

## Fast $^{31}\text{P}$ metabolic imaging of human muscle

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### Introduction

Phosphocreatine (PCr) and Adenosine triphosphate (ATP) are important metabolites involved in the energy metabolism. Due to the low intrinsic SNR of the  $^{31}\text{P}$  nucleus, 3D  $^{31}\text{P}$ -MR spectroscopic imaging (MRSI) at clinical MR systems (1.5 and 3T) requires long measurement times. The increased sensitivity available at 7T provides opportunities for direct  $^{31}\text{P}$  metabolic imaging. Generally, MRI of tissues or organs with multiple resonances results in chemical shift artefacts in the frequency-encoding direction (water-fat shift in regular MRI). If one is not interested in the complete  $^{31}\text{P}$  spectrum selected resonances can be excited and completely spatially separated in the frequency-encode direction within one image by choosing an appropriate imaging bandwidth. The large chemical shift dispersion between two resonances (e.g. PCr and ATP) is then exploited to create one image in which both metabolites are displayed next to each other (equivalent to an extreme water-fat shift in proton MRI).

Here we combined a 3D gradient echo imaging sequence (GRE) with a dual frequency selective Shinnar-Le Roux (SLR) excitation pulse for direct fast  $^{31}\text{P}$  metabolic imaging. The SLR pulse selectively excites the PCr and  $\beta$ -ATP resonances simultaneously. With proper choice of imaging bandwidth, one wide field of view (FOV) image contains both a PCr and a  $\beta$ -ATP map, separated by their chemical shift difference.

### Method

The  $^{31}\text{P}$  MRI sequence consists of an unlocalised 3D gradient echo (GRE) sequence using a frequency-selective Shinnar-Le Roux (SLR) pulse for excitation. The excitation pulse (duration 10 ms) symmetrically selects two frequency bands of 350Hz (ramps of 150Hz). By positioning the carrier frequency of the SLR pulse exactly in between the resonances of PCr and  $\beta$ -ATP (0 ppm and 16.4ppm), these two resonances are excited (Fig.1). By choosing the FOV more than twice the size of the object and adapting the imaging bandwidth (Hz/pixel) to the imaging matrix of the  $^{31}\text{P}$  GRE sequence, the PCr and ATP images are separated within one image. At a bandwidth of 300Hz/pixel and a 3D matrix size of 16x16x20, it is possible to obtain a 3D image set of PCr and ATP of the upper leg within 3:14 minutes (TR=300ms, TE=7.1ms, 2 averages, voxel size=31.3mm\*31.3mm\*20.0mm) (Fig.2). By increasing the matrix size to 32x32x20mm and decreasing the bandwidth to 160Hz/pixel we could obtain a high resolution image set of PCr in the upper leg in only 3.14 minutes (Fig.3).

Measurements of the quadriceps femoris of one healthy male volunteer were performed at a 7T Magnetom whole body MR system (Siemens Medical Solutions, Erlangen, Germany) operating at 120.299 MHz for  $^{31}\text{P}$ . A circularly polarized  $^1\text{H}$  birdcage head coil was used for anatomical MRI and an in-house developed double loop quadrature TxRx surface coil (fixed on top of the upper leg) was used for  $^{31}\text{P}$  imaging. The  $^{31}\text{P}$  surface coil provides an elliptical coil profile.

A simple PCr recovery curve was measured by acquiring  $^{31}\text{P}$  images of PCr and ATP before (resting state), during and after a moderate exercise inside the scanner. The subject was asked to contract the quadriceps 30sec before and during one measurement. This measurement was followed by two measurements during which the subject relaxed the quadriceps. A region of interest was drawn inside the vastus lateralis and image intensities of 4 subsequent slices in the leg were averaged and plotted against time (Fig.4).

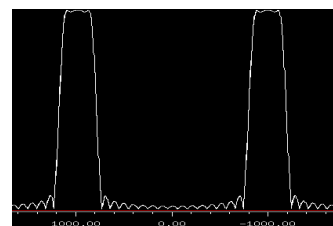


Figure 1. Shinnar-Le Roux optimized dual frequency selective pulse profile. The two passbands are separated by 1972 Hz, 16.4 ppm of the  $^{31}\text{P}$  spectrum at 7T

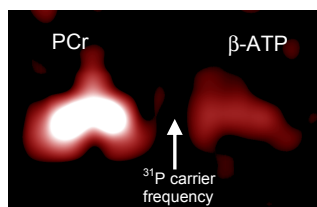


Figure 2. Separated PCr and  $\beta$ -ATP signals of the upper leg

### Results and Discussion

The principle of separating the PCr and the  $\beta$ -ATP signal on the basis of their chemical shift difference within one image worked well. The PCr signal allows for high resolution imaging, whereas the SNR of  $\beta$ -ATP is too low to obtain an image with high resolution, because of its low concentration and short  $T_2^*$ . Signals conventionally acquired with MRSI are now visualized without any further post-processing. As the spectral dimension of conventional MRSI is omitted no spectra need to be fitted, only an accurate calculated translation in the frequency encoding direction could match the  $^{31}\text{P}$  images to anatomical MRI. As the flip angle and repetition time can be varied, acquisition time can be short and the data analysis simple. Maps of the PCr to ATP ratio can be constructed by taking the ratio of the appropriate image sections. The method can be further optimized by adjusting the pulse shape and duration to shorten echo time or to excite other resonances simultaneously.

In the recovery experiment we illustrated the potential for clinical use of the method by observing a decrease of PCr in the quadriceps of the volunteer during exercise and a fast return to normal PCr level afterwards. The ATP-level remained stable (Fig.4).

### Conclusion

Direct  $^{31}\text{P}$  metabolic imaging with a dual frequency selective excitation at 7T enables studies of phosphorylated compounds with high spatial and temporal resolution. The chemical shift dispersion between phosphorylated resonances can be exploited to obtain MR images containing a separated map of multiple metabolite resonances. Besides the examination of muscles, this concept can also be applied to the brain, and even further expanded to other MR-detectable nuclei.

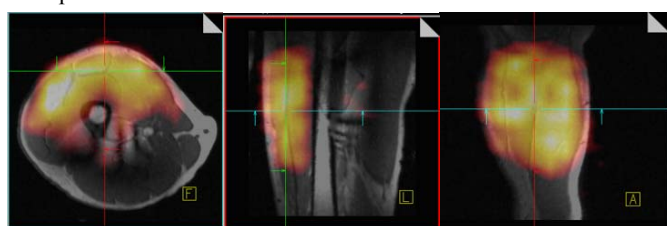


Figure 3. High resolution 3D PCr image set matched with an anatomical image of the upper leg of a volunteer

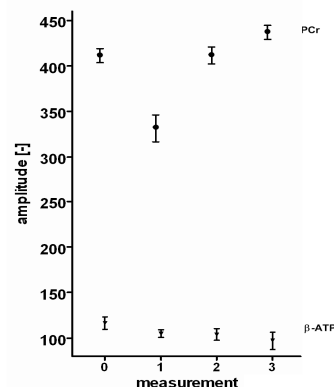


Figure 4. PCr and  $\beta$ -ATP signal of the vastus lateralis before (0), during (1) and after (2,3) moderate exercise