Multiparametric Imaging Analysis
Magnetic Resonance Spectroscopy

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KEYWORDS

• Magnetic resonance spectroscopy • *N*-acetyl aspartate • Choline • Glioma • Cerebral metastasis • Lactate • 2-Hydroxyglutarate • Brain tumor

KEY POINTS

- Magnetic resonance spectroscopy (MRS) is a noninvasive technique that allows the study of metabolic processes and chemical environment in the brain parenchyma.
- MRS is one of the few diagnostic techniques that can be used for evaluation of low-grade neoplastic processes and for their differentiation from non-neoplastic entities.
- Despite many technical and reimbursement challenges to its use in routine clinical practice, MRS will continue to develop as an important and sensitive imaging tool for assessment of intracranial pathologies.

DISCUSSION OF PROBLEM/CLINICAL PRESENTATION

MRS allows the qualitative and quantitative assessment of specific metabolites in the brain parenchyma or intracranial extra-axial spaces. MRS analysis of brain tumors can be performed using ^{1}H (proton) MRS or, less frequently, with ^{31}P (phosphorus) or ^{13}C (carbon) MRS techniques. For ^{1}H MRS, the most common metabolites evaluated in routine clinical practice include *N*-acetyl aspartate (NAA), choline-containing compounds (Cho), creatine (Cr), myo-inositol (mI), lipid (Lip), and lactate (Lac) (**Table 1**). NAA is considered a neuronal metabolite and is decreased in processes with neuronal destruction or dysfunction.[1] Cr is a metabolite related to the cellular energy metabolism and is considered relatively stable in different pathologic processes affecting the central nervous system and useful as a reference metabolite. Cho are related to membrane turnover and their elevation is indicative of a process that results in increased glial proliferation and membrane synthesis (as seen with cellular proliferative disorders).[2,3] Lip peaks are often indicative of areas of necrosis and Lac peaks are directly originated from processes resulting in anaerobic metabolism. mI can be a marker of astrocytic metabolism and can be seen elevated in certain pathologic processes (see **Table 1**).

Common diagnostic problems encountered in routine clinical brain tumor imaging can be summarized as follows.

Is It Neoplastic or Not?

Non-neoplastic processes, including malformations of cortical development (such as focal

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Table 1
Metabolites evaluated with magnetic resonance spectroscopy in brain tumor imaging

Metabolite	Peak Configuration	Resonance (ppm)	Best Echo Time for Detection	Clinical Associations
NAA	Singlet	2.0	Short or long TE	Neuronal marker (not seen in non-neural brain tumors)
Cho	Singlet	3.22	Short or long TE	Membrane turnover marker and cellular proliferation
Cr	Singlets	3.03 and 3.9	Short or long TE	Cellular energy byproduct. Lower in necrosis[63]
mI	Multiplets	3.56	Short TE	Low-grade gliomas, gliomatosis[4]
Lip	Broad peaks	0.9, 1.3	Short TE	Tuberculomas, PCNSL, radiation necrosis
Lac	Doublet	1.33	1.5T = inverted at 135–144 ms 3T = 288 ms	Anaerobic metabolism marker Prominent if necrosis or hypoxia
Glx	Multiplets	2.1–2.4 ppm; 3.7 ppm	Short TE	Detected in GBM, astrocytomas and oligodendrogliomas
Taurine	Triplets	3.4	Short TE	Medulloblastomas
Alanine	Doublet	1.47	1.5 T = 144 ms	Meningiomas
Citrate[30,64]	Multiplets	2.6	3T = 35 ms and inverts at 97 ms	Gliomas, particularly aggressive pediatric types
Gly[65–67]	Singlet	3.55	3T = 160 ms[67]	Low-grade gliomas, central neurocytomas
2HG[31,68]	Multiplets	1.85, 2.01, 2.28, and 4.05	Best seen with spectral editing techniques 3T = 97 ms[68]	IDH mutations

Adapted from Chronaiou I, Stensjoen AL, Sjobakk TE, et al. Impacts of MR spectroscopic imaging on glioma patient management. Acta Oncol 2014;53(5):583.

cortical dysplasia) (**Fig. 1**), hamartomas, cerebral infarcts, infectious pathologies, inflammatory diseases (including demyelinating and vasculitic processes), and vascular pathologies (including capillary telangiectasias and cavernous malformations), can be difficult to differentiate from intra-axial or extra-axial intracranial neoplastic processes in conventional magnetic resonance (MR) studies (**Table 2**). MRS is a useful imaging tool to help in the differentiation and characterization of these pathologies. Neoplastic processes have metabolic byproducts related to their mitotic activity (Cho) and neuronal dysfunction (NAA) that can be detected by MRS and improve the accuracy of the clinical diagnosis (**Fig. 2**). The closer the MR spectrum is to a normal spectrum the more likely that the intracranial lesion is a benign process or developmental anomaly (see **Fig. 1**). There is significant overlap in the Cho/NAA ratios, however, between non-neoplastic processes, such as tumefactive demyelinating lesions, infarcts, and infectious processes with neoplastic pathologies. Specific metabolic markers have been identified that may make this distinction more reliable (eg, glutamate/glutamine [Glx] for demyelination or 2-hydroxyglutarate [2HG] for isocitrate dehydrogenase [IDH] 1–mutant gliomas).

Is the Lesion a Primary or a Secondary Brain Tumor?

Several studies have shown the utility of MRS, particularly using the multivoxel technique for differentiation of glioblastoma from an intracerebral metastasis.[4] The assessment of normal-appearing brain parenchyma in the immediate