Magnetization transfer ratio (MTR) imaging in the presence of fat

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PURPOSE: Magnetization transfer (MT) contrast including magnetization transfer ratio (MTR) may provide high sensitivity for detecting disease-induced changes in macromolecular tissue content that is not assessable by conventional MRI [1]. One of the potential confounders of body MT applications is tissue fat, which was previously shown to affect apparent MT parameters in liver imaging [2]. Recent studies of MT networks in fatty tissues suggests that off-resonance MT saturation will have no detectable effect on the detected fat signal due to the absence of an MT pathway from fat to water or to protein and membrane phospholipid protons [3,4]. The absence of a MT effect in fat and its distinct relaxation properties may impact significantly MTR estimates in tissues with a natural abundance of macromolecules and fatty infiltrations. Multi-echo chemical shift encoded (CSE) imaging has been demonstrated to provide robust separation of fat and water in the presence of confounding factors [5,6]. The absence of MT effects in fat makes fat signal consistent between images both with (MTon) and without (MToff) MT saturation, which may allow CSE-based removal of the confounding fat signal for unbiased MT imaging. In this work, we study the effects of tissue fat on MTR estimates, and propose to improve the robustness of MT imaging by removing fat effects through the use of multi-echo CSE.

METHODS: Numerical simulations were performed to model MTon and MToff signals in a mixture of fat and water as a function of echo time (TE) in a spoiled gradient echo sequence with fat fractions (FF) up to 40%. The simulations were based on an MTR=0.3 and *in vivo* signal levels separately measured for fat and water at 3T. Imaging was performed on a 3T clinical MRI (MR750w, GE Healthcare, Waukesha, WI). Physical phantoms containing mixes of 2% agar, water, and fat (peanut oil) [5] were imaged by a MT SPGR sequence with MT preparation at 3kHz (MTon) and 100kHz (MToff). A post-surgical bariatric patient volunteer and normal volunteers were imaged using consecutive respiratory-gated CSE acquisitions (IDEAL) [5] with MT preparation at 1.5 kHz (MTon) and 100 kHz (MToff). Total acquisition time for combination of both MT-CSE sequences was ~5min. Data were first reconstructed to generate independent fat and water images [8] followed by MTR calculation (MTR = (MToff – MTon)/MToff).

Figure 1. Surface plot of the percent error in MTR as a function of FF and TE (the surface plot is clipped at +/-100% levels for improved visualization).

RESULTS: The simulations show that apparent MTR significantly varies with both FF and TE (Fig. 1). MTR error is linearly increasing with FF even for in-phase TEs (0 & 2.3ms) reaching -60% error for the maximum FF studied. As the fat and water approach out-of-phase echo time (TE=1.15 ms), the dependence becomes more complicated and reaches the highest errors (including two singularities) at the out-of-phase TE. The physical phantom results are shown in Figure 2. Fat images from MToff and MTon CSE were identical confirming insensitivity of the fat signal component to off-resonance irradiation (results not shown). MTR images from the fat+agar phantoms at different TEs show oscillating MTR in each individual object due to TE-dependent fat/water chemical shift signal interference. Note MTR variations in each individual echo image despite the fact that same 2% agar solution was used in all objects and there is both overestimation and underestimation of MTR predicted in Fig. 1 depending on FF and TE compared to CSE MTR. MTR calculated from CSE water images show uniform MTR across all fat fractions, which is consistent with uniform macromolecular composition (agar) of the phantoms. Results in the bariatric volunteer demonstrate a similar inconsistency of MTR with echo time (Fig. 3) measured at a location of 12% FF in the liver. MTR measured from CSE images was found to remove the confounding fat signal providing higher MTR.

CONCLUSION: We have demonstrated the challenge in evaluating MT properties in fat-containing tissues due to complicated chemical shift related interference of fat signal, which confounds the measurement of the MT-induced attenuation of water signal by macromolecular tissue content. It is important to note the presence of error in MTR with increasing fat fractions even at in-phase TEs. The complicated dependence of MTR on FF and TE may reduce specificity of MT imaging to macromolecular content, which is known to vary at different stages of cirrhotic liver disease [9]. To resolve this confounder, we demonstrated the use of a CSE-MRI method to spectrally separate signal due to water and fat both in physical phantoms and an initial volunteer study. We conclude that MT measurements in fatty tissues should take into account potential fat and have demonstrated that CSE-based fat/water separation is a promising approach to avoid FF-dependent MTR bias, and dependence of apparent MTR values on pulse sequence parameters such as TE.

References: [1] Wolff et al. MRM 1989:10:135-144. [2] Komu et al. Physiol Meas. 1994:63:713-718 [3] Chen et. al. MRM 2006:55:1246. [4] Chen et. al. MRM 2010:63:713. [5] Reeder et al. MRM 2005: 54:636–644. [6] Meisamy et al. Radiology 2011 :258 :767-775. [7] Hines et al. JMRI 2009 :30 :1215-1222. [8] Hernando et al. MRM 2010:63:79-90. [9] Yarnykh V et al. ISMRM 2012, A392.
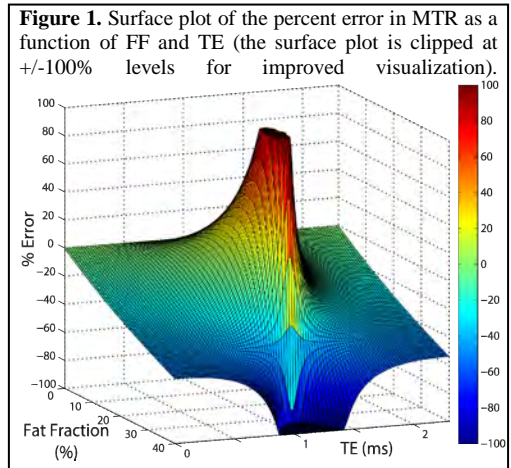
Figure 2. Top: MTRs from fat+agar phantoms at different echo times. **Bottom left:** MTR from CSE-separated MTon and MToff images. **Bottom right:** Location of phantoms with different fat fractions.
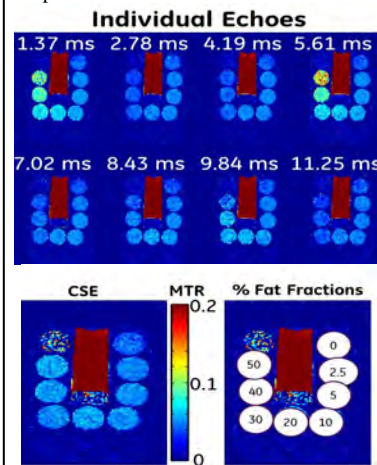

Figure 3. Results of volunteer CSE MTR experiments. MTR plot was taken from a liver ROI with 12% fat fraction. Note varying MTR values vs. echo time, and their underestimation compared to CSE MTR.