MR Spectroscopy and Spectroscopic Imaging of the Brain: Principles and Applications

Hyeon-Man Baek, Ph.D

Bioimaging Research Team, Korea Basic Science Institute, Ochang, Korea; Department of Bio-analytical science, University of Science & Technology, Daejeon, Korea

Abstract:

In vivo magnetic resonance spectroscopy (MRS) and the related technique of magnetic resonance spectroscopic imaging (MRSI) are widely used in both clinical and preclinical (e.g., animal model) research for the non-invasive evaluation of brain metabolism. They are also used in medical practice, although their ultimate clinical value continues to be a source of discussion. This presentation reviews the general information content of brain spectra and commonly used protocols for both MRS and MRSI and also touches on data analysis methods and quantitation.

In vivo MRS of the human brain has developed rapidly since its first observation in the 1980s (1, 2). Early studies in both humans and animals focused on the 31P nucleus which allowed the measurement of energy metabolites such as phosphocreatine and ATP, as well as inorganic phosphate and phosphoesters. With the development of improved techniques for spatial localization and water suppression, proton MRS became more prevalent in the 1990s because of its higher sensitivity and greater convenience (since it can be performed without hardware modification on most MRI machines, unlike MRS of other nuclei) (3). While interest remains, particularly at high magnetic field strengths, in nuclei such as 31P, 23Na, and 13C (particularly for isotopically labeled and/or hyper-polarized molecules (4)), the vast majority of brain MRS studies use the proton. Because of its relatively low sensitivity, only small, mobile molecules which are present in millimolar quantities are generally detectable in an in vivo MR spectrum. At commonly used field strengths such as 1.5 or 3.0 T, only signals from choline (Cho), creatine (Cr), and N-acetylaspartate (NAA) are observed in normal brain at long echo times (e.g., 140 or 280 ms), while compounds such as lactate, alanine, or others may be detectable in pathological conditions which increase their concentration (5). At short echo times (e.g., 35 ms or less) other compounds such as glutamate, glutamine, myo-inositol, as well as lipids and macromolecular resonances, are detectable.

MR spectroscopy is traditionally performed in the clinical environment using a single-voxel (SV) approach. On occasion, 2D or 3D MR spectroscopic imaging (MRSI) may be performed in conjunction with (usually) PRESS-based localization (6, 7). The

PRESS sequence is usually performed to restrict the signal localization to the sub-region of the brain of interest, which allows smaller fields-of-view to be used, avoids artifacts from peripheral regions, and reduces the number of spectra that need to be processed. However, this approach also suffers several drawbacks, including lack of coverage of potentially important brain regions, chemical shift displacement artifacts at the edge of the PRESS voxel, and dependence on the operator of correct voxel placement. For these reasons, over the years there has been development of alternative MRSI techniques which either have whole-slice, multi-slice, or 3D whole-brain coverage. Whole-brain coverage at high spatial resolution should be the goal for clinical applications (since, a priori, the location and extent of a metabolic abnormality may not be known ahead of time), but important challenges to this methodology are the need to perform it in clinically reasonable scan times, to optimize and simplify data analysis, quantitation, and visualization software. In addition, recognizing and removing artifacts is an important step for clinical implementation in order to avoid incorrect interpretation by clinicians. Because extended spatial coverage at high resolution leads to long encoding-times, high speed acquisition techniques such as echo-planar spectroscopic imaging (EPSI) are required (8), preferably also in combination with parallel imaging acceleration such as SENSE or GRAPPA (9-11). Also, high-resolution multi-dimensional data sets (particularly those recorded with 32-channel coils) are large (e.g. > 5GB not unusual) so attention equally needs to be paid to acceleration of the reconstruction and data transfer.

In general, MRSI is more sensitive to imperfections and artifacts than conventional MRI, because the signals to be measured are small, often contaminated by much larger unwanted artifact signals (water and lipid), and also has a much more stringent requirement on field homogeneity. Field inhomogeneity may arise from several reasons, including the air-tissue interfaces within the cranium, post-surgical effects, hemorrhage, or incorrect adjustment of shim currents. Generally, this will manifest as decreased signal on MRSI, but may occasionally give increased signal if it leads to residual water or lipid contamination in the spectrum. Importantly, various ‘quality’ measures may be derived from the MRSI data itself which can help in interpreting metabolic images and deciding if focal signal intensities are real or artifact (12). Such quality measures may include metabolite or water peak linewidth, water peak intensity, or an uncertainty measure from spectral curve-fitting (e.g. Cramer-Rao Lower Bounds (CRLB)). Finally, atlas-based analysis methods and integration of spectra across voxels may improve spectral quality (particularly signal-to-noise ratio (SNR)) compared to analysis of individual voxels from the dataset.

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