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Evaluation of brain energy metabolism and intracellular pH level using phosphorus (^{31}P) MR spectroscopy

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Abstract. Evaluation of brain tumor metabolism is an important issue in brain tumor studies. Phosphorus magnetic resonance spectroscopy (31P-MRS) allows noninvasive examination of metabolic changes occurring in pathologic brain tissue by measuring intracellular pH level based on obtained spectra of phosphorus-containing metabolites involved in cell membrane phospholipids turnover. The purpose of this study was pHmetry of brain tumors using 31P MRS.

The mean pH level of the control group of healthy volunteers (N=23) was 6.963 ± 0.044 . Measured PME/PDE= 1.17 ± 0.20 .

31P MRS demonstrates highly reproducible results opening prospective for comparative studies with the diseased groups (mainly gliomas) and further translation to the clinical practice.

1. Introduction

Methods of magnetic resonance spectroscopy (MRS) along with conventional MRI are widely used in diagnosis of brain lesions. The method of phosphorus (^{31}P) MRS allows to study energy metabolism of brain tissue by obtaining spectra of phosphorus-containing metabolites. These metabolites play an important role in the energy cell metabolism and their concentration in the white and gray matter is quite high. It is also supposed that ^{31}P MRS is able to detect brain pathology at the earliest stages of structural change, which can be visualized on anatomical images later. Also 31P MRS allows assessing intracellular pH level of brain tissue noninvasively.

The purpose of this study was evaluation of brain energy metabolism and intracellular pH level using 31P MRS.

2. Methods and materials

All measurements were performed on 3T GE Signa 3.0 MR System using a twin 1H-31P coil (figure 1 a). The study included 23 healthy volunteers aged from 19 to 28 y.o. (mean age 25 ± 1.84 ; 15 males, 8 females). Region of interest (6x6x2 cm) was located similarly in all subjects and did not contain large blood vessels and brain ventricles (figure 1 b). Signals from outside of the ROI were suppressed by targeting of presaturation areas. After that, the parameters of the coil were tuned by phosphocreatine peak at phosphorous frequency (51.7 MHz) and 31PMR spectroscopy was performed for 12 minutes. The phosphorus spectra were processed in the SAGE software by GE. Calculation of intracellular pH was carried out according to the formula obtained by Petroff et al [1], where δPi is the chemical shift of inorganic phosphate (Pi) relative to the peak of phosphocreatine (PCr) (figure 2):



$$pH = 6.77 + \log\left(\frac{\delta Pi - 3.29}{5.68 - \delta Pi}\right) \quad (1)$$

3. Results

The stable phosphorus spectra of the normal brain tissue were obtained. The peaks of main metabolites were identified. Intracellular pH level was measured for each volunteer. The phospholipids integrity was calculated by measuring PME/PDE ratio. The results are shown in table 1.

Table 1. The mean value of pH level and PME/PDE ratio

PME/PDE	1.17±0.20
pH	6.963±0.044



Figure 1 (a). Twin 1H-31P coil.

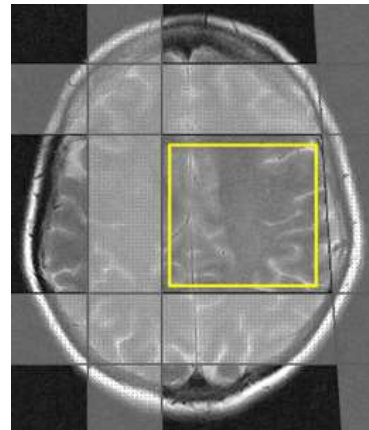


Figure 1 (b). Region of interest (ROI).

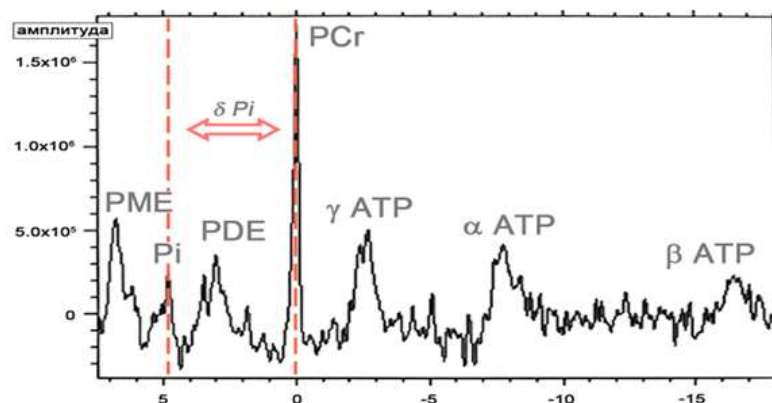


Figure 2. Determination of the chemical shift of inorganic phosphate relative to the peak of phosphocreatine on the example of the phosphorus spectrum of a healthy volunteer, male 25 years old (explanations in the text).

4. Discussion

The highest peak of the spectrum is phosphocreatine (PCr). There are three peaks of adenosine triphosphate (ATP) to the right of PCr. There is a peak of phosphodiester (PDE) to the left of PCr. This peak can be elevated in case of increased degradation of cell membrane phospholipids [2]. The peaks next to PDE are inorganic phosphate (Pi) and phosphomonoesters (PME). The main components of PME peak are phosphocholine and phosphoethanolamine. They are precursors of cell membrane phospholipids and involved in biosynthesis of phosphoglycerides [3]. PCr and ATP are high-energy phosphate compounds, whereas PME, PDE and Pi are low-energy phosphates. Comparisons of their indicators are often used in the assessment of brain metabolism.

The PME / PDE ratio can serve as an index of cell membrane phospholipids metabolism. It reflects changes in the membrane synthesis rate and cell membrane phospholipids turnover. Thus, it can be regarded as a marker of malignancy or continued tumor growth or tumor response [4, 5]. However, the results of measurement of the digital values of PME/PDE ratio are different in previous studies. For instance, in our study the mean of the ratio PME/PDE was 1.17 ± 0.20 . It differs from the result obtained by Ha D. et al. which was 0.47 ± 0.07 [3]. The cause of this variance might be a difference in technical parameters of MRI system, such as magnetic strength, and/or a difference in ROI sizes.

The mean intracellular pH value was 6.963 ± 0.04 (the median value was 6.945, the minimum was 6.89, and the maximum was 7.05). This is lower than values obtained by Maintz D. et al, Ha D. et al, Wenger K. et al [4, 3, 6] and were 7.04 ± 0.01 ; 7.07 ± 0.1 ; 7.017 ± 0.026 respectively. However, the maximum pH value in our study (7.05) is within the range. This variation of values may be explained by the fact that pH level changes with age [7]. Our group of healthy volunteers was young and uniform in age.

Limitation of ³¹P MRS are related to the identification complexity of the main metabolites peaks in vivo studies and numerous artifacts, most often caused by metal implants, blood flow and patient movements

³¹P MRS could be an important tool to study pathogenic pathways of brain lesions in the long term. In order to adapt this method to the clinical setting further investigation are required.

5. Conclusions

³¹P MRS is an advanced noninvasive method that demonstrates highly reproducible results, reflecting important information about the metabolic processes and intracellular pH level of brain tissue in health and disease.

Acknowledgements

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