Fat content quantification errors using multiple gradient echo imaging: A phantom and simulation study

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Introduction

In the past decade, the incidence increase of obesity, diabetes and lipid metabolism disorders involved an epidemic increase of Non-Alcoholic Fatty Liver Diseases (NAFLD) which may affect from 10 to 30% of adults and 13% of children in the occidental population. NAFLD can evolve to Non-Alcoholic Steato-Hepatitis (NASH) and may lead to liver fibrosis up to cirrhosis from which complications involve 15,000 deaths per year in France [1-2]. A clinical follow-up of NAFLD evolution would be very valuable. While the histology after liver biopsy is the gold standard for liver steatosis assessment, inherent risk, interobserver variability and sampling errors of this method are inappropriate. Several MR quantification methods have been proposed for liver fat content quantification including ^{1}H spectroscopy, in- and out-of-phase dual-gradient echo, three-point Dixon IDEAL or multiple gradient echoes [3-6]. Dual- or multiple- gradient echo sequences are routinely performed in clinical practice but accuracy can be affected by T_2* decay, T_1 saturation and multiple spectral components of fat. This work investigated fat content quantification error using different models based on multiple gradient echo imaging. This work presents some computer simulations, phantom study and example of in-vivo application on selected patients with histological results.

Material and method

MR acquisitions were performed on a 1.5 T Magnetom Symphony *(Siemens Medical Solutions, Erlangen, Germany)*. MRI protocol was composed of two sequences. A 2D in- and out-of-phase dual-echo FLASH sequence with the following parameters : TE/TR/flip angle, 2.38 [OP], 4.76 [IP] ms/188 ms/70°; 208 x 256 matrix; 244 x 400mm² FOV; 400 Hz.pixel^{-1} bandwidth and 5 mm slice thickness in axial plane. A 2D multiple echo FLASH sequence with the following parameters: 6 first OP echoes and 6 first IP echoes; TR/TE, 219/n x 2.38 ms with n = 1,…,12; 208 x 256 matrix; 244 x 400 mm^2 FOV; 500 Hz.pixel^{-1} bandwidth and 8 mm slice thickness in axial plane. Sequence was performed twice with 15° and 70° flip angles.

Computer simulation was performed using Matlab *7.5 (Mathworks, Natick, Mass)*. Different tissue relaxation times and 2D FLASH sequence parameters were simulated for 2 point-Dixon method associated with dual-echo MR acquisition as well as bi-exponential model with T_2* correction and bi-exponential model with T_1 and T_2* correction both associated with multiple gradient-echo acquisition and finally a mono-exponential model with multi-spectral T_2* correction.

A fat-water phantom was built using a cubic plastic container filled with equal volumes (2.8 L) of olive oil and doped water with 1.8 mM.L^{-1} of ferumoxtran-10 to obtained relaxation times close to physiologic values at 1.5T (measured T_1/T_2*, 340/10 ms for fat and 580/16 ms for water – non published data). In order to acquire on a unique slice with a linear variation of fat content (0 to 100%), a coronal oblique slice was positioned at the oil-water interface.

Additionally, three patients with chronic liver diseases and different histological fat results (0, 20 and 30%) were enrolled for in-vivo assessment. Acquisitions were performed in breath-hold with previously described MR acquisition protocol. For each model, regression coefficient r-value and p-value were calculated to evaluate model-based fat quantification reliability with regard to histological results.

Results

Simulation showed a systematic underestimation of fat content with 2 point-Dixon method when liver T_2*-values decrease. The mean relative error (MRE) between estimated and true fat content was estimated at 15.6, 27.7 and 35.6 % for average T_2*-values of 20, 15 and 10 msec respectively whereas MRE was constant (around 8%) with bi-exponential T_2* corrected model with moderated T_1 saturation (15° flip angle). However, with 70° flip angle, fat was systematically overestimated by 22.3% and 27.8% MRE for 300 and 500 ms T_1 difference between fat and water respectively (Fig. 1). Concerning bi-exponential T_2*- and T_1-corrected model, MRE was 8.6% with 15° flip angle. Fat was systematically overestimated with 70° flip angle (MRE of 17.9 and 22.6% for 300 and 500 msec T_1 difference between fat and water respectively). Experimentally measured phantom T_2*- and T_1-values were 35 ± 5/ 210 ± 11 ms and 70 ±7/ 610 ± 15 ms for fat and water respectively. Fat quantification results confirmed computer simulation with 10.2, 20.4%, MRE for bi-exponential T_2*-corrected model with 15° and 70° flip angle respectively. MRE was 12.1 and 19.3% for bi-exponential T_1- and T_2*-corrected model with 15° and 70° flip angle respectively. Another model, the mono-exponential multi-spectral model was evaluated and MRE was estimated at 10.4%. In-vivo study results were summarized in Table.1.

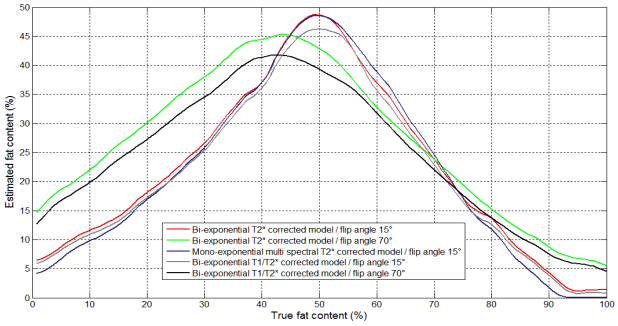

Figure 1: Fat content percentage measured on the fat-water phantom and estimated with the different quantification models.

Table 1: Confrontation between estimated fat content with several quantification models and histological results from in vitro-study.

Fat content (%) / Models	Patient #1	Patient #2	Patient #3	r-value	p-value
Histological results	**30.0**	**20.0**	**0**		
Bi-exponential T2* w/70°	27.1	17.4	2.7	0.78	**0.05**
Bi-exponential T2* w/15°	19.5	14,3	1.6	0.61	**0.03**
Multi-spectral T2* w/15°	21.1	15.8	1.8	0.7	**0.03**
Bi-exponential T1-T2* w/15°	24,5	19.3	2.2	0.87	0.07
Bi-exponential T1-T2* w/70°	29.8	23.2	4.4	0.65	**0.05**

Discussion

Computer simulation showed the limitation of quantification accuracy for in- and out-of-phase dual-gradient echo based fat estimation method due to T_2* decay variations. It is commonly the case in fatty liver disease when iron deposition is present and shorten T_2*-value or at 3.0T with T_2*-values shorter than at 1.5T. This behavior is fixed with bi-exponential T_2*-corrected or T_2*- and T_1-corrected model using multiple echo acquisition and taking into account T_2* and proton density of fat and water components independently. Simulation with 70° flip angle showed a systematic fat content overestimation with an MRE increase with larger fat to water T_1 differences. It is minimized with low flip angle limiting water saturation effect. Phantom measurements confirmed the later simulations. However, multiple gradient echo acquisitions acquired with two different flip angles allowed to resolve dominant component ambiguity due to magnitude images (for example, out-of-phase magnitude image with 90% fat content is similar to 10% fat content). Based on MRE parameters, simulated values were in agreement with experimental values measured on the phantom. In-vivo application showed a good correlation (R≈0.99) between presented models and histological results. Regression coefficients could be still improved with multiple-exponential T2* model. Fat content determined using proton density ratio has also to be corrected to be directly compared with surface ratio measured with histology. In conclusion, multiple gradient echo acquisitions with two different flip angles associated with a model correcting for T_1 saturation and T_2* decay appears to be a simple but effective non-invasive method available on all clinical systems to monitor patients with chronic liver diseases.

References

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