Clinical Imaging of Tumor Metabolism with ^{1}H Magnetic Resonance Spectroscopy

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KEYWORDS

• ^{1}H magnetic resonance spectroscopy metabolites • Choline • Magnetic resonance spectroscopic imaging • Brain tumor • Prostate cancer • Breast cancer • Hepatocellular carcinoma

KEY POINTS

- Magnetic resonance spectroscopy (MRS) is able to determine the tissue chemical composition of a certain tissue, providing clinical valuable information for oncologic molecular imaging.
- Clinical MRS is mainly based on ^{1}H protons, which is technically challenging and needs robust quality control of sequence design, acquisition including artifact identification and postprocessing, and quantification steps for clinical implementation.
- MRS increases the overall diagnostic accuracy in multiparametric evaluation of brain tumors and is a key tool especially for lesion characterization, tumor grading, and assessment of local extension, as well as for treatment monitoring.
- MRS has been included in routine clinical MR imaging protocols for prostate cancer assessment for years, although its role is now under debate because of limited reproducibility, complex interpretation, and long acquisition time.
- Choline has emerged as a metabolic hallmark of malignancy in tumors of breast, the musculoskeletal system, and other abdominopelvic organs.

INTRODUCTION

Magnetic resonance spectroscopy (MRS) creates a specific spectral curve of the area of interest, because of its ability to depict the tissue chemical composition and analyze the radiofrequency signals generated by the precession frequency of different active molecules in an external magnetic field (B_0). In recent years, MRS has gradually been introduced into clinical practice. The capability of MRS to noninvasively determine the concentration of different metabolites in a certain tissue provides powerful biological information not given by other

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functional techniques performed with MR imaging, such as diffusion-weighted imaging (DWI) or dynamic contrast-enhanced (DCE) MR imaging. MRS can study different endogenous metabolites, such as phosphorus (^{31}P), carbon (^{13}C), sodium (^{23}Na), fluor (^{19}F), or hydrogen (^{1}H) protons. However, because of the high ^{1}H concentration in the human body and the absence of need for additional hardware, ^{1}H is the preferred option for most clinical applications, which also provides a higher signal-to-noise ratio (SNR).

The characterization and posttreatment follow-up of tumors in different regions is the most common clinical application of ^{1}H MRS. ^{1}H MRS has been used for tumor assessment of the central nervous system (CNS) for years, integrated as part of a multiparametric MR imaging protocol; in some clinical scenarios, it is the only tool with discriminative value.[1] Recent technical advances have favored the spread of ^{1}H MRS outside the brain. However, this technique has been integrated in clinical settings only in selected anatomic features, such as the prostate, where MRS has been successfully performed for cancer assessment.[2] This slow expansion is mainly because of technical difficulties that limit reproducibility between different centers. The use of MRS for evaluation of other anatomic areas, such as the breast or the musculoskeletal system, is emerging strongly but is still limited to a few centers with sufficient expertise. The implementation of MRS for evaluation of other abdominopelvic organs is progressing even more slowly, because this technique is prone to motion artifacts, but progress is steady and there have been promising results. For all these reasons, MRS has to be considered in the battery of functional MR imaging techniques for evaluation of cancer, because it provides unique biochemical information and can create a specific metabolic fingerprint of different malignancies.

In this review, the focus is on the principles and technical adjustments necessary to perform ^{1}H MRS in different organs; the clinical experience for the assessment of cancer in the brain and body is also analyzed.

Physical Bases

MRS is based on the same MR principle as conventional MR imaging and can excite and acquire information from nuclei with spin equal to half during the relaxation process. Unlike conventional MR imaging, in which frequency information of the received signal is used for imaging encoding, in MRS, this information is sensitive to the magnetic field shielding of the electron surrounding the nucleus. This property allows MRS to distinguish between different molecular bonds, and therefore, between different chemical compounds. MRS can use this capability to observe in vivo several metabolites, which provides biochemical information from living tissues.

A nucleus inside a molecular bond fills a magnetic field shielding, resulting in the combination of external magnetic field and the molecular bond electron shielding, which can be expressed as:

$$\omega_i = \gamma(1 - \sigma_i)B_o \quad \textbf{(1)}$$

where ω_i represents the MR frequency of a specific molecular bond, σ_i is the electron shielding of a this bond, γ represents the gyromagnetic ratio, and B_0 represents the external magnetic field.

From Equation 1, it can be observed that the direct comparison of peak position inside MRS spectra depends on the external magnetic field, making it difficult to compare spectra results acquired at different magnetic field strengths. To overcome this limitation, a new scale called parts per million (ppm) (Equation 2) allows direct comparison of the electron shielding, avoiding any dependency with the external magnetic field.

$$\text{ppm} = \frac{\omega - \omega_0}{\omega_0} \times 10^6 = \frac{\sigma - \sigma_0}{1 - \sigma_0} \times 10^6 \quad \textbf{(2)}$$

Information from MRS is normally represented as a spectroscopic signal (**Fig. 1**) with different peaks located in a specific frequency position (or ppm) that are associated with a particular molecular bond, and therefore, with a determined metabolite. **Fig. 1**A shows a conventional ^{1}H spectrum of the brain of a healthy volunteer, in which different peaks associated with defined metabolites can be distinguished.

Clinical Information

MRS is able to obtain information from metabolites that are present at the cellular level with millimolar concentrations ($\sim 1e^{-4}$ times less concentration than water). Those metabolites that have less than millimolar concentration are difficult to be detected in a conventional MRS experiment due to their decrease in signal in the noise range. Lack of MRS signal, due to low concentration of the metabolites, needs to be compensated during MRS acquisition, limiting the minimum voxel size or increasing the number of repetitions to average the signal to reduce noise contamination.

Most of the relevant proton metabolites that can be found in a conventional MR spectrum are described in **Table 1**.