ERETIC with automatic phase adjustment and eddy current correction compensation

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Introduction

ERETIC (Electrical REference To access Invivo Concentrations) has proven to be a reliable and accurate method for the quantification of metabolite concentrations *in vivo* in single voxel MRS [1, 2]. In this approach, the areas of the metabolite resonances are converted into absolute concentrations by comparing them to an artificially generated signal, which is recorded together with the metabolite signal and is calibrated in a phantom once per study. As a further development and simplification of the phantom replacement method [3] it has, especially in the presence of lesions or pathological disorders, considerable advantages compared to methods using internal references [4]. Eddy currents, arising from switching field gradients, can strongly corrupt the identification of metabolite peaks and falsify the quantification results. Klose [5] proposed to use the signal of the unsuppressed water acquired in an additional scan (reference scan) to correct for eddy current effects. The correction is accomplished by dividing the time domain signal of the actual scan by the phase factor of the reference scan signal at each data point. It is a widely used approach, and it is highly desirable to combine ERETIC with the Klose correction in order to obtain reliable quantification results. So far this was only possible if the fitting of the metabolites and of the ERETIC peak were carried out on differently post processed spectra, or by accepting errors in the fitting of the ERETIC peak, since this artificial peak gets distorted by the eddy current correction. Either way, it was necessary to fit the metabolites and the ERETIC peak separately or to adapt fitting parameters to every spectrum because of the unsteady phase difference between the metabolite and the ERETIC signal.

In this work, we combine ERETIC and the Klose correction with no need for additional post processing and without losses in the accuracy of the quantification results. For the first time the ERETIC peak and the metabolites peaks are simultaneously quantifiable using standardized freely or commercially available algorithms as LCModel [6].

Materials and Methods

In the setup used here [2] the electrical reference signal is generated by the spectrometer itself. An amplitude modulated RF pulse is sent through an auxiliary channel and transmitted over an optical system to the coil. To avoid lineshape distortions of the ERETIC peak in the eddy current corrected spectra, this RF pulse is modified between the water reference scan and the acquisition of the water suppressed spectra, without prolonging the measurement time. Directly after the water reference scan the time-dependent phase of the complex water signal is calculated at every time point and added to the ERETIC signal by frequency modulation of the RF pulse. In a sense, an inverse Klose correction is thus applied to the ERETIC signal. In the subsequent scan of the water suppressed signal, the ERETIC signal then has the same time-dependent phase distortion as all metabolite signals that experience eddy current effects. To obtain the same zero-order phase for the ERETIC signal as for the water signal (and thus as for the metabolites), the phase of the RF pulse is initially measured and set to zero in an additional preparation step. After that, the phase of the water signal from the reference scan at the first time point is added as a constant phase to the RF pulse.

This method was implemented in the control software of a Philips Achieva 3T human MRI scanner (Philips Healthcare, Best, The Netherlands) and validated by performing 10 scans each in the centrum semiovale of two different healthy volunteers, alternatingly with and without the modifications described above. Scan parameters were as follows: TR/TE 2359ms/27ms, 128 spectral averages divided in 8 dynamics, 4 unsuppressed water scans in each dynamic, 25x25x25 mm^3 voxel size using PRESS localization. All signals were corrected for eddy current effects using the Klose approach and fitted using LCModel with simulated basis sets. The ERETIC peak is fitted by simulating a peak with a Gaussian-Lorentzian lineshape using the CHISMU control parameter in LCModel.

Results and Discussion

With the modifications for the ERETIC signal proposed here, after eddy current correction, the ERETIC peak is automatically in phase with all the other metabolites and shows no line distortion. Therefore the ERETIC peak can be readily fitted with LCModel (**Fig. 1.a**) without the need of changing fit parameters from scan to scan. The obtained values for the resonance area are very stable over all 5 scans in both volunteers as indicated by the coefficient of variation (CV), summarized in **table 1.** The tNAA/ERETIC ratios are as stable as the tNAA/Water ratios. On the other hand, in absence of phase and inverse Klose correction to the ERETIC signal, a reasonable fit is not achieved, even when larger standard deviations for the shift and the FWHM of the simulated peaks are allowed. As shown in **Fig. 1.b**, the fit may fail completely, due to too pronounced differences in lineshape and phase between the measured ERETIC peak and the simulated peak. In other instances the fit is partly successful, although a significant residuum remains (**Fig. 1.c**). In this case the disturbed baseline compromises the fit of the other metabolites.

		mean [a.u.]	CV [%]
V1	ERETIC area	29.4	0.3
	tNAA/ERETIC	0.338	3.0
	tNAA/Water	0.618	2.9
V2	ERETIC area	31.3	0.4
	tNAA/ERETIC	0.306	1.0
	tNAA/Water	0.548	1.4

Table 1. *Comparison of ERETIC areas and ratios obtained in two healthy volunteers (V1, V2)*

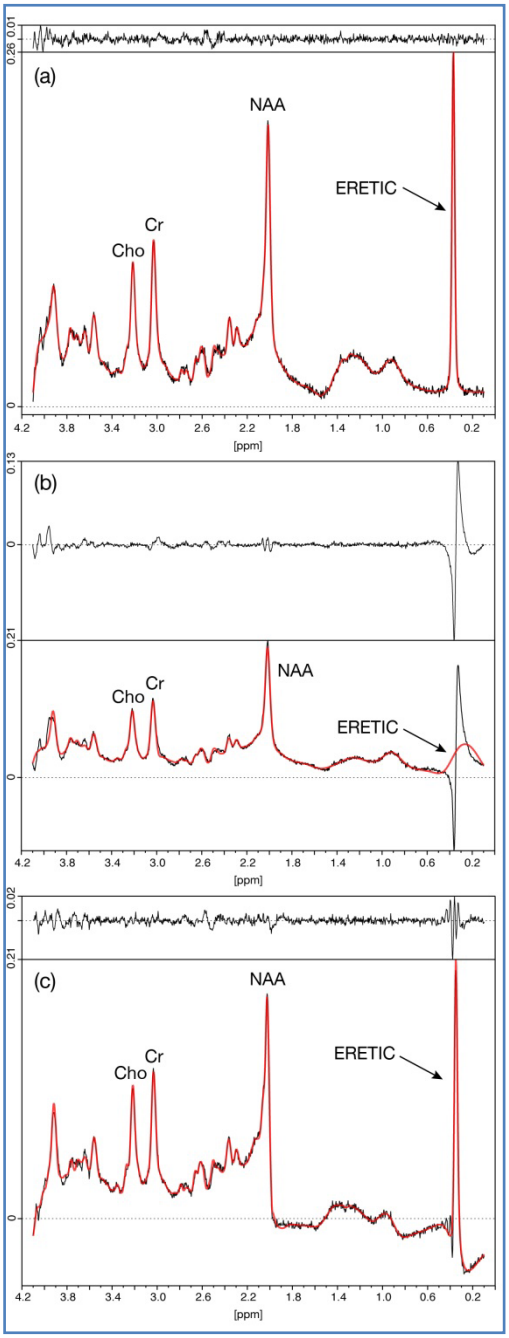

Figure 1. *PRESS spectra from one volunteer (V2) with the ERETIC peak at 0.35 ppm. (a) with the described modifications of the ERETIC signal and (b) and (c) without. The red line indicates the fit, the underlying black line indicates the measured signal. In the small box above each spectrum, the residuum is shown.*

It is a great advantage of the method proposed here, that the ERETIC peak can be fitted using a peak simulated with LCModel, instead of including the ERETIC peak in the simulated basis sets. In this way, the lineshape function used in LCModel is not influenced by the ERETIC peak and the metabolite fit results aren't influenced by the presence of the artificial signal. ***In Conclusion***, we increased the usability of ERETIC by implementing an automatic phase correction and eddy current correction compensation. With this fitting and data handling become far less demanding, which is an important step towards clinical applicability of ERETIC.

[1] Barantin et al., Magn Reson Med (1997); 38:179-182
[2] Heinzer-Schweizer et al., NMR Biomed (2010); 23:406-413
[3] Buchli et al., Magn Reson Med (1994); 32:447-452
[4] Helms, Magn Reson Med (2001); 46:256-263
[5] Klose, Magn Reson Med (1990); 14:26-30
[6] Provencher, NMR Biomed (2001); 14:260-2