF TEXTURE ANALYSIS IN PREDICTING HISTOPATHOLOGICAL OUTCOME IN PATIENTS WITH BRAIN MASSES USING CT AND MRI IMAGING

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ABSTRACT

Objectives: Brain tumors, particularly gliomas, are difficult to differentiate radiologically, whether they are benign or malignant, which usually requires histopathological examination. Texture analysis (TA), a method for quantification of heterogeneity of the tumor, can be used as a tool for this differentiation. This study aims to elucidate possible associations between computed tomography (CT) scan or magnetic resonance imaging TA (MRI TA) of brain tumors and their histopathological diagnosis.

Methods: A total of 20 patients with brain tumor were retrospectively studied. A detailed history was taken so that only pre-treatment CT/MRI scans were included to avoid heterogeneity of the sample. Patients from all age groups and sexes were included. Postcontrast images with the largest cross-section of the tumor were processed for TA (using texRAD software).

Results: In this study, it was found that for World Health Organisation (WHO) grade I and II brain tumors, mean and mean of positive pixel (MPP) are high and Kurtosis is low when compared with WHO grade III and IV. The strongest differences on unfiltered images were found for mean and MPP (p=0.049) and on medium-level filter for Kurtosis (p=0.049).

Conclusion: TA has a great potential to improve the diagnosis and stratification of patients of brain tumors. It can also give information regarding the underlying growth patterns, and hormonal/tumor markers, may add inputs in decisions regarding therapeutic efficacy, follow-up before and after treatment and prognosis, thus helping in the management of the patient.

Keywords: Texture analysis, Low-grade gliomas, High-grade gliomas, Computed tomography scan, Magnetic resonance imaging.

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INTRODUCTION

Texture analysis (TA) is a technique for quantification of heterogeneity in radiological images and is an important element in the growing field of radiomics [1]. This tool that helps to extract extensive data from radiology images [2]. TA has proven useful in medical diagnostic imaging, especially in oncological imaging to differentiate between benign and malignant tumors [3]. This imaging technique reflects the tumor heterogeneity as seen on the histopathological examination [4]. TA was initially applied to simple radiographs in 1973 [5], subsequently to ultrasound images, and later to computed tomography (CT) and magnetic resonance imaging (MRI), with an increasing number of positron emission tomography studies. The initial implementation of TA to predict patient survival by grading the tumor was suggested by Ganeshan *et al*. [6]. Computed tomography texture analysis (CTTA) uses the statistical distribution of pixel values within the tumor as a substitute marker of tumor heterogeneity, which recognizes feature of malignancy, tumor aggressiveness, and treatment response in patients with cancer. TA of MRI data from cerebral tumors has been shown to be an important tool for characterizing the microenvironment within these neoplasms [7,8]. TA is now entering the area of personalized medicine. Therefore, this study was conducted to elucidate possible associations between MRI TA of brain tumors and their histopathological diagnosis.

METHODS

The present study was done at Dr. B. Nanavati Super-speciality Hospital, a tertiary care center in Mumbai, after getting approval from the Chairman, Academic Committee, Scientific Committee, and Ethical Committee of Dr. B. Nanavati Super-speciality Hospital. This retrospective observational study of 1 year, included 20 cases of brain tumors undergoing pre-treatment MR study. Cases of all age groups, irrespective of sex, were included. Patients having a history of claustrophobia, metallic implant insertion, cardiac pacemakers, and metallic foreign-body *in situ*, patients with contrast allergy and medical renal disease were excluded from the study. The protocol was explained to the patients and the relatives in the language best understood by them and informed written consent was obtained from all patients or relatives prior to the CT/MRI examination.

MRI for all brain lesions was done on GE 3 Tesla 750w discovery whole-body MR system using a circularly polarized phased array head coil. Initially, each patient was subjected to routine Spin Echo (SE) sequences. Axial T1W/TSE, Axial T2W/TSE, Coronal T2W/TSE, Sagittal T2W/TSE, Axial T2W/FFE, FLAIR Axial, Axial T1W/FFE, Coronal T1W/FFE, Sagittal T1W/FFE, DWI and/or CISS/3D sequences were obtained with varying slice thickness. For the contrast study, 5 mL of gadobutrol 1.0 mmol/mL (0.2 mL/kg body weight in pediatric age group) was injected intravenously at the rate of 2 mL/s followed by 10 mL of saline flush and postcontrast T1 axial and 3D brain volume (BRAVO) T1-weighted postcontrast sequences were obtained. Postprocessing of the T1 postcontrast image showing the maximum cross-section of the lesion was done with the help of inbuilt texRAD software.

TA was performed on cross-sectional images. The study coordinator reviewed the surgical reports and the CT/MRI images obtained during percutaneous biopsy to ensure that only pathologically proven lesions

were included in the study. CT and MR images were anonymized and transferred to a dedicated workstation for CTTA and MRTA, respectively. Textural features were extracted using commercially available research software (TexRAD, version 3.9, Feedback Plc, Cambridge, UK) which applies a two-step filtration-histogram approach. Axial postcontrast CT and MR images were used for TA. Histogram parameters included for this study were mean (average value of the pixels), standard deviations, entropy (indicator of irregularity), mean of positive pixel (MPP), skewness (indicating asymmetry of the histogram), and kurtosis (indicating the peak of the histogram). The data was coded and entered into Microsoft Excel spreadsheet. The Mann–Whitney *U* test was used to compare the distribution of MRTA parameters in brain tumors. Receiver operating characteristics analyses were performed for the most discriminative features to assess the performance of the diagnosis. Texture parameters that were shown to be statistically significant were then entered in a binary logistic regression (forward conditional). The statistical significance level was set at $p<0.05$. Statistical analysis was conducted using SPSS software (version 18.0; SPSS, Chicago, IL).

RESULTS

Of the total 20 cases studied, a maximum number of patients were those aged between 60 and 70 years (30%) and >70 years (20%) (Table 1), with majority of them being of the female sex (55%).

15 out of the 20 cases were intra-axial in location and the remaining were extra-axial in location. Maximum tumors were recorded in the right frontal region (35%), followed by left Parietal region (20%), (Table 2). About 45% of the cases were diagnosed with high-grade gliomas (HGGs) on histopathological examination, followed by meningioma (40%), Schwannoma (5%), and low-grade gliomas (LGG) (5%).

For Mean (on un filtered images) greater than or equal to 4044.91, TA can differentiate World Health Organization (WHO) low-grade from WHO high-grade tumors with sensitivity of approximately 83% and specificity of approximately 80% with area under the curve (AUC 0.759 and p=0.025 (Fig. 1 and Table 3).

For MPP (on unfiltered images) greater than or equal to 4044.91, TA can differentiate WHO low grade from WHO high-grade tumors with a sensitivity of approximately 83% and specificity of approximately 80% with AUC 0.759 and p=0.025 (Fig. 2 and Table 4).

For Kurtosis (on medium-level filter) greater than or equal to 0.1, TA can differentiate WHO high grade from WHO low grade tumors with sensitivity of approximately 70%and specificity of approximately 84% with AUC 0.759 and p=0.023 (Fig. 3 and Table 5).

Representative case

28-year-old lady with right frontal lesion processed for TA. Mean (on unfiltered images): 1960.54 MPP (on unfiltered images): 3779.21 Kurtosis (on medium-level filter): 1.25. Based on the results obtained from our study, the above parameters are more in favor of HGG. These findings were confirmed with histopathology reports of the patient (Fig. 4).

DISCUSSION

The incidence of central nervous system (CNS) tumors in India ranges from 5 to 10/100,000 population, with an increasing trend and accounts for 2% of malignancies [8].

More than 80% of all primary brain tumors are diagnosed in people older than 40 years. The average age for brain tumor diagnosis is 61 years [9]. In the present study, maximum numbers of patients were in the age group of 60–70 years (30%), followed by >70 years (20%), which was comparable with the study done by Ghosh *et al*. having majority of the patients in 6th decade (38%), followed by 7th decade (22%) [10]. Saha *et al*., in their study, also reported most of cases (44%) were above the age of 50 years [11].

Table 1: Distribution of cases according to age

Age in years	Number of cases (n)	Percentage
<20	1	5
20–30	3	15
30–40	2	10
40–50	2	10
50–60	2	10
60–70	6	30
>70	4	20

Table 2: Distribution of cases according to location of tumor

Location	Number of cases (n)	Percentage
Left cerebellum	1	5
Left frontal	3	15
Left occipital	1	5
Left parietal	4	20
Left temporal	1	5
Right frontal	7	35
Right parietal	2	10
Right temporal	1	5

Table 3: Test results of ROC curve depicting sensitivity and specificity of difference in mean values

Area	Standard error	Asymptotic significance	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.759	0.116	0.025	0.532	0.986

ROC: Receiver operating characteristic

Table 4: Test results of ROC curve depicting sensitivity and specificity of difference in MPP values

Area	Standard error	Asymptotic significance	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.759	0.116	0.025	0.532	0.986

ROC: Receiver operating characteristic

According to the WHO classification, CNS tumors are classified into four grades, where I to II are low-grade and III to IV are high grade. The limited survival chances for brain cancer patient, mainly WHO high-grade tumors is very low [12,13]. Grading of the tumors is important as it helps the treating doctor to determine the appropriate treatment strategy and predict the prognosis and outcome of the disease [14].

TA is a method used for quantifying the spatial distributions of intensities or heterogeneity in images. TA holds promise in the field of oncology diagnosis, including quantifying tumor heterogeneity and tumor grading. In the present study, nine patients of HGG (Grade III and IV), eight patients of meningiomas, including atypical meningiomas), two patients of LGG (Grade I and II), and one patient of Schwannoma (Grade I) were included and their T1 postcontrast MRI images were processed for TA.

In the present study, Mean and Most Probable Point were high and Kurtosis was low for low-grade tumors, compared with high-grade tumors. Similar statistical findings were seen in the study by Tessamma and Ananda Resmi Based on T2-weighted imaging, their study indicated that contrast, intensity and entropy, kurtosis, and spectral energy showed differences between low- and high-grade tumors [15].

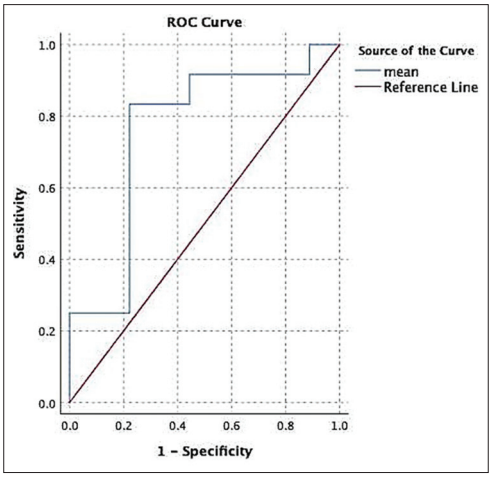


Fig. 1: Receiver operating characteristic curve depicting sensitivity and specificity of difference in mean values

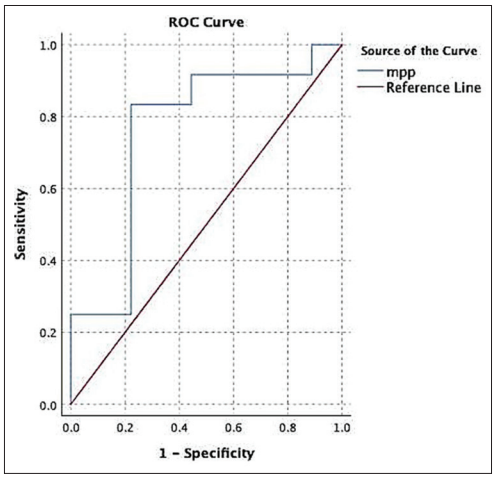


Fig. 2: Receiver operating characteristic curve depicting sensitivity and specificity of difference in mean of positive pixel valuesa

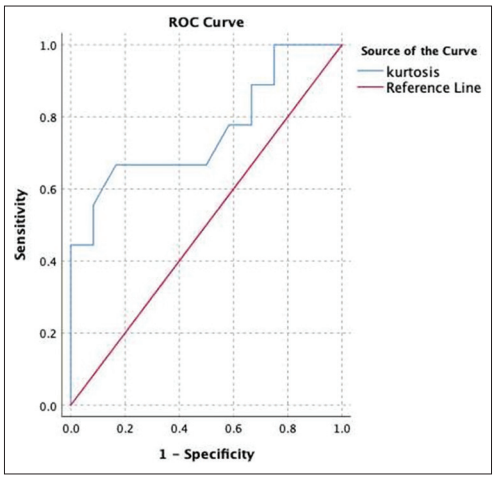
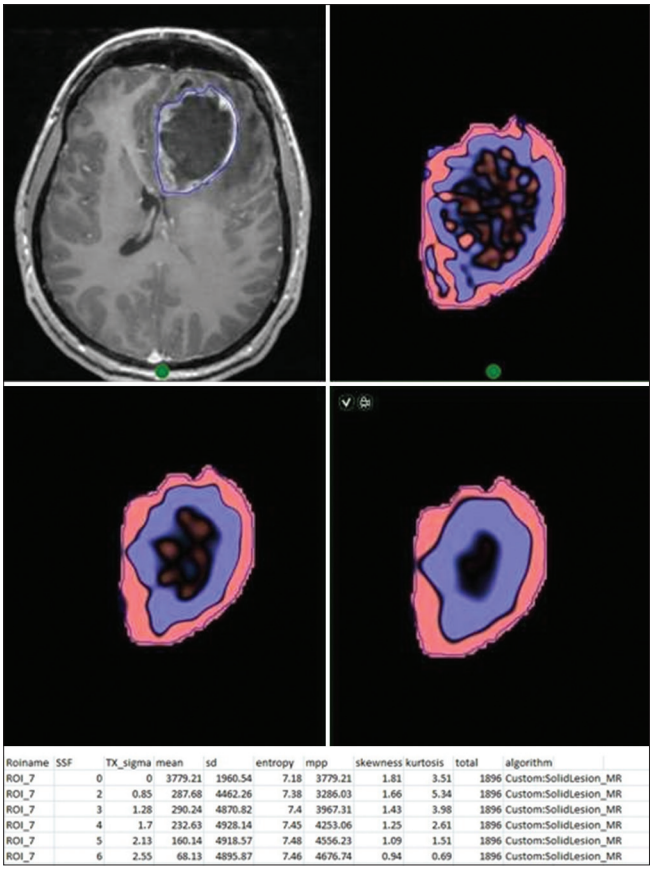


Fig. 3: Receiver operating characteristic curve depicting sensitivity and specificity of difference in Kurtosis values

Similar findings were noted in the study done by Ryu *et al.* which suggested high entropy, high skewness, and low fifth percentile values of the apparent diffusion coefficient histograms, based on the entire tumor volumes, could be used to differentiate between high- and LGGs [16].



Roiname	SSF	TX_sigma	mean	sd	entropy	mpp	skewness	kurtosis	total	algorithm
ROI_7	0	0	3779.21	1960.54	7.18	3779.21	1.81	3.51	1896	Custom:SolidLesion_MR
ROI_7	2	0.85	287.68	4462.26	7.38	3286.03	1.66	5.34	1896	Custom:SolidLesion_MR
ROI_7	3	1.28	290.24	4870.82	7.4	3967.31	1.43	3.98	1896	Custom:SolidLesion_MR
ROI_7	4	1.7	232.63	4928.14	7.45	4253.06	1.25	2.61	1896	Custom:SolidLesion_MR
ROI_7	5	2.13	160.14	4918.57	7.48	4556.23	1.09	1.51	1896	Custom:SolidLesion_MR
ROI_7	6	2.55	68.13	4895.87	7.46	4676.74	0.94	0.69	1896	Custom:SolidLesion_MR

Fig. 4: Magnetic resonance post contrast BRAVO image

Table 5: Test results of ROC curve depicting sensitivity and specificity of difference in MPP values

Area	Standard error	Asymptotic significance	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.759	0.114	0.023	0.536	0.982

ROC: Receiver operating characteristic

A meta-analytical study for systematically evaluating the accuracy of TA in discriminating LGGs from HGGs was conducted by Wang *et al*. The findings of the meta-analysis showed that the pooled sensitivity and specificity of TA were 0.93 and 0.86, respectively. The AUC was 0.96. The results of this study demonstrated that TA had high diagnostic performance in ruling out HGGs in discriminating gliomas [17].

Our findings also correlated with the study done by Zacharaki *et al*., that textural parameters extracted from the brain lesions in FLAIR seem to be significant for glioma grading [18].

Some discrepancies were noted with the previously done studies, likely due to the fact that we used different MRI sequence and different software (texRAD) for extracting texture parameters and also due to subjective error in interpretation of the radiological images.

The results of the present study look promising as the sensitivity achieved is approximately 83% and specificity is 80%, with AUC 0.759 and p=0.025 for Mean and MPP (on unfiltered images) for differentiating WHO low grade from WHO high-grade tumors. For Kurtosis also (on a medium-level filter), the present study achieved sensitivity of approximately 70% and specificity of approximately 84%

with AUC 0.759 and p=0.023 to differentiate WHO high grade from WHO low-grade tumors.

CONCLUSION

This study reveals the usefulness of three texture parameters (Mean, MPP, and Kurtosis) in differentiating the WHO low-grade and high-grade brain tumors. From this, we conclude that one single texture parameter is not sufficient to describe the gross heterogeneity of a tumor. Textural analysis using multimodalities will be more helpful for the diagnosis and grading of various tumors.

Limitation

In the current study, we used the manual segmentation method to draw ROI, which can be limited by inter- and intra-observer reproducibility.

Recommendation

By leveraging the specific properties of various functional MRI and CT imaging techniques, TA can be used to quantify different tissue properties. TA could provide insight on the distribution or longitudinal development of tumor vascularisation and diffusion.

AUTHOR CONTRIBUTION

All the authors contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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