Non-Invasive Multi-Parametric in vivo Mapping of the Brain Tumors and Brain Metastases

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Abstract — However, magnetic resonance (MR) is a well-known non-invasive medical tool, its modalities are not routinely used in the clinical oncologic practice. The multi-modal comprehensive set of computer-evaluated quantitative MR parameters of the brain tissue in patients with suspected intracranial tumors could provide more recent, more accurate and wealthier information about the tumor tissue. Most helpful are in this regard, proton and phosphorus magnetic resonance spectroscopy (1H and 31P MRS), relaxometry of T2 values, dynamic- contrast enhancement MRI (DCE MRI), and diffusion-weighted MRI (DWI). Their measurement techniques, evaluating methods as well as clustering multi-parametric analysis could be key instruments in diagnostic of intracranial tumors.

Keywords—Brain tumor; cancer metastases to brain; magnetic resonance; MRS; T2 relaxation; DCE MRI, DWI

I. INTRODUCTION

The standard in the diagnosis of brain tumors and brain cancer metastases is to use magnetic resonance imaging (MRI), which can help to estimate the tumor nature and the degree of its malignancy, although, this determination can be subjective and not always accurate [1], [2]. The computer quantification processes also data obtained from MR but uses the computer algorithm.

The mathematical algorithm does not process optical information useful for diagnostic radiologists as it is the case of clinical MRI, but the exact values of the specified parameters for a specific area in the healthy or tumorous brain tissue. Exact computer evaluation of these parameters helps to estimate histological type of tumor and the degree of malignancy in a specific way [3]-[5]. The MR parameters bring useful information about the healthy or tumorous brain tissue and so increase the sensitivity and specificity of measurements [6], [7]. Moreover, the new MR methods could be widely applied for monitoring of the brain tumors and help to set targeted therapy [8], [9]. High informative contribution and individualization of therapeutic approach could also have economic impacts in savings for medicaments and other medical equipment.

Proton magnetic resonance spectroscopy (1H MRS) requires recording the signal of resonating ¹H nuclei in specific chemical compounds, which transform into the form of metabolites peaks (Fig.1) [10], [11]. In this way, 1H MRS provides to noninvasively investigate the brain tissue metabolism in vivo, allow to get information about neuronal function (e.g., concentration of the most abundant neurotransmitters, glutamate -Glutamine -Gln), and γ-aminobutyric acid -GABA) and neural viability (typical marker is tNAA, N-acetylaspartate and N-acetyl-aspartyl-glutamate), about the membrane changes (signal of choline-containing components, tCho), as well as about cellular biochemical and energetic processes (peaks of myoinositol -ml or creatine-containing compounds, tCr), [1], [12], [13]. Alternation of brain metabolite (i.e., increased lactate, lipids or macromolecules), can be also detected by 1H MRS and thus indicate pathological tissue changes, even long before it becomes noticeable [14], [15]. Accurate spectra evaluation is challenging and usually performed by specific software, e.g. LModel (Provencher) [16], jMRUI (MRUI Project) [17], jSIPRO (jSIPRO package) [18] and other home-made tools. Many studies declare that by using 1H MRS it is possible to clearly distinguish some histological types and grades of malignancy of brain tumors [19], [20].

Phosphorus magnetic resonance spectroscopy (31P MRS) allows evaluating spectral peaks of compounds, which function groups contain resonating phosphorus (31P) nuclei [4], [5], [21]. Thus is possible to investigate levels of important brain metabolites including (Fig.1): energy markers
- phosphocreatine (PCr), inorganic phosphate (Pi) and peaks of adenosine triphosphates: α-ATP, β- and γ-ATP; metabolites of membrane phospholipids synthesis - phosphomonoesters (PME) and metabolites of membrane phospholipids degradation - phosphodiester (PDE), [22] - [24]. The most widespread evaluated software is in this case jMRUI (MRUI Project) [17], however, various in-house-developed software’s using Matlab (Math Works, Natick, MA), Bash (Software Foundation, Boston, MA), or MINC (MINC tools, McConnell Brain Imaging Centre, Montreal, Canada) have been so far developed [25]. That, 31P MRS is an appropriate oncologic tool has been declared in many previous studies, which show that in the brain tumor tissue, it can be observed an increase in cell proliferation (increased levels of PME, PDE), increased energy consumption (increased levels of ATP and Pi; decreased PCr) and the presence of anaerobic metabolism (alkaline intracellular pH) [24], [26], [27].

**Fig. 1 Non-invasive investigation of the brain tumorous tissue in vivo using 1H and 31P MRS enables to analyze alternation in specific metabolites. These spectra were measured on 1.5T MR scanner and evaluated by LCModel for 1H MRS (version 6.2-1L) and jMRUI (version 5.0-219) for 31P MRS**

**Relaxometry, or mapping of T2 relaxation time** is based on evaluating tissue-characteristic T2 values, which reflect mobility and chemical environment of analyzed brain structure [28] - [30]. Thus it enables a noninvasive investigation of tissue microstructure, its intra- and extracellular fluid volume [7], [31], [32]. Measurements are carried out as series of different T2-weighted MRI, and subsequently by a range of possible methodologies and software’s calculate appropriate characteristic tissue parameters or their maps (Fig.2) [33] - [35].

The relaxometry in tumors reach different T2 values than in healthy tissue, while their reflect changes in chemical composition of the tissue [36] - [39].

**Fig. 2 Non-invasive investigation of the brain tumorous tissue in vivo using relaxometry (T2-mapping) enables to analyze cellular density and microvascularity of the tissue. These data were measured on 1.5T MR scanner and evaluated by in-house-developed package using Matlab (Math Works, Natick, MA)**

**Diffusion - weighted MRI (DWI)** allows evaluating the diffusion of water molecules within microstructures insight the brain. By applying the MR pulse set, the reduced water diffusion in the tissue is represented as an increased signal on MRI [40] - [42], which could, in fact, be evaluated in each in-house-developed software. DWI distinguish tumors due its typically increased cellularity, and hence a slowing movement of water molecules [5], [40]. When DWI is measured in various directions, there is obtain more information (e.g., apparent diffusion coefficient, ADC, related to cell size and density; fractional anisotropy, FA, reflected spatial tissue organization), which could be presented as a diffusion tensor imaging (DTI or tractography) - visualization of the tract of axons in brain tissue [11], [32], [42]. It has been shown that the ADC and FA values contribute to the identification of the tumor process, as well as DTI enable determinate tumor position (Fig.3) [43], [44].

**Fig 3 Non-invasive investigation of the brain tumorous tissue in vivo using DWI and DCE MRI enables to analyze chemical composition of the tissue. These data were measured on 1.5T MR scanner and evaluated by in-house-developed package using Matlab (Math Works, Natick, MA)**

**Dynamic-contrast enhancement MR imaging (DCE MRI)** is a series of 3D T1-weighted MR images measured before and after intravenous administration of contrast medium. The gadolinium-based contrast agent is a paramagnetic substance that causes shortening of the T1 relaxation time [9], [40], and [45]. Therefore, the DCE MRI can differentiate tissues due to accumulation of contrast medium, reflecting the increased tissue vascularity [5], [46], [47]. The measured dynamic data could be evaluated in the form of kinetic curves (Fig.3) and in appropriate software (e.g., JIM-Xinapse Systems Ltd., Northants. UK) [48] it is
possible to obtain various physical parameters describing the tissue angiogenesis [49], [50]. The DCE MRI brings knowledge about the tissues pharmacokinetic properties and physiological parameters such as perfusion, the state of the blood-brain barrier, microvasculature or vascular wall permeability [51] - [53].

II. CONCLUSION

In conclusion, MR modalities are worldwide accepted non-invasive clinical methods and should gradually be integrated into the medical practice. They provide unique anatomical, morphological, as well as biochemical analysis of the tissue allowing more precise localization, more detailed and faster diagnosis and monitoring of the brain tumors [2], [11], [32], [44]. To achieve this target, it is crucial the optimal technical engineering approach.

REFERENCES


