CEST-Dixon MRI for Sensitive and Accurate Measurement of Amide Proton Transfer in Humans at 3T

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Introduction

Chemical exchange saturation transfer (CEST) MRI based *in vivo* detection of endogenous cytosolic proteins or peptides [1] is enabled by chemical exchange between amide protons (3.5 ppm) and the bulk water. The signal of amide proton transfer (APT) reflects protein concentrations as well as local pH via the exchange rate. Promising clinical applications of APT-CEST MRI are envisioned in oncology (metabolic pathology in tumors [2]) and in neurology (ischemic acidosis in stroke patients [1]). Detection of amide protons is based on a signal asymmetry analysis with symmetric RF saturation offset frequency around the water resonance, which is strongly biased in the presence of local magnetic field inhomogeneity δB_0. For correction, either a full CEST spectrum (20-40 frequency offsets) is interpolated to derive the actual water resonance [3], resulting in a strong scan time penalty, or a separate, precise B_0 mapping sequence is applied [4]. Separate B_0 mapping scans require precautions, such that f_0 (reference value to the water resonance), or shimming is not changed before/during the actual CEST acquisition, and they are error prone in the presence of water and fat compartments. We propose to acquire APT-CEST MRI using a multi gradient-echo sequence and to derive δB_0 by a Dixon [5] technique. Multiple echoes can be averaged to harvest the CEST signal with optimal contrast-to-noise-ratio (CNR) after the long saturation pulse. In this work, we also addressed practical issues with respect to hardware-limited duration of the saturation pulse on clinical scanners [6]. Feasibility of precise APT-CEST mapping in the human head is demonstrated using a clinical 3T scanner.

Methods

The study was performed on a 3T clinical whole-body scanner (Achieva, Philips Healthcare, NL) using an 8-channel head coil for signal reception and the body-coil for RF transmission. Acquisition software was modified to use the low-power mode of the RF amplifier, which allows arbitrarily long saturation pulses (typically used for MRS proton-decoupling, 500 W maximum, 100% duty-cycle). A multi-echo T1-weighted 2D GRE sequence was used: matrix 128^2, resolution $1.41\times1.41\times6.0$ mm^3, 6 echoes, TR=1031 ms, TE_1=1.9 ms, ΔTE=3.04 ms, pixel bandwidth 1532 Hz, 6 saturation frequency points in steps of 80 Hz around $\Delta\omega=\pm448$ Hz (3.5 ppm) and one off-resonant (S_0, $\Delta\omega$=-20 kHz), saturation pulse-train t_{sat}=1000 ms (16×62.5 ms, sinc-gauss), $B_{1,rms}$=1.4 μT, local SAR_{max}=3.2 W/kg, SENSE factor R=3, 5½ minutes scanning time. δB_0 maps for all saturation offsets were calculated by iterative Dixon reconstruction [5] and subsequently combined to a single map for correction. Images at different frequency offsets (average over all echoes) were co-registered using rigid-body translations to compensate for head motion. Maps of the asymmetric magnetization transfer ratio $MTR_{asym}=(S[-\Delta\omega]-S[+\Delta\omega])/S_0$ were calculated based on δB_0 corrected, point-by-point interpolated images $S[-\Delta\omega]$ and $S[+\Delta\omega]$. *In vivo* feasibility was tested in 2 human volunteers, from whom informed consent was obtained.

Results and Discussion

CEST-Dixon-MRI was successfully completed in two volunteers. Required pulse angles were reached with RF power levels below 500 W (maximum B_1 field of 4.1 μT) under the weak loading conditions for the body-coil (human head). Imaging parameters where solely constrained by clinical SAR regulations. The uncorrected APT map in Fig.1a was calculated from the frequency points at $\Delta\omega=\pm448$ Hz as well as S_0 and shows a strong influence of δB_0. The Dixon B_0 map is displayed in Fig.1c and reveals a water resonance range of 150 Hz. With the B_0 map directly derived from the CEST scan, there is no overall frequency offset, such that zero-valued positions correspond to exactly symmetrical off-resonant saturation, where no correction is necessary (compare to discussion in [4]). The corrected APT-CEST map in Fig.1b demonstrates a uniform response in the healthy brain (except for a major vessel at the bottom and some border effects) and thus provides an excellent basis for lesion detection. The applied interpolation of data from multiple $\Delta\omega$-values enhances CNR and gives room for SENSE acceleration to keep the acquisition within a clinically acceptable time frame. Translation of the low-power-mode concept for long CEST saturation pulses to other regions of the human body is under investigation.

Conclusion

A precise APT measurement in the human brain is demonstrated on a clinical 3T MRI scanner using a multi-GRE CEST-Dixon technique with intrinsic B_0-field correction, which was completed in less than 6 minutes.

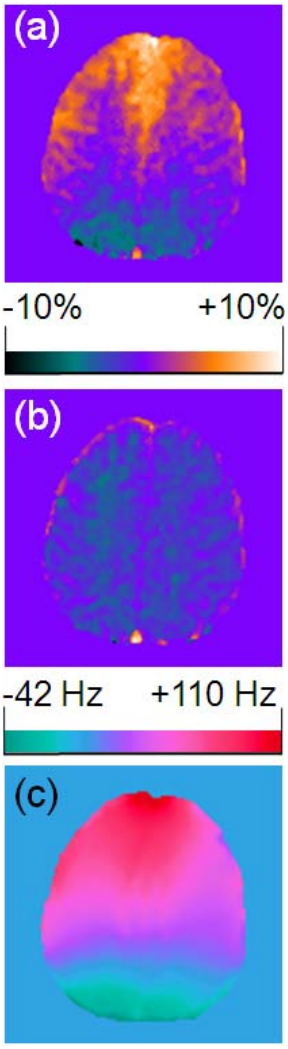

Figure 1: A very uniform APT-CEST map (b) is obtained in the healthy human brain using a multi-gradient-echo CEST-Dixon technique with intrinsic correction of B_0 inhomogeneity. The uncorrected APT map (a) is dominated by systematic errors due to B_0 induced asymmetry. The B_0-map (c) was derived by iterative Dixon reconstruction from the same image data.

References

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