Introduction

Magnetic Resonance Spectroscopy of the brain reveals a wealth of metabolic information, not only from a single region of interest (single voxel MRS), but spatially mapped over potentially the entire brain as well (MRSI). Particularly for relatively highly concentrated compounds in the brain with weakly or non-coupled spin systems with relatively long T2 relaxation properties, like the methyl proton spins in NAA at 2 ppm, in total creatine at 3.0 ppm or in total choline at 3.2 ppm, MRSI has successfully been applied in research studies as well as in clinical practice [1].

For compounds at either low concentrations, coupled spin systems, short T2 relaxation, or with partially overlapping signals of other compounds, MRSI requires challenging acquisition methods before their content can be obtained accurately [2]. High field proton MRS with proper B0 shimming is used to enhance the sensitivity and to reduce overlapping resonances, while short echo times (TE) are used to minimize the effect of spin evolution of coupled spins and T2 relaxation [3]. However, when applied in spectroscopic imaging, these techniques require good water suppression, but even more important, excellent outer volume suppression to exclude contaminating signals from outside the region of interest [4].

Since the range in chemical shift of the proton spins in most metabolites is small, and almost all different metabolites have hydrogen nuclei, the chance of overlapping resonances is high even at high field strengths. Therefore, the higher chemical shift dispersion of other isotopes in these molecules may be explored to distinguish even more and different metabolites than obtained with 1H MRS. For instance, 31P MRSI can be applied to obtain many compounds in energy metabolism [5], or metabolism involved in cell proliferation (i.e. choline metabolism) [6]. In fact, by using saturation transfer techniques [7] even chemical exchange rates can be quantified and mapped over the brain. Although the intrinsic sensitivity for these isotopes is less than for 1H spins, SNR can be enhanced substantially for some compounds by taking advantage of Nuclear Overhauser Enhancement (NOE) or polarization transfer techniques [8].

This course addresses the challenges in obtaining accurate MRSI data of the brain, focusing on excluding signal contamination in short TE 1H MRSI (from mice to men), and illustrating the potential of SNR enhanced phosphorus MRSI in the human brain.

High field Proton MRSI of the brain at short TE

When regions of interest are selected that exclude large susceptibility transitions, B0 shimming can be excellent over the entire region of interest. As such, spectral resolution will be optimal, and chemical shift selective water suppression can be obtained easily. However, outside the region of interest, in general the B0 shim will not be optimal, resulting in substantial artifacts related to off resonance signals. Water suppression will be insufficient with a high probability that residual signal may shift into the spectral range of the metabolites of interest [2]. These signals will contaminate the spectra in the region of interest due to voxel bleeding caused by spatial Fourier transform. Another potential artifact may originate from highly concentrated lipids at the skull, generally outside the region of interest. With chemical shift selective water suppression techniques only, these signals will not be attenuated and may therefore leak into the voxels of interest by spatial Fourier transform as well.

Exclusion of signals from spins outside the region of interest can be realized most effectively by volume selective perturbation of the spins of interest before applying the phase encoding
Figure 2. Illustration of the chemical shift displacement artifact (CSDA) of spins with a difference of 2.7 ppm in chemical shift (i.e. water versus NAA) using a PRESS sequence at 3T (left) or at 7T (right) with a maximum B1 of 27 μT.

An alternative in excluding signals originating from outside the region of interest would be to use outer volume suppression prior to excitation of all spins. Although intrinsically less effective as STEAM, PRESS or LASER, when combined with phase encoding at a field of view (FOV) that includes also the tissue outside the region of interest, the combined suppression can be superb. Pulse acquire MRSI with a minor acquisition delay can be applied to obtain the FID with Localized Outer Volume Suppression (FIDLOVS) with hardly any CSDA or losses due to T2 relaxation or spin evolution [14]. In fact, when these OVS pulses are realized with RF shimmed multi transmit coils [15], or omitted with constrained B0 shimming, RF power deposition can be reduced even further (Figure 3 [16]).

Figure 3: MRSI dataset obtained at 7T from the human brain with a pulse acquire sequence and RF shimmed OVS [16].

SNR enhanced phosphorus MRSI of the human brain

Although textbooks may imply that the sensitivity in detecting 31P compared to 1H spins is related by the third power of the gyromagnetic ratio of these nuclear spins (i.e. magnetic moment, population difference, and flux-changes in the coil), the actual sensitivity difference in vivo at high fields is substantially less. Since tissue losses dominate at high fields, even in the detection of 31P spins, the flux-changes in the coil remain approximately constant for both frequencies. When using 1H to 31P polarization transfer techniques, also the population difference can be transferred leading to an overall sensitivity difference of approximately linear to the gyromagnetic ratio of these nuclear spins (i.e. 2.4 fold per nucleus). Increasing the spatial resolution by 34% in all 3 dimensions would result in approximately an equal SNR per nucleus.

As the number of metabolites that contain 31P nuclei is substantially less than the ones that contain 1H nuclei, and the spectral range is larger than in 1H MRS, the chance of overlapping resonances is substantially less in 31P MRS. Figure 4a shows an example of a 31P MRSI dataset obtained from the human brain, clearly illustrating resonances of PCr, Pi, ATP, PC, PE, GPE, and
GPC. Using $^1$H to $^{31}$P polarization transfer, clearly the gain in SNR of some compounds can be appreciated (Figure 4b) [8]

![Figure 4: localized $^{31}$P MR spectra obtained from the human brain at 3T clearly visualizing resonances of energy metabolites (ATP, P Cr and Pi (a)) as well as compounds involved in cell proliferation (PE, PC, GPE, GPC (b)), which SNR can be increased using $^1$H to $^{31}$P polarization transfer (c).](image)

**Conclusion**

MRSI at high fields can map substantially more metabolites than NAA over the brain. Excluding signals outside the region of interest with sequences at short TE can provide accurate proton MRSI datasets. Even MRSI of other nuclear spins, like $^{31}$P can be obtained with high SNR mapped over the human brain.

**References**