Correlation of Magnetic Resonance Spectroscopy with Histopathology of Brain Biopsies

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Abstract: The pathology of human tissue can be determined by magnetic resonance spectroscopy (MRS) but it was a controversial field for over 20 years. Now MRS on human biopsies identifies disease processes, neoplastic status, and prognostic variables with high accuracy. The MRS databases were compared with careful and specialized histology. The MR method is fast, accurate, and robust and for most organs complements routine histopathological diagnosis. Study was performed to evaluate the rule of Magnetic Resonance Spectroscopy in diagnosis of brain tumors compare by histopathology. A total of 38 patients were examined in this study. The data collected from three hospitals in Khartoum state from 2014 to July 2015. The patients were examined with the own department protocol using Magnetic resonance machine. The study founded that (86.8%) of patients examined by Spectroscopy have same results compare to the histopathology results. Conclusion: MRS is an accurate, noninvasive diagnostic technique for quantifying brain tumors.

Keywords: Brain-tumors, Spectroscopy, Histopathology, Metabolite

1. Introduction

As stated The incidence of brain tumors (BTs) increases annually by (De Moor, Janet S., et al 2013); [1]There are approximately 2,500 new diagnosed case per year in the USA and the incidence of brain tumors has increased slightly over the recent decades which is possibly ascribed to improved diagnostic imaging technologies (Gill, S. K., Panigrahy et al 2013). [2] Despite the fact that the actual incidence and prevalence worldwide is still remains in accurately measured or detected, with 80% of patients with malignant brain tumors die from the disease.

At present, brain biopsy represents the reference standard for diagnosing brain mass, although the drawbacks of this invasive technique are well known. It is associated with morbidity and mortality, it has sampling errors, and it is not appropriate for screening, longitudinal monitoring, or evaluating treatment response [3]. Among the currently available imaging modalities, magnetic resonance imaging (MRI) and ¹H MR spectroscopy (MRS) are the most reproducible, safe, and accurate imaging techniques that can be used in clinical trials and epidemiologic studies [4]. However, MRS has limited clinical applicability or availability because it requires sophisticated post processing methods, and not every MRI is routinely equipped with MRS capabilities. Recent improvements in MRI can provide the magnetic resonance imaging estimated proton density fat fraction (MRI-PDFF), which is a novel biomarker that has demonstrated robust correlation and equivalency with MRS [5-6].

In addition, MRI-PDFF allows fat mapping of the entire liver, and it can be used with any clinical MRI platform, where as MRS measures fat biochemically in small regions of interest (ROIs). To the best of our knowledge, few studies have used MRS and histology to investigate brain content in patients with BTs [7-8].

2. Materials and Methods

The study was performed in Royal Care hospital in Khartoum State 38 patients (20 males, 18 females; age range, 4–80 years) have been examined using MRI scanner (1.5 tesla- Toshiba Avantage-Japan 2009).

2.1 MRI protocol

All the cases were examined in supine position with standard circularly polarized head coil using the following sequences. Axial and Sagittal T1WI (550/8.7 ms) TR/TE spin echo. Coronal T2WI (5000/96 ms) TR/TE spin echo. Axial FALIR (9000/92/ms) TR/TE spin echo. 5 mm section thickness, 230-230 Field of view (FOV) and 256-256 matrix size

All of cases which require contrast administration to confirm tumor diagnosis, intravenous administration of Gadolinium- DTPA, contrast enhanced T1WI in axial, sagittal and coronal planes was performed. About 38 cases with confirmed diagnosis MRS were done using single voxel technique.
2.2 MRS protocol

Two localization methods have been performed, each has a different TE. Data were acquired using Point Resolved Spectroscopy (PRESS) pulse sequence and spectroscopic localization has been performed on post contrast T1WI with automatic shimming. All the MR Spectroscopy was performed using single voxel technique initially post contrast imaging was done to localize the tumors and then voxel was placed on volume of interest.

Measurement parameters used in 2D-MRSI were TR/TE: 1500/135 ms, (FOV): 120 _ 120 mm, section thickness: 10 mm and total scan time was 7 min. The Region of interest (ROI) was carefully placed to avoid strong interference from subcutaneous fat and lipids of the skull, and outer volume suppression (OVS) slabs outside the ROI was used to further reduce the potential for artifact. Measurement parameters used in SVS scans were 1500/35 ms (TR/TE) and voxel size was about 1.5 cm3. The total Scan time was 3.14 min. 1.2.

Analysis of the spectroscopic data: The main metabolites identified by MRS are (NAA) at 2.02 ppm, (Cr) at 3.0 ppm and (Cho) at 3.2 ppm. Concerning lipids and lactate (LL) were qualitatively defined and estimated their sum between 0.9 and 1.3 parts per mil (ppm). The following metabolite ratio was calculated using the standard commercial software. A spectrum was excluded for analysis if integration of any peak could not be accomplished using the automated analysis software.

3. Results

The diagnostic findings of MRS depend on the following: (High Choline indicate brain malignancy, weak NAA signal refers to replacement of healthy brain tissue by tumor cells, level of Cr refers to high energy metabolism and Lac refers to anaerobic metabolism).

| Metabolite     | Major resonance (ppm) | Physiological significant                                      | Increase                  | Decrease                  |
|----------------|------------------------|----------------------------------------------------------------|---------------------------|---------------------------|
| NAA            | 2.0                    | Marker of neuronal health. See only in neuronal tissues         | Rarely in canavan disease | Neural damage             |
| Cho            | 3.2                    | Marker of membrane synthesis and NO of cells                   | Active tumors growth      | HIV & Liver disease       |
| Cr             | 3.0                    | Energy metabolism. stable in many disease                      | Trauma                    | Tumors & hypoxia          |
| Lipids (Lip)   | 0.8 - 1.4              | Normally not present or very low                                | Necrotic tumors, stroke and abscess | -                         |
| Lactate (Lac)  | 1.3                    | Normally not present or very low                                | Necrotic tumors, stroke and abscess | -                         |
| Glutamate & Glutamine (Glx) | 2.1 - 2.6  | Regulation of neurotransmitter activity                      | Hepatic encephalopathy& severe hypoxia | -                         |
| Myo-inositol (MI) | 3.5                  | Used as astrocytes marker                                    | Glioma, Alzheimer and glimatosis | Hepatic encephalopathy   |

MRS (single or multi-voxel technique) is noninvasive diagnostic procedure for brain metabolite that could register the pattern of tissue with chemical compounds (Choline compounds (Cho), Creatine and Phosphocreatine (Cr), N-Acetyl-Aspartate (NAA), and Lactate (Lac)) and map out the spatial distribution of metabolites within the brain.

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![Figure 1](image1.png) **Figure 1:** Shows the gender distribution in this study.
MR spectroscopy is a powerful tool for evaluating patients with brain tumors by interpretations the MR spectroscopy findings for the specific diagnosis. The study showed that male patients are more than female patients, the most common brain pathologies diagnosed by MR spectroscopy is malignancy followed by benign.

Our results suggest that MRS is an accurate, noninvasive diagnostic technique for quantifying brain tumors.

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