Evaluation of Quantification of Fat in the Presence of SPIO and Gd-EOB-DTPA; Experimental Phantom Study

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Purpose

It should be considered an accurate quantification of liver fat content using a 1.5T MRI in order to prevent the development of NASH (Non Alcoholic Steato Hepatitis).

T2*-corrected Dixon MRI can quantify liver fat content in the presence of iron.

The aim of this study is to investigate three-point T2*-corrected Dixon magnetic resonance (MR) imaging for accurate quantification of fat content in the presence of iron and Gd-EOB-DTPA.

Background

Recently, more and more people have been developing NASH (Non Alcoholic Steato Hepatitis). 10 to 20 percent of people who are infected with NASH, will develop fatty liver hepatitis and cirrhosis, eventually progressing to liver cancer (1,2).

Generally, non-invasive MRI and invasive biopsies are used in the quantification of fatty liver. MR spectroscopy is also used in the quantification of tissue's fat percentage.

Recently, it has become more common to use MR contrast agent of Gd-EOB-DTPA for detecting hepatic tumors. Using this contrast medium it takes about 10 to 20 minutes after intravenous injection to acquire hepatocyte phase images (3). And during this 10 to 20 minutes after IV of Gd-EOB-DTPA, we usually get T2-weighted images and diffusion-weighted images. So, under the clinical site, these methods for quantifying hepatic fat content maybe performed after injection of contrast media. There is no paper about studying for fat quantification of liver containing Gd-EOB-DTPA.

The most accurate quantification fat suppression method is the Dixon method in all methods (4). Chemical shift MRI uses the difference in resonance frequency between water and lipids (roughly 224Hz) to show the difference between tissue containing water from tissue containing both water and lipids. Using this formula, Dixon developed a reconstruction algorithm to distinguish a fatty liver from a healthy liver and thought to be useful in determining the percent of fat in the liver. After Dixon experiments several other researchers have advanced the Dixon technique to quantify liver fat content using calibration by liver biopsy. However, these studies are limited by the small number of patients. Disadvantages of the Dixon technique and its variations is that they don't correct for potentially confounding T2* effects, and results are limited in the presence of hepatic iron (5).
**Methods and Materials**

**Phantoms**

In order to simulate human fatty liver including lipid droplets in liver cells, we used an emulsion method, so that the mixture of agar gel emulsion is distributed uniformly fat micelles. First, sodium dodecyl sulfate 43mmol/L of emulsifier was dissolved in deionized water at room temperature. Then using a magnetic hot plate 2%w/v of agar was dissolved into the solution.

30mL of this agar solution was injected into 50mL polypropylene containers (50mL jar Aiboi). Then various amounts of iron, canola oil and Gd-EOB-DTPA (Nihon Schering Co) was slowly added and created a mixed solution.

We made three sets of phantoms.

1. First set of phantoms containing FFs (Fat fractions) of 0%, 10%, 20%, 30%, 40%, 50% plus 0 or 11.2mgFe/mL iron of SPIO (ferucarbotran ; Nihon Schering Co), corresponding to no and excessive iron deposition, respectively, plus 0.2mmom/mL Gd-EOB-DTPA respectively.

2. Second set of phantoms FFs was fixed at 10%, plus 0.2mmolGd/mL Gd-EOB-DTPA and varying the amount of iron, containing 0, 2.8, 5.6, 8.4, 11.2, and 14.0mgFe/mL iron.

3. Third set of phantoms FFs was fixed at 10% and 11.2µgFe/mL iron, the concentrate of Gd-EOB-DTPA was changed to 0,0.05,0.1,0.15,0.2,0.25mmolGd/mL. The values of FFs and iron concentrations were selected to represent physiologic ranges seen in normal and pathologic human livers (6).

**Study sequence and Signal analysis**

MRI was performed at 1.5 T MR unit (PHLIPS AchieVal 1.5T Dual 32ch) using three-point Dixon (TR/TE1/TE2/TE3 of 280/2.4/4.6/9.2milliseconds), using a body phased array coil, flip angle of 10 degrees. slice thickness, 5 mm, field of view of 400 mm.

Signal analysis was performed using Image J 1.45. Setting ROI and we measured the signal intensity(SI). We estimated T2* according to below formula (1).

\[ T2^* = \frac{(TE_3-TE_2)}{\ln(SI_2/SI_3)} \quad (1) \]

Where \( SI_2 \) and \( SI_3 \) are signal intensities obtained at echo 2 and echo 3, respectively.
T2* correction factors F1 and F2 for the data of echo 1 and 2 were calculated according to formula (2)

$$F_1 = \exp\left[\frac{TE_1}{T2^*}\right] \quad F_2 = \exp\left[\frac{TE_2}{T2^*}\right]$$  \hspace{1cm} (2)

Then, calculate corrected signal intensity and obtain real FFs (fat fractions).

FFs were estimated without T2*-correction and with T2*-correction. For statistical analysis we used Spearman correlation.
Results

**Fig. 1:** Comparison of real FFs and predicted FFs

References:

Real FFs and predicted FFs are quite similar ($r_{\text{spearman}} = 0.98$)
Correlation between real fat and FFs containing SPIO(iron) was $r_{\text{spearman}}=0.73$

Iron effects on fat quantification was corrected with T2* relaxation effects. ($r_{\text{spearman}}=0.96$)

Real FFs and Predicted FFs containing Gd-EOB-DTPA(0.2mmolGd/mL) are similar($r_{\text{spearman}}= 0.95$). However, Predicted FFs were a little underestimated.

Real FFs and Predicted FFs containing iron and Gd-EOB-DTPA are similar($r_{\text{spearman}}= 0.97$) with slightly variations of fat percentage.
**Fig. 3:** Comparison of real FFs fixed at 10%, and predicted FFs, containing SPIO(11.2µgFe/mL) and concentrations various Gd-EOB-DTPA, corrected with T2* relaxation effects.

**References:** - Tokyo/JP

Comparison of FFs fixed at 10%, and predicted FFs, containing iron and various concentration of Gd-EOB-DTPA are similar if the concentration of Gd-EOB-DTPA changes.

Comparison of FFs fixed at 10%, and predicted FFs, containing various concentration of Gd-EOB-DTPA are similar if the concentration of Gd-EOB-DTPA changes.

**DISCUSSION**

T2*-corrected Dixon MR imaging is a noninvasive tool used for correcting the influence of SPIO on fat quantification in our phantom study that was reported by J-P Ku“hn, for quantification of hepatic fat content (5). We consider there is a possibility for quantification of fat in the liver containing Gd-EOB-DTPA using correction for T2* relaxation effects. Then in the following order, increasing with accuracy, Gd-EOB-DTPA< SPIO<Gd-EOB-DTPA plus SPIO (Fig.2). To increase the accuracy, correction for T1 relaxation should be required.
Fig. 1: 1 Comparison of real FFs and predicted FFs

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**Fig. 2:** Comparison of real FFs and predicted FFs containing iron and Gd-EOB-DTPA corrected with T2*relaxation effects.

**Fig. 3:** Comparison of real FFs fixed at 10%, and predicted FFs, containing SPIO(11.2µgFe/mL) and concentrations various Gd-EOB-DTPA, corrected with T2* relaxation effects.
Conclusion

When doing the quantification of liver fat fractions there is a possibility of accurate quantification using correction for $T_2^*$ relaxation effects of Gd-EOB-DTPA as has been proved for iron. Also studying correction for $T_1$ is required.
References


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