Quantitative Fat Imaging for Evaluating Diffuse Liver Diseases

Correcting for challenging confounding factors

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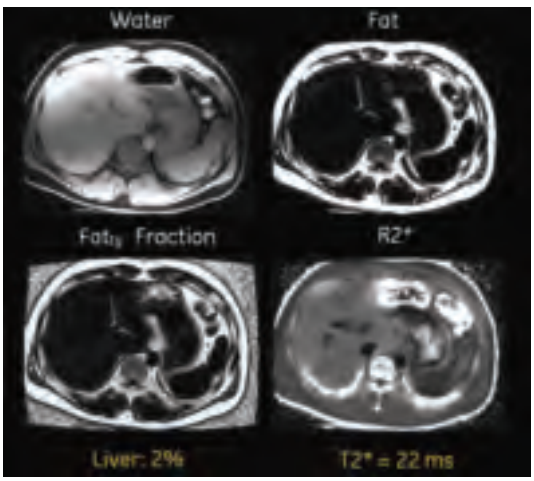
Hepatic steatosis, the intracellular accumulation of triglycerides (triglyceride fat) in hepatocytes, is a common and often asymptomatic condition. An estimated 20 to 80 million Americans have nonalcoholic fatty liver disease (NAFLD), which is the most common chronic liver disease in the United States.[1] Steatosis is now recognized to play a causative role in important hepatic and systemic metabolic disorders. For example, recent data have shown that 5% to 15% of patients with NAFLD present with established cirrhosis on liver biopsy and that 4% to 5% of individuals with isolated steatosis eventually develop cirrhosis. The risk of developing cirrhosis is significantly higher in nonalcoholic steatohepatitis (NASH), the aggressive subset of NAFLD characterized by the presence of inflammation and fibrosis, in addition to steatosis.[2]

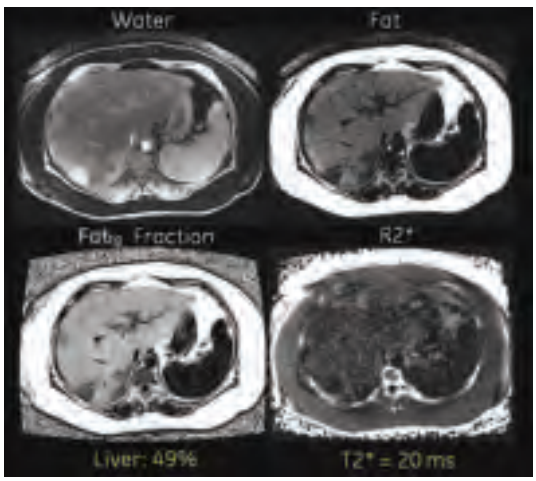
In other studies, 20% to 50% of individuals with steatosis subsequently became diabetic,[3,4] suggesting a causative role of steatosis in the development of type II diabetes. Recent studies also demonstrate that NAFLD is an independent risk factor for cardiovascular mortality beginning at age 45.[5] Finally, there is emerging evidence of a relationship between hepatic steatosis and an increased risk of malignancy—7% of patients with NAFLD-related cirrhosis developed hepatocellular carcinoma (HCC) over a 10-year timeframe.[6] Because of the high prevalence of NAFLD in the general population, it is estimated that more than 50,000 Americans might eventually develop NAFLD-related HCC.[7]

In summary, hepatic steatosis has important implications for many hepatic and systemic disorders. Fortunately, steatosis can be reversible, and reduction in liver fat may diminish many of its associated risks. Given the often silent, asymptomatic nature of this disease, accurate non-invasive approaches are needed for the assessment of liver fat.

Healthy volunteer



Fatty liver



Fatty liver images are courtesy of Dr. Claude Sirlin, University of California, San Diego, CA.

Figure 1. This healthy volunteer has 2% triglyceride fat fraction vs. diseased fatty liver patient has 49% triglyceride fat fraction. T2* values are around 20 ms for both livers.

A promising MR-based technique

IDEAL IQ provides volumetric whole-liver coverage in a single breath-hold and generates estimated T2* and triglyceride fat fraction maps in a non-invasive manner. It is intended for breath-held abdominal imaging to evaluate diffuse liver diseases such as hepatic steatosis of the liver and corrects for challenging confounding factors such as T2* decay. The technique is designed for water-triglyceride fat separation with simultaneous T2* correction and estimation based on the IDEAL technique. Six gradient echoes are typically collected using the 3D Fast SPGR sequence in one or two repetitions. The IDEAL IQ reconstruction produces water and triglyceride fat images, and relative triglyceride fat fraction and R2* maps from the six echo source data.

T2* correction and estimation

T2* decay causes signal dephasing and T2* in liver can be shorter than the normal range in cases of iron overload. It has been assumed that T2* decay results in negligible signal loss among the echoes in conventional Dixon methods, but it can be significant on the time scale of Dixon echo shifts leading to substantial errors in hepatic fat estimates (Figure 2).

IDEAL IQ uses a novel construct of a "complex field map" to include the effects of T2* into the signal model (Figure 3). By acquiring six echoes and estimating the complex field map using an iterative least square method, it is possible to achieve simultaneous water-triglyceride fat decomposition and T2* estimation in a single breath-hold.[8]

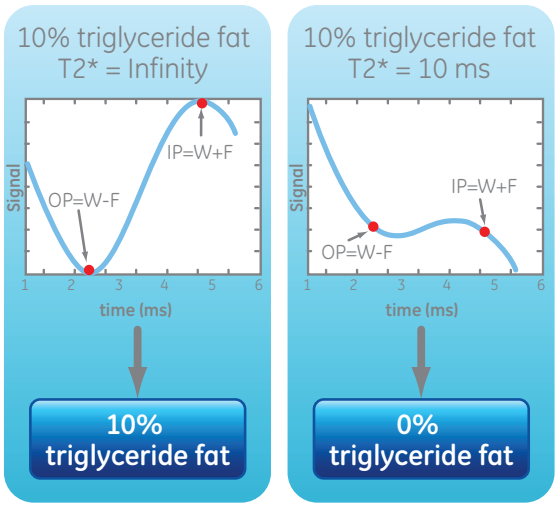


Figure 2. Signal level plots as a function of time using typical in-phase (IP) and out-of-phase (OP) imaging with and without T2* effects. IP and OP images would have been sufficient to calculate the triglyceride fat fraction if there were no T2* effects. However, with the T2* effects, the signal's decay will result in under-estimation of triglyceride fat fraction.

Multi-peak fat spectrum modeling

Conventional chemical shift-based water-fat separation methods use a relatively simple signal model that assumes both water and fat have a single resonance frequency. However, it is well known that fat has multiple spectral peaks, at least six of which can be resolved at clinical field strengths (Figure 4). This inaccuracy in the signal model results in two undesired effects. First, water and fat are incompletely separated. Second, methods designed to

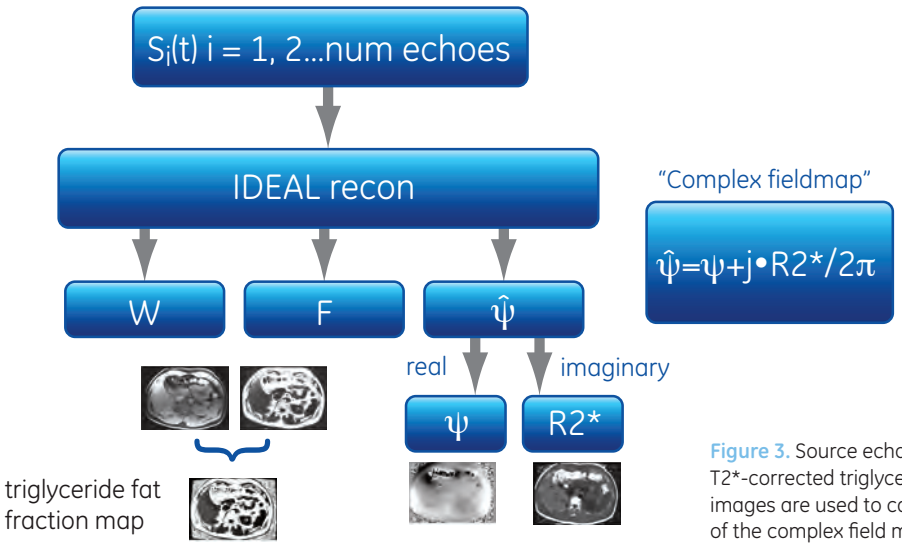


Figure 3. Source echoes are decomposed into T2*-corrected water, T2*-corrected triglyceride fat, and complex field map. The water and fat images are used to calculate a triglyceride fat fraction map. The real part of the complex field map corresponds to B_0 field inhomogeneity, while the imaginary part contains information on R2* (=1/T2*).

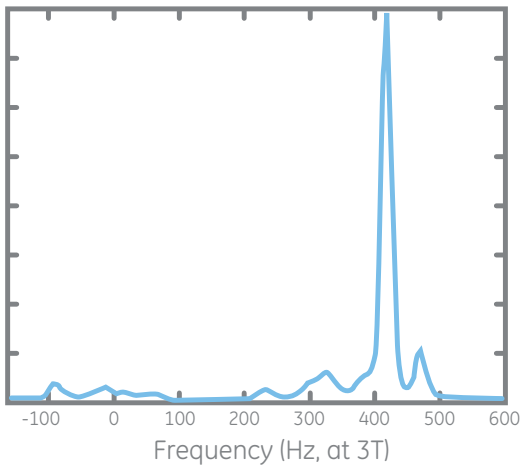


Figure 4. A representative spectra in subcutaneous fat at 3T. The spectra were shifted and displayed such that the main fat peak is at 420 Hz relative to water.

estimate T2* in the presence of fat incorrectly estimate the T2* decay in tissues containing fat. In IDEAL IQ, a more accurate multi-frequency model of triglyceride fat is included:

$$s(t) = (\rho_w + \rho f \sum \alpha_p \bullet e^{j2\pi f_p t} \bullet e^{j2\pi \Psi t}$$

where f_p is the resonance frequency of the p-th fat peak (relative to water), α_p is the relative amplitude of the p-th peak such that $\sum \alpha_p = 1$, and ψ is the complex field map as shown above. The IDEAL algorithm is easily modified to accommodate the multi-frequency representation of the fat signal,[9] and leads to improved accuracy in triglyceride fat fraction measurement.[10] Furthermore, R2* is more accurately estimated in the presence of fat (Figure 5).

Dr. Scott B. Reeder

Scott B. Reeder, MD, PhD, is the Section Chief of MRI and Cardiovascular Imaging, and Director of the UW clinical MRI fellowship. He joined UW-Madison in 2005 from Stanford University where he completed his radiology residency and a fellowship in abdominal and cardiovascular imaging. Previously, he completed medical school at Johns Hopkins in Baltimore, where he also received his Masters and PhD in Biomedical Engineering. He is originally from Canada where he received his BScE in Engineering Physics at Queen's University in Kingston, Ontario. In addition to his clinical duties, Dr. Reeder is also the Director of the UW Liver Imaging Research Program, an active NIH-funded group that performs research in technical development and translation of new imaging methods to assess liver disease. Specific areas of research interests include development of new MRI methods for quantification of abdominal adiposity, liver fat, liver iron overload, and other features of diffuse liver disease, quantification of perfusion in liver tumors, hemodynamics of portal hypertension, and the use of new contrast agents in liver and biliary diseases.

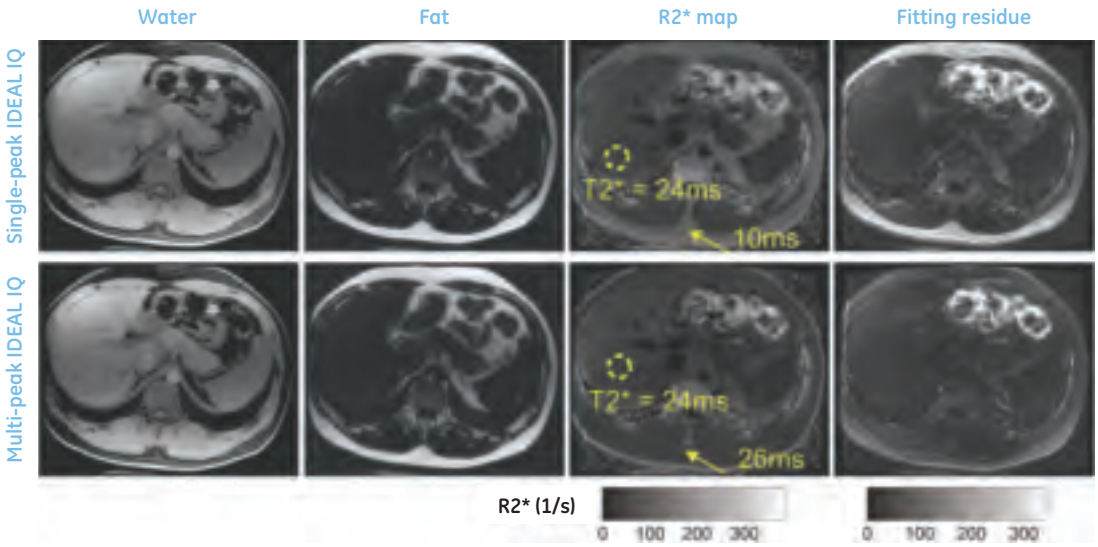


Figure 5. Top: single-peak model; bottom: multiple-peak model. As can be seen from the R2* maps, single-peak model results in an erroneous estimate of T2* in the subcutaneous fat (average T2* = 10 ms). In contrast, R2* map with the multiple-peak model shows an improved T2* estimate (averaged T2* = 26 ms). The T2* values in the liver remain the same because there is no fat in the liver. As expected, the residue maps show significant improvement of the fitting in adipose tissues when using the multiple-frequency model of fat.

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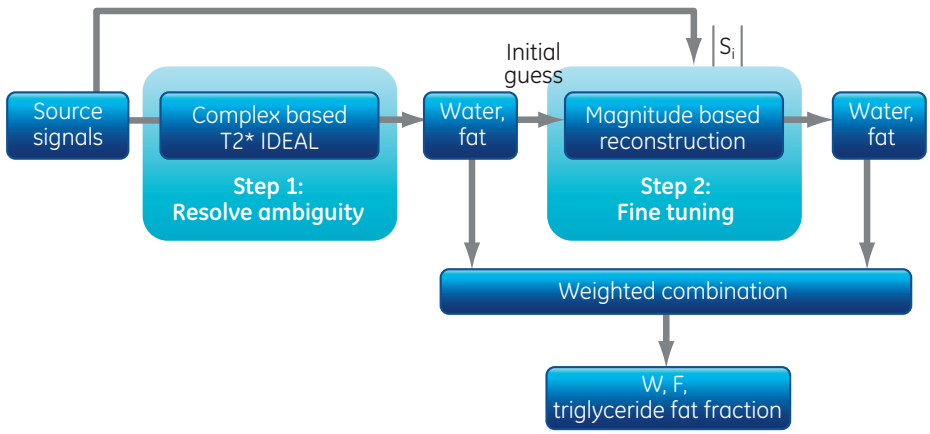

Figure 6. Flow diagram of the complex-based and magnitude-based hybrid approach. The second step relies on the results from the first step for initial conditioning of the fit. The results from the two steps are combined to provide robust and accurate water-fat separation.

Magnitude-based reconstruction

Chemical shift-based, water-fat separation techniques rely on different water-fat phase shifts generated at multiple echo times to estimate the B_0 field inhomogeneity map and the water and fat images. Such methods that utilize complex data may be sensitive to phase errors in the source images due to system imperfections such as eddy currents. Although the effect of these phase errors is acceptable for most qualitative applications, they may create clinically important errors for some applications such as fat quantification.

Water-fat separation can also be achieved using only the magnitude of the complex source signals. Magnitude methods are insensitive to phase errors in the source images; however, the water-fat ambiguity of chemical shift methods cannot be resolved when phase information is discarded. As a result, magnitude-based methods cannot uniquely determine the triglyceride fat fraction for values over 50%. IDEAL IQ uses a hybrid water-triglyceride fat separation approach that combines the strengths of both complex and magnitude reconstruction approaches (Figure 6). Using the hybrid method, the effects of phase errors can be removed without introducing water-fat ambiguity.[11]

Combining all these techniques, IDEAL IQ enables accurate estimation of relative triglyceride fat fraction map and R2* map. ■

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