Specialty area: Preclinical Imaging

Dave Morse David.Morse@Moffitt.org

Highlights

- Principles of Magnetic Resonance Spectroscopy (MRS) and Spectroscopic Imaging (MRSI) relative to magnetic resonance imaging (MRI): Chemical shift (spectral width), MR visible nuclei (natural abundance and gyromagnetic ratio, hyperpolarization); and pixels vs. voxel volumes.

- Technical considerations specific to MRS: Special coils (tuning); voxel dimensions (shimming, sequences: e.g. ISIS).

- Review preclinical applications of MRS: In vivo microenvironment, metabolism (tumor pH, glycolysis, lipid and phospholipid); (early) therapeutic response.

SPECTROSCOPY

- TARGET AUDIENCE: Basic science and translational researchers and clinicians with an interest in preclinical in vivo studies involving the tissue or tumor microenvironment, metabolism and therapy response.

- OUTCOME/OBJECTIVES: Understand the principles, technical challenges and applications of in vivo MRS in preclinical studies.

- PURPOSE: MRS methodology provides tools for quantifying microenvironmental and metabolic parameters related to distinct pathologies, and to non-invasively observe dynamic changes in these parameters, in vivo, as related to enzymatic activities or therapeutic interventions in real-time.

- PRINCIPLES: Unlike MRI, where image pixel values are typically generated from the spatially localized proton signal, which is predominately composed of water and fat, in vivo MRS allows for the quantification of metabolites that are of much lower natural abundance within a “voxel” volume. Individual metabolites are separated on a spectrum within the frequency range examined and the degree of separation is a function of “chemical shift.” For proton spectroscopy, the water peak must be suppressed to resolve the metabolite peaks of lower abundance. In addition to ^{1}H, a number of additional MR visible nuclei can be observed based on their natural abundance and gyromagnetic ratio, increasing the number of natural metabolites that can be studied by MRS. Dynamic nuclear polarization (DNP) has allowed for the hyperpolarization of contrast agents, greatly increasing the signal to noise ratio, allowing for MRI of signal from nuclei other that ^{1}H, e.g. ^{13}C. However, hyperpolarization can also be used for enhanced spectroscopic studies that enable the quantification of substrate metabolism in vivo. In addition to MRS where the spectrum is generated from a single ”voxel” volume, MRSI allows for the generation of images based on metabolite quantifications generated from a number of adjacent spatially localized “voxel” volumes.

- TECHNICAL CONSIDERATIONS: Major technical considerations in MRS will be briefly covered, which generally involve the need for special coils that can be dual tuned to the ^{1}H resonance frequency for MRI and to frequencies for other nuclei to generate the spectrum. MR images are needed for volume selection methods, e.g. ISIS. Shimming is of greater importance for MRS relative to MRI and fat and water suppression (1H MRS) may be needed. Sophisticated analyses e.g. deconvolution algorithms, may be needed for quantification of the different elements within in vivo spectra as peak resolution from tissue signals is low relative to NMR of extract samples.

- APPLICATIONS: Multiple MRS and MRSI approaches have been employed to non-invasively measure pH levels in the in vivo tissue microenvironment. These include the use of measurable agents that have peaks with pH sensitive chemical shift and quantification of the conversion of hyperpolarized ^{13}C-labeled bicarbonate to CO_2. Metabolism studies have included the in vivo quantification of intermediates of glycolysis, lipid metabolism and of phosphatidylcholine anabolism and catabolism. Changes in these metabolite levels have been studied in the context of therapy response. The ability to use DNP to hyperpolarize metabolic substrates has greatly enhanced studies of metabolism, allowing for the in vivo non-invasive quantification of enzyme activities, increasing the potential for clinical translation and use of this technology for diagnosis and early detection of therapeutic response.

- CONCLUSION: In vivo MRS and MRSI of small animal models can be used to explore basic research questions related to the tissue and tumor microenvironment, metabolism and to follow early therapy response. There is also potential for translation and use of in vivo spectroscopy applications for use in the clinic for diagnosis and to follow early therapy response for guidance of patient care.

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- Technical considerations for MRS

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- Microenvironment (pH)

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- Metabolism (glycolysis, pentose phosphate, lipid, phospholipid)

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- Therapy response (Pyruvate-Lactate, tCho/lipids, PCho)

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