Quantitative Fat Imaging for Evaluating Diffuse Liver Diseases

Correcting for challenging confounding factors

By Kenji Asano, ME1, PSD/Application Architect; Ersin Bayram, PhD1, Body MR Applications Development Manager; Huanzhou Yu, PhD1, Scientist; and Scott B. Reeder, MD, PhD2, Section Chief of MRI and Cardiovascular Imaging

1GE Healthcare, Waukesha, WI; 2University of Wisconsin, Madison, WI

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.

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

**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
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:

\[ s(t) = \left( \rho_w + \rho f \sum \alpha_p \right) e^{i2\pi f \tau} e^{i2\pi \psi} \]

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

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.

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.
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 $R^*_2$ map.

**Magnitude-based reconstruction**

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**References**