Effects of Fat Particle Size on R2* in Fat-Water-SPIO Emulsion Phantoms: Implications for Fat Quantification with Phantoms

C. D. Hines[1], C. Roen[1], D. Hernando[1], and S. B. Reeder[1,2]
[1]Radiology, University of Wisconsin-Madison, Madison, WI, United States, [2]Biomedical Engineering, University of Wisconsin-Madison, Madison, WI, United States

Introduction: It is well established that T_2* correction is necessary for accurate quantification of fat using chemical shift based water-fat separation methods[1,2,3]. Both single T_2* correction (assumes water and fat share a common T_2*)[1,2] and independent T_2* correction methods have been described[3,4]. Recently, it was shown that independent T_2* correction improves the accuracy of fat quantification in a water-fat-SPIO phantom[3] compared to single T_2* correction, because the R_2* of water and fat were affected by the SPIOs very differently[3,5]. However, fat particle sizes were very large (~250μm), and extrapolation of the phantom results to in vivo fat quantification may not be valid. The purpose of this work is to investigate the impact of fat particle size on the behavior of R_2* of water and fat in the context of T_2* correction for fat quantification.

Methods: A homogeneous fat-water-SPIO emulsion phantom of constant 30% fat by volume (% v/v) was constructed with varying particle sizes of fat[6]. The fat source of the phantom consisted of peanut oil supplemented with 225mg/mL soy lecithin (Fisher Scientific), as a source of phosphatidylcholine. The water source consisted of 1.8% (v/v) glycerol, 4mM gadobenate dimeglumine (MultiHance, Bracco Inc.), and 4mM sodium azide in water. To alter particle sizes of fat, 0.0, 0.025, 0.05, 0.075 and 0.1% (v/v) tween-80 was added. SPIOs (Feridex, Bayer Healthcare, Wayne, NJ) were added in final concentrations of 0, 10, and 20 μg Fe/mL. A total of fifteen emulsion vials comprised the phantom (5 particle sizes x 3 iron concentrations). Concentrations of tween were chosen such that fat particles would be on the order of hepatocytes (mean diameter = 25μm[7]).

Mixtures of fat, water, tween and iron were passed through a microfluidizer (Microfluidics Corp.) to homogenize and produce the emulsions[8]. Fat particle size was measured using a particle sizer (Zeta Potential Particle Sizer, NICOMP), and micrographs of the emulsions were acquired at 100x.

Imaging was performed at 1.5T (Signa HDxt, GE Healthcare) using an investigational version of a quantitative chemical shift based water-fat separation method (3D-IDEAL-SPGR[9]) in a single channel quadrature head coil. Imaging parameters included: 16 echoes, first TE = 1.3ms, echo spacing = 2.2ms, TR = 63.8ms, flip = 5° to minimize T_1 bias[10], BW= ±142.86kHz, FOV=26x18.2cm, 7mm slices, 10 slices, and 256x256 matrix for a true spatial resolution of 1.0x0.7x7.0mm. An on-line quantitative fat-water reconstruction was used to reconstruct fat-fraction images corrected for eddy currents[11], noise bias[8], T_2* decay[3], and multiple spectral fat peaks[1,2]. As part of the T_2* correction independent estimates T_2* for water and fat were obtained[3].

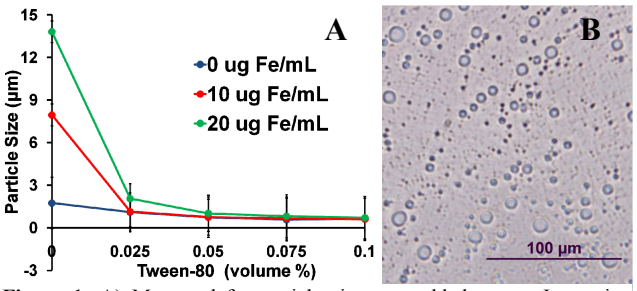

Figure 1: A) Measured fat particle sizes vs. added tween. Increasing amounts of tween produce smaller fat particles. Error bars represent standard deviation. B) 100x micrograph of emulsion with 10 ug Fe/mL and 0.05% tween. The presence of lipid particles is clearly seen.

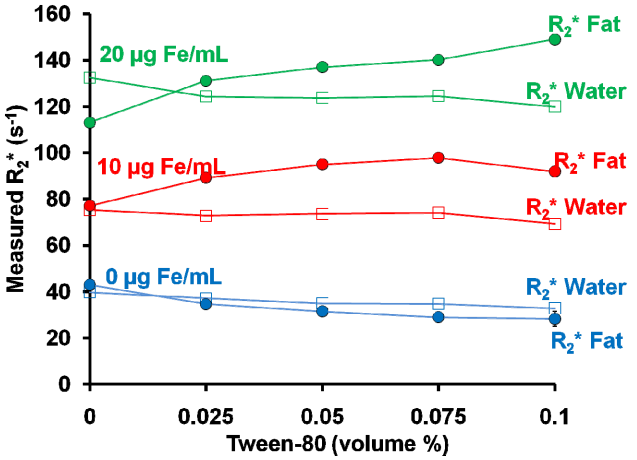

Figure 2: R_2* values of fat increase with decreasing fat particle size in the presence of iron, as lipids in smaller particles are more greatly affected by iron. In the absence of iron, R_2* of fat and water are approximately equal. Measured R_2* water (empty squares) and R_2* fat (filled circles) using independent T_2* correction for emulsions with 0 μg Fe/mL (blue), 10 μg Fe/mL (red), and 20 μg Fe/mL (green).

Results: Fig. 1A plots measured fat particle sizes with increasing amounts of tween for each iron concentration. Fig. 1B confirms the presence of spherical fat droplets in the emulsion.

Fig. 2 plots measured R_2* values of fat and water for each iron concentration versus amount of tween. In the absence of iron (blue), R_2* of fat and water are approximately equal. Higher R_2* values are seen for both fat and water in the presence of increased iron, although water R_2* remains relatively unaffected by fat particle size. In the presence of iron, lipids in smaller particles are more affected by surrounding water-soluble iron and have higher and increasing R_2* values than water with increasing iron concentration. This phenomenon is likely due to the sequestration of signal-generating lipid tails residing in the hydrophobic core of lipid droplets that require iron to be closer proximity to fat in order to have an effect on the fat signal.

Discussion: In this work, a novel phantom consisting of homogeneous fat and water emulsions with controlled particle sizes of fat in the presence of iron was described for use in fat quantification. Results demonstrate that in the presence of iron, fat and water have different R_2* behaviors, which is dependent on the fat particle size. Therefore, it may not be valid to readily extend results from fat-water-iron phantoms to in vivo fat tissue quantification. For example, the fat particles used in this phantom are closer to those experienced in vivo, and unlike past reports with much larger particle size, the relative difference between R_2* of water and fat may be smaller. Large fat particle sizes in phantoms may lead to large differences between the R_2* of water and fat, necessitating independent correction of R_2* for water and fat signals. In vivo, however, where fat vacuoles are much smaller and on the order of measured fat particles in this work, the relative differences in R_2* of water and fat may be smaller. With small particle sizes and hence more similar R_2* values, the increased complexity from independent T_2* correction may be unnecessary and single T_2* methods may suffice for accurate fat quantification. Future work will analyze R_2* values in patients with microvesicular and macrovesicular steatosis with iron overload, and its impact on the choice of T_2* correction methods in vivo.

References: [1] Yu et al. JMRI 2007 [2] Bydder et al. MRI 2008 [3] Chebrolu et al. MRM 2010 [5] O'Reagan et al. Radiology 2008 [5] Hines et al. JMRI 2009 [6] Fox et al. Colloids and Surfaces B: Biointerfaces 2008 [7] Suriawinata A. Histology for Pathologists, 3rd edition. [8] Fang et al. Colloids and Surfaces B: Biointerfaces 1993 [9] Reeder et al. JMRI 2007 [10] Liu et al. MRM 2007 [11] Yu et al. ISMRM 2009 #462
Acknowledgements: This work was supported by the NIH (R01 DK083380, R01 DK088925, and RC1 EB010384), the Coulter Foundation, and GE Healthcare.