## Effects of T1, T2, and Spectral Complexity on In- and Out-of-Phase Imaging: A systematic approach by computer simulation

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where IP is the 1<sup>st</sup> in-phase echo, and OP is the 1<sup>st</sup> out-of-phase echo. In practice, however, these assumptions may not hold, in which case the method is prone to systematic errors. Using computer simulation, the errors due to these effects were modeled using realistic values of T1, T2, and the lipid MR spectrum. For simplicity and expository purposes  $B_0$  field and other inhomogeneity effects were not considered here.

**METHODS**: MR spectroscopy was performed on corn oil using a spin-echo sequence with long TR (3sec) at 9 different TEs. Four major peaks (**Table 1**) were identified in accord with prior knowledge, and the peak areas were estimated using AMARES algorithm [4, 5] after correcting for T2 decay.

$s(TE) = \left  P_w \exp\left(\frac{-TE}{T2_w^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\sin\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right] + \exp\left(\frac{-TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{-TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{-TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\sin\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{-TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\sin\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{-TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\sin\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{-TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\sin\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{-TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{-TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{-TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) \left(\frac{(1 - \exp(-TR / T1_w))\cos\alpha}{1 - \exp(-TR / T1_w)\cos\alpha}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) \left(\frac{TE}{T2_f^{(r)}}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right) + \exp\left(\frac{TE}{T2_f^{(r)}}\right)$	$\frac{\exp(-TR/TI_f))\sin\alpha}{\exp(-TR/TI_f)\cos\alpha} \sum_{n=1}^{N} P_n \exp(i\omega_n TE) \dots \dots [Eqn]$
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The MR signal was modeled as a sum of signals of various frequencies (Eqn 2), the water and the  $\alpha_{,\alpha_{n}}$  Flip angle and frequency of n<sup>th</sup> fat component dominant CH<sub>2</sub> peaks in the 2-component model, and the water and the four main fat peaks in the 5-component models, with P<sub>n</sub>'s weighted by the observed peak areas (**Table 1**). Fat components were assumed to have common T1<sub>f</sub> and T2<sub>f</sub> values, which may differ from those of water. The signal intensity over time after excitation was generated with varying fat fraction, given by (P<sub>1</sub>+P<sub>2</sub>+...)/(P<sub>w</sub>+P<sub>1</sub>+P<sub>2</sub>+...), from 0 to 1. Six different cases were simulated for each of 2- and 5-component models: (A) long T1 and long T2 to simulate an ideal situation where **Eqn. 1** is accurate, (B) T1<sub>w</sub>  $\neq$  T1<sub>f</sub> to isolate the T1 effect, (C) T2<sub>w</sub>  $\neq$  T2<sub>f</sub>, to isolate the T2 effect, (D) T1<sub>w</sub>  $\neq$  T1<sub>f</sub> and T2<sup>\*</sup><sub>w</sub>  $\neq$  T2<sup>\*</sup><sub>f</sub>, to simulate an asymmetric spin-echo sequence, (E) T1<sub>w</sub>  $\neq$  T1<sub>f</sub> and T2<sup>\*</sup><sub>w</sub>  $\neq$  T2<sup>\*</sup><sub>f</sub>, to simulate a short T2<sup>\*</sup> environment (e.g. Fe overload) in a gradient-echo sequence. The fat fraction was estimated by **Eqn. 1**, and plotted against the true fat

fraction defined by the simulation. Due to fat-water dominance ambiguity of the IP-OP method, the fat fraction could only be given as modulo min(f, 1-f). The error of the fat quantification was illustrated as deviation from the diagonal lines, which represent exact correspondence between estimated and true fat fraction. For all simulations, flip angles were  $20^{\circ}$  and  $70^{\circ}$ , and TR = 150msec.

 Figrue 1
 Table 1: Major Fat Spectral Peaks

 ppm
 Relative Area (Pn)

 5.3
 0.2

 2.1
 0.4

 1.3
 1

 0.9
 0.2

proton densities of water and n<sup>th</sup> fat component T1, T2 values of water, and each of fat components

 $\begin{array}{c} P_w, P_n \\ T1_w, T1_f, T2_w, T2_f \end{array}$ 

**RESULTS**: The simulations illustrate the following observations: (1) T1 effects, including high flip-angle, generally cause overestimation of fat fraction (**Fig. 2 and 3, B, D-F**). (2) T2 effects cause underestimation of fat in low-fat range, and overestimation in high-fat range (**C-F**). (3) The 5-component model predicts



**CONCLUSION:** (1) A simple Dixon IP-OP fat quantification may be inaccurate over realistic values of T1, T2, (or  $T2^*$ ), and it is prone to systematic errors due to these effects. (2) The previously under-recognized effect of fat-fat interference (due to its multiple spectrum components) can contribute to the errors in fat estimation.

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