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REVIEW PAPER

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Clinical application of advanced neuroimaging techniques – Magnetic Resonance Spectroscopy

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ABSTRACT

Continuous scientific research and the increasing saturation of the medical market in Poland implements the possibilities of using advanced MR techniques including MRS in everyday practice. This method, which has so far been used primarily for research purposes, can bring measurable benefits to patients not only in terms of clarifying diagnosis and narrowing differential diagnosis, but also monitoring the course of various diseases and their treatment. Here we present the basic principles of performing and interpreting spectroscopic spectra and possible clinical applications and development prospects of MRS. The literature reviewed both Polish and foreign articles both historically and in the past 10 years. The paper presents methodological issues related to the proper performance of magnetic resonance spectroscopy (MRS) and spectral composition and the role of major metabolites, as well as current clinical applications and directions of MRS development.

Keywords. spectroscopy, MR, SVS, CSI

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Introduction

The dynamic development of magnetic resonance over the past 30 years has led to the tumultuous development of diagnostic methods based on medical imaging. In the present era, we are no longer limited to structural imaging, showing anatomy and enabling detection of pathological changes in the central nervous system, mainly for CT and MR, but we also have the possibility (unfortunately not widely used) of imaging processes below the actual spatial MR resolution, based on advanced techniques such as Magnetic Resonance Spectroscopy (MRS), Diffusion Weighted Imaging (DWI), Diffusion Tensor Imaging (DTI), Perfusion Weighted Imaging (PWI), Susceptibility Weighted Imaging (SWI), and Functional Magnetic Resonance Imaging (fMRI). MRS is a non-invasive method of testing both *in vitro* and *in vivo* compounds in normal and pathological tissues, allowing for a semi-quantitative assessment of their metabolic composition and thus allowing for a biochemical evaluation of the various processes occurring in the body such as neoplastic lesions, degenerative processes, ischemic changes and many others.[1]

The basic phenomenon used in MRS is the so-called "chemical shift" and signal splitting associated with the shielding of hydrogen nuclei (^{1}H) and the local chemical environment respectively. The intensity of the signal corresponds to the amount of chemical compound present. The frequency differences are directly proportional to the magnitude of the external magnetic field B_0. The chemical shift of a peak measured in parts per million (ppm) reflects shielding factors in the magnetic environment of the molecule which may shift the position of the peak. The chemical shift in ppm is a dimensionless quantity obtained by dividing frequency in Hertz (Hz) by the field strength which makes it independent of the magnitude of the applied magnetic field. MRS uses signals not only of the ^{1}H nuclei, but also other nuclides such as ^{13}C, ^{15}N, ^{19}F, ^{23}Na and ^{31}P. Compared to ^{1}H MRS (hydrogen spectroscopy), other spectrometers such as those designed to study nucleic acids are characterized by lower sensitivity and require a significant prolongation of study time due to the significantly lower concentrations of these elements in the tissues. ^{1}H MRS is performed in standard MR systems with conventional RF coils, and additional spectrum detection and transmission equipment is required to obtain spectrum from ^{13}C, ^{19}F and ^{31}P. In practice, the most commonly used is ^{1}H MRS due to the key role of hydrogen in living organisms, although obtaining satisfactory spectra is associated with a rather complicated process and requires appropriate equipment, at least 1.5 T MR and appropriate software. As a result of the MRS study, we obtain the resonance spectra of the area of interest in coordinates (amplitude of the signal/shift) composed of so-called bands or peaks that have a location and shape specific to the metabolite, and the field size under each peak determines the amount of metabolite.[2] MRS allows you to study both simple and complex chemical compounds and, consequently, cells in both physiological and pathological states.[3] Practical use of MRS requires the use of a method for recording the spectrum from a selected region, referred to as "voxel" or more precisely as VOI (volume of interest). We have two location methods: SVS (single voxel spectroscopy); CSI (multi-voxel chemical shift imaging) or MVS (multi voxel spectroscopy) - multiple voxels - 2D/3D spectroscopy. The VOI should be adjusted so that it does not go beyond the test area. In SVS, the voxel can cover an area such as a small lesion and are limited if used in areas that undergoes changes in size (<1 cm), near bone, sinuses, fluid reservoirs, or blood since the results of the study are distorted. By using the SVS method, you can change the intensity of a solid magnetic field in a position-dependent manner, allowing you to record the spectrum from the selected voxel. The advantage of SVS is the high homogeneity of the test area, the ease of selectively in suppressing the water signal, the high signal to noise ratio (S/N ratio) and the short test time (4-8 min.). The sequences used in the SVS include: ISIS (Image-Selected *in vivo* Spectroscopy), STEAM (Stimulated Echo Acquisition Mode), PRESS (Point-Resolved Localized Spectroscopy).[4]

Multi-voxel CSI allows for the simultaneous recording of spectra from many adjacent voxels, allowing for spatial mapping of individual metabolites in the examined organ layer.[5] CSI allows for a large-scale assessment of a large area of both tumor and uncertain zones and edema and normal brain (tumor border evaluation), and is also important in biopsy planning. The advantage of CSI is the smaller voxel volume, larger coverage area, and higher spatial resolution. The need for long echoes (TEs) limits the information obtained to three major spectral spikes (N-acetyl aspartate - NAA, choline compounds - Cho, creatine and its derivatives - Cr). Also, adjacent voxel image contamination, and lower signal-to-noise are disadvantages of multi-voxel CSI.

Fundamental to achieving high sensitivity and resolution, the MRS study selects appropriate echoes and repetition times (TE and TR) and voxel size and position. TE spectrum time is recorded at different values (most commonly used are 20 ms, 30 ms, 135 ms, 144 ms and 270 ms). MRS spectra recorded at short TEs contain signals from most metabolites, whereas long TEs are used when lipid and intercellular signal is required, but the MRS spectrum is limited to NAA, Cr and Cho signals (**Figure 1**). Levels of metabolites and their ratios recorded with short and long TEs can vary. Fundamental to the high sensitivity and resolution of the MRS study is the selection of suitable TE and TR times and the size and position of the voxel.

The size of voxel in practice is usually 2×2×2 cm i.e. 8 cm^3. A small voxel volume gives better spectral resolution and field homogeneity, but increases test time (smaller vol-

ume → weaker signal → greater repetition). The greater voxel volume results in greater heterogeneity of the field associated with averaging the spectrum of healthy and pathologically altered tissues, which interferes with the proper proportions of metabolites and may falsify the results.

The strongest signal in the ^{1}H MRS spectrum is derived from water protons, which determines the need to suppress it so that it can record signals from other compounds. A similar problem applies to areas where fatty tissue predominates. The purpose is the CHESS (Chemical Shift-Selected Sequence) sequence. It is necessary to use a variety of correction techniques for FID (Free Induction Decay), undesirable signals, noise and deformation associated with acquisition to obtain the correct spectral spectrum. The stages of processing the resonant time domain signal (prior to Fourier transformation) are: offset correction (removal of the constant electrical current generated by the electronic circuit while the FID signal has disappeared to zero), zero filling (the signal is extrapolated by the addition of zero points, which improves resolution of the spectrum), apodization (signal multiplication by appropriate signal-to-noise correction functions). Phase conversion of the resonance signal in the frequency domain (after Fourier transform) is comprised of: phase correction (to obtain pure absorption spectrum), baseline correction (elimination of device artifacts and spectrum of large non-mobile molecules that underline baseline outlines). Calculation of the surface area under the resonance bands of metabolites (by calculating the value of the surface area under the resonance band curve) is the most direct and fast quantitative spectrum analysis method, however, this requires a lat baseline and well separated bands. Determining the molar concentrations of a substance on the basis of integrals of the corresponding resonant bands requires calibration, which encounters significant difficulties in *in vivo* studies. Because of these problems, the quantitative MRS results are most often used as the quotient of the intensity of the resonant signals of individual metabolites.[6] Calculation of absolute amounts of metabolites is possible in dedicated programs such as the LC Model.[7]

Proton spectra (^{1}H MRS) consists of peaks representing the most commonly occurring chemical compounds at a predetermined position – ppm: [1]

1. NAA - N-Acetyl Aspartate (2.02 ppm)
2. Cr + PCr - Creatine and Phosphocreatine (3.03 ppm, 3.93 ppm)
3. Choline compounds (3.20 ppm, 3.22-3.23 ppm)
4. I / m - Inositol, Myo-inositol (3.56 ppm, 4.06 ppm)
5. Glx - Glutamates, GABA, Glucose (2.0-2.45ppm, 3.60-3.80 ppm)

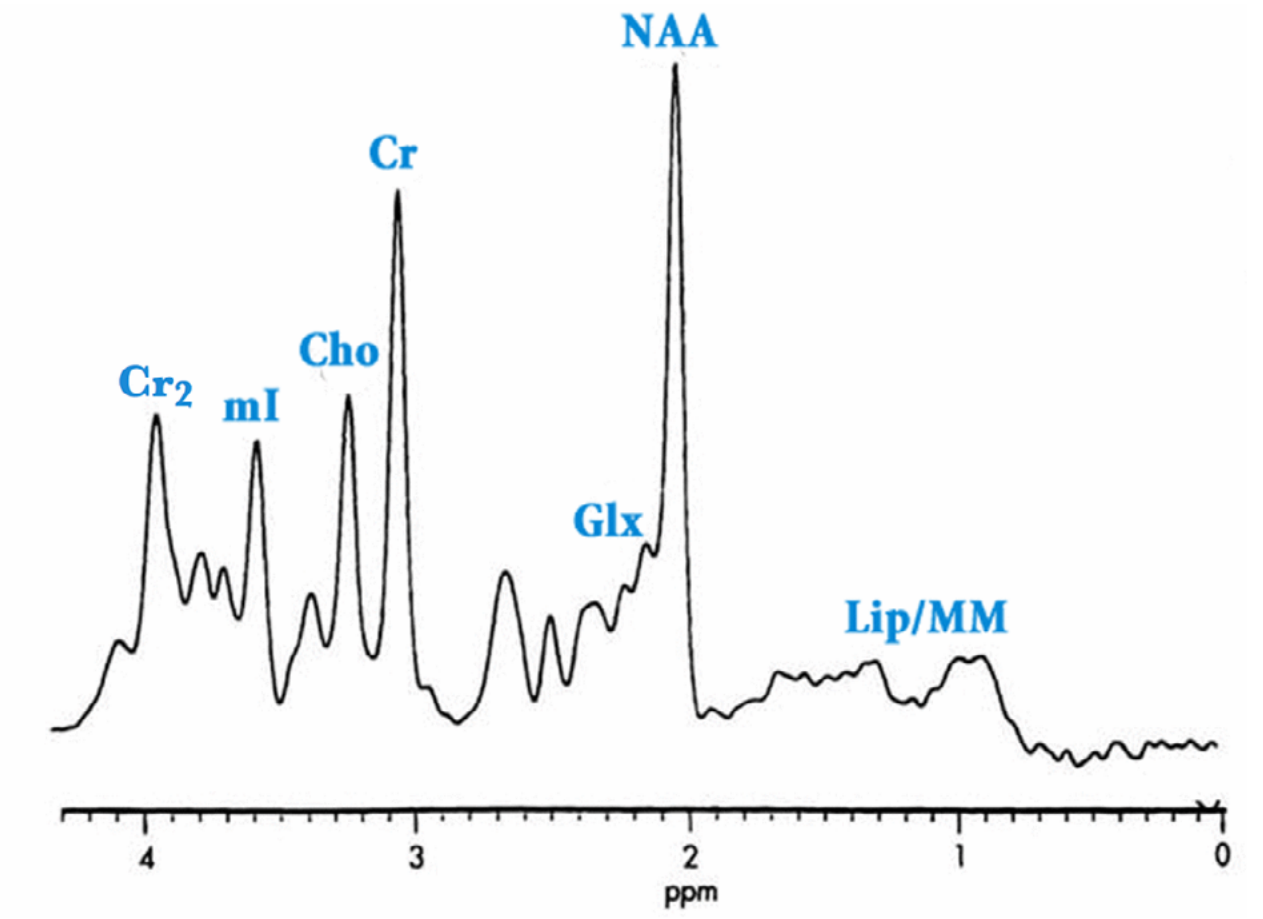

Figure 1. MRS spectrum sample

6. Gly-glycine (3.56 ppm)
7. Ala - alanine (1.48 ppm)
8. Tau - taurine (3.21 ppm, 3.28 ppm, 3.35 ppm)
9. Lac - lactic acid (1.30 ppm)
10. Lip-lipids (0.90 ppm, 1.30 ppm, 2.00 ppm)

NAA (N-acetyl aspartate) is a marker of nerve cells (axons). N-acetyl aspartate participates in the process of neuronal protein synthesis, metabolism of neurotransmitters, and participation in the synthesis of fatty compounds in the myelin sheath. It is present in a healthy cerebral cortex and in glial tumors. Its level is lower in most diseases except Canavan disease. It does not occur in non-electrocardiomous tumors such as metastases, meninges, neuroblastomas, striatum and the central part of glial tumors and malignant lymphomas.

Cr + PCr (creatine and phosphocreatine) is a marker of cellular energy processes and an indicator of the proper functioning and use and storage of energy in a cell. It is a reservoir for high energy phosphate groups, maintains a normal ATP/ADP ratio and is used as an additional energy carrier between mitochondria and other cellular structures. The concentration of Cr is stable, hence it is used to calculate ratios with other metabolites for objective spectral estimation. The total Cr concentration decreases in all brain tumors compared to normal tissue, although it is relatively higher in neuroectodermal tumors.

Cho (choline) is a marker of the metabolism of cell membranes and myelin. The increase in its concentration may result from the breakdown of cell membranes (inflammation, demyelination, infarction, tumor necrosis) or their increased synthesis (tumor cell proliferation). It is a precursor of acetylcholine and phosphatidylcholine. The dominant spike in the brain of a healthy newborn, decreases in concentration with age. Pathological changes cause large fluctuations in the choline peak. The Cho / NAA ratio is particularly important when the level of Cr decreases as a result of pathological processes.[8]

I/mI (inositol, phosphatidylinositol, polyphosphoric inositol and monophosphoric inositol, myo-inositol) is a marker of astrocytic asthma. The suggested role is regulation of osmosis and maintenance of normal cell volume. The mI band is well visible in the brain of a healthy newborn. Increased concentration means astrocytoma astrocytosis (post-glial or post-inflammatory glare, benign astrocytomas or neuroblastoma). The highest concentration of I is in neuroblastomas, hence the possibility of neuroblastoma differentiation in ^{1}H MRS.

Glx (glutamine, glutamate, glutamic acid, γ-aminobutyric acid, glucose) are considered markers of focal ischemia and hypoxia (nerve cell death markers). Glutamine is a major neurotransmitter that stimulates the brain and plays a role in mitochondrial metabolism. Glutamate concentrations increase during periprocedural stroke, appear rapidly in cells devoid of oxygenation, in epileptic foci. Changes in glutamic acid and glutamate levels are also observed in neurodegenerative diseases such as Alzheimer's disease.

Gly (glycine) is considered to be a marker of glial tumors that is observed in neuroanatomical tumors such as glioblastoma, medulloblastoma, ependymoma. It is important in the differential diagnosis of glial tumors with metastatic tumors.

Ala (alanine). Alanine levels increase in meninges, gliomas and pituitary adenomas.

Tau (taurine) is an amino acid, neurotransmitter and has cytoprotective properties. It occurs only in PNET (primitive neuroectodermal tumor), lacking in other tumors and healthy brain tissue.

Lac (lactic acid) is a marker of anaerobic processes and does not occur under physiological conditions. It appears in the foci of cell necrosis (tumors, ischemia) and in infectious processes (abscesses), as well as in diffuse lesions of the axons and mitochondrial metabolic disorders.

Lip (lipids) also do not occur under physiological conditions. They appear in pathological changes associated with acute destruction of myelin and in cell necrosis sites.

Clinical applications of proton spectroscopy - ^{1}H MRS:
1. In brain cancer[9-14]
- assessment of histological character of gliomas,
- assessment of the extent and borders of the brain tumor,
- determining the degree of malignancy of glial tumors,
- assessment of malignant transformation of benign glial tumors,
- differentiation of primary brain tumors and metastases,
- differentiation of tumors,
- differentiation of low grade gliomas with ischemic lesions,
- planning stereotactic biopsy of brain tumors,
- evaluation of the completeness of surgery,
- assessment of tumor recurrence,
- differentiation of recurrence with radiation necrosis,
- evaluation of radio- and tumor chemistry and monitoring of oncological therapy,

2. In degenerative brain diseases
3. In multiple sclerosis
4. In infectious diseases of the brain (abscess, ADEM, HIV, toxoplasmosis)
5. In metabolic diseases

6. In brain trauma
7. In ischemic brain diseases
8. In epilepsy
9. In psychiatry

Clinical applications of ^{1}H MRS in the assessment of histological characterization of gliomas[10,12]

Astrocytoma - decreased concentrations of N-acetyl aspartate (NAA) and NAA/Cr ratio, high choline content (Cho) and increase in Cho/NAA and Cho/Cr ratio, lipids (Lip) and lactate (Lac) may appear, although not very high. Elevated myo-inositol concentration (ml) - peak mI is inversely proportional to tumor grade.

Oligodendroglioma shows decreased concentrations of N-acetyl aspartate (NAA) and NAA/Cr ratio, high choline content (Cho) and an increased Cho/NAA and Cho/Cr ratio. Lipid and lactate content (Lac) may be selected but not high. It can be differentiated with other gliomas quantitatively on the basis of elevated glutamine and glutamate metabolites (Glx) using short TE time.

Ependymoma shows decrease of N-acetyl aspartate (NAA) and NAA/Cr ratio, choline growth (Cho) and Ch/NAA, Cho/Cr ratios, myo-inositol (mI), glycine (Gly) and taurine (Tau).

Glioblastoma Multiforme (GBM) shows significant decreased N-acetyl aspartate (NAA) and NAA/Cr ratio, very high choline levels (Cho) and elevated Cho/Cr and Cho/NAA ratios. Dominant high peaks of free lipids and lactate (Lip+Lac), in tumors with extensive necrosis foci. High concentrations of choline (Cho) and Cho/NAA are indications of the degree of malignancy of the tumor. Glioblast multiforme is a disease of the entire brain, and changes in MRS may also occur outside the maximum contrast enhancement areas of the tumor. Assessment of the extent and boundaries of GBM is essential for operative and radiotherapy. It has been demonstrated that structural MR examination is in some types of tumors (GBM) insufficient in assessing their limits, hence the need to test in the IHMRS environment around the tumor strengthening region for evaluation of choline (Cho) and N-acetyl aspartate (NAA) (MRI fusion map with CM and ^{1}H MRS-CSI).

Clinical application of ^{1}H MRS in determining the degree of malignancy of glial tumors[10,11]

^{1}H MRS allows non-invasive determination of the type and degree of malignancy of the glial tumor on the basis of comparison of metabolite concentrations in the tumor and the white matter of the opposite brain tissue. In general, N-acetyl aspartate (NAA) and creatine (Cr) concentrations, cholecystolone (Cho) and Cho/NAA and Cho/Cr ratios, myo-inositol (mI) and glycine (Gly) and lactate (Lac) and Lipids (Lip), typically occur in the areas of necrosis. The intensity of these changes correlates with the degree of tumor malignancy, particularly choline growth (cell proliferation and membrane degradation) and lipids (disintegration), and the decrease in N-acetyl aspartate (nerve cell loss). The NAA/Cho ratio of less than 1.6 is a high grade malignant glioma. In the G3-G4 glioblastoma necropsy area, Cr also decreased and Cho/Cr increased (G1-2=2.05±0.18, G3=2.58±0.11, G4=5.1±0.89). Lipid (Lip) growth is observed in G3-G4 gliomas. The tendency to increase Cho/Cr and Ch/NAA ratios in tumor surrounding tissue was also noted in case of its malignant nature. MRS spectroscopy makes it possible to differentiate between G2 and G4, but it is more difficult to differentiate G2 from G3 and G3 from G4.

Clinical application of ^{1}H MRS in evaluation of malignant malignant tumors[10-12]

The decrease in N-acetyl aspartate (NAA) and high choline growth (Cho) and the appearance of lactate (lac) and lipids (Lip) as well as the decrease in myo-inositol (mI) levels suggest that they are malignant.

Clinical application of ^{1}H MRS in differentiating glial tumors and metastases

Glucose levels (Cho) and Cho/Cr and Cho/NAA levels increase due to environmental stimulation, and N-acetyl aspartate (NAA) level decreases with G3-G4. In the context of metastasis due to angioedema, the Cho/NAA ratio is preserved. Metastases are characterized by the growth of free (moving) lipids (Lip) and the absence of other brain metabolites. Increasing lactate concentration (Lac) is not a pathogenic phenomenon in this case. Diagnostic problems may arise with differentiation of GBM-derived metastases in which necrosis and disintegration are prevalent, especially if SVS voxel in the GBM carries necrotic tissue, and in the metastases will be fragments of healthy tissues.

Clinical application of ^{1}H MRS in differentiation of other tumors[13]

Tumors have low or zero N-acetyl aspartate (NAA) because the tumor is of mesenchymal origin. In sequences with short TE 20-30 ms visible glutamate growth (Glx). In sequences with short and long echoes (TE 20-30 ms and 135-136 ms), high choline concentration (Cho) and alanine peaks (Ala) and Lactates (Lac) are observed. Syphilis - high levels of the compound inositol (I/mI), which makes it possible to differentiate with mucin.

PNET (Primitive NeuroEctodermal Tumor) - high concentration of choline (Cho), lipid (Lip) and lactate (Lac), visible taurine (Tau), which is pathognomonic for PNET.

Central Neurocytoma - high concentration of choline (Cho) and glycine (Gly).

Gliomatosis cerebri - increases in choline (Cho) and myosinolytic (mI) and high creatine (Cr) and conse-

quently decreases the Cho/Cr ratio, as opposed to Low Grade Glioma (LGG) (Cho) and increased Cho/Cr ratio.

Based on the ^{1}H MRS-CSI maps, especially in the case of non-contrast-enhancing stereotactic biopsies, we estimate where the highest Cho/Cr and Cho/NAA levels exist. We evaluate the completeness of surgery based on ^{1}H MRS-CSI maps, evaluate the tissue for residues of high choline concentration (Cho) and Cho/NAA. The assessment of tumor recurrence and differentiation with radiation necrosis and tumor radioscopy and oncological monitoring are transposed on the basis of the following criteria: resumption of Cho/Cr and Cho/NAA ratios; Necrosis - markedly low values of N-acetyl aspartate (NAA), choline (Cho) and creatine (Cr) compared to healthy tissue. For recurrence, choline concentration (Cho) and N-acetyl aspartate (NAA) decrease, but in early changes after radiotherapy also increases choline (Cho) concentration. The fall of lactate (Lac) and "moving" lipids (lipids) during radiotherapy is a good indicator of brain tumor radioactivity. The presence of blood, air and fluid in the post-operative box results in distortion of ^{1}H MRS results.

Clinical applications of ^{1}H MRS in cerebral degenerative diseases and differentiation of dementia syndromes[15,16]
AD (Alzheimer Disease) - increase in myo-inositol (mI) and decrease of N-acetyl aspartate (NAA), a significant ratio of these values in the hippocampus and temporo-parietal cortex.
FTD (Fronto-Temporal Dementia) - decrease of N-acetylasparaginate (NAA) and Glutamate (Glx) and increase of myosinolytic (mI) in the gray matter of the temporal-parietal and central region.
PD (Parkinson Disease) - decrease in NAA/Cr ratio in the temporo-parietal cortex, black essence, basal nucleus, striatum and occipital lobe.
HD (Huntington Disease) - decrease in N-acetyl aspartate (NAA) and increased lactate (Lac) levels in the striatal, occipital and frontal cortex, NAA/Cho ratio decrease in basal and brain cortex.

Clinical applications of ^{1}H MRS in multiple sclerosis[17,18]
In the acute phase, demyelinating MSs show a slight decrease in N-acetyl aspartate (NAA), which over time returns to normal, and contrast-enhanced MSs also exhibit choline (Cho) and lipid (Lip) growth. In the phase of chronic MS focus hyposensitivity in T_1 dependent images show a decrease in N-acetyl aspartate (NAA) and increase in myo-inositol (mI). It has now been demonstrated that white matter with normal MR signal may exhibit elevated choline (lipid) and lipid (Lip) and N-acetyl aspartate (NAA) levels in MS, which correlates better with functional damage than MS in T_2 dependent images. ^{1}H MRS seems to be helpful in assessing axonal lesions and demyelination, and together with DTIs, it can better monitor the evolution of MS lesions.

Clinical applications of ^{1}H MRS in cerebral infectious diseases[19]
Chunks - Very low concentration or absence of choline (Cho), creatine (Cr) and N-acetyl aspartate (NAA), lipid and lactate levels (Lip, Lac), and alanine peak (Ala).
ADEM - normal choline levels (Cho) and lipid level (Lip) and N-acetyl aspartate (NAA) drop, which returns to normal after treatment.
HIV - decline in NAA/Cr ratio and increase in Cho/Cr and mI/Cr ratios (ability to monitor HIV treatment).
Toxoplasmosis - increase in lipid and lactate concentrations (Lip, Lac) and no other metabolites.

Clinical applications of ^{1}H MRS in metabolic diseases[14]
Mitochondrial diseases (Leigh, Kearns-Sayre Syndrome, Mitochondrial Encephalopathy, lactic acidosis, MELAS, MERRF) associated with cellular respiratory disorders lead to anaerobic glycolysis and lactate accumulation in the brain and in ^{1}H MRS we can prove the presence of a lactate (Lac) normal brain.
Peroxisomal diseases (Adrenoleukodystrophy, Zellweger's syndrome) lead to nerve cell damage, which is manifested in ^{1}H MRS by N-acetyl aspartate (NAA) and glutamate (Glx) and choline (Cho) growth. ^{1}H MRS plays a special role in discriminating patients for bone marrow transplantation in the early stages of disease before the onset of neurological symptoms, and can also be used to screen for early demyelination.
Phenylketonuria - phenylalanine peaks in ^{1}H MRS with short TE time at 7.37 ppm can be demonstrated; other metabolites are normally normal.
Disease "Maple Syrup" - can be shown to increase the leucine peaks, isoleucine and valine at 0.9 ppm.
Canavan disease - damage to the enzyme aspartoacylase leads to an increase in the concentration of N-acetyl aspartate (NAA).
Alexandra's disease - leads to a decrease in the concentration of N-acetyl aspartate (NAA) and an increase in lactate concentration (Lac).

Clinical applications of ^{1}H MRS in brain injury [14]
As a result of spilled axonal injury and depression of nerve cell metabolism, N-acetyl aspartate (NAA) declines. In fact, the white brain after N-acetyl aspartate (NAA) falls back to normal NAA levels. Contrary to this, in fact, the gray matter of the brain decreases the concentration of NAA is progressing. Likewise, the concentration of choline (Cho) increases after trauma and its level is maintained in elevated gray matter affected. In adult patients with normal-looking white matter, the NAA/Cr ratio correlates with the severity of injury and is a predictor of neurological damage.

Clinical applications of ^{1}H MRS in ischemic diseases[14]
At the acute and subacute stage of the ischemia, the level of N-acetyl aspartate (NAA) gradually decreases, while the concentration of choline, lactate and glutamate (Cho, Lac and Glx) is increasing. Lacs (lac) grow shortly after the infarction within a few hours and may persist for as long as the chronic phase. In the chronic phase, a very large decrease in N-acetyl aspartate (NAA) and myosinosis (mI) is evident. Phosphoric spectroscopy (^{31}P MRS) in ischemia decreases the ratio of phosphocreatine to inorganic phosphorus (PCr/Pi).

Clinical applications of ^{1}H MRS in epilepsy[20]
N-acetyl aspartate (NAA) drop and drop in NAA/Cr ratio and Glx concentration (glutamine/glutamate complex). Lactation increases (Lac) is observed in the epilepsy camp and can last several hours. During laparoscopic, lactate elevation (Lac) is also used to evaluate lateralization of epileptic activity.

Clinical applications of ^{1}H MRS in psychiatry[21-24]
Schizophrenia - decrease in NAA/Cr ratio in the prefrontal cortex, hills and hippocampus, glutamate elevation (Glx) in the initial stage of the disease and fall in the chronic stage.
Depression - increase of Cho/Cr ratio in the real white frontal lobe, subcortical nucleus, myo-inositol decrease (mI) in the prefrontal cortex, Glx level (glutamate) decreased in the prefrontal cortex and increased in the occipital lobes.
Cyclophrenia - increase of myoinositol concentration (mI) in the frontal and frontal cortex of the rump, decrease of N-acetyl aspartate (NAA) in the prefrontal cortex and hippocampus, glutamate increase (Glx) in the prefrontal cortex during mania and choline increase in course of depression.

Due to device limitations and economic aspects, the use of Phosphor Spectroscopy ^{31}P MRS is currently largely limited to research, although in the near future this method will probably be more widely used in the evaluation of the musculoskeletal, cardiac and liver systems.[25,26] Spectra obtained from brain tissue consists of 7 peaks:
γ-ATP - gamma adenosine triphosphate
Pi - Inorganic phosphate
α-ATP - alpha adenosine triphosphate
PDE - phosphodiester
β-ATP - beta adenosine triphosphate
PME - phosphomonoesters
PCr - phosphocreatine

Analysis of ATP, PCr and Pi peaks allows us to determine the concentration of high energy intracellular compounds and the intensification of energy transformation processes. PCr/Pi is an indicator of the oxygen potential of the cell. The chemical shift Pi relative to PCr determines the intracellular pH. The mutual position of phosphates γ and α in ATP allows the calculation of intracellular magnesium concentration.

Current trends in spectroscopy are: finding new clinically important markers (eg GABA, taurine, glucose), applying dynamic and 3D spectroscopy, developing a metabolite mapping program (CSI), and assessing responses to pharmacological treatment such as lithium (mI) antiepileptic (GABA level).

Although proton MR spectroscopy in many cases is not able to answer the clinical questions in many cases, and in most brain pathologies, NAA (except Canava disease) and choline growth are likely to be affected. MR studies widen the possibilities of predicting histological origin and degree of malignancy of tumor processes and intensification or differentiation of other diseases of the nervous system. MR spectroscopy, based on other elements, is still an active research area with hopes to expand the possibilities of disease differentiation in clinical applications in the near future.

References

1. Bertoldo D, Watcharakorn A, Castillo M. Brain proton magnetic resonance spectroscopy. Introduction and overview. Neuroimag Clin N Am. 2013;23:359-80.
2. Jansen JFA, Backes WH, Nicolay K, Kooi ME. ^{1}H MR spectroscopy of the brain : absolute quantification of metabolites. Radiology. 2006;240:318-32.
3. Posse S, Otazo R, Dager SR, Alger J. MR spectroscopis imaging : principles and recent advances. J Magn Reson Imaging. 2013;37:1301-25.
4. Moonen CT, von Kienlinvan M, van Zijl PC, et al. Comparison of single-shot localization methods (STEAM and PRESS) for in vivo proton NMR spectroscopy. NMR Biomed. 1989;2:201-7.
5. Maudsley AA, Darkazanli A, Alger JR, et al. Comprehensive processing, display and analysis for in vivo MR spectroscopic imaging. NMR Biomed. 2006;19:492-503.
6. Klose U. Measurement sequences for single proton MR scpectroscopy. Eur J Radiol. 2008;67:194-201.
7. LC Model website. http://lcmodel.ca. Assessed November 18 2016, Updated January 9, 2017.
8. Sobiecka B, Urbanik A. The role of choline (Cho) in the diagnostics and differentiation of brain tumours with H MRS technique. Pol J Radiol. 2009;74:7.
9. Oz G, Alger R, Barker PB, et al. Clinical proton MR spectroscopy in central nervous system disorders. Radiology. 2014;270:658-79.
10. Herminghaus S, Dierks T, Pilatus U, et al. Determination of histopathological tumor grade in neuroepithelial brain tumors by using spectral pattern analysis of in vivo spectroscopic data. Journal of Neurosurgery. 2003;1:74-81.

11. Julià-Sapé M, Griffiths JR, Tate RA. Classification of brain tumours from MR spectra: the INTERPRET collaboration and its outcomes. NMR in Biomedicine. 2015;28:12,1772-87.
12. Jaskólski DJ, Fortuniak J, Majos A, et al. Magnetic resonance spectroscopy in intracranial tumours of glial origin. Neurol Neurochir Pol. 2013;47:438-49.
13. Jaskólski DJ, Fortuniak J, Stefańczyk L, et al. Differential diagnosis of intracranial meningiomas based on magnetic resonance spectroscopy. Neurol Neurochir Pol. 2013;47: 247-55.
14. Semantic Scholar - An academic search engine for scientific articles. https://pdfs.semanticscholar.org. Updated January 12, 2017.
15. Magierski R, Sobów T, Kłoszewska I. Spektroskopia MR w chorobach zwyrodnieniowych ośrodkowego układu nerwowego. Post Psych Neurol. 2005;14:155-163.
16. Urbanik A. Diagnostyka otępienia przy pomocy protonowej spektroskopii MR. Przegl Lek. 2010;67:237.
17. Szafirska M, Urbanik A, Róg T. Zmiany metaboliczne w obrębie blaszek u chorych na stwardnienie rozsiane - ocena w technice protonowej spektroskopii MR (1HMRS). Prz Lek. 2013;70:328-34.
18. Szafirska M, Urbanik A. Rola rezonansu magnetycznego w diagnostyce stwardnienia rozsianego. Ogólnopol Prz Med. 2012;3:48-53.
19. Podsiadło L, Urbanik A, Garlicki A, et al. 1H MRS application in the evaluation of CNS in the patents with AIDS. Pol J Radiol. 2003;68:5-9.
20. Michalska J, Kociemba W, Steinborn B, et al. Rola spektroskopii rezonansu magnetycznego w padaczce. Neur Dziecięca. 2008;34:61-4.
21. Silverstone PH, McGrath BM, Kim H. Bipolar disorder and myo-inositol: a review of the magnetic resonance spectroscopy findings. Bipolar Disord. 2005;7:1-10.
22. Renshow PF, Lafer B, Babb SM, et al. Basal ganglia choline levels in depression and response due to fluoxetine treatment: in vivo proton magnetic resonance spectroscopy study. Biol Psychiatry 1997;41:837-43.
23. Rachel W, Siwek M, Dudek D, et al. Protonowa spektroskopia rezonansu magnetycznego w zaburzeniach afektywnych. Neuropsychiatria i Neuropsychologia. 2008;3:29.
24. Herman-Sucharska I, Werewka-Maczuga A, Urbanik A, et al. Ocena przydatności protonowej spektroskopii MR w diagnostyce i monitorowaniu leczenia choroby afektywnej jednobiegunowej Przegl Lek. 2010;67:4.
25. Karcz P, Urbanik A. Spektroskopia protonowa mięśni podudzia przed i po wysiłku fizycznym. Przegl Lek. 2013;70:286-92.
26. Zaleska T, Walecki J, Michalak M, Michalak E. Spektroskopia magnetycznego rezonansu w kardiologii. Medical Science Review - Diagnostyka Obrazowa. 2002;1:20-4.