Quantification of liver steatosis in MRI: available techniques and use of transverse magnetization decay curve in patients with iron overload

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Learning objectives

Steatosis, the accumulation of fat-containing vacuoles within hepatocytes, is a key histologic feature of fatty liver disease. Liver biopsy, the current standard of reference for the assessment of steatosis, is invasive and has sampling errors, in this context MRI is emerging as a valuable non-invasive tool for early detection and monitoring of liver fat. Several MRI-based techniques are currently in clinical use for the detection and quantification of fat fraction (FF), allowing the separation of the MRI signal into fat and water signal components.[1]

The objectives of this work are:

- Illustrate the available techniques for the evaluation of liver steatosis with MRI imaging.
- Outline the advantages, for patients with iron overload, of a quantification method based on the fitting of the transverse magnetization decay curve.
- Compare the results obtained with this technique with the results obtained with the 2-point Dixon method.
Background

The basic MRI techniques for fat detection can be grouped into three categories, with each technique taking advantage of a different physical property [1]:

1. **Chemical shift imaging**: a standard nonselective radiofrequency pulse is applied to tissues and water and fat proton species are excited, but the water signal precesses faster than the fat signal.
2. **Frequency-selective imaging**: a presaturation pulse is applied around the resonance frequency of fat prior to the section excitation pulse to eliminate fat signal from the generated image.
3. **MR spectroscopy**: data are collected in the absence of a gradient, such that the frequency content of the observed signal reflects the native precessional frequencies of various molecules as water (H$_2$O), fat (eg, CH$_2$), and others. In effect, MR spectroscopy directly measures the chemical composition of tissue on the basis of the frequency composition of the signal arising from the voxel of interest.

In this work we focus our attention on the chemical shift imaging. One of the most commonly used MRI methods for fat detection and quantification is gradient recalled echo imaging using Dixon's 2-point technique [2]. This method assumes a simplified two component system wherein the observed MR signal is the summation of two signal sources: fat protons and water protons, which are characterized by a distinct chemical shift of approximately 3.5 parts-per-million (ppm). Images are acquired at two echo times (TEs) at which the signals from fat protons and water protons are presumed to be exactly in-phase (IP) and out-of-phase (OP). The fat fraction (FF), which is the ratio of the signal from fat protons to the signal from all protons, is then obtained by the following:

$$\text{FF} = \frac{\text{IP-OP}}{2 \times \text{IP}}$$

where IP and OP are the pixel intensities of in-phase and out-phase images.

There are several confounders in the accurate measurement of FF measurements and these include: $T_1$ relaxation, $T_2^*$ relaxation, fat spectral complexity, etc. Since these images are acquired with TEs that are short relative to the $T_2^*$ of healthy liver (approximately 30 ms at 1.5 T), it is normally assumed that $T_2^*$ decay is negligible and all signal variation between the two TEs is due to the phase interference of the fat and water protons. $T_2^*$ is then particularly relevant for liver imaging since steatosis can be in many cases associated to iron overload, which causes $T_2^*$ signal decay. [3]
In literature [4,5] a method based on a biexponential curve-fitting model has been used to derive the relative signal contributions from fat and water. The oscillation in signal intensity - for tissues containing lipid and water- as a function of echo time and the simultaneous $T_2^*$ decay may be modeled with the following equation [5]:

$$|S| = |S_w e^{-t/T_2^*_{w}} + S_f e^{-t/T_2^*_{f}+i##t}|$$

where $S_w$ and $S_f$ are the components of the signal from water and fat, respectively, and $T_2^*_{w}$ and $T_2^*_{f}$ are their respective decay constants, while $t$ is the time after excitation and $#$ is the difference in frequency between fat and water.
Imaging findings OR Procedure details

Patients with mild and/or moderate iron overload were imaged with a 1.5T MRI with the following sequences:

- $T_2^*$ multigradient echo (echo train of 16 echos and 1.15 ms echo spacing, TE 1.15-18.4 ms, slice thickness 10mm, gap 0mm)
- $T_1$ LAVA
- $T_1$ fSGPR dual echo (slice thickness 7mm, gap 1mm).

Quantification of fat was performed both measuring the evolution of the signal with echo time (fitting of the transverse magnetization) and evaluating the FF with the 2-point Dixon technique.

In order to perform the fitting of the transverse magnetization signal and the FF mapping, a publicly available software (C-Iron, Camelot Biomedical Systems, http://c-iron.camelotbio.com) was used: in the $T_2^*$ images a freehand ROI was drawn from a transverse midhepatic slice excluding large blood vessels. Pixels where the estimation of the $T_2^*$ or FF is unreliable (according to a statistical criterion) are automatically excluded from the computation.

In order to apply the 2-point Dixon method, the $T_1$ fSGPR dual echo images were considered: a circular ROI was drawn in a homogeneous region of liver and the pixel intensities of in-phase and out-phase images were measured to calculate the fat fraction as described in Background section.

A comparison of the FF evaluated by the 2-point Dixon technique and the curve-fitting method was then performed.

**PATIENT 1**

We can observe in the $T_1$ dual echo sequence a heterogeneous steatosis (Fig. 1 on page 7). With the Dixon method the FF results 24% in the posterior right lobe and 9% in the anterior right liver lobe. The fat fraction calculated with C-Iron is 22% with a standard deviation of 4% (Fig. 2 on page 7). The patient has a low iron overload with a $T_2^*$ of about 8-9 ms.

**PATIENT 2**

We can appreciate homogeneous steatosis except for a small paracolecistic area of less steatosis (Fig. 3 on page 8). The FF calculated by Dixon method is 18-19% whereas
C-Iron gives a FF of 22% with a 4% standard deviation (Fig. 4 on page 9). The patient has a low iron overload with a T$_2^*$ of about 12 ms.

**PATIENT 3**

Patient with cirrhosis. In the T$_1$ dual echo images we can appreciate the iron overload causing reduced signal in the in-phase image compared to the out-of-phase image (Fig. 5 on page 10, the opposite behaviour of steatosis). The FF with the Dixon method is not assessable because of the iron overload. C-Iron detects no steatosis (Fig. 6 on page 11) and a heterogeneous T$_2^*$ distribution due to cirrhosis (Fig. 7 on page 12).

**PATIENT 4**

Patient with severe iron overload (T$_2^*$ about 2ms, i.e. LIC$_{dw}$=14 mg/g). FF is not evaluable both with the Dixon method and C-Iron because of the iron burden (Fig. 8 on page 13). However, the T$_2^*$ decay and the simultaneous oscillation in signal intensity as a function of echo time can be detected and interpreted as steatosis (Fig. 9 on page 14).

**PATIENT 5**

Patient with T$_2^*$ of 12-13 ms. FF with the Dixon method: 6% (Fig. 10 on page 15), with C-Iron 11±4% (Fig. 11 on page 16).
Fig. 1: PATIENT 1: in-phase (top) and out-of-phase (bottom) T1 dual echo images.

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Fig. 2: PATIENT 1: Fat Fraction map calculated by C-Iron.

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**Fig. 3:** PATIENT 2: in-phase (top) and out-of-phase (bottom) T1 dual echo images.

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Fig. 4: PATIENT 2: Fat Fraction map calculated by C-Iron.

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Fig. 5: PATIENT 3: in-phase (top) and out-of-phase (bottom) T1 dual echo images.

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Fig. 6: PATIENT 3: Fat Fraction map calculated by C-Iron.

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**Fig. 7:** PATIENT 3: Iron overload map calculated by C-Iron.

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**Fig. 8:** PATIENT 4: in-phase (top) and out-of-phase (bottom) T1 dual echo images.

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**Fig. 9:** PATIENT 4: Fat Fraction map calculated by C-Iron.

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Fig. 10: PATIENT 5: in-phase (top) and out-of-phase (bottom) T1 dual echo images.

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Fig. 11: PATIENT 5: Fat Fraction map calculated by C-Iron.

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Conclusion

The software C-Iron provides more complete information for patients with liver steatosis since it calculates a map instead of a fat fraction value averaged on a liver region of interest. Moreover, our findings are in accordance with the literature: in presence of iron, the dual echo method underestimates FF with respect to the T$_2^*$ curve-fitting method.
References


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