THE ROLE OF MR SPECTROSCOPY IN NEUROONCOLOGY

Kozić D, Ostojić J, Bjelan M, Koprivšek K

University of Novi Sad School of Medicine, Institute of Oncology, Diagnostic Imaging Centre, Sremska Kamenica, Novi Sad, Serbia

Abstract: Magnetic resonance spectroscopy (MRS) is a diagnostic tool that provides information related to brain’s metabolic activity. Literature data suggest that elevation of the ratio between the choline and creatine (the Cho/Cr ratio), the reduction of the ratio between n-acetyl-aspartate acid and creatine (the NAA/Cr ratio), increase of the ratio between myo-inositol and creatine (the MI/Cr ratio), and the presence of lipids and lactate are useful diagnostic markers in grading tumors as well as in the prediction of tumor malignancy potential. Two additional important roles of MRS are differentiation between recurrent tumor and radiation necrosis and evaluation of peritumoral region.

Key words: magnetic resonance spectroscopy, tumor evaluation, brain metabolism.

Introduction

The role of magnetic resonance imaging (MRI) and computerized tomography in detecting neoplastic processes of the central nervous system is well known. The numerous studies in the last decade have proved the importance of magnetic resonance spectroscopy (MRS) in further categorization of human brain tumours [1].

Basic principles

MRS is a diagnostic tool that provides information regarding "brain chemistry". The most frequently used nuclei are hydrogen, sodium and phosphorus. Due to its better signal to noise ratio compared to other nuclei, hydrogen (proton) MRS is today most widely applied in clinical practice.
Two types of proton MRS are routinely performed – single voxel and multivoxel MRS. Single voxel imaging involves the sampling of only one region of tissue (Figure 1), while in the multivoxel method, also referred to as chemical shift imaging, spectroscopic information is obtained from multiple adjacent areas, over a large volume of interest (Figure 2).

Figure 1 – Single voxel MRS in the grey matter (a) and white matter (b) of the normal brain parenchyma

Figure 2 – Multivoxel MR spectroscopy of the supratentorial brain parenchyma
While MRI creates an image, MRS creates a graph, or "spectrum" showing the types and quantities of the chemicals within the brain parenchyma (Figure 3). Metabolites that are most frequently identified in MRS are: N-acetyl aspartate (NAA), a neuronal marker located on the scale at 2.0 ppm, choline (Cho), a marker of the cell membrane function, at 3.2 ppm, creatine (Cr), a marker of energy storage in the brain, at 3.0 ppm, lactate, a product of anaerobic glycolysis, at 1.3 ppm, lipids – markers of brain tissue destruction, between 0.9 and 1.4 ppm, neurotransmitters – glutamine/glutamate compound, between 2.2 and 2.4 ppm and myo-inositol (MI), glial cell marker, at 3.5 ppm. In order to obtain the spectrum of metabolites, water elimination is necessary.

The water suppression is usually done using the CHESS (Chemical Shift Selective Imaging), while the excitation of the metabolites is done using three-pulse schemes such as STEAM (stimulated echo acquisition model) or PRESS (point resolved spectroscopy) which excites a 3-dimensional box in the brain. Using shorter echo times (~30 msec) increases the signal to noise ratio (SNR), and therefore more metabolites can be detected. To avoid lipid contami-
nations, longer echo times (e.g. ~270ms) are also used, which comes at the cost of decreased SNR, still good enough for reliable estimation of the main metabolites like NAA, Cr and Cho.

The most widely accepted method in the evaluation of spectra is to determine the absolute metabolic ratios [2]. The normal Cho/Cr ratio is up to 1.2, while any value above 1.5 is considered abnormal. Normal NAA/Cr ratio is 2.0, while any value below 1.6 is considered abnormal. Normal NAA/Cho ratio is 1.6.

Characteristics of MRS in gliomas and non-glial tumours

Gliomas are the most frequent primary neoplasms of the central nervous system and are classified into four grades by the World Health Organization (WHO). Tumour grading is very important for preoperative treatment planning. Conventional MRI may fail to accurately determine the glioma grade, especially between grade II and grade III.

In almost all patients with brain tumours MRS is abnormal at presentation. The reduction of NAA is compatible with the loss of neuronal elements since they are destroyed or replaced by tumour cells. The reduction of the Cr peak is a less prominent finding, most likely consistent with altered brain metabolism. The elevation of the choline peak in brain tumours is associated with an increase in membrane synthesis and accelerated cell proliferation. The rise of the MI peak in the tumoural region is most compatible with proliferation of glial tissue since this metabolite is found to be related with the breakdown of myelin. Elevated lactate is commonly seen in glioblastoma multiforme, suggesting the presence of tumour hypoxia [3–5]. Although the aforementioned findings are seen in both low-grade and high-grade tumours, marked elevation of the Cho/Cr ratio and a more prominent drop of the NAA peak suggests the presence of high-grade glioma (Figure 4 and 5). Complete lack of NAA and Cr peaks may suggest a non-glial origin of the neoplasm. Elevated Cho and lipid peaks are typical of metastatic disease of the brain (Figure 6), while a "choline only" spectrum is characteristic of non-glial intraaxial neoplasms [6, 7]. The additional presence of alanine is seen in meningiomas [8].

Extensive literature data show that Cho/Cr, NAA/Cr and MI/Cr ratios and the presence of lipids and lactate are useful in grading tumors and prediction of tumour malignancy potential. The presence of necrosis is considered an important factor in distinction between anaplastic astrocytoma (grade 3) and glioblastoma multiforme (grade 4). The presence of lipids suggests necrosis within neoplastic tissue due to membrane breakdown [1].

It has been reported that NAA level is reduced to 40–70% of its normal value in astrocytomas, with a trend of more prominent NAA level decrease with the advanced tumor grade [9–12]. However Bulakbasi et al. could not find any statistically significant relation between the decrease in NAA level and the tumour grade [3]. Oya et al. evaluated the utility of proton MRS in bone and soft tissue tumours, in order to detect whether or not a NAA signal could be recognized at 2.0–2.1 ppm. The signal was not found in neurofibroma (9/9), schwannoma (6/6), pheochromocytoma (2/2) and other mesenchimal tumours of non-neuroectodermal origin [13].

Figure 4 – Astrocytoma grade 3, with significantly increased Cho/Cr ratio and markedly reduced NAA

Figure 5 – Glioblastoma multiforme. Extremely increased Cho/Cr ratio with complete absence of NAA, compatible with severe neuronal destruction
Also, even in high-grade gliomas, both Cho and Cr peaks are usually well defined and separated while in extraaxial tumours the Cr peak is either completely not detected or presents with a "shoulder"-like appearance at the bottom of the Cho peak. Information obtained from MR spectroscopy, consistent with a rather typical "extraaxial neoplasm pattern" could be quite a reliable indicator that helps in the differentiation between glioma and the non-glial nature of the unusual malignant cranial tumour [14, 15]. In the investigation of Moller-Hartman et al. the additive information from MR spectroscopy led to a 15.4% higher number of correct diagnoses and to a 6.2% lower number of incorrect diagnoses compared to MR imaging alone, while 16% fewer equivocal diagnoses were also observed [11]. In the study that included 164 patients, neither MRI nor MRS alone provided a degree of accuracy sufficient for reliable preoperative differential diagnosis of brain tumours. However, by combining these two modalities, a high level of diagnostic accuracy was achieved [15].

Multivoxel MRS might be useful in detailed evaluation of the metabolic profile in large gliomas, and might have an advantage over stereotactic biopsy since primary tumours are often histopathologically heterogenous and may have components of varying grades of malignancy within the tumour.

*Figure 6 – Brain metastatic disease associated with elevated choline and lipid peaks*

**Other roles of MRS in neurooncology**

Two additional important roles of MRS are differentiation between recurrent tumours and radiation necrosis and evaluation of the peritumoral region. Increase in Cho and glutamine-glutamate peaks in the peritumoral zone that appears normal on conventional MRI, correlates with high-grade gliomas and poor prognosis. Evaluation of the peritumoral zone could also be helpful in
differentiating between metastatic disease and high-grade glioma, since the peritumoral zone adjacent to metastasis shows no significant elevation of the two aforementioned metabolites.

Due to disruption of the blood brain barrier, contrast enhancement is evident in both radiation necrosis and recurrent high-grade gliomas. Elevation of Cho peak and Cho/Cr ratio above 1.7 suggests the recurrent neoplasm [16].

**MRS and evidence-based medicine**

Unfortunately, MRS is still not considered a proven evidence-based diagnostic modality. An assessment of MRS prepared by the Tuft’s New England Medical Center Evidence-Based Practice Center for the Agency for Healthcare Research and Quality, by the Center for Medicare and Medical Services and by the BlueCross BlueShield Association Technology Evaluation Center, concluded that MRS was a beneficial non-invasive diagnostic tool for some of the proposed indications, but with still insufficient evidence to permit conclusions regarding diagnostic applications [17].

**Acknowledgement**

This work has been supported by the Ministry of Science and Technological Development of Serbia, Scientific Project Number 175022.

**REFERENCES**


Резиме

УЛОГАТА НА MR СПЕКТРОСКОПИЈАТА ВО НЕВРООНКОЛОГИЈАТА

КОЗИЈ Д., ОСТОЈИЋ Ј., БЈЕЛАН М., КОПРИВШЕК К.

Медицински факултет, Универзитет во Нови Сад,
Институт за онкологија, Дијагностички центар,
Сремска Каменица, Нови Сад, Србија

Апстракт: Спектроскопското снимање со магнетна резонанса (ССМР) претставува дијагностичка алатка која овозможува да се добијат информација поврзани со метаболитската активност на мозокот. Досегашните резултати од стручната литература сугерираат дека покачениот срзмер меѓу холинот и креатинот (или Cho/Cr срзмер), покачениот срзмер меѓу Н-ацитевно-асперативната киселина и креатинот (или NAA/Cr срзмер), покачениот срзмер меѓу мионоситолот и креатинот (или MI/Cr срзмер), како и присуството на липиди и лактати, не се само корисни дијагностички маркери за мозочни тумори, туку и за предвидување на малигнит потенцијал на туморот. Две дополнително важни улоги на ССМР се можностите за диференцијација меѓу повторувачки тумор и некроза од зрачење, како и евалуација на ткивото околу туморот.

Клинички зборови: спектроскопија со магнетна резонанса, евалуација на тумори, мозочен метаболизам.

Corresponding Author:

Kozić D.,
Institute of Oncology
University of Novi Sad School of Medicine
Sremska Kamenica,
Novi Sad, Serbia
E-mail: dusko.b.kozic@gmail.com

Прилоги, Одн. бил. мед. науки, XXXIII/I (2012), 425–433