Quantification of susceptibility-induced fat resonance shift on chemical shift-based water/fat separation of skeletal muscle

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Introduction: The quantification of skeletal muscle fatty infiltration is important in assessing risk factors for metabolic abnormalities (like obesity and diabetes) [1] and in monitoring the progression of myopathies [2]. Muscular fat includes intramyocellular lipids (IMCLs) that are approximated as spherical droplets within myocytes and extramyocellular lipids (EMCLs) that are approximated as strands of fat in the annular interstitial space between myocytes [3,4]. Magnetic resonance spectroscopy measurements have shown that the chemical shift difference between water and EMCL is changing with the orientation of surrounding myocytes due to bulk magnetic susceptibility effects [3,5]. Chemical shift based water/fat separation techniques [6] have been recently employed to quantify the spatial distribution of muscular fat [2,7], relying on a precalibrated multi-peak fat spectrum model [8]. Because of the in general low contribution of IMCL to the total muscular fat, chemical shift based water/fat separation approaches investigate primarily the EMCL compartment. Since the orientation of the extracellular fat strands depends on the orientation of the surrounding myocytes, the EMCL compartment spectrum shifts due to susceptibility effects. Quantification of this fat resonance shift would provide information about the microscopic characteristics of the measured lipids (orientation, shape). Goal of the present work is to characterize the effect of susceptibility-induced fat resonance shift on quantitative chemical shift-based approaches and to propose an algorithm to quantify the resonance shift.

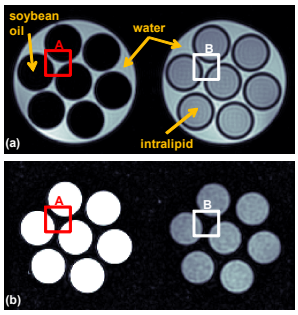

Fig. 1: Susceptibility effect phantom: (a) water and (b) fat images.

Materials & Methods: Model formulation: The multi-peak T_2* IDEAL signal model [8] is enhanced by introducing a susceptibility-induced resonance shift Δx in the precalibrated multi-peak fat spectrum. If a_p are the relative amplitudes of the P peaks of the fat spectrum at the frequencies Δf_p, the proposed signal model is:

$$S(t)=\left[\rho_w+\rho_f\sum_{p=1}^{P}a_p\exp\left(j2\pi\left(\Delta f_p+\Delta x\right)t\right)\right]\exp\left(j2\pi\psi t\right)\exp\left(-t/T_2^*\right) \qquad (1)$$

Because of the low values of Δx (betwen -25 and 12 Hz at 3 T [3]) the signal is affected by the presence of the resonance shift primarily at longer echo times (TEs). Therefore, the problem of Eq. (1) can be solved in two steps. The first step assumes Δx=0 and solves for water (ρ_w), fat (ρ_f), fieldmap (ψ) and T_2* using the multi-peak T_2* IDEAL algorithm at short TEs [8]. The second step solves the full problem of Eq. (1) and extracts Δx, using as initial estimates the results of the first step and Δx=0, and updating the parameter estimates based on a first order Taylor's approximation, similarly to the way it has been previously done in estimating separate T_2* values for water and fat [9]. The second step uses all acquired time points at both short and long TEs.

MRI measurements: A water-fat phantom was constructed containing 2 samples. Sample 1 (left cylinder in Fig. 1) contained 7 cylindrical vials of soybean oil immersed in water simulating EMCL-muscle interfaces. Sample 2 (right cylinder in Fig. 1) contained 7 cylindrical vials of Intralipid 20% fat emulsion in water simulating IMCL-muscle interfaces. A quadrature knee coil was used to scan the phantom and the calf muscle of a healthy volunteer on a 3 T GE scanner. The phantom was scanned at seven different orientations with respect to B_o (quantified by the angle θ between the phantom axis and B_o). An investigational version of 16-point IDEAL in a 3D SPGR sequence was used with parameters: FOV=13 cm, TR/TE/ΔTE=17/1.7/0.8 ms, flip angle= 2º, matrix 128x128, 4 mm slice thickness. Given the knowledge of Δf_p as determined by spectroscopy, the precalibrated a_p values were derived using the 16-point multi-species IDEAL algorithm [8] in fat only regions (soybean oil region for the phantom and subcutaneous fat region for the *in vivo* data).

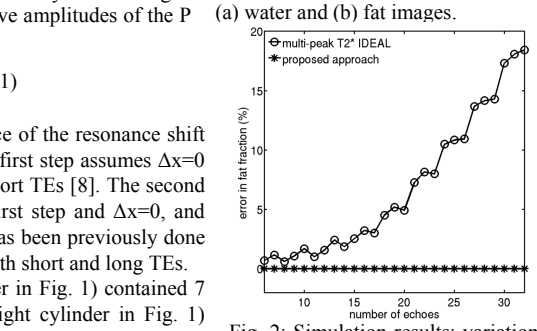

Fig. 2: Simulation results: variation of the error in fat fraction with the number of echoes when Δx=-25 Hz.

Results: Simulations: The bias in the fat fraction caused by the susceptibility induced fat resonance shift is simulated for a nominal fat fraction of 50% for acquisitions with constant echo shift (ΔTE=0.8 ms) and a variable number of echoes (nTE) between 6 and 32. The bias in fat fraction induced by the presence of the resonance shift is below 2% for 6 echoes and increases as nTE increases, when the multi-peak T_2* IDEAL model is used (Fig. 2). The bias is totally removed using the proposed approach independently of nTE.

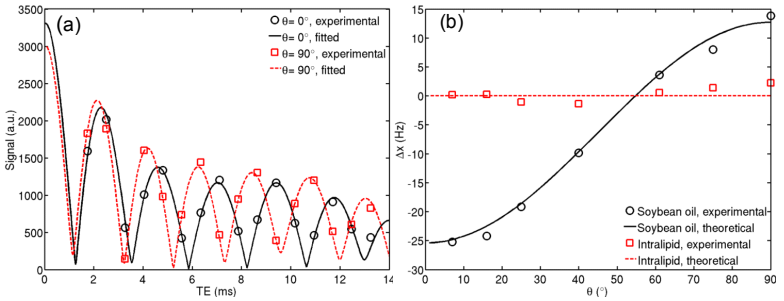

Fig. 3: Phantom results: (a) time evolution of magnitude signal in ROI A with θ=0º and 90º, and (b) variation of extracted fat resonance shift with phantom orientation for ROIs A, B.

Phantom results: ROIs A and B are placed in the interface of the surrounding water with the soybean oil and Intralipid vials respectively (Fig. 1). The variation of the gradient echo signal as a function of echo time is shown in Fig. 3a for ROI A and two different orientations of the phantom with B_o (θ=0º and θ=90º). There is an obvious water-fat frequency difference on the ROI A signal between the two different orientations (Fig. 3a). The water-fat separation problem is solved using the proposed algorithm estimating Δx. Fig. 3b shows that the variation of the experimental Δx with the angle θ for ROIs A and B is in good agreement with the expected theoretical results. The theoretical curve for the soybean oil is derived using the analytical expression for the fat resonance shift induced by cylindrical inclusions with susceptibility difference $\Delta\chi$ from the surrounding medium $\Delta B_z/B_o=(\Delta\chi/6)\,(3\cos^2(\theta)-1)$ where $\Delta\chi$=0.61 ppm [3]. There is no susceptibility-induced fat resonance shift expected for the spherical lipids of the Intralipid (Fig. 3b).

In vivo results: Fig. 4 shows the time evolution of the in *vivo* gradient echo magnitude signal for ROIs in the soleus (SOL) and medial gastrocnemius (MG). The apparent frequency shift is due to the different pennation angles of the two muscles. The proposed approach predicts Δx_{SOL}= -11 Hz, Δx_{MG}= -28 Hz (which is consistent with the lower pennation angle of MG compared to SOL) and the fitted results show good agreement with the experimental data.

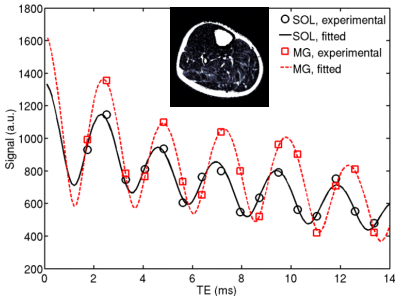

Fig. 4: *In vivo* results: time evolution of magnitude signal in SOL and MG ROIs.

Discussion & Conclusion: The effect of susceptibility induced fat resonance shift leads to low fat fraction bias in standard quantitative chemical shift based water/fat separation acquisitions where a low number of echo time points and short TEs are used. However, the effect is amplified at longer TEs. We have proposed a novel algorithm to quantify the susceptibility induced fat resonance shift. The proposed approach presents potential for extracting information about the orientation of the lipid strands and for discriminating increased intracellular lipid storage versus extracellular fatty infiltration. The algorithm could be also used to detect temperature-induced frequency shifts. More work would be required in order to characterize the noise performance of the proposed approach especially at low and high fat fractions.

References: [1] Gallagher et al, AJCN 81:903, 2005, [2] Wren et al, AJR 190:W8, 2008, [3] Szczepaniak et al, MRM 47:607, 2002, [4] Boesch et al, MRM 37:484, 1997, [5] Schick et al, MRM 29:158, 1993, [6] Reeder et al, MRM 51:35, 2004, [7] Karampinos et al, ISMRM 2010, p.418, [8] Yu et al, MRM 60:1122, 2008, [9] Chebrolu et al, MRM 63:849, 2010.

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