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^{1}H MRS spectroscopy in brain tumors – in search of the highest efficacy

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Summary

Many thousands of published papers, a lot of communications and daily practice show the outstanding role of proton spectroscopy (^{1}H MRS) in neurooncology. Paradoxically, in several clinical centres (neurosurgery ones) we can observe the lack of full acceptance of the reliability of this method. Presumably, the reason for this attitude lies in non-uniform methodology and quite superficial treatment of spectroscopic results. At the beginning of this paper, we would like to stress that fortunately, there is a certain number of publications which order criteria of tumor's malignancy, its tissue characterisation and the degree of malignancy. In this paper we intend to point out the proper ways of improving reliability of ^{1}H MRS in brain tumor diagnosis. Obviously, the quality of spectroscopic exams is influenced by methodology and manner of result interpretation (e.g. just simple visual inspection of MRS spectra is not sufficient for correct diagnosis).

Currently, imaging diagnosis of brain tumors is based on many modalities (DTI, perfusion CT, MR, PET, SPECT) which are sufficiently effective in detection and differentiation of the lesions; in this context, we can say that ^{1}H MRS spectroscopy constitutes the element of multimodal diagnostic approach for brain tumors.

Nevertheless, the current papers concerning MR spectroscopy stress its significant role in making therapeutic decision, particularly as an alternative for surgery treatment and solution of the recurrence of tumor or/and extent of the tumor's spreading. Over 15 years of experience with ^{1}H MRS in diagnosis of brain tumors convinced us that these methods have very high diagnostic and decision-making value provided that it is properly applied and interpreted correctly. It is also important to choose the statistic methods that will show the best discriminators (markers) for particular pathologies. Authors' intention is to recommend the best ways to form the right diagnosis considering technological requirements, methodology and result interpretation.

Key words: magnetic resonance • spectroscopy • brain tumors

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Technical Aspects

Magnetic resonance spectroscopy is based on the phenomenon called "chemical shift". The resonance frequency of a certain atomic nucleus is to a small (but measurable) degree changed by the surrounding chemical bonds and, owing to that, the identification of particular molecules is possible.

The features of MRS spectrum, such as the number of resonance lines, their position, the volume under each of them, depend on chemical structure of the examined compound. Analysis of spectrum can lead to identifying the compounds and their proportions in the studied sample. It enables studying simple and complex chemical compounds, as well as the metabolism of living cells in physiologic and pathologic states. The description of spectrum usually requires using a standard substance (internal substance). In the *in vivo* ^{1}H MRS examinations the role is played by phosphocreatinin.

The most common spectroscopic techniques used in clinical practice are proton spectroscopy (^{1}H MRS) and phosphor spectroscopy (^{31}PMRS) [1–8] as those elements play the vital role in the assessment of metabolic turnover. The first one provides information about various metabolic disorders (acethylaspartate acid – nervous cells marker, creatinin – related to metabolic changes, choline – element of cell membranes, lactates – markers of anaerobic metabolism). The second one enables evaluation of energetic condition of the cells (phosphate compounds, mono- and biphosphate, phosphocreatinin, adenosine triphosphate ATP) and has application more in ischemic diagnosis than in oncology. Proton MR spectroscopy can be performed on most 1.5 T clinical MR equipment. There are two standard methods for data acquisition: single voxel spectroscopy (SVS) and multi-voxel spectroscopy (chemical shift imaging CSI)

Single Voxel Spectroscopy (SVS) – The Key Method Constantly

Single Voxel Spectroscopy enables registering the spectrum of selected volume, called the "volume of interest" (VOI) or voxel; this method is still most precise in locating the tissue which is examined. The SVS VOI localization methods include: ISIS (Image-Selected *In-Vivo* Spectroscopy), STEAM (Stimulated Echo Acquisition Mode), PRESS (Point-Resolved Localized Spectroscopy); these methods has not changes till now.

Generally, the PRESS technique is recommended. As we know, it is a sequence of 3 pulses: 90°–180°–180°. A double spin-echo method enables good localization and strong suppression of signals outside the selected voxel, while long duration of echo ensures a better visualization of metabolites with long relaxation time.

Typical SVS spectroscopy protocols at 1.5 T:
1. **Metabolite ratios** (clinical): repetition time (TR): 1–1.5s, the number of averages: 128, voxel size: 1.5×2×2 cm, acquisition time: 2–3 min;
2. **Semi-quantitative**: repetition time (TR): 2s, the number of averages: 192, voxel size: 1×1×1.5 cm, acquisition time: 7 min;
3. **Quantitative**: repetition time (TR): from 3s to 6s, the number of averages: 192, voxel size: 1×1×1.5 cm, acquisition time 10 min (for TR=3s).

They represent a compromise between TR (this should ideally be long to minimize T1 losses), number of averages or phase encodes (ideally large to achieve better SNR and/or spatial resolution) and acquisition time (which is short for the clinical sequences, and long for the more quantitative sequences).

Echo Time (TE) is dependent on examine metabolites. In many molecules, non-equivalent protons interact with each other in a phenomenon know as J-coupling. The result, in simple cases, is the splitting of peaks into doublets, triplets, etc. Furthermore, there is a time-dependence to J-coupling. In short TE spectra, the various components of a J-coupled lineshape are in phase, and add coherently. At longer TE values, the different components get out of phase. Some parts of a lineshape may be pointing up while other parts are pointing down. For example, in lactate is a doublet centred at 1.33 ppm and quartet centred at 4.11 ppm. The doublet lines are in phase and pointed upward for short TE, out of phase with each other and other non-coupled peaks for TE=67 ms, in phase with each other but inverted with respect to the rest of spectrum at TE=135 ms, and pointed upward again at TE=270 ms. For more complicated J-coupled molecules one must examine them at short TE values before J-coupling causes irreversible destruction of signal, much like a short T2. NAA, creatine, and choline all have uncoupled methyl group protons, so these molecules can be examined using either long or short TE spectra. Lactate is most easily detected at short TEs or at multiples of 135ms. Glutamine, glutamate, and myo-inositol are easily seen at short TEs. Unfortunately, lipids and macromolecules contribute a rolling baseline to short spectra. Eddy currents and out-of-voxel artefact are worse at short TE, as is spectral overlap. For this reasons longer-TE spectra are easier to acquire and analyze. Thus, one often obtains two spectra from the same region.

Among SVS advantages are: high homogeneity of the field of the examined volume, easy selective water-suppression, high signal-noise ratio (S/N), and relatively short duration of the examination (around 4–8 minutes).

Multi-Voxel Spectroscopy – Still Valid But More Time-Consuming And Not So Good Resolution

Multi-voxel spectroscopy or the CSI (Chemical Shift Imaging) is a technique, which visualizes the chemical shift in one measurement period and collects spectroscopic signals from multiple small voxels located within a large examined area. The registered signals form a map of spatial distribution of the metabolites.

Typical CSI spectroscopy protocols at 1.5 T:
1. **Semi-quantitative** (clinical): TR: 2s, matrix: 16×16, FOV (field of view): 24 cm, voxel size: 1.5×1.5×1.5 cm, acquisition time: 8 min;
2. **Quantitative**: TR: 3s, matrix: 24×24, FOV: 32 cm, voxel size: 1.3×1.3×1.5 cm, acquisition time: 29 min;

They represent a compromise between a quality of imaging and acquisition time.

The major disadvantage is that the shape of individual voxels is less well defined than in single voxel techniques, and the necessity of long echo-durations limits the amount of received data to 3 bands of metabolites. CSI is also more sensitive to heterogeneity of the magnetic field and to fat tissue-derived artefacts [9]. Long time necessary for acquisition of the CSI data limits the use of this method in clinical practice.

Preprocessing Techniques – Where Trouble May Begin

Because of the fact that the FID signal contains a lot of noises, unwanted signals and deformations connected with acquisition, application of various corrective techniques is inevitable.

The first stage of pre-processing is conducted in time domain (before the Fourier transformation). It includes: offset cor-

rection, eddy current correction, zero filling and apodization (multiplying the signal with appropriate S/N corrective functions). The next stage of processing the resonance spectrum, after the Fourier transformation (in frequency domain - FD), is based on the phase and baseline correction, and on calculating the area below the resonance bands of certain substances. In medical applications such procedures are usually carried out automatically with the use of software supplied by the tomography producer. This is the oldest, but still the fastest and straightforward method to quantify the spectrum lines. Most importantly, it is line-shape independent. However, this method is prone to many mistakes and its use is limited to well-resolved peaks with good S/N ratio on a flat baseline. Accurate quantification of the *in vivo* spectra requires mathematical fit of the observed spectrum in order to disentangle the overlapping lines and to reliably estimate their area. Proper phase and baseline correction is the preliminary condition for correctness of this analysis. An introduction of the common processing methods in *in vivo* MR spectra is given in a few references [10].

Calculation of molar concentrations of the substances on the basis of integrals of corresponding resonance lines requires calibration. In view of the problems with reliable calculations of molar concentrations, the quantitative MRS results are often presented as intensity quotients of resonance signals of particular metabolites (Metabolite Ratios, MR). Nevertheless, the MR must be interpreted with caution as, despite the fact that the metabolites proportion is enclosed within certain range, it does not mean that particular metabolites concentration has changed [11]. One of the programs enabling calculation of total metabolites concentration is LCModel (Linear Combination of Model spectra). It matches linear combination of signals from single metabolites with spectrum of compounds measured independently. LCModel is especially useful for short TE (time of echo) and high concentration metabolites – myoinositol, glutamine. The disadvantages include difficulties with accessibility to the source code (the reason being commerciality of the program) and time-consuming manual adjustment.

Recently, more attention has been paid to time-domain quantification methods [12–14]. The visual interpretation of the measured MRS signals and the fitting results are best done in the frequency domain.

There exist a huge amount of software dedicated to MRS. We only mention a few of them: jMRUI quatitation package (quantitation methods: VARPRO, AMARES, QUEST), AQSES-GUI package, education MATLAB NMR data processing package (NMRLAB).

Statistic Methods Supporting Diagnosis – Crucial Impact On Diagnostic Success

Various methods have been suggested for classification of spectra into groups used for diagnosis and prognosis. Classification is often achieved using logistic regression (LR), linear and quadratic discriminates (LDA, QDA) and Fisher criteria, the K-nearest neighbour classifier (KNN) or the Parzen density estimator, classification and regression tree (CART), random forest (RF), genetic algorithm, artificial neural networks (ANN) and support vector machines (SVM). Linear discriminant analysis (LDA) is a technique that has been widely used in spectroscopy for pattern recognition and has obtained good results for many applications including brain tumor classification. SVS have recently gained prominence in the field of machine learning and pattern classification [15]. The important advantage of SVM is that it offers a possibility to train generalizable, nonlinear classifiers in high dimensional spaces using a small training set.

Innovations In MR Spectroscopy

More and more efforts are being put into developing fast spectroscopic imaging techniques, such as Turbo Spectroscopic Imaging (TSI), echoplanar magnetic resonance spectroscopic imaging (EP-MRSI), spiral MRSI, parallel spectroscopic imaging using SENSE. Further research effort will thus aim at investigating the potential of fast, highly resolved MRSI at high field, as well as at achieving whole-brain coverage by 3D acquisition.

Functional Spectroscopy (fMRS)

The development of fast imaging techniques in spectroscopy enabled observation of dynamic metabolic processes in brain. The fMRS scanning requires the same equipment as fMRI but uses a different kind of software made for recording various levels of chemical substances. The main difference between the aforementioned techniques is that fMRS measures the changes of metabolites, while the fMRI - blood oxygenation (BOLD). One of the substances that can be measured by fMRS is the lactate, considered as determinant of anaerobic metabolism. The idea of observing the lactate in fMRS is based on the following mechanism: increased electric activity of region of the brain (caused by a certain task) uses up the energy and that leads to the growth of nutrients consumption (i.a. oxygen, glucose) and increase of blood flow. Metabolism is increased and so is the lactate (which is a by-product). The disadvantage of this method is a relatively long measuring time and actually small lactate signal, which still makes the optimization of spatial resolution a challenge, if the SNR is to be maintained at the a sufficient level [15].

Multinuclear Spectroscopy – Not Only Proton Spectrocopy

The MR spectroscopy uses spectra of various elements. Apart from the aforementioned hydrogen spectroscopy (^{1}H MRS) and phosphoric spectroscopy (^{31}PMRS), the carbon (^{13}C MRS) and fluoric (^{19}FMRS) spectroscopy are also used [16]. Compared to the ^{1}H other nuclei, especially ^{31}P and ^{13}C, are less sensitive. Nuclid spectra with appropriate S/N require a much longer measuring time. The carbon, phosphor and fluorine spectra need additional device/tool for detection and transmission, which operates on resonance frequency of nuclei of our interest. A typical spectrum of the aforementioned nuclids is complex; it has a wide band of chemical shift and contains signals, which are split into multiplets. [17].

Hyperpolarized ^{13}C

The main reason for general low sensitivity of NMR techniques is low polarization of nuclei in thermal balance;

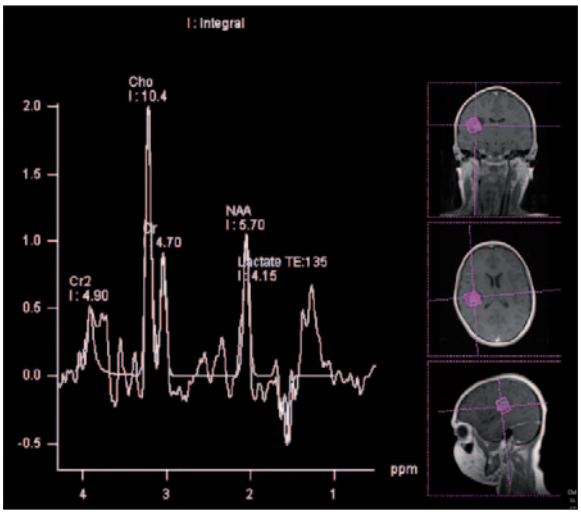


Figure 1. 12-year-old girl with AA scheduled for surgery. [1]H MRS (long TE-135 ms) reveals extremely high level/ratio of Cho, presence of Lac, Lip and low level of NAA.

even in the high fields only one in 105 of nuclei contributes to the measured signal. However, it is possible to improve polarization of selected nuclei by a factor of 100000 or more. The enhancement of polarization can be obtained by increasing the magnetic field. Another idea to improve the polarization is to create artificial non-equilibrium arrangement of the nuclei. The state of hyperpolarization, in which the difference in population of spins of high or low energy increases by a few rows compared to the balance state does not depend on the outer magnetic field. Hyperpolarization concerns mainly the organic substances containing ^{13}C or the following nuclei: ^{3}He, ^{129}Xe and ^{15}N. There are two methods of hyperpolarization: DNP (dynamic nuclear polarization) and PHIP (para-hydrogen-induced polarization). Hyperpolarization enlarges signal amplitude what results in reduction of scanning time to a few seconds. [18].

Clinical Aspects

Considerable amount of papers concerning the value of [1]H MRS in brain tumors was published in many countries around the world during the last 10 years, unfortunately less than 100 contain broad clinical material, sufficient statistics and current point of view on tumors in [1]H MRS. An excellent reference material concerning this issue could be accessed in the paper published by W. Hollingworth et al [19]

Owing to literature data and our own experience of more than 10 years,we have made an effort to categorize publications according to the several following main clinical subgroups: metastasis versus high-grade astrocytoma, high vs low-grade astrocytoma, tumor extent before treatment, neoplastic vs nonneoplastic lesions, recurrent or residual tumor versus treatment-related change; the aforementioned topics allow us to list the most important problems concerning [1]H MRS in the diagnostics of brain tumors. The following topics could establish the formal applications for [1]H MRS in brain tumors diagnosis:

1. Diagnosis of brain tumors and selection from nontumoral pathology, tumors classification and grading.

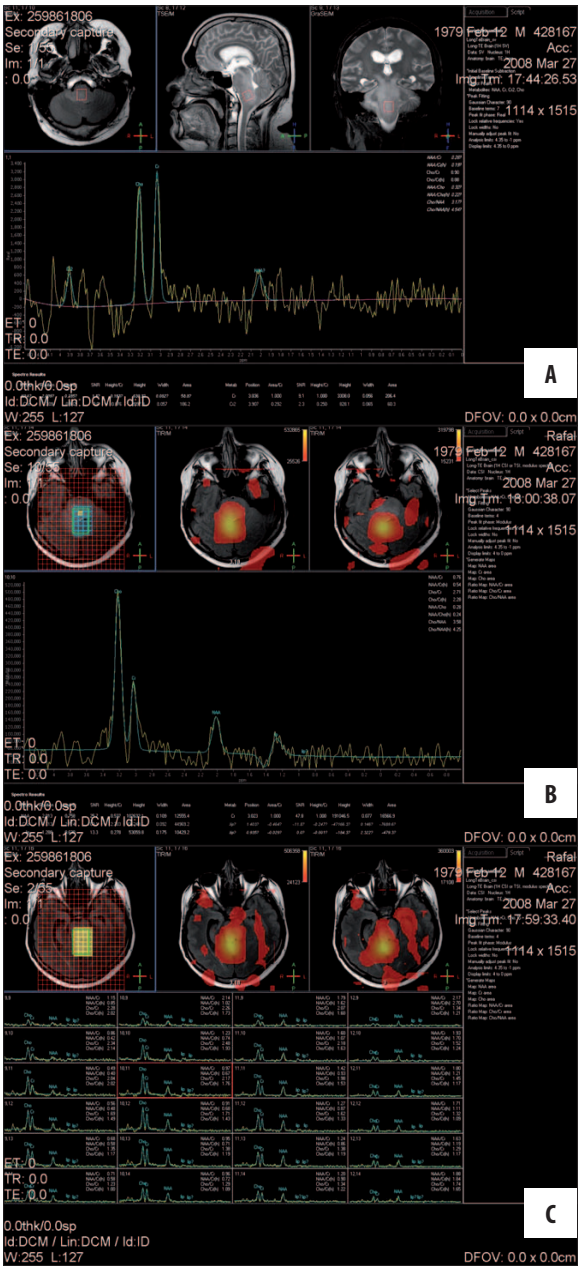
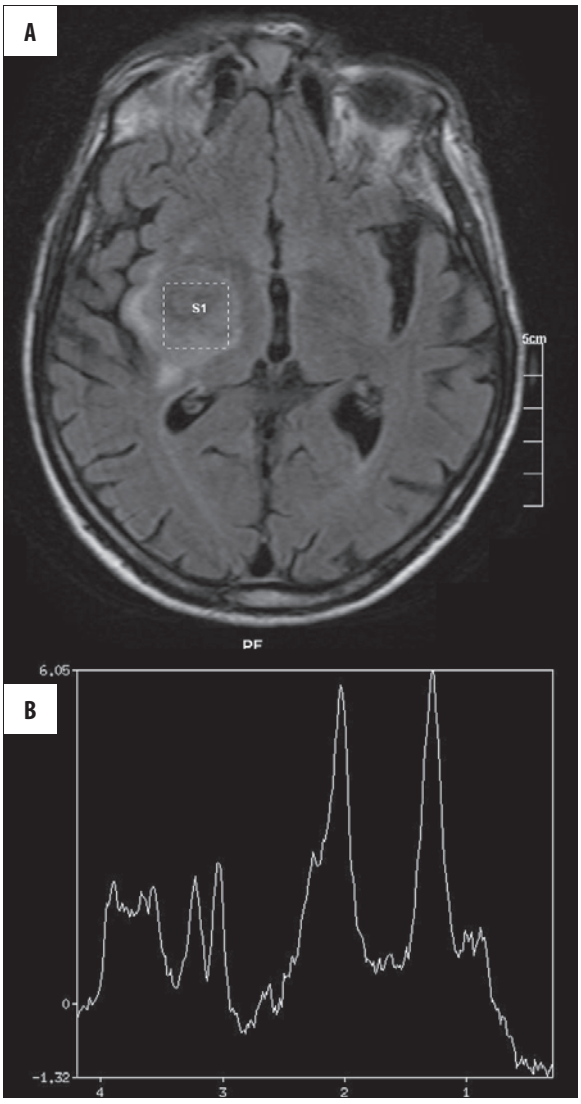


Figure 2. 26-year-old man with pontine glioma (AA, confirmed by biopsy) after many courses of radiotherapy. [1]H MRS, SVS and CSI show elevation of Cho and Lac; owning to colored mapping of metabolites distribution obtained from CSI, extension of Cho elevation areas is observed.

2. Detection of tumor recurrence vs radiation necrosis, differentiate delayed radiation necrosis from recurrent tumor.
3. Evaluation of the extent of tumors infiltration (uncertain zone).

In terms of point 1 one is able to state, rather roughly, that commonly analyzed types of tumor ratios and/or metabolites concentrations, are more or less different from control group. These ratios of particular metabolites to Cr are as follows: Lip/Cr, Lac/Cr, Ala/Cr NAA/Cr, Cho/Cr, mI/Cr,Glx/Cr and ratios of those metabolites to



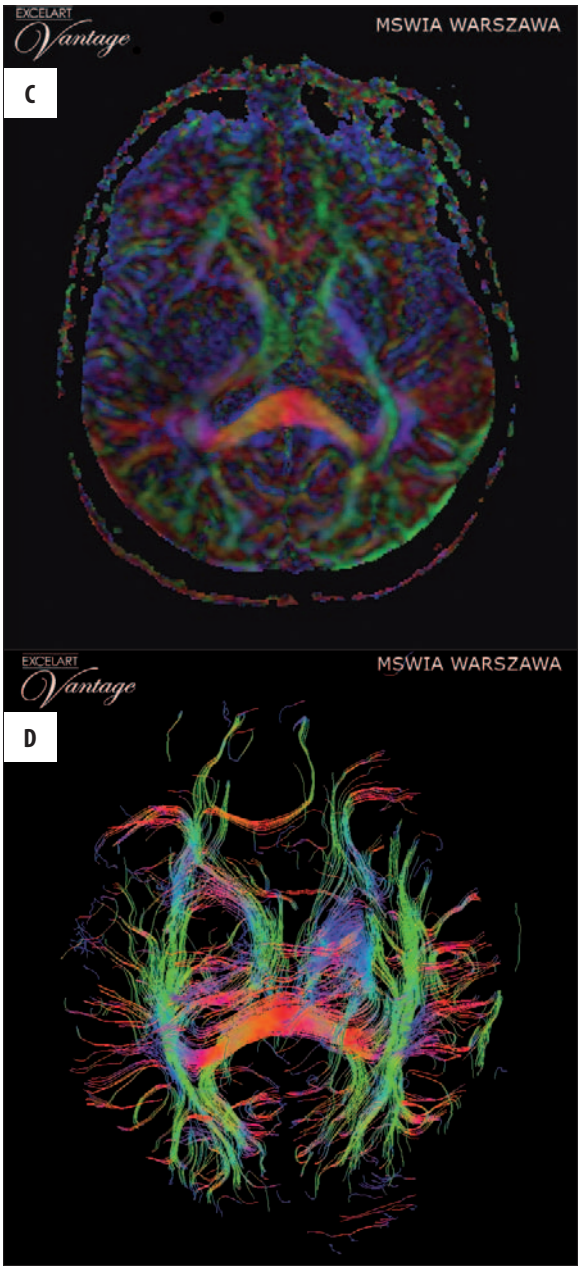


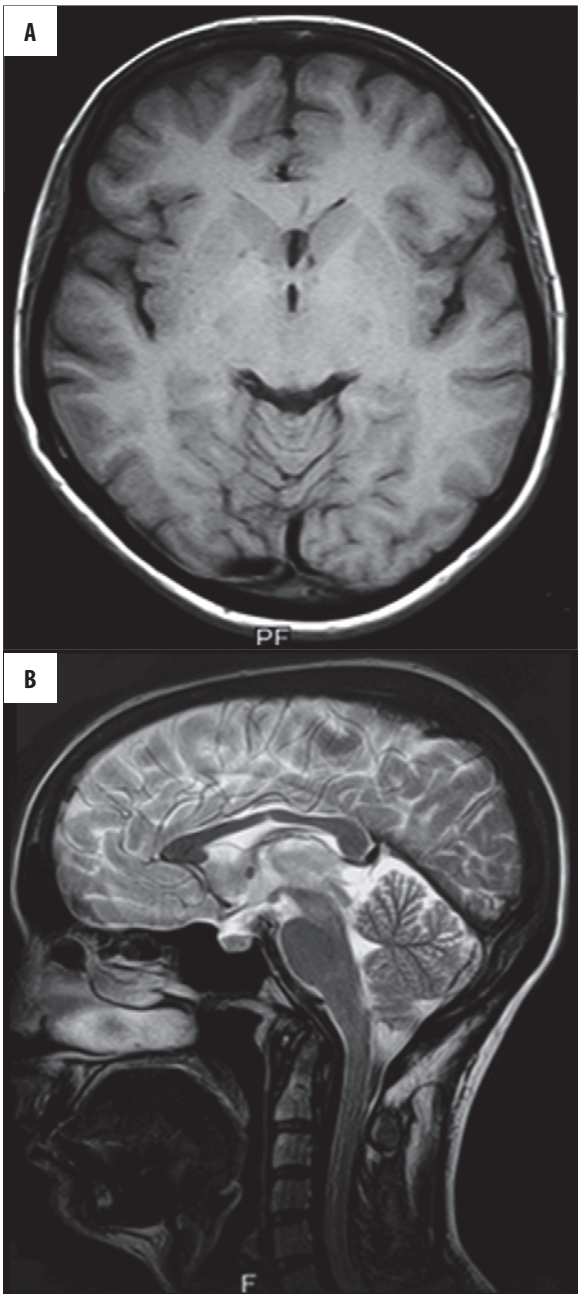
Figure 3. 59-year-old man with left side hemiparesis and two seizures, reported a few month ago; surgery and histopathology confirmed metastatic tumor (lung carcinoma). (**A**) MRI (FLAIR) revealed oval tumor in the right hemisphere surrounded by edema zone; (**B**) ^{1}H MRS is characterized by expression of Lac and Lip, elevation of Cho/Cr ratio, also one can observe relatively high level of NAA (and ratio to Cr). (**C,D**) Preoperative DTI (FA images and Tractography) demonstrated displacement and compression of motor fiber pyramidal tracts, without features of infiltration.

unsuppressed water. High-grade gliomas, mostly anaplastic astrocytoma (III) and glioblastoma multiforme (IV) tended to have higher Cho/Cr, Cho/NAA, Lac/Cr and Lip/Cr and low/or extremely low/ NAA/Cr and mI/Cr; these tumors are well differentiated from the rest of astrocytic tumors mainly by the presence of a broad resonance centred at 0.9 and 1.3 ppm attributable to lipids (Lip) and presence of increased concentration of Lac and Cho (Figures 1,2).

Increased Lip concentration is significantly recognized in high grade astrocytoma, can be treated however as a marker of AA and GBM; this would agree with the findings that high grade gliomas contain mobile lipids,the amounts of which correlate with the extent of cell necrosis on microscopy [20].

Studies using ^{1}H MRS indicate a similar correlation between metabolic profile *in vivo* and the histological grade of gliomas and indicate that also lactates (Lac) are more likely to be present in high-grade tumors not only of glial origin, especially metastases [1–3,19] (Figure 3).

One of the most important spectroscopic marker of tumor's growth is Cho, the presence of which in low and high grade glioma is acknowledged by many authors [1,20,22] (Figure 4.) However, an enthusiastic approach to the value of Cho as a marker of tumor's malignancy is lowered by the fact that Cho may result from the degradation of cell membrane but also because of the proliferation of cells. [2,19,20].



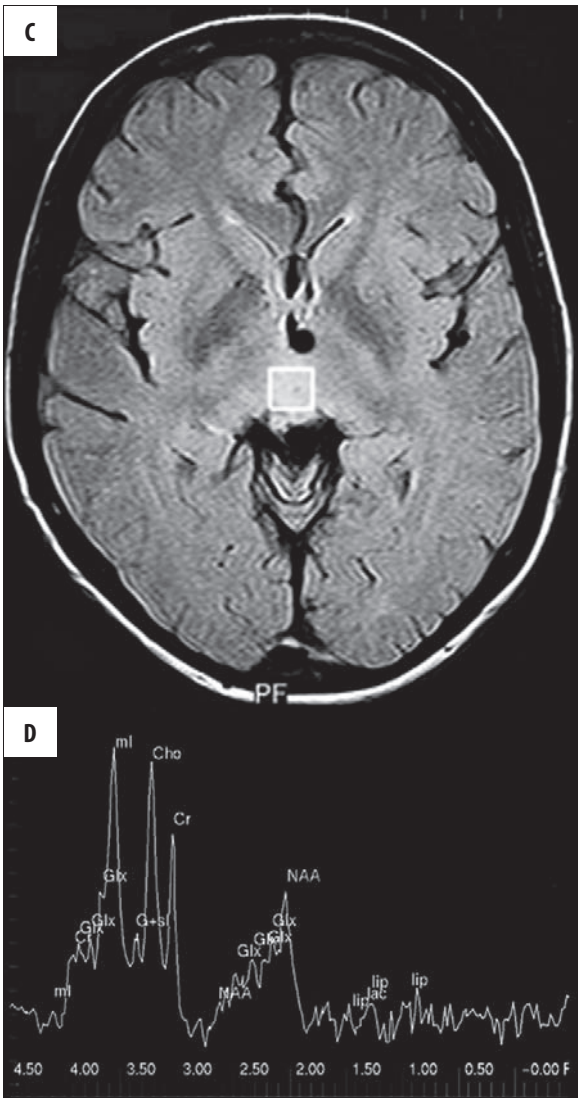


Figure 4. 35-year-old women with tectal glioma (astrocytoma), confirmed by biopsy, revealed in MRI (see sagittal plane). [1]H MRS showed high mI/Cr and Cho/Cr ratio from tectal region (suspected of tumor) suggestive of low grade glioma.

In majority of [1]H MRs studies based on abundant material deriving our own and from the cooperating centers (over 250 pts in 2004–2007), proton spectroscopy was very accurate in differentiating high and low grade gliomas achieving sensitivity no less than 95% and specificity 92%. Results differences among all centers were not significant; our experience indicates that diagnostic accuracy diminished in the differentiation grade III and grade IV tumors. Knowledge of tumor grading influences therapeutic decisions and should be constituted also by non-invasive diagnostic methods like [1]H MRS. The ratios of maximum Cho/NAA,Cho/Cr and minimum NAA/Cr are highly correlated with tumor grade except for the difference between GBM and AA

No Lac or Lip peak was detected in the solid part of low-grade tumors found only in high-grade gliomas, which suggests that Lip and Lac peaks may have discriminatory power.

Because the presence of mobile lipids in high grade astrocytomas correlates with necrosis and the latter with prognosis, it is strongly possible that mobile lipids in anaplastic glioma can act as a marker for tumors likely to exhibit more aggressive behaviour [4,19,21]. Although large amounts of lipids appear to be specific for anaplastic gliomas or GBM,however their absence does not exclude either of them.

One of the true markers of low grade astrocytoma (LGA) is myoinositol (mI) which indicates proliferation of glial cells and also Cho (Figures 4,5); elevated mI is observed exclusively in this type of tumor. However, in malignant glioma mI decreases due to prevalence of rapid growth and necrosis [20]; Cho has usually slightly lower concentration

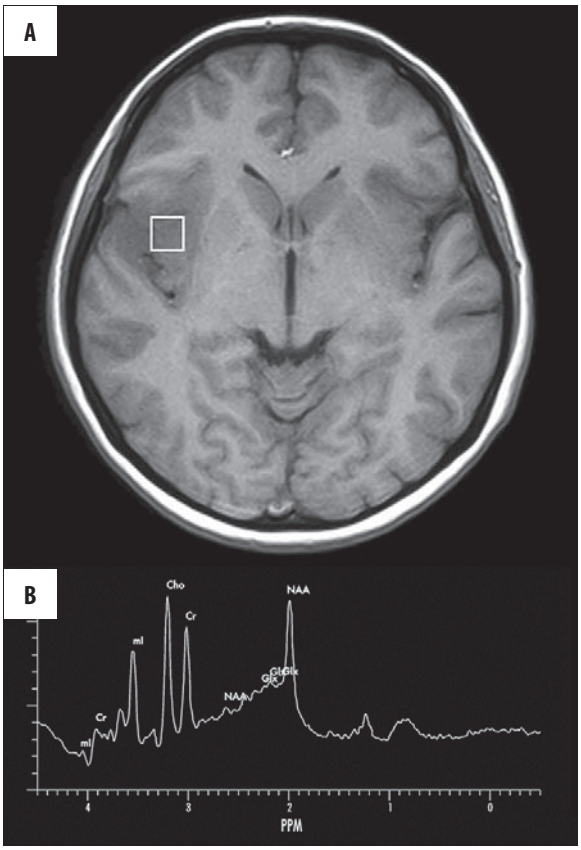


Figure 5. 45-year-old man suffered from first-time episode of epilepsy. ^{1}H MRS obtained from the area of tumor reveals spectrum typical for low grade glioma: elevation of Cho and mI, slightly decreased NAA level. Histopathology confirmed the presence of oligodendroglioma.

in LGA, which we can explain as a result of lower proliferation power and slower cell's destruction in comparison with malignant tumors.

Apart from the fact that ^{1}H MRS is moving forward we are practically able to differentiate several intrancranial tumors, limited to four types: low and high glioma,meningioma and metastases. For example, in meningioma (MEN) alanine (Ala) is the most characteristic peak (1.4–1.5 ppm); this resonance shows high levels of statistical significance for all of Ala compartments.

Other findings characteristic of MEN are:
1. Increase of Cho with respect to LGA,GBM and MET.
2. Increase of Glx in reference to LGA and AA.
3. The lack of Lip 1.3 with respect to MET or GBM.

The strongest discriminative performance between intracranial tumors (Lip,Lac, Ala, NAA, Cho, mI) can be performed in many algorithms, which are widely discussed in chapter entitled "Technical Consideration".

Development of *in vivo* ^{1}H MRS for noninvasively predicting and /or detecting tumor response to therapy at an early stage requires identification of metabolites concentration of which correlates with tumor response to therapy,or those which indicates the failure of treatment.

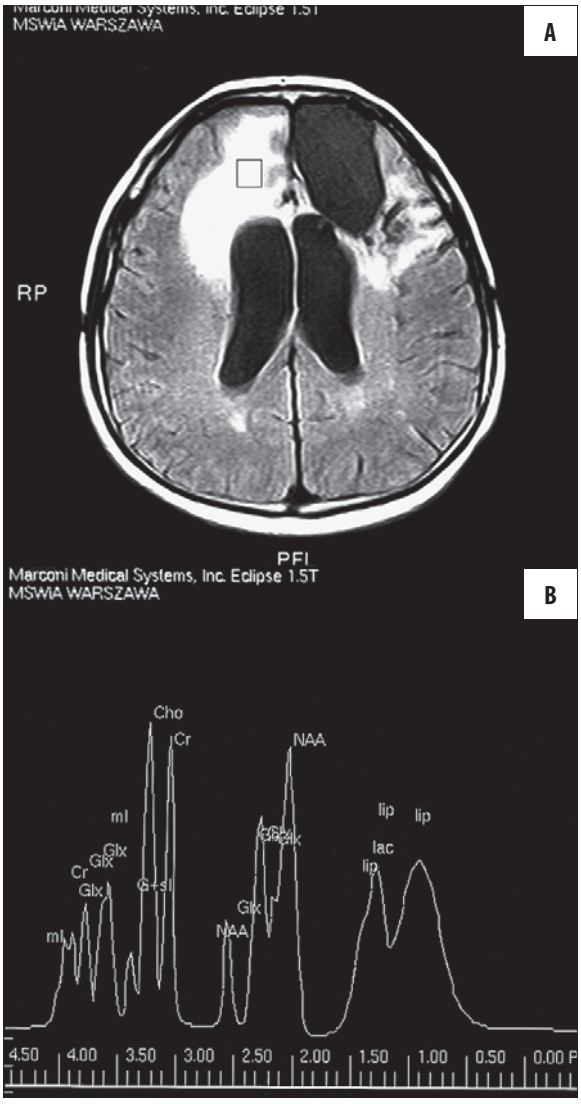


Figure 6. 69-year-old man after surgical removal of GBM in left frontal lobe. The surgery was performed in 2005 and recently we have observed increased frequency of seizures.

In the most studies the ratios of resonance signals assigned to the major ^{1}H MRS – visible metabolites: NAA, Cho, Cr, mI, Lac and Li (methylene group) were evaluated before, during and after post-surgical fractionated radiotherapy (usually 60 and <40 Gy respectively), which was performed in brain's region close to and more distant from the tumor bed; most of researchers reported that four metabolites such as Lac,NAA,Cho and mI can be treated as a markers of local irradiation injury, while diminishing of Lac concentration indicates radiation response; mechanism leading to decreasing of lactate concentration is probably connected with increased blood flow and /or decreased glycolysis activity of tumor's tissue. Choline is the second metabolite which can be a marker for failure of radiotherapy; there are findings which suggest that increasing Cho/Cr and Cho/NAA ratio and increasing of Lac concentration indicates radiotherapy failure and early tumor recurrence [22–25].

^{1}H MRS is valuable method in distinguishing recurrent tumor from treatment related changes (Figures 6,7) In most

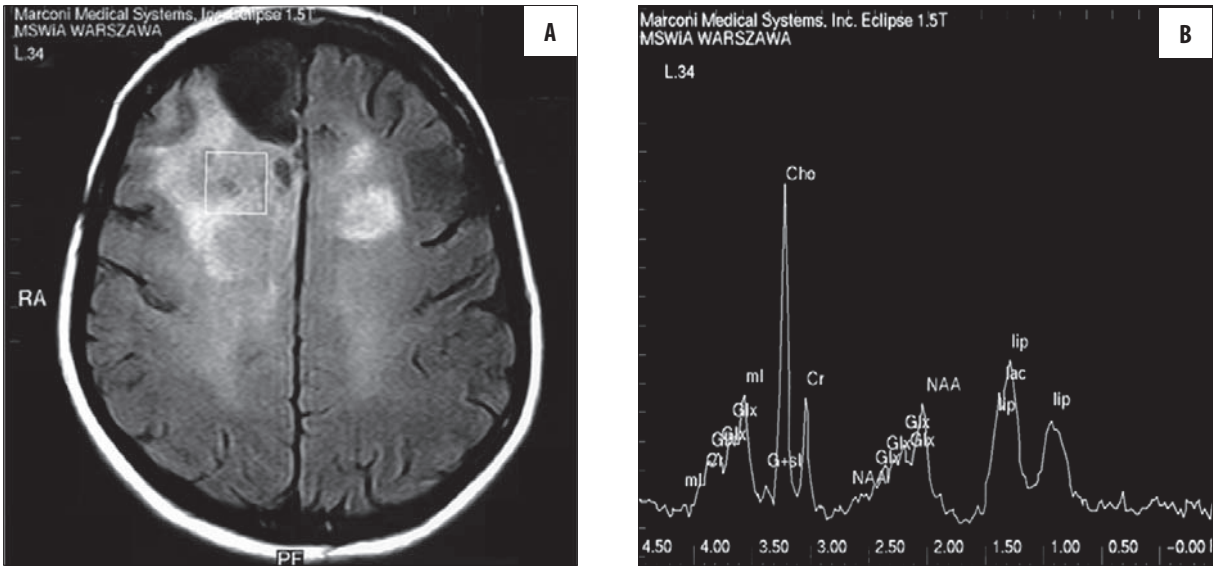


Figure 7. 40-year-old man underwent surgery for anaplactic glioma in 2006. Treated with intensive radiotherapy he hasn't shown signs of recurrence till now. [1]H MRS obtained from right frontal lobe revealed spectrum from. VOI located in adjacent to resection area performed five month after MRI examination which showed, without doubt, recurrence of tumor; Spectrum from the VOI located in this area is typical for the proliferation of the tumor showing elevation of Cho, Lac and Lip, depressed of NAA and Cr due to radiotherapy (leucomacia).

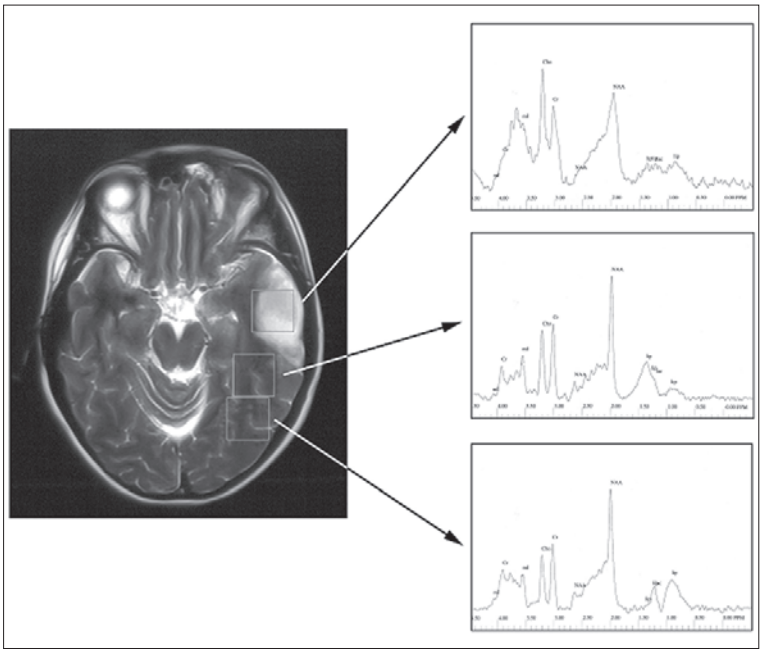


Figure 8. 32-year-old woman underwent surgery due to temporal brain tumor. Low grade glioma was diagnosed. [1]H MRS reveals spectra from solid part of tumor, from border zone and tissue distant from the tumor. There are no signs of recurrence after more than five years since the surgery.

patients from those group increased choline peak and ratio to Cr has been noticed; following several studies quoted by Hollingworth [19] an increased Cho peak was higher than 80% sensitive and more than 85% specific in distinguishing tumor from radiation – induced necrosis; However, many authors note that PET has much higher sensitivity (95%) and specificity (100%) than [1]H MRS in this matter. It can be assumed that fusion of [1]H MRS and CT or MR perfusion are able to improve accuracy in this crucial problem.

MRI reveals post-surgical cavity in the left frontal lobe and extensive area of brain tissue destroyed after radiotherapy (leucomalacia); no mass effect and no edema. [1]H MRS: spectrum from the VOI located in this area is typical for the proliferation of the tumor showing elevation of Cho, Lac and Lip.

The determination of tumor boundaries, especially in high-grade glioma is critically important for the proper planning of treatment. However, the standard diagnostic imaging methods do not enable precise outlining of the extension of tumor cell infiltration into the surrounding tissue (uncertain zone), which appears normal on standard diagnostic MR images (Figures 8,9). Many papers [23–25] reported that [1]H MRS demonstration of metabolic changes in peritumoral zone can modify treatment for cerebral glioma (pre-surgical planning, extension of post-surgical radiotherapy) and allows to predict risk of early recurrence, because the peritumoral

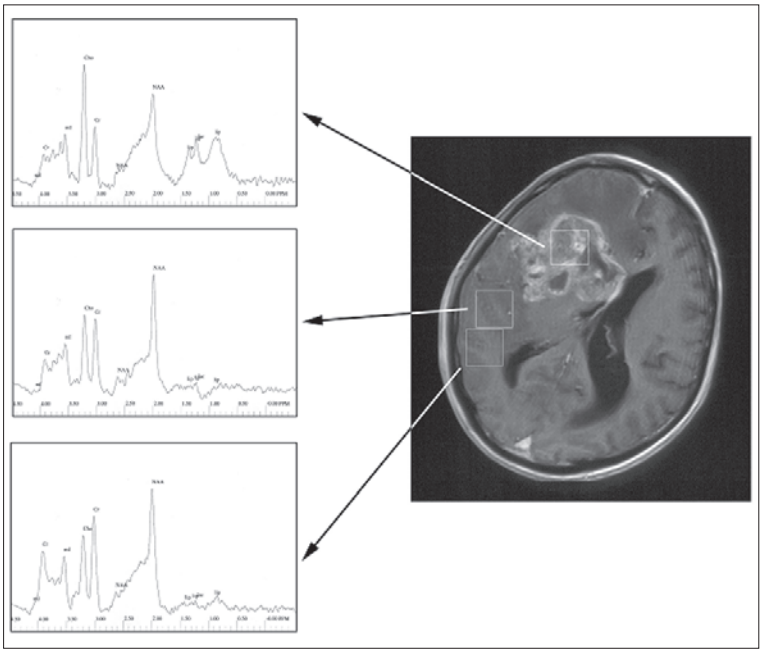


Figure 9. 55 year old man with GBM, confirmed during the surgery. ^{1}H MRS obtained inside the tumor and adjacent tissue indicate tumor infiltration besides apparent tumor. Survival period since surgery till death was 7 months.

zone is most often the starting point for postoperative recurrence of glioma. The clinical importance of the peritumoral zone for future neuropathologic changes has been known for many years; it is assumed that malignant gliomas are not strictly focal lesions, but are also characterized by the cerebral spreading of malignant cells along the axons, perivascular spaces and/or through the subarachnoid space.

Connclusions

Above discussed aspects, considerations and technical possibilities, as well as methodological requirements, guidelines and clinical applications of proton spectroscopy strengthens our belief in the power of this method used in neurooncological diagnosis.

References:

1. Walecki J, Grieb P, Chojnacka E et al: *In vivo* ^{1}H MRS. in intracranial tumors. Pol J Radiol, 1998; 63(3): 225
2. Pieniążek P, Sokół M, Przeorek C: Spektroskopia protonowa magnetycznego rezonansu jądrowego – aspekty metodologiczne o ograniczenia w badaniach mózgu. Rez Magn Med., 1998; 6(1): 11
3. Gajewicz W et al: The use of proton MRS in the differential diagnosis of brain tumors and tumor – like processes. Med Sci Monit, 2003; 9: 97–105
4. Peeling J, Sutherland G: High resolution ^{1}H NMR spectroscopy studies of extracts of human celebral neoplasms. Magn Reson Med, 1992; 24: 123
5. Backer PB, Doris DM: *In vivo* proton MR spectroscopy of the human brain. Progress in Nuclear Magnetic Resonance Spectroscopy, 2006; 49: 99–128
6. Tzika A et al: Biochemical characterization of pediatric brain tumors by using *in vivo* and *ex vivo* magnetic resonance spectroscopy. J Neurosurg, 2002; 96: 1023–31
7. Hubesh B et al: P-31 MR spectroscopy of normal human brain and brain tumors. Radiology, 1990; 174: 401–9
8. Albers MJ et al: Proton-decoupled ^{31}P MRS in untreated pediatric brain tumors. Magnetic Resonance in Medicine, 2004; 53: 22–29
9. Klose U, Bultmann E, Jiru F, Nagele T: CSI-Measurements of the Human Brain at 3T. Magnetom Flash, 2/2005, 46
10. in't Zandt H, van Der Graaf M, Heerschap A: Common processing of *in vivo* MR spectra., NMR, Biomed, 2001; 14(4): 224–32
11. Bottomley PA: The trouble with spectroscopy papers. Radiology, 1991; 181: 344–50
12. Poullet J, Sima DM, Simonetti AW et al: An automated quantitation of short echo time MRS spectra in an open source software environment: AQSES, NMR Biomed, 2007; 20(5): 493–504
13. Ratiney H, Sdika M, Coenradie Y et al: Time-domain semi-parametric estimation based on a metabolite basis set, NMR Biomed, 2005; 18(1): 1-13
14. Elster C, Schubert F, Link A et al: Quantitative magnetic resonance spectroscopy: Semi-parametric modeling and determination of uncertainties, Magn Reson Med, 2005; 53: 1288–96
15. Richards TL: Functional Magnetic Resonance Imaging and Spectroscopic Imaging of the Brain: Application of fMRI and fMRS to Reading Disabilities and Education *http://faculty.washington.edu/toddr/Anonftp/fmrifmrs.doc*
16. Liebfritz D: Basic biochemistry and high resolution NMR. Syllabus 18, ESMRRMB, 12, 1999
17. Salibi N, Boettcher U: Multinuclear MR Spectroscopy at 3 Tesla. Magnetom Flash 2005; 2: 82
18. Mansson S et al: 13C imaging – a new diagnostic platform. Eur Radiol, 2006; 16: 57–67
19. Hollingworth W et al: A Systematic Literature Review of MRS for the Characterization of Brain Tumors. AJNR, 2006; 27: 1404–10
20. Yang D et al: Cerebral glioma: prospective comparison of multivoxel 2D chemical – shift imaging proton MRS,echoplanar perfusion and diffusion – weighted MRI.Neuroradiology, 2002; 44: 656–66
21. Majos C et al: Proton magnetic resonance spectroscopy (1H MRS) of human brain tumors: assessment of differences between tumor types and its applicability in brain tumor categorization.Eur Radiol, 2003; 13: 582–91
22. Walecki J et al: Role of short TE 1H-MRS in monitoring of post-operation irradiated patients. Eur J Radiol, 1999; 30: 154–61
23. Burtscher I: 1H MRS and preoperative diagnostic accuracy: an evaluation of pts with intracranial mass lesions who underwent stereotactic biopsy. Phd Thesis, Lund Univ, Sweden, 1999
24. Bhujwalla ZM et al: Detection of tumor response to radiation therapy by *in vivo* proton MR spectroscopy. Int J Radiat Oncol Biol Phys, 1996; 36: 635–39
25. Tarnawski R et al: ^{1}H MRS *in vivo* predicts the early treatment outcome of postoperative radiotherapy for malignant gliomas. Int J Radiat Oncol boil Phys, 2002; 1271–76