Quantitation of Localized ^{31}P Magnetic Resonance Spectra Based on the Reciprocity Principle

Roland KREIS[1], Johannes SLOTBOOM[1], Joachim PIETZ[2], Bruno JUNG[1], Chris BOESCH[1]
[1]University & Inselspital, Dept.Clin.Research, Div. MR-Spectroscopy & Methodology, Bern, Switzerland; [2]Pediatric Neurology, University Heidelberg, Germany;

Introduction
Absolute quantitation increases the information content of clinical MR spectroscopy (MRS). For ^{1}H-MRS, water referencing is the easiest way of signal calibration. As none of the ^{31}P-containing metabolites is necessarily constant in pathology, other methods have been suggested for absolute quantitation of ^{31}P-MRS, either based on external standards, external reference signals, the ^{1}H-water signal or phantom replacement techniques with coil load matching (c.f. Refs in [1]). Here, it is suggested to use a B_1-insensitive excitation and to calibrate receive sensitivity based on the reciprocity principle [2,3] using a local measurement of the power required for a standardized B_1 field.

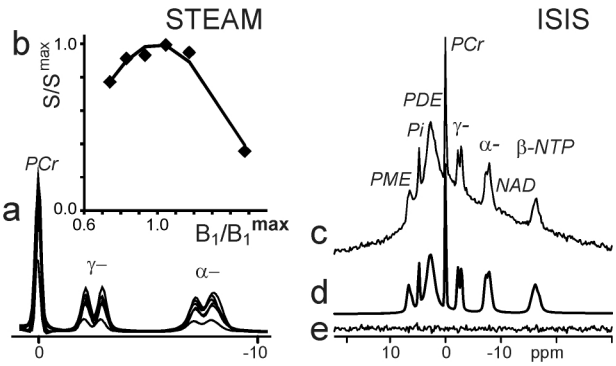
Theory
Thus the technique consists of two parts. First, a series of ^{31}P-MR spectra are recorded with a short-TE STEAM sequence using a range of flip angles. The voltage V_{max} required to obtain the maximum signal S_{max} is taken as a measure of the local B_1 field, incl. B_1 inhomogeneity and coil loading. The ^{31}P-signal can be approximated with a $\sin^3$ dependence on B_1. Changes in the slice profiles as function of B_1 can be neglected (only the position of the signal maximum is used). Second, the spectra to be quantitated are recorded with ISIS using adiabatic pulses. These spectra are fitted and the areas converted to absolute units based on the reciprocity principle [2]. The reciprocity principle states that - for matched transmit/receive coils - the external voltage needed to produce a given B_1 field at a given location is inversely proportional to the voltage induced in the coil by a given B_1 field occurring as a spin response. The MR signals can thus be calibrated through division by V_{max}. The absolute concentration c of each metabolite i in mmol/kg wet weight is obtained from:

$$c = A / (f_{T1} f_{T2} f_{CSF} f_d f_{Bl} f_c f_P f_T \rho) \quad ,$$

with: A: peak area; f_{T1}:T_1 saturation correction; f_{T2}: T_2 correction (minimal for very short dead time); f_{CSF}: Correction for inclusion of CSF spaces (P_i content in CSF taken care of); f_d: Correction factor for potential changes in detector gain (controlled by regular phantom measurements); f_{Bl}: B_1 correction (= $1/V_{max}$); f_c: calibration constant to convert into mmol/kg (phantom with known concentration of ^{31}P-metabolites); f_P: Number of ^{31}P nuclei in metabolite i ; f_T: Temperature factor ($\propto$ 1/T[K]); ρ brain density.
Data modeling using prior knowledge constraints is an integral part of the suggested quantification procedure. Prior knowledge enters in the form of fixed relations between different parts of the spectrum of a single component (e.g. nucleotide triphosphates, NTP) or in the choice of model functions for broad unresolved resonances. Many model parameters were determined on summed spectra and kept at fixed relations when fitting single spectra with much lower SNR.

Materials & Subjects
Clinical MR scanner (1.5T Signa, General Electric) with double tuned bird cage ^{1}H/^{31}P head coil (quadrature for ^{31}P). ***ISIS:*** adiabatic full passage inversion pulses, adiabatic half passage excitation and crusher pulse after detection, 5000 Hz spectral width, 2048 data points, TR = 4s *in vivo* and 2 to 30s *in vitro*. ***STEAM:*** 10 ms TE, 14 ms TM, 5 s TR. **Data processing:** automatic zero and first order (144°) phasing, 4 Hz broadening. Fitting with TDFDFIT [4] using a model that takes truncation effects into account. It included: Phosphocreatine (PCr), the NTP resonances, NAD, inorganic phosphate (P_i), phosphomono- (PME), and -di-ester (PDE), and a model of the phospholipid (PL) baseline. All peaks were set up as one or several Voigt lines.
Cerebral spectra were recorded in 10 healthy **subjects** (5m, 5f) from a supraventricular ROI (70 cm^3).

Results
The results are illustrated in the Figure. Parts a and b contain the STEAM data for a single subject (fitted spectra and course of amplitudes of 6 scans with differing B_1). On the right, the summed ISIS data are plotted (c: raw sum spectrum, d: fit excluding the PL baseline, e: residues). The resulting tissue concentrations of ^{31}P-Metabolites, ^{23}Mg and pH are in good agreement with the published literature values [mmol/kg]: e.g. PCr: 2.72±0.11 (range of lit.values: 2.8-3.4); NTP: 2.41±0.15 (2.2-2.8); Pi: 0.95±0.09 (0.9-1.2). The inter-examination/interindividual standard deviations are smaller than in virtually all previous quantitative studies.
The PDE content was 16% lower for women than for men (p=0.05), while the ratio of PCr vs. the total ^{31}P-metabolite signal was found to be significantly larger for women than for men (p=0.01).



Discussion & Conclusions
The presented method allows for the determination of absolute concentrations of ^{31}P containing metabolites. *Advantages:* i) not necessary to acquire spectra from an external standard (→ less problems with B_1-field inhomogeneity), ii) no lengthy calibration measurements with sophisticated phantoms or under accurately matched coil-loading conditions (→ simple calibration). *Disadvantages:* i) requires additional *in vivo* measurements to determine the local B_1 field. (Other, less time-consuming algorithms than STEAM measurements may improve the method); ii) works only with transmit/receive coils with a reasonably constant B_1 over the ROI; iii) singular variations in receive sensitivity (hardware failure) may produce wrong results (long-term variations can be controlled by regular phantom checks).
The gender differences found may be related to differences in ROI content and must be verified in a larger study population.
In conclusion, the presented technique provides a means to obtain quantitative ^{31}P-MR spectra routinely, particularly in a clinical setting, where lengthy calibration measurements cannot be recorded for each patient. The low inter-examination variations should lead to better definition of deviations with respect to the norm in individual patients and improved monitoring of changes in single subjects.

References
1. Hajek, *Quart. Magn. Res. in Biol. Med.* **II,** 165-193 (1995).
2. Hoult, *Concepts Magn. Reson.* **12,** 173-187 (2000).
3. Michaelis et al *Radiology* **187,** 219-227 (1992).
4. Slotboom et al *Magn. Reson. Med.* **39,** 899-911 (1998).

Supported by the Swiss National Foundation (31-43280.95).