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METHODOLOGY AND CLINICAL SIGNIFICANCE OF MAGNETIC RESONANCE SPECTROSCOPY

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Annotation: The clinical application of magnetic resonance spectroscopy (MRS) has long been limited by its low sensitivity. In recent years, the development of clinical MRI systems with high magnetic field strengths, such as three Tesla, and the sensitivity of their pulses with optimized radiofrequency have significantly improved. As a result, in vivo MRS has become an increasingly common technique in the clinic. In particular, a description of the main resonances present in brain MR spectra is given, along with several examples of deviations from the normal spectral pattern associated with inborn errors of metabolism. In addition, the possible role of MRS in oncology is illustrated by examples of MR spectra of brain tumors.

Keywords: Magnetic resonance spectroscopy, MRS, diagnostics, Methodology, Metabolism, Brain diseases.

МЕТОДИКА И КЛИНИЧЕСКОЕ ЗНАЧЕНИЕ МАГНИТНО-РЕЗОНАНСНОЙ СПЕКТРОСКОПИИ

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Аннотация: Клиническое применение магнитно-резонансной спектроскопии (МРС) долгое время ограничивалось ее низкой чувствительностью. В последние годы значительно улучшилась разработка клинических МРТ-систем с высокой напряженностью магнитного поля, таких как три Тесла, и чувствительность их импульсов с оптимизированной радиочастотой. В результате МРС in vivo стала все более распространенной методикой в клинической практике. В частности, дается описание основных резонансов, присутствующих в МР-спектрах головного мозга, наряду с несколькими примерами отклонений от нормального спектрального паттерна, связанных с врожденными нарушениями метаболизма. Кроме того, возможная роль МРС в онкологии иллюстрируется примерами МР-спектров опухолей головного мозга.

Ключевые слова: Магнитно-резонансная спектроскопия, МРС, диагностика, методология, метаболизм, заболевания головного мозга.

Relevance. Magnetic resonance (MR) spectroscopy is commonly known as an analytical technique for identifying molecules in chemistry and determining

their biophysical properties. The main clinical application of nuclear magnetic resonance is to obtain detailed anatomical images of the human body using magnetic resonance imaging. However, not only MRI, but also NMR spectroscopy has several clinical and biomedical applications. When NMR is used in vivo, and in particular in the clinic, the convention is to omit the term "nuclear" from the name, since the inclusion of this part can lead to false associations with nuclear medicine, radioactive materials, and ionizing agents. Therefore, in vivo NMR spectroscopy is called magnetic resonance spectroscopy (MRS). As in its application in chemistry, MRS allows the detection of relatively small molecules, typically at concentrations of 0.5–10 mM, with sufficient flexibility inside or outside cells or extracellular spaces. The resulting MR spectra provide information about metabolic pathways and their changes, making MRS a well-suited technique for monitoring metabolic changes due to disease and monitoring treatment. This review provides an overview of in vivo MRS methodology and clinical cases, from which those familiar with the chemical applications of MR spectroscopy can learn about its clinical application. The main focus is on 1H MRS of the human brain, which is the main clinical application of MRS. Since it is not possible to provide a complete description of all biomedical applications of in vivo MRS, this review is limited to examples of human brain MRS in the detection of inborn errors of metabolism, brain cancer diagnosis, and research.

Materials and Methods. MR spectra can be obtained using various nuclei of several metabolites in the human body, such as 1H, 31P, 19F, 13C, 23Na, all of which can provide valuable metabolic and physiological information. However, in biomedicine, 1H MRS is mainly used due to the high sensitivity of the 1H nucleus, the almost 100% availability of this isotope, and the abundance of this nucleus in most metabolites. In addition, 1H MRS can be performed relatively easily using standard radiofrequency (RF) coils of clinical MR imaging systems designed for diagnostic MR imaging. In fact, the MR signal of 1H nuclei in water and fat are used to obtain MR images. Common clinical MR systems have magnetic field strengths ranging from 0.2 to 3 Tesla (T). In MRS applications, it is usually the smaller metabolite signals that are of interest, rather than the water and fat signals, that are of interest, so a sufficiently strong magnetic field is required. Therefore, most clinical MRS measurements are performed using MR systems with field strengths of 1.5 T or higher. In particular, the advent of clinical MR systems with field strengths of 3 T has improved the signal-to-noise ratio in MR spectra and made it possible to obtain spectra from smaller volumes.

Results and Discussion. For 1H MRS, an RF body coil mounted inside a magnetic bore can be used as an RF transmitter in conjunction with another coil placed on the surface or around the body to receive the RF signal. Another possibility is to use a transmit-receive coil used for both transmission and reception. In recent years, many improvements have been made to MR coil design, such as the development of various phased array designs, which have led to increased sensitivity. A smaller surface area than the coil provides higher MRS, but the sensitive region is much smaller. In the phased array coil concept, a higher

MRS can be combined with an extended field of view (FOV) by combining multiple surface coils. For MRS using cores other than 1H, standard MR coils cannot be used, but special coils tuned to the desired core must be purchased or built. These often consist of multiple coils, one of which is tuned to the desired core, such as 31P or 13C, and the other tuned to 1H for separation or polarization transfer. For all MRI and MRS examinations, some safety precautions should be taken against potential hazards arising from the main magnetic field, changing magnetic field gradients, or RF radiation. No harmful physiological effects are known to result from the main magnetic field of 1.5-3 T clinical MR systems, but the strong magnetic field attracts ferromagnetic objects. It should be determined whether the patient has an implanted electronic device such as a pacemaker or internal defibrillator, or other magnetic materials such as cochlear implants or ferromagnetic aneurysm clips. Also, the presence of metal fragments in critical locations, e.g., in the eye or brain, is a contraindication for MRI examination. And even a doctor entering the room with loose metal objects such as pens or scissors in his pocket can pose a risk to the patient lying in the magnet, as these objects can be directed towards the patient by the strong forces of the magnetic field. In addition, watches and credit cards should be left outside the room, as they can be damaged by the magnetic field.

Changing magnetic field gradients causes acoustic noise, for which patients should wear ear protection. In addition, rapid gradient changes can cause nerve stimulation, but such rapid changes are not commonly used in MRS, and the gradients used in clinical scanners are monitored and a warning is issued if the gradient changes are too rapid. The net effect may be a slight warming of the patient (1-2C) by the RF radiation. The amount of energy absorbed per tissue mass, defined as the Specific Absorption Rate (SAR), is also monitored and strictly limited in clinical MR systems. One non-safety-related contraindication is claustrophobia. Patients with severe claustrophobia, as well as patients who are not able to lie still, such as young children, may need to be sedated or anesthetized for the MRI scan. MRS data acquisition. Typically, an MRS scan begins with the acquisition of some anatomical MR images of the organ of interest. These MR images are then used as a guide to select the tissue volume from which the MR spectrum will be acquired. In single voxel spectroscopy (SVS), this can be a single volume located in a tumor or a specific location where metabolism may be disturbed due to the patient's disease. Another option is magnetic resonance spectroscopic imaging (MRSI), originally introduced as chemical shift imaging, in which a large volume is divided into several small voxels, each of which generates a spectrum simultaneously. This technique, which is a kind of hybrid of MRS and MRI, is suitable for determining spatial distributions, for example, for identifying the area affected by tumor infiltration. In 1H MRS, methods such as chemical shift water suppression (CHESS; Haase et al. 1985) or water suppression enhanced by T1 effects (WET; Ogg et al. 1994) are usually used to suppress the water signal when acquiring metabolite spectra. Additionally, a spectrum is obtained without water suppression, which can be used for line shape correction and quantification.

The main SVS techniques used to obtain 1H MR spectra, mainly applied to the brain, are point-resolution spectroscopy (PRESS; Ordidge et al. 1985; Bottomley 1987) and stimulated echo acquisition. The main difference between STEAM and PRESS is that in STEAM, a stimulated echo is acquired with three 90 pulses and a second echo is acquired with a 90-excitation pulse, followed by two 180 refocusing pulses in PRESS. In both methods, each of the three pulses is combined with a gradient in the X, Y, or Z direction, which is used to select a slice in that direction. Only the signal of a quadrature sound (one voxel) is focused and acquired in all three slices. The echo time (TE) can be changed by changing the delay times between pulses. If a longer TE is used, the signal is reduced due to T2 and the phase of the multilet signals is shifted due to J-coupling. For quantitative measurements, a combination of a short echo time and a long repetition time (TR) is usually used to obtain signals with minimal signal loss due to T2- and T1-weighting. Longer TE measurements are used only to obtain a limited number of sharp (often single) resonance spectra, which are relatively easy to analyze. TEs of 135–144 ms are often used because this results in a spectrum in which the doublet signal of lactate, which has a J-coupling constant of approximately 7 Hz, is completely inverted.

Results. A key difference between the two SVS pulse sequences is that half of the signal is not used in STEAM by the stimulated echo acquisition, which results in a 50% lower SNR compared to PRESS. A disadvantage of PRESS volume selection has long been the use of two 180 pulses. Because of the limited maximum pulse intensity, the pulse length of a 180 pulse is usually longer than 90 pulses or the pulse shape is tailored to limit its length. Therefore, the presence of these two 180 pulses does not allow for very short TEs, they lead to a less optimal slice selection profile, and their bandwidth is smaller, causing a larger chemical shift (CSD) artifact. This CSD artifact arises from the fact that signals with different chemical shifts experience different (frequency-coded) slice selections and therefore do not originate from exactly the same volume. This effect is amplified at high magnetic field strengths. For these reasons, STEAM is the method of choice for data acquisition with short TE and precise volume selection. However, recently the characteristics of the 180 pulses used in PRESS have been increasingly improved, e.g., by numerical optimization (Schulte et al. 2008) or by replacing each 180 pulses with two adiabatic pulses (Scheenen et al. 2008). These developments, together with the very significant factor of SNR increase compared to STEAM, have made the PRESS sequence currently the most popular SVS sequence for 1H MRS. The main disadvantage of MRSI is the presence of voxel bleeding, i.e., the voxel spectrum can be contaminated with signals originating from neighboring voxels of positive and negative intensity due to the shape of the point spread function associated with the limited matrix size used in MRSI (Brown 1992). The effect of voxel bleeding can be reduced by using special filters before the Fourier transform (FT) in the spatial domain, but this increases the size of the voxels. Typically, SVS is used when precise quantification is required, and MRSI is used to obtain information about spatial distributions.

Conclusions: It has been shown that MRI is not limited to applications in chemistry, but that MRS is also a valuable tool in the clinic. With the current availability of MR scanners with sufficiently high field strengths, such as 3T, combined with optimized pulse sequences and RF, the initially limited sensitivity of in vivo MRS has been greatly improved. This, combined with the unique metabolic information provided by MRS, will ensure that this technique will be routinely used in the clinic in the future.

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