Introduction: Accurate quantification of fat with MRI is challenging, affected by confounding factors that include: $T_2^*$ decay, the spectral complexity of fat, $T_1$ related bias, and noise related bias. New MRI methods attempting to address confounding factors require validation in fat-water phantoms with accurately known fat-fractions over a physiologically expected range. In this work we describe the construction of a fat-water-iron phantom for the purpose of validating new MRI fat quantification techniques. Results using a multi-echo chemical shift based fat-water separation method (IDEAL) including $T_2^*$ correction and accurate spectral modeling are shown.

Methods: A fat-water-iron phantom comprised of 49 20mL vials in varying true fat volume percentages (0, 2.5, 5, 10, 20, 30, 40, 50 and 100) and iron concentrations (0, 10, 20, 30, 40, and 50 μg/mL) was constructed. Appropriate volumes of peanut oil were dispensed by weight into vials, assuming the known density of peanut oil (0.916 g/cm$^3$). Aliquots (0-89.5 μL) of iron (Feridex, Bayer Healthcare) was added to shorten $T_2^*$ for rigorous validation of $T_2^*$ correction methods. 43mM sodium dodecyl sulfate (surfactant) and 43mM sodium chloride were dissolved in distilled, deionized water at room temperature. 3.75mM sodium azide was added to suppress microbial growth, and 0.3mM Gd-BOPTA (MultiHance, Bracco Inc.) was added to shorten the $T_1$ of water to approximately 600ms to more closely match physiologic values of $T_1^*$. Agar (2.0% w/v) was added over heat until melted. The resultant “water solution” comprised the water fraction of the phantom.

Water solution aliquots were measured in graduated cylinders, quickly poured into the vials containing peanut oil and Feridex, and mixed through gentle inversion for approximately 2 minutes. Upon cooling, the emulsion stiffened and formed a solid gel at room temperature. Accurate measurement of the fat-fraction required correction for volume contraction that occurred during cooling. This was performed by pouring all intended water solution volumes into graduated cylinders, and measuring the true volume once the solution had cooled. Fat-fractions and iron concentrations were re-calculated to reflect the actual volume of the water mixture present.

Imaging was performed at 1.5T (TwinSpeed HDx, GE Healthcare, Waukesha, WI) using an investigational version of the 3D spoiled gradient echo (SPGR) IDEAL acquisition in a quadrature single channel head coil. The exam consisted of three multi-echo IDEAL acquisitions: 6-echo, 9-echo, and 16-echo, all with echo spacing of 2.3ms (TE1 = 1.6ms). Imaging parameters for multi-echo IDEAL included: flip = 5° (to avoid $T_1$ related bias), TR = 16.4, 23.3, and 42.7ms, respectively, BW = ±100kHz, FOV = 35 x 35cm, slice = 8mm, and 256x256 matrix. PRESS (Point RESolved Spectroscopy) spectra were acquired on vials with no iron, and all iron concentrations for 30% fat. PRESS sequences were acquired without water suppression using a voxel size of 12 cm$^3$, TE/TR = 26/3500ms, BW = ±2500Hz, and 2048 readout points.

A modified IDEAL water/fat reconstruction using a self-calibrated fat signal evolution model that takes multiple spectral peaks of fat into account was used for subsequent online calculation of fat-fraction. This algorithm uses a magnitude discrimination method to calculate fat-fraction, free from noise bias. Reconstructions were performed with and without a $T_2^*$ correction method that assumes a common $T_2^*$ between water and fat. Images were also reconstructed with single and multiple spectral peaks of fat ("MP"). Spectra were post-processed using Matlab (Mathworks, Natick, MA) to integrate water and total area under the fat peaks to obtain PRESS fat-fraction.

Results: Figure 1 displays the correlation between known and PRESS fat-fractions, indicating excellent agreement and validation of the fat content of the vials, which was the same at all iron concentrations. One-way ANOVA tests showed no statistically significant differences between 6-, 9-, and 16-echo IDEAL acquisitions for all fat-fractions and $R_2^*$ values. A significant understimation of fat-fraction is seen in data when accurate spectral mapping of fat was not used (Figure 2). When accurate spectral modeling was included, $T_2^*$ correction showed improved agreement with known fat-fractions compared to data without $T_2^*$ correction (Figure 3). The apparent fat-fraction increases with increasing iron concentrations, although this effect is less pronounced with accurate spectral modeling and $T_2^*$ correction. For increasing iron concentrations, spectroscopy results showed a diminishing water peak, in addition to the expected line broadening of both water and fat peaks. Figures include standard error bars, but are smaller than the symbol size in the plots.

Discussion and Conclusion: The phantom described in this work provided a stable and accurate tool for validation of fat quantification imaging methods under development by our group. Specifically, this work demonstrated the necessity of accurate spectral modeling of fat and the need for $T_2^*$ correction. At higher iron concentrations, the single $T_2^*$ correction method shows deviations from expected fat-fractions reflecting a breakdown in the assumption that the $T_2^*$ of water and fat are equal, likely due to preferential shortening of the water $T_2^*$ caused by a lack of mixing of SPIO’s in fat. A “dual” $T_2^*$ correction method for improved accuracy of fat quantification at high iron concentrations will be presented elsewhere.

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