Direct ^{31}P Magnetic Resonance Imaging Applying the Nuclear Overhauser Effect

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Target Audience: Scientists and physicians interested in the field of non-proton MRI.

Purpose: Phosphorus (^{31}P) can be found in a couple of biomolecules in the human body. Especially phosphocreatine (PCr) and adenosine triphosphate (ATP) play a crucial role in physiological processes such as energy metabolism. Due to the distinct chemical shift of ^{31}P in these molecules, it is possible to image their spatial distribution using frequency selective excitation techniques in MRI [1,2]. In the human calf muscle these metabolites feature concentrations of ~30mM/l of PCr and ~10mM/l of ATP [3]. In comparison to ^{1}H the *in-vivo* signal of ^{31}P is four orders of magnitude smaller. For that reason this work focuses on the Nuclear Overhauser Effect (NOE) to increase the SNR of ^{31}P MRI [4].

Methods: ^{31}P-MRI was conducted on a 3T whole body MR system (Magnetom TIM Trio, Siemens Healthcare, Erlangen, Germany) using a double-resonant (^{31}P/^{1}H) quadrature birdcage coil (Rapid Biomed GmbH, Rimpar, Germany).
Phantom-study: Solutions of different phosphorous metabolites and distilled water were examined. The concentrations of phosphocholine (PC), inorganic phosphate (Pi) and PCr were 500mM/l and of ATP 250mM/l. Therefore, a standard FLASH sequence (TR=70ms, TE=4.8ms, FA=10°, 32 averages, TA=1min, resolution: 8×8×10mm^3, 16 averages) with and without preceded ^{1}H NOE pulses (10 pulses, 5ms duration, FA=90°, 1ms pause) was used to determine the NOE enhancement factors whereas the whole phosphorous spectrum was excited (c.f. Tab. 1).
Muscle-imaging: Calf muscle images of four healthy volunteers were acquired using a frequency selective 3D ^{31}P FLASH sequence (TR=53ms, TE=8.3ms, FA=7°, TA=33min, resolution: 1cm isotropic resolution, 50 averages) with preceded ^{1}H NOE pulses (6 pulses, 5ms duration, FA=90°, 1ms pause). Frequency selective excitation was achieved by a Gaussian RF pulse (3ppm FWHM bandwidth for PCr). To represent the anatomy of the calf, ^{1}H FLASH images are displayed in the background (c.f. Fig. 1). To determine the required bandwidth of the excitation pulse a spatially nonselective spectroscopy FID sequence (TR=1500ms, TE=0.185ms, 100 averages, FA=35°) was performed prior to the measurements (c.f. Fig. 2).

Results and Discussion: The theoretical NOE enhancement factor predicted for phosphorus is 2.2 [5]. The measured factors are given in the following passages.
Phantom-study: The phosphorous metabolites feature different NOE enhancement factors (c.f. Tab. 1) depending on various parameters e.g. dipole-dipole coupling. The highest effect was found in PCr with a NOE factor of 1.7.
Muscle-imaging: Transversal slices of the calf (c.f. Fig. 1) illustrate that PCr can mainly be found in muscle tissue. The SNR gain applying the NOE could be calculated to a factor of 1.4 determined by ROIs in muscle tissue and in the background. Reference phantoms of Pi (top right) and PCr (bottom right) with concentrations of 100mM/l were added to demonstrate the selective excitation. As expected a signal could only be detected in the tube containing PCr. The chemical shifts of the phosphorous metabolites (c.f. Fig. 2) differ from the literature values *in-vivo* due to sloping pH-values [5]. The two peaks of the PCr signal occured due to inaccurate shimming but do not influence the frequency selective images.

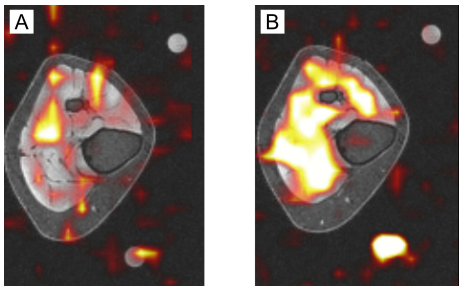

Fig. 1: Transversal slice of the human calf muscle from a healthy volunteer. Anatomical information is represented by a ^{1}H FLASH image (1.3mm isotropic resolution). In the overlay the PCr image is superimposed in colorscale (1cm isotropic resolution; interpolatied to match the resolution of the ^{1}H image). *A*: frequency selective ^{31}P FLASH, *B*: frequency selective ^{31}P FLASH with NOE pulses.

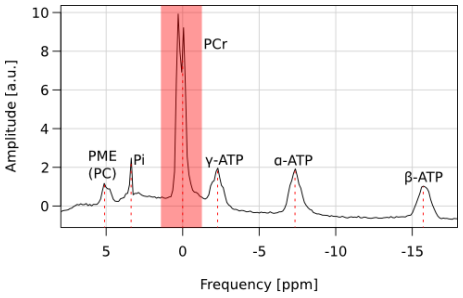

Fig. 2: ^{31}P spectrum of the human calf muscle examined with an FID sequence. The red marked area indicates the selective excitation pulse used in the ^{31}P FLASH sequence.

Tab. 1: Chemical shift and enhancement factors gained by the NOE for several phosphorous metabolites measured in phantom solutions.

	PC	Pi	PCr	γ-ATP	α-ATP	β-ATP
Chemical shift [ppm]	5.1	3.4	0	-2.3	-7.3	-15.7
NOE factor	1.1	1.2	1.7	1.3	1.3	1.1

Conclusion and Outlook: In this work ^{31}P/^{1}H images were acquired using a frequency selective 3D imaging sequence with signal amplification by ^{1}H NOE pulses. PCr-MRI of the calf muscle at 3T is possible in clinically feasible measurement times (~30min) and an isotropic spatial resolution of 1cm. In this imaging experiment the NOE yields an SNR gain of a factor up to 1.4 *in-vivo* and 1.7 in phantom studies. In the future we will investigate interleaved excitation [2] with additional NOE pulses to achieve shorter acquisition times than in CSI sequences.

References: [1] Ernst et al., J Comput Assist Tomo (1993) 17(5):673-680; [2] Lu et al., Magnet Reson Med (2013) 69:538-544; [3] Kemp et al., NMR Biomed (2007) 20:555-565; [4] Bachert et al., Magnet Reson Med (1990) 15:165-172; [5] Haacke et al., J Wiley & Sons (1999).

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