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Comparison of diagnostic accuracy of magnetic resonance spectroscopy with conventional magnetic resonance imaging for brain tumors and correlation with histopathology as gold standard

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***Abstract*---**Background; Despite a large number of revolutionized advancements in Imaging technology clinicians are unable to get hundred percent accurate results. Multiple limitations have been observed in Imaging modalities. Multiple published trials are available online on the evaluations of these imaging modalities individually and

in combinations to find out the level of accuracy of these technologies. Objective; This study was design to compare the diagnostic accuracy of MR Spectroscopy with MRI which is a conventional diagnostic tool for brain tumor diagnosis while keeping the Histopathology evaluation as Gold Standard. Methodology; The patients who fulfilled the inclusion criteria were included in study. All scans were carried out on GE 1.5 Tesla MR Scanner using head coil. Axial T1W, T2W, Fluid Attenuated Inversion Recovery (FLAIR), Sagittal T2W, Coronal Fluid Attenuation. Inversion Recovery (FLAIR) and T1W post- contrast Axial, Coronal and Sagittal images were acquired. MR spectroscopy was performed through single voxel technique. Final diagnosis was made on histopathology results. The reports of biopsy were co related with radiological diagnosis of MRI and MRS. Results; The study was conducted with 150 suspected cases. There were 85(56.7%) males and 65(43.3%) females. Histopathology 100(66.7%) cases were confirmed positive and 50(33.3%) negative. When diagnosis through MRI compared with Histopathology it was noted that the sensitivity of MRI was 74.0% and the specificity 82.0% with an accuracy of 76.6%. When diagnosis on MRS was compared with histopathology as gold standard, the sensitivity was 89.0% and specificity of 96.0% with the accuracy of MRS in diagnosis was 91.3%. Conclusion; Magnetic Resonance Spectroscopy (MRS) is a rigorous, non-invasive, safe and convenient imaging modality for the evaluation of brain tumors as compared to Magnetic Resonance Imaging (MRI).

***Keywords*---**diagnostic accuracy, magnetic resonance spectroscopy, conventional magnetic resonance imaging, brain tumors, histopathology.

Introduction

Brain tumors can develop largely from inside the neural tissue or as metastases from a distant source. Primary brain tumors are seen in more than half of all intracranial lesions. In 2011, the incidence of all primary malignant and non-malignant brain and CNS cancers was 18.71 cases per 100,000 (7.3 for malignant tumors and 11.52 for non-malignant tumors)(Ostrom et al., 2011). The comparable appearances of brain tumors and other diseased entities on CT and MRI make diagnosis difficult. Patients with brain tumors may remain asymptomatic as in low grade gliomas or may present with non-specific signs and symptoms that may be focal or generalized. Low grade gliomas with no surrounding edema mostly remain asymptomatic for years. The onset and duration of symptoms and signs and symptoms of mass effect as compression on the ventricles or herniation of brain and pattern of cranial nerves involvement suggests the location of tumor (Neugut et al., 2019). The MRI gradient-echo (GRE) sequence is just as excellent as CT for detecting calcifications and acute and chronic hemorrhages. However, because both look dark on the GRE sequence, calcifications may be misdiagnosed as persistent bleeding. Calcifications provide nonspecific signal intensities on conventional MRI T1W and T2W images. For these reasons, despite the hazards of ionizing radiation, CT remains the preferred

modality in clinical practice(Zulfiqar et al., 2012). MRI can detect even tiny isodense lesions on CT, however poor delineation of calcifications and bleeding is a significant drawback. Although MRI with contrast is a good tool for seeing and characterizing many malignancies, there are situations when a diagnostic challenge exists due to similarities and unusual characteristics of brain lesions(Chen et al., 2014). As a result, patients must undergo invasive surgical procedures for biopsy to rule out malignancy. MRS, also known as nuclear magnetic resonance spectroscopy (NMR), is a cutting-edge technology that provides information about the metabolism of live brain metabolites.

Magnetic resonance spectroscopy is a non-invasive analytical technique for distinguishing benign from malignant tumors and defining malignant neoplasms. It is possible to do it as part of standard MR imaging using commercially accessible MRI machines(Horská and Barker, 2010). Instead of pictures, MRS data is processed to produce a graph or spectrum with a sequence of peaks that indicate the kinds and quantities of distinct chemical metabolites in brain tissue in vivo. The metabolites detected by MRS have previously found chemical changes in nuclear MR spectra. Signals from H protons in water are muted in the MRS method, enabling H protons in other molecules to be detected(Dhillon et al., 2018). N-Acetylaspartate (NAA), Choline (Cho), and Creatine are the metabolites of a typical healthy brain (Cr). Peak heights on an MR spectroscopy graph show the concentration of these metabolites (i.e. area under the peak), and peak position identifies the individual metabolite.

NAA is of neuronal and axonal origin, with a peak resonance frequency of 2.02 ppm. A decrease in peak height indicates the loss or malfunctioning of normal neural tissue. The highest resonance frequency of creatine (Cr) is 3.0ppm, and this metabolite is the energy marker of neurons. The choline (Cho) peak demonstrates higher cell membrane production and breakdown, implying enhanced membrane turnover in rapidly proliferating cells, as seen in cancer. Its maximum value is 3.2ppm. Choline levels are related to tumor cellular density and tumour penetration into adjacent brain tissue. As a result, elevated choline levels also delineate tumour borders in treatment planning(Minati et al., 2010).

Furthermore, a lactate peak (doublet) at 1.35ppm is a sign of ischemia and anaerobic glycolysis, as seen in infarction and necrotic tumors, among other things. In granulomatous infections, it is also high in foamy macrophages. The lipid peak resonates at 0.9-1.3ppm and is caused by cell membrane disintegration, which releases lipid droplets, as in necrosis. These peaks do not appear in the typical brain spectrum. The neuronal function and membrane turnover within the volume of interest can be linked to underlying disease by examining the relative peaks and ratios of their concentrations. MRS will help not only in categorizing disease inside the brain, but also in calculating the impact of anti-tumor therapy by detecting aberrant metabolite ratios in chosen voxels(Horská and Barker, 2010).

Methodology

This was cross-sectional study carried out at Department of Radiology, Shaikh Zayed Hospital, PGMI Lahore. Total 150 patients of both genders and with clinical

suspicion of brain tumors were recruited for this study by convenient sampling technique.

Sampling criteria

Patients between age of 20 to 65 years who were referred from indoor, outdoor and emergency department with sign symptoms of brain tumor or non-specific MRI and CT scan reports were recruited. All patients with life expectancy less than three years, Recurrent tumors, with any sympathetic device like pace makers and patients having contra-indication of MRI were excluded.

Data collection and Analysis procedure

A dually signed Performa was used to record the data of all variables from the patients fulfilling the inclusion criteria. All scans were done on GE 1.5 Tesla MR Scanner using head coil. Axial T1, T2, Sagittal T2, Coronal Fluid Attenuation Inversion Recovery (FLAIR) and post-contrast (if recommended/ needed and appropriate) Axial, Coronal and Sagittal images were acquired. MR spectroscopy was performed through single voxel technique. After water suppression, a point-resolved spectroscopy (PRESS) technique was used for localization and the studies were obtained with TE and TR of 135 and 1500 respectively. The collected information was entered in SPSS v23.0. Data for age was recorded using Mean ± standard deviation. Data for gender and positivity in MRI and MRS and on histopathology were recorded using frequency and percentage with 95% confidence interval. Sensitivity, Specificity, PTV, NPV and accuracy of MRI and MRS against histopathology findings were reported by using percentage with 95% confidence interval.

Results

Demographic characters of participants showing the case of age was like most number participants 77 (51.3%) were more than 50 years of age and in this age group most of the participants were female, Despite in overall number the majority 85(56.7%) were adult males and 65(43.3%) were adult females. The study was divided into two major age groups. There were 33cases (22%) with average age 20-35 years. The other age group 36-50 years had 40(26.7%) cases.

Age groups	Frequency	Percent
20-35 years	33	22.0
36-50 years	40	26.7
≥50 years	77	51.3
Total	150	100.0

Table 1 Demographic characters

Histopathology of 100(66.7%) cases confirmed positive and 50(33.3%) negative for MR Spectroscopy. On comparison of conventional MRI with contrast, and Histopathology it was observed that the sensitivity of MRI was 74.0% and the specificity 82.0%.

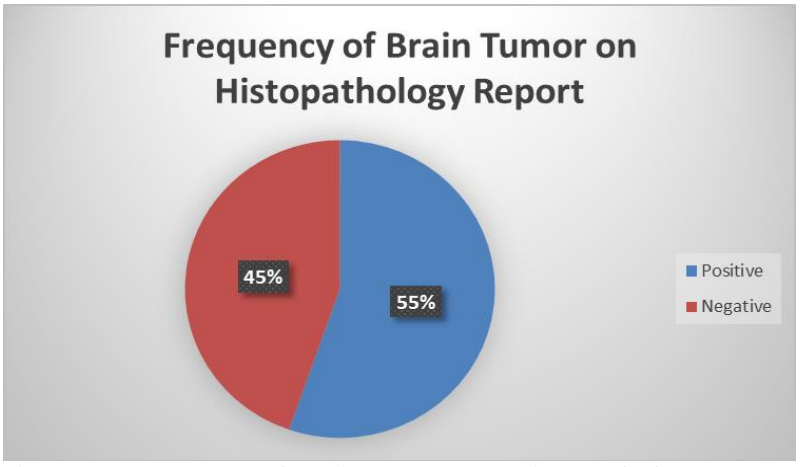

Figure 1 Frequency of Brain Tumor on Histopathology Report

Keeping histopathology as gold standard and comparing the results of MR Spectroscopy the sensitivity of 89.0% and specificity of 96.0% was found to be at a higher diagnostic level as compared to conventional MRI alone. The PPV was 97.8% and NPV was 81.3%. The accuracy of MRS in diagnosis was recorded to be 91.3%. Keeping histopathology as gold standard and comparing the results of MR Spectroscopy the sensitivity of 89.0% and specificity of 96.0% was found to be at a higher diagnostic level as compared to conventional MRI alone. The PPV was 97.8% and NPV was 81.3%. The accuracy of MRS in diagnosis was recorded to be 91.3%.

Brain tumor on MRI	Brain tumor on Histopathology		P-value
	Positive	Negative	
Positive	74	9	< 0.001
Negative	26	41	
Total	100	50	

Table 2 MRI comparison with histopathology reports

On comparison the findings of MRI accuracy while comparing with histopathology results as standard were as Sensitivity 74%, Specificity 82%, Positive prediction 89.1%, negative prediction61.1%, Accuracy 76.6% and prevalence was 66.6%. When comparison was made for MRS and Histopathology 45 cases matched for grade 1 and 47 cases showed a match for grade 2 tumors. All the remaining 50 cases matched for negative results. The kappa statistics was 0.920 with a p-value < 0.001 and grading matched for 94.7% cases between MRS and histopathology.

Brain tumor on MRS	Brain tumor on Histopathology		P-value
	Positive	Negative	
Positive	89	2	< 0.001
Negative	11	48	
Total	100	50	

Table 3 MRS comparison with Histopathology reports

On comparison with Histopathology reports the MRS technology was having sensitivity 89.0%, Specificity 96%, positive predictive value 97%, Prediction of negative results was 81.3%, accuracy rate 91.3% and prevalence was 66.6%. Histopathology grading showed 48 cases to be grade 1 and 52 cases to be grade 2 gliomas. The grading on MRI was similar for 75(50.0%) cases, out of which 15(20.0%) were negative for malignancy. The study thus concluded that MRS significantly improves characterization of brain tumors compared to conventional MRI for all diagnostic measures with p-values <0.001

Discussion

Conventional MRI is helpful for the first examination of brain tumors, but in certain cases, it may not seem to be effective for discriminating between tumor types or identifying tumor grade(Upadhyay and Waldman, 2011). The MRI's perplexing results pave the path for the application of MRS. In a study of mass lesions, Moller Hartmann et all found that adding MRS improved diagnostic accuracy from 55 to 70%(Möller-Hartmann et al., 2002).use of golden methods of detection like biopsy can be reduced by using modern techniques like MRS(Sibtain et al., 2007).through MRS type of lesions can also be diagnosed by providing chemical profile of cerebral lesions. For the identification of brain lesions, MRI had a sensitivity of 74.0% and a specificity of 82.0%, with a diagnostic accuracy of 76.6%. In this work, Lord et al. demonstrated findings for diagnosing high-grade glioma using conventional MRI. The sensitivity and positive predictive value values (72.5%, 86.1%) were close to those found in our study (74.0%, 89.1%), however the specificity and negative predictive value values (65.0%, 44.0%) were significantly lower than those found in our study (82.0%, 61.1%)(Lord et al., 2018). MRS is becoming more important in diagnosing many neurological and neurosurgical problems. In their investigation, Mahmud et al. discovered MRI specificity and sensitivity of 84 and 75%, respectively, which is close to our findings. It has been demonstrated that including an MR Spectroscopy sequence can increase the diagnosis accuracy of brain malignancies(Rafique et al., 2022). In their investigation, Jesrani et al. discovered that sensitivity was 87.5%, specificity was 93.3%, positive predictive value was 95.5%, negative predictive value was 89.7%, and accuracy was 92.1% using MRS, which corresponds to the results observed in our study(Musawar et al., 2022). Alam et al. observed 93.02% sensitivity, 70% specificity, 93.02% positive predictive value, 70% negative predictive value, and 88.67% diagnostic accuracy in another study, which is similar to the accuracy recorded in our study(Alam et al., 2011). In another investigation, Amin et al. found that MRS had equal sensitivity (90.7%), specificity (94.4%), and diagnostic accuracy (91.5%)(Amin et al., 2019). In comparison to histology, the sensitivity, specificity rate, and diagnostic accuracy of MR Spectroscopy were 89.0%, 96.0%, and 91.3%, respectively. In the current study, the PPV of MR Spectroscopy was 97.8% and the NPV was 81.2%. Other investigations with brain lesions revealed MRS sensitivity ranging from 79 to 100% and specificity ranging from 74 to 100%. The PPV varied from 92 to 100%, whereas the NPV ranged from 60 to 100%(Anderson et al., 2014). The fundamental benefit of single voxel MR spectroscopy is that invasive biopsy procedures in patients with brain tumors can be avoided. High specificity and PPV of MR spectroscopy are desirable for this purpose to minimize false positive results that may lead to needless neoplastic intervention by the

surgeon. Our study has a high specificity (96.0%) and PPV (97.8%). The primary benefit of single voxel MR spectroscopy is that invasive biopsy procedures in patients with brain tumors can be avoided. High specificity and PPV of MR spectroscopy are desired for this purpose to minimize false positive results that may lead to needless neoplastic intervention by the surgeon. The specificity (96.0%) and PPV (97.8%) in our research are pretty high.

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