ERETIC based in vivo ^{1}H MRSI quantification

N. Zoelch[1], S. Heinzer-Schweizer[2], P. Boesiger[1], and A. Henning[1]
[1]Institute for Biomedical Engineering, University and ETH Zurich, Zurich, Switzerland, [2]Philips AG Healthcare, Zurich, Switzerland

Introduction

Quantification of metabolite concentrations from spectroscopic images has been performed by a variety of approaches:
Absolute quantification based on internal water referencing [1] is the current method of choice. It accounts for B1 variations across the field of view but imposes problems when assessing diseases that lead to alteration of tissue water concentration [2] and relaxation behavior. Methods using external references for absolute quantification [3] often suffer from susceptibility problems and resonances of interest being obscured by the reference signal. Just like the phantom replacement methods, whose main drawback is the need for an additional carefully calibrated scan, methods using external references have never been established for routine clinical diagnostics, although they were successfully used for many scientific studies. The ERETIC (Electric REfrence To acess In vivo Concentrations) method was introduced by Barantin et al. [4] and since then has been proven to be a reliable and accurate method for the assessment of metabolite concentrations *in vitro* [4, 5] and *in vivo* in single voxel MRS [4, 6]. The advantage of this approach is its insensitivity to changes in coil loading conditions, receiver gain settings and data processing. Also, the quantification can be performed simultaneously with the acquisition of the spectra. Unlike internal reference standards, the ERETIC method is also applicable in lesions or in the presence of pathological disorders and can be combined with localization without scan time prolongation. ***In this work*** a modified ERETIC method has been developed to enable quantification of metabolite concentrations in spectroscopic images (MRSI). Together with the acquisition of a B_1 map, an accurate quantification of absolute metabolite concentrations can be achieved.

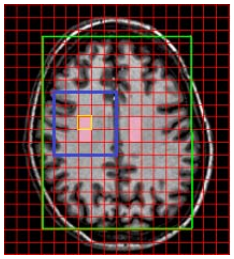

Figure 1: 18x20 voxel transversal slice.

Materials and Methods

All experiments were performed on a Philips Achieva 3T human MRI scanner (Philips Healthcare, Best, Netherlands) with a modified commercial transmit/receive birdcage proton coil [6]. Two-dimensional (2D) spin-echo MRSI localized by OVS [7] data were obtained from a 12 mm transversal slice (FOV: 170 mm x 190 mm, 18x20 voxels) that was planned on a T1-weighted FFE image (see Fig. 1).

ERETIC Layout and Setting: The ERETIC Setup for in vivo 1H MRS is described in detail and has been validated in [6]. In the present work the ERETIC pulse shape was set to Voigt; the frequency offset was chosen to be zero ppm, because no other metabolite signals are expected there. The amplitude, phase and decay time constant of the ERETIC signal were adjusted to obtain a peak-shape similar to the N-acetyl aspartate (NAA) peak.

ERETIC and MRSI: In case of MRSI, a defined phase as well as a defined spatial response function and hence stable and comparable signal amplitudes can only be achieved, when the ERETIC signal is placed in a predefined voxel. For this purpose an additional variable phase was calculated for every phase encoding step and added to the ERETIC signal to imitate phase encoding. The additional phase offset was determined by calculating the phase encoding gradient zeroth moment in the chosen voxel.

Quantification: Unsmoothed spectra including the ERETIC peak were fitted using the AMARES approach of jMRUI [8] after water removal by HLSVD filtering. In order to determine absolute concentrations of NAA, creatine (Cre) and choline (Cho) *in vivo*, the ERETIC signal was calibrated *in vitro* using the a phantom with physiological brain metabolite levels. The *in vivo* metabolite concentration is then calculated according to [6]

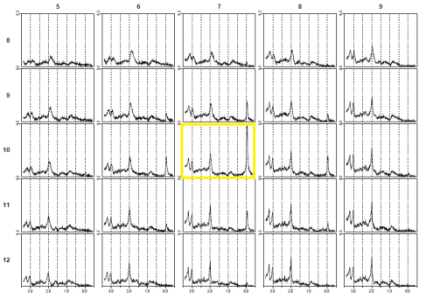

Figure 2: A subset of voxel spectra with the ERETIC peak at 0 ppm in voxel (7, 10).

$$C_m = C_{m,cal} * \frac{A_{ERETIC,cal}}{A_{m,cal} * f_{s,cal} * f_{c,cal} * f_{o,cal}} * \frac{A_m * f_s * f_c * f_o}{A_{ERETIC}}$$

where *C* is concentration, *A* the measured peak area and *f* a correction factor. Subscript *cal* indicates the values obtained by *in vitro* calibration, and *s, c, o* are the corrections with respect to sequence, coil and other parameters. To correct for inhomogeneities of the RF field and differences in power optimization, standard Philips B_1 maps were recorded. From these, the actual fraction b1(x,y) of the desired maximum B_1 strength (20 μT) were extracted for each voxel. The sequence correction factor is then calculated according to

$$f_s = \frac{1 - e^{-\frac{TR}{T1,m}}}{1 - \cos\left(b1(x,y) * \frac{\pi}{2}\right) e^{-\frac{TR}{T1,m}}} * \sin\left(b1(x,y) * \frac{\pi}{2}\right) * \left|\cos(b1(x,y) * \pi)\right| * e^{-\frac{TE}{T2,m}}$$

	tCho	tCr	tNAA
Us	1.79 ± 0.22	5.41 ± 0.63	10.49 ± 1.00
[9]	1.65 ± 0.25	6.69 ± 0.37	12.13 ± 0.78
[10]	1.68 ± 0.27	5.7 ± 0.6	10.6 ± 0.8
[11]	1.8 ± 0.3	6.1 ± 0.8	11.2 ± 1.2
[12]	1.83 ± 0.14	6.63 ± 0.31	9.47 ± 0.42

Table 1: Averaged quantification results from 4 white matter voxels compared to literature values.

TR is the repetition time and TE the echo time. *In vivo* T_1 und T_2 relaxation times were taken from [9] while for the in vitro calibration T_1 and T_2 relaxation times were experimentally determined. The first factor of the correction factor f_s describes repetition time induced saturation effects. The second and third factor account for imperfections of the π/2 –pulses and π -pulses, respectively. The last factor corrects for T_2 relaxation. Coil correction can be considered as f_c=1 since coil loading is intrinsically accounted for by the ERETIC method. Finally, a temperature correction f_o must be applied to correct for the different equilibrium magnetization at different temperatures.

Results and Discussion

Figure 2 shows a subset of voxel spectra in the range from -0.4 ppm to 3.4 ppm acquired in the brain of a volunteer. The chosen subset is indicated with a blue box in Figure 1. The ERETIC peaks appears in the intended voxel (column 7, row 10, yellow box in Fig.1 & Fig. 2) with the phase adjusted to the phase of the metabolites peaks. Due to the point spread function of this particular experiment, the ERETIC peak becomes also visible in neighboring voxels. Quantification results from 4 white matter voxels (indicated in pink in Figure 1) are presented in Table 1. Obtained average metabolite levels are in agreement with literature values from SV ^{1}H MRS studies. A reproducibility study and cross validation with the internal water reference method in multiple volunteers as well as establishment of a more sophisticated fitting approach including macromolecule and spline baseline fit is ongoing.

In conclusion, the ERETIC method was successfully implemented and tested for in vivo ^{1}H MRSI quantification.

References.
[1] Thulborn & Ackermann, J Magn Res (1983); 55:357-371
[2] Helms, Magn Reson Med (2001); 46:256-263
[3] Kreis et al., J Magn Res Ser B(1993); 102:9-19
[4] Barantin et al., Magn Reson Med (1997); 38:179-182
[5] Marro et al., J Magn Res (2008); 194:67-75
[6] Heinzer-Schweizer et al., NMR Biomed (2010); 23:406-413
[7] Henning et al., Magn Reson Med (2008); 59:40-51
[8] Stefan et al., Meas Sci Technol (2009); 20
[9] Baker et al., J Magn Reson Imag (2008); 27:489-49
[10] Pouwels et al., Magn Reson Med (1998); 39:53-60
[11] Michealis et al.,Radiology (1993); 187:219-227
[12] Kaiser et al., Neurobiol Aging (2005); 26:665-672