Mitigating bias and variance associated with fat signal in quantitative DCE of the breast

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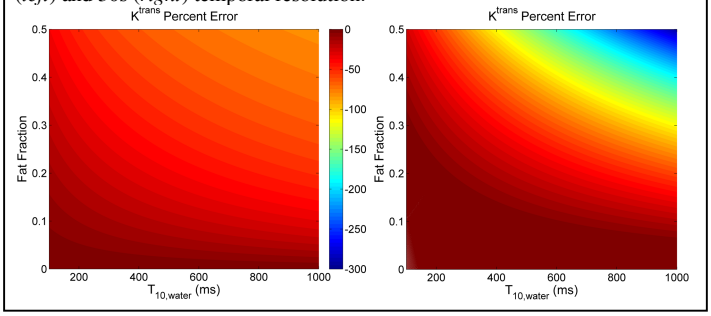
Target Audience: Medical physicists studying quantitative pharmacokinetic modeling and body/breast imaging radiologists.

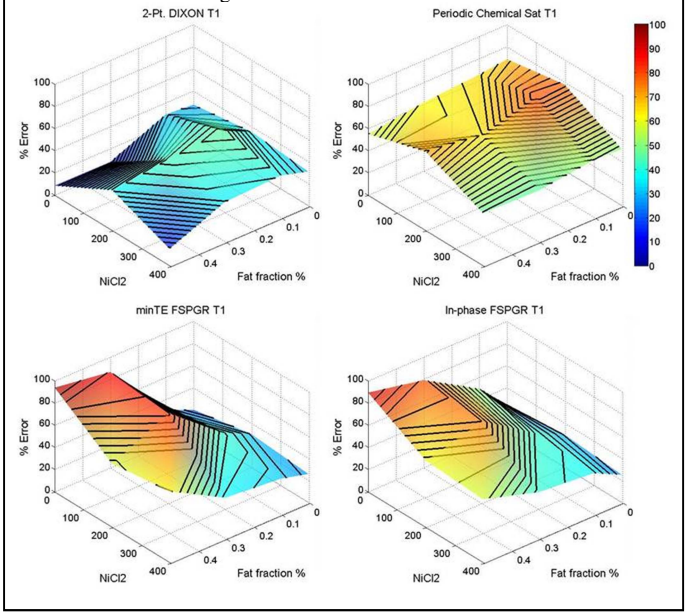
Purpose: Effective diagnostic breast imaging requires robust separation or suppression of the MR signal originating from fatty tissues to allow proper assessment of the water signal and contrast enhancement of tissues of interest. Cancers presenting as non-mass enhancement on breast MRI are particularly challenging, commonly resulting in fatty tissue co-mingled with suspicious enhancement. Fat separation or suppression is very important in quantitative imaging with T_1 correction, where current models, such as the general kinetic model (GKM) [1], fail to account for the complex signal characteristics arising from voxels containing both MR visible fat and water signals. Intermittent chemical saturation pulses are often used clinically balancing temporal resolution and quality of fat suppression, but these techniques rely on imaging conditions that are often difficult to achieve consistently across patients or for longitudinal imaging in the same patient, *i.e.*, uniform B_1 and B_0 magnetic fields within the imaging volume. Achieving these requirements becomes challenging when moving to 3 T, due to dielectric effects and patient geometry. Improved time-resolved imaging methods [2] now allow much greater temporal-spatial resolution, which can also be used to acquire data at multiple echo times (TE), facilitating 2-point Dixon methods that have previously been show to provide greater robustness in the setting of non-uniform B_1 fields [3]. ***In this work,*** we evaluate the feasibility of using a 2-point Dixon method for mitigating the bias and variance from combined fat-water signals in quantitative DCE of the breast.

Figure 1. Simulation results showing estimated percent error in K^{trans} fit using the GKM as a function of relative fat concentration and native water T_1 at 5s (*left*) and 30s (*right*) temporal resolution.



Methods: Simple simulations were performed to evaluate the bias introduced in pharmacokinetic (PK) parameter estimates from a combined fat-water signal. All simulations assumed the fat and water signals to be in-phase with a fat fraction of 0-50%, $T_{1,fat}$ of 260ms, and $T_{1,tissue}$ ranging from 200-1000ms. PK simulations were performed using a vascular input function (VIF) [4] and the general kinetic model to create gadolinium concentration [Gd] curves from tissue for a single K^{trans}, v_e, and v_p value from which the signal intensity was estimated from the tissue curve for the range of fat fractions and $T_{1,tissue}$ values described previously at temporal resolutions of 5 and 30s. Imaging was performed on a 1.5T clinical MRI system (MR450w, GE Healthcare, Waukesha, WI). Separate image volumes were collected at multiple flip angles (2, 5, 10, 15, 20, 25, and 30 degrees) using 3 separate acquisitions including a minimum TE fast spoiled gradient echo (FSPGR), an SPGR with a TE of 4.2ms, at which fat and water are in phase, and a dual-echo FSPGR with in and out of phase TEs. A phantom containing four mixtures (0, 10, 30, and 50%) of fat and water was prepared [5]. Three sets of these fat water mixtures were prepared, two containing $NiCl_2$ concentrations of 197 and 394 mg/L, corresponding to T_1 values, in aqueous solution, of 800 and 400ms, respectively, relevant to *in vivo* measurements. Images were analyzed using the open-source quantitative image analysis tool QUATTRO [6] to estimate T_1 values using ROIs circumscribed within each of the 12 vials. A multi-echo chemical shift encoded (IDEAL-IQ) acquisition was performed to measure the local fat fraction [7]. The T_1 of fat and water were also measured in each phantom using a multi-TR/TE single-voxel spectroscopy acquisition [8].

Figure 2. Contoured surface plots of the absolute error between fitted T_1 from imaging vs. spectroscopy as a function of fat fraction and NiCl2 concentration. Note the greatest error



Results: *Simulations:* Figure 1 illustrates the results of the PK simulations. The simulation results suggest that bias increases with increasing fat fraction and increasing difference between $T_{1,fat}$ and $T_{1,tissue}$, with a maximum absolute bias of in Ktrans of 82% and 293% at the 5s and 30s temporal resolutions. *Phantoms:* Surface plots of the percent error in the measured T_1 between imaging methods compared to spectroscopy show the greatest errors occur when using the minimum TE FSPGR acquisition, and use of a 2-point Dixon separation method decreased the bias (Fig. 2).

Conclusions: Conventional DCE-MR breast imaging and PK modeling necessitates suppression or separation of signal from fat for both visualization and quantitation, respectively. Others have shown that 2-point Dixon methods can provide more robust fat saturation, and in this work we demonstrated that this method reduces bias in quantitative DCE modeling in the presence of fat. Simulation results suggest the errors in Ktrans due to fat signal are within the same range as temporal resolution improvements in going from 30 s to 5 s.

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