

# Adult Brain Tumors

## Clinical Applications of Magnetic Resonance Spectroscopy



Lara A. Brandão, MD<sup>a,b,\*</sup>, Mauricio Castillo, MD<sup>c</sup>

### KEYWORDS

- Proton magnetic resonance spectroscopy (H-MRS) • Adult brain tumors • Tumor histology
- Tumor grade • Tumor extension • Tumor progression • Therapeutic response
- Differential diagnosis

### KEY POINTS

- Proton magnetic resonance spectroscopy (H-MRS) may be helpful in suggesting tumor histology and tumor grade and may better define tumor extension and the ideal site for biopsy compared with conventional magnetic resonance imaging.
- Combining H-MRS with other advanced imaging techniques such as diffusion-weighted imaging, perfusion-weighted imaging, and permeability maps improves diagnostic accuracy for intraaxial brain tumors.
- Short echo time allows for recognition of more metabolites than long echo time, which is important for differential diagnosis of brain masses and grading tumors.
- Higher choline (Cho) levels and lower myoinositol (Myo)/creatine (Cr) ratio are seen in more malignant tumors compared with lower-grade tumors.
- Lactate is directly related to tumor grade in adult brain tumors. However, lactate is found in essentially all pediatric brain tumors regardless of histologic grade.
- Gliomas are often invasive and show increased Cho levels in surrounding tissues, which may be used to distinguish these lesions from metastases.
- When lipids and lactate are found in a solid lesion, lymphoma should be suggested.
- A prominent lipid peak is seen in lymphomatosis cerebri, whereas a significant increase in Myo is characteristic of gliomatosis cerebri.
- A significant increase in the Cho peak and the presence of lipids and lactate are commonly seen in pilocytic astrocytoma, a grade I tumor.
- Typically, higher levels of Cho occur in grade III gliomas; whereas, in glioblastoma multiforme, the Cho levels may be much lower as a result of necrosis.
- If the Cho/N-acetylaspartate ratio is increased outside the area of enhancement, tumor infiltration can be diagnosed.
- An increase in Cho-containing compounds after radiation therapy may be seen in radiation necrosis misclassified as tumors.
- H-MRS in specific cases improves the accuracy and level of confidence in differentiating neoplastic from nonneoplastic masses.

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<sup>a</sup> Clínica Felipe Mattoso, Av. Das Américas 700, sala 320, Barra da Tijuca, Rio de Janeiro 30112011, Brazil;

<sup>b</sup> Clínica IRM- Ressonância Magnética, Rua Capitão Salomão 44 Humaitá, Rio de Janeiro 22271040, Brazil;

<sup>c</sup> Division of Neuroradiology, Department of Radiology, University of North Carolina School of Medicine, Room 3326, Old Infirmary Building, Manning Drive, Chapel Hill, NC 27599-7510, USA

\* Corresponding author. Clínica Felipe Mattoso, Av. Das Américas 700, sala 320, Barra da Tijuca, Rio de Janeiro, CEP 30112011, Brazil.

E-mail address: larabrandao.rad@terra.com.br

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## INTRODUCTION

Localized proton magnetic resonance spectroscopy (H-MRS) of the human brain, first reported more than 20 years ago,<sup>1–3</sup> is a mature methodology used clinically worldwide for evaluation of brain tumors.<sup>4</sup> H-MRS may help with differential diagnosis, histologic grading, degree of infiltration, tumor recurrence, and response to treatment mainly when radiation necrosis develops and is indistinguishable from tumor by conventional magnetic resonance (MR) imaging.<sup>5</sup> Combining H-MRS with other advanced imaging techniques such as diffusion-weighted (DW) imaging, perfusion-weighted (PW) imaging, and permeability maps improves diagnostic accuracy for intraaxial brain tumors.<sup>6–8</sup>

## TECHNIQUE

### *Short Echo Time Versus Long Echo Time*

Different H-MRS parameters may be optimized and 1 of the most relevant is echo time (TE).<sup>9</sup> Short TE allows for recognition of more metabolites than long TE, which is important for differential diagnosis of brain masses and grading tumors. For example, myoinositol (Myo), a marker for low-grade gliomas, is only seen on short TE acquisitions.<sup>5</sup>

### *Multivoxel MRS Versus Single-Voxel MRS*

A key consideration for brain tumor evaluations is their metabolic inhomogeneity. Multivoxel (MV) techniques, also called chemical shift imaging (CSI),<sup>10</sup> simultaneously record spectra from multiple regions and therefore map the spatial distribution of metabolites.<sup>11</sup> MV H-MRS provides smaller volumes of interest compared with single-voxel (SV), avoiding sampling error. For these reasons, high-resolution MV MRS such as MRS imaging is often favored for evaluating brain tumors.<sup>5,12</sup> Nevertheless, SV H-MRS has some advantages compared with MV techniques.<sup>13</sup> SV H-MRS is quicker and easier to obtain in standard clinical settings, providing the opportunity to obtain more than 1 spectrum (ie, spectra at 2 different TEs) in a reasonable amount of time. Evaluating spectra at both short and long TE improves the level of accuracy in differentiating focal brain lesions.<sup>13</sup> SV H-MRS provides better quality spectra compared with MRS imaging. The authors recommend that both techniques be used in the evaluation of brain masses (Fig. 1).

## SPECTRAL PATTERN OF TUMORS

The spectral pattern of intracranial tumors may vary according to histology and malignancy grade and is discussed here.<sup>14–18</sup>

### *Reduction in N-Acetylaspartate Levels and in N-Acetylaspartate/Creatine Ratio*

Reduction in N-acetylaspartate (NAA) levels and NAA/creatine (Cr) ratio is observed in tumors, indicating decreased viability and number of neurons (see Fig. 1; Fig. 2). The reader should bear in mind that in low-grade gliomas, the spectral pattern might be similar to that of normal brain (Fig. 3).<sup>19</sup> Absence of NAA in an intraaxial tumor generally implies an origin outside the central nervous system (metastasis) (Fig. 4) or a highly malignant tumor that has destroyed all neurons in that location (Fig. 5).<sup>5</sup>

### *Decreased Cr Levels*

Decrease in Cr may occur, representing energy failure in aggressive malignant neoplasms (see Figs. 1 and 2).

### *Increase in Choline Levels and in Choline/NAA and Choline/Cr Ratios*

An increase in choline (Cho) levels is shown by an increase in the Cho/NAA or Cho/Cr ratio, rather than its absolute concentration. Increased Cho is associated with higher turnover in the cell membrane and higher cell density resulting from proliferation of tumor cells (see Figs. 1 and 2).<sup>20,21</sup> In tumors, Cho levels correlate with the degree of malignancy and are linearly correlated with cell density (the inverse of what is seen with the apparent diffusion coefficient [ADC]) instead of the proliferative index. Higher Cho levels are seen in more malignant tumors (see Figs. 1 and 2) and lower levels in lower-grade tumors (see Fig. 3). Cho is usually higher in the center of a solid mass and decreases peripherally. Cho is consistently low in necrotic areas (see Fig. 5).<sup>5</sup>

### *Myo*

Myo is a glial marker because it is primarily synthesized in glial cells, almost only in astrocytes. The Myo/Cr ratio is usually higher in lower-grade (see Fig. 3) than in higher-grade tumors (see Fig. 2).<sup>22</sup>

### *Lactate Peak*

Increased lactate levels are likely the result of anaerobic glycolysis, although they can also be due to insufficient blood flow leading to ischemia or necrosis.<sup>23,24</sup> Lactate is directly related to tumor grade in adult brain tumors, with higher peaks seen in higher-grade tumors (see Fig. 2). However, lactate is found in essentially all pediatric brain tumors regardless of histologic grade.

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