In-vivo measurement of absolute metabolite concentrations using the ERETIC method

S. Heinzer-Schweizer[1], N. De Zanche[1,2], M. Pavan[1], G. Mens[3], U. Sturzenegger[4], A. Henning[1], and P. Boesiger[1]

[1]Institute for Biomedical Engineering, University and ETH Zurich, Zurich, Switzerland, [2]Department of Medical Physics, Cross Cancer Institute and University of Alberta, Edmonton, Canada, [3]Philips Healthcare, Best, Netherlands, [4]Philips AG Healthcare, Zurich, Switzerland

Introduction

Magnetic resonance spectroscopy (MRS) is an established technique to assess metabolite distributions in vivo. Relative quantification is widely used, but it has the major disadvantage of ambiguities whenever several metabolite concentrations change simultaneously. Hence absolute quantification is an indispensable tool to precisely determine metabolite changes for clinical diagnostics and physiological studies. Calibration with ERETIC (Electric REference To access In vivo Concentrations), whereby a synthetic reference signal is injected during the acquisition of spectra, has been proven to be an accurate method for the assessment of absolute concentration in vitro[1] and was discussed as a potentially powerful tool for in-vivo measurements[2]. *In this work*, quantitative values of in-vivo metabolite concentrations in several volunteerns have been obtained using the ERETIC method. Brain ^{1}H MRS spectra were acquired and cross-validated against the internal water reference method. In addition, a previous implementation [3] has been perfected by substitution of the suggested electrical by an optical signal transmission line from the RF amplifier to the RF coil to eliminate random fluctuations of the ERETIC signal intensity due to parasitic coupling. An auxiliary RF channel was used for signal transmission and standard channels remained available for NOE enhancement and proton decoupling, which will be important for the future application of the method to in vivo ^{31}P and ^{13}C MRS. In-vivo brain spectra were acquired on a clinical 3T Philips scanner using a transmit/receive volume head coil. Brain ^{1}H MRS quantification results based on the ERETIC approach are in good accordance with values obtained by the internal water reference method as well as literature values.

Materials and Methods

The ERETIC pulse shape, phase, decay time constant, amplitude and frequency can be adjusted directly at the scanner console. Phase cycling for single voxel spectra and phase encoding for the acquisition of CSI spectra can also be applied, thus fully implementing a synthetic NMR signal. Frequency updates during a scan with multiple averages result in a simultaneous update of the ERETIC signal. The broadband tune channel of the system is used to generate the ERETIC signal at any given resonance frequency. Variations in the ERETIC signal depending on patient loading were avoided by placing the loop as close as possible to the receiver coil in order to couple the signal inductively and to avoid electric coupling effects. Loop dimensions were minimal so that the transmitted ERETIC signal remained stable with varying coil loading. Coupling through electric fields is further reduced by using an end-capped birdcage coil whose RF mirror separates the load from the ERETIC loop and provides stable grounding. A directly modulated RF-over-optical-fiber link [Figure 2] was used to transmit the ERETIC signal from the spectrometer to the coupling loop. The link consists of a light emitting diode (LED), a polymer optical fiber and a photodiode detector. The ERETIC signal, which is generated by the RF amplifier, modulates the optical carrier in the service room and travels through the optical fiber, which enters the scanner room's Faraday shield through a waveguide. The fiber ends behind the RF coil inside the scanner bore where the electrical signal is finally recovered by a photodiode, which is connected to the ERETIC loop [Figure 1]. This setup guarantees that only signal that is coupled through the ERETIC loop will be picked up by the receive coil and that all sources of parasitic coupling are eliminated.

In-vivo brain metabolite concentrations were assessed on five subjects (age = 28±3.9 years). Single voxel PRESS (TR=2500ms, TE= 47ms) spectra were acquired in the centrum semiovale (CSO) of the brain, followed by metabolite signal fitting and internal water referencing. The signals were corrected for the temperature difference between the phantom and the in-vivo measurement, and a volume correction was performed. Furthermore, T_1 and T_2 corrections were made to account for difference regarding T_1 and T_2 relaxation times of the GE 'braino' phantom compared to brain tissue. A water reference scan was acquired for all spectra to quantify all metabolite concentrations with the internal water reference method, which is the current gold-standard method for quantification of ^{1}H spectra in healthy tissue.

Results

The use of an optical transmission system enables a stable and reproducible ERETIC signal intensity since random fluctuations in ERETIC signal coupling to the receiver coil due to changes in position of cables and highly dielectric human tissue are avoided. In-vivo ERETIC quantification results from the centrum semiovale of five subjects are in good agreement with values obtained by using the internal water reference standard [Figure 3] as well as with literature values. The product-moment correlations of the absolute concentration values determined with internal water referencing and ERETIC are 0.98 for NAA, 0.93 for Cho and 0.91 for Cre and indicate that the two methods correspond well to each other in healthy tissue.

Discussion

Through the use of an optical RF transmission setup, the signal source is kept outside of the scanner room and parasitic coupling is avoided. Therefore, stable and reproducible measurements can be performed with a reference signal amplitude that is independent of cable positioning. The primary advantage of ERETIC is its independence of loading, matching and receiver gain, while quantification results are obtained in a single scan. The above results suggest that ERETIC is a promising approach for disease states, in which water content changes and assumptions about the water concentration become unreliable, so that the use of the internal water reference method for the determination of tissue metabolite concentrations is inappropriate.

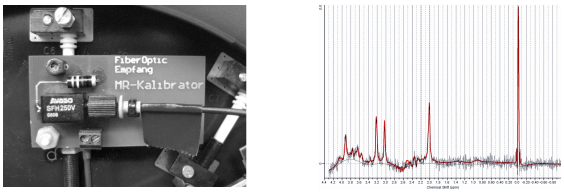


Figure 1 (left) The ERETIC loop is placed at the back of the RF mirror of the birdcage coil. (right) LCModel quantification of an in-vivo ^{1}H brain spectrum with the ERETIC signal positioned at 0.0ppm.

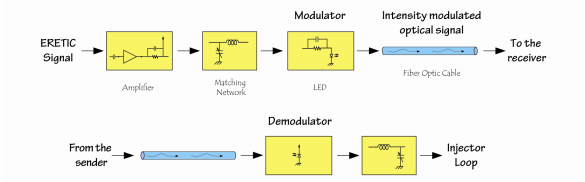
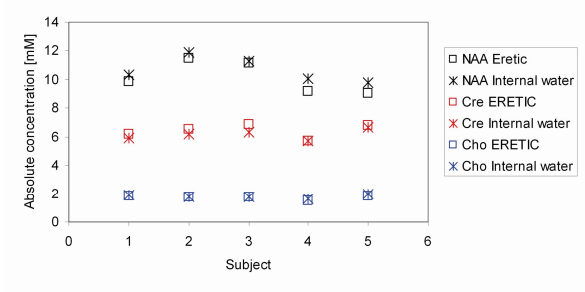


Figure 2 Schematic of the optical setup. The signal is amplified before it is sent to the scanner room and finally reaches the injector loop.



	NAA concentration/mM		Cho concentration/mM		Cre concentration/mM	
	ERETIC	Internal water	ERETIC	Internal water	ERETIC	Internal water
S1	9.88	10.35	1.86	1.91	6.21	5.93
S2	11.49	11.95	1.75	1.78	6.54	6.15
S3	11.16	11.28	1.76	1.73	6.85	6.29
S4	9.15	10.08	1.50	1.60	5.72	5.71
S5	9.06	9.77	1.87	1.96	6.81	6.67
Average (± 1 SD)	10.15±1.0	10.68±0.90	1.75±0.13	1.80±0.14	6.42±0.42	6.15±0.36

Figure 3 / Table 1 Metabolite concentrations determined with the ERETIC and internal water reference method. The values are in good agreement with one another.

[1] Barantin et Al., Magnetic Resonance in Medicine 38, 1997
[2] Marro et al., Journal of Magnetic Resonance 194, 2008
[3] Schweizer et al., Proc ISMRM 193, 2008