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Hepatic fat quantification using automated six-point Dixon: Comparison with conventional chemical shift based sequences and computed tomography☆

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ABSTRACT

Purpose: To compare automated six-point Dixon (6-p-Dixon) MRI comparing with dual-echo chemical-shift-imaging (CSI) and CT for hepatic fat fraction in phantoms and clinical study.
Materials and methods: Phantoms and fifty-nine patients were examined both MRI and CT for quantitative fat measurements.
Results: In phantom study, linear regression between fat concentration and 6-p-Dixon showed good agreement. In clinical study, linear regression between 6-p-Dixon and dual-echo CSI showed good agreement. CT attenuation value was strongly correlated with 6-p-Dixon ($R^2 = 0.852$; $P < 0.001$) and dual-echo CSI ($R^2 = 0.812$; $P < 0.001$).
Conclusion: Automated 6-p-Dixon and dual-echo CSI were accurate correlation with CT attenuation value of liver parenchyma. 6-p-Dixon has the potential for automated hepatic fat quantification.

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is a common cause of chronic liver disease, and is recognized as a potentially progressive liver disease encompassing the mild form, simple steatosis, and the progressive form, nonalcoholic steatohepatitis (NASH). NASH is a more advanced form of the disease that includes inflammation and fibrosis and is a potential precursor of cirrhosis and hepatocellular carcinoma (HCC). At present, the diagnosis of NAFLD and NASH currently relies on liver biopsy as the gold standard for assessment of the degree of steatosis and inflammation, and the microscopic tissue fat content is estimated by the number of fat-containing hepatocytes [1,2]. Liver biopsy, however, is an invasive approach that provides limited sampling locations, sampling errors, interobserver variability and is not suitable for screening or frequent monitoring [3,4].

Ultrasonography (US) remains the first method for evaluation of the presence and severity of hepatic steatosis with a low sensitivity and specificity. Because it is operator- and machine-dependent, US has limited repeatability and reproducibility [5]. Computed tomography (CT) is the other imaging method for determining liver fat, which is based on X-ray penetration of the tissue. Unlike the US features mentioned above, X-ray attenuation can be measured objectively and with high precision [6–8]. However, several factors other than fat (e.g., presence of iron, copper, fibrosis, and edema; ingestion of drugs such as amiodarone and gold) affect CT attenuation values, resulting in unavoidable errors in fat quantification [8] and low sensitivity for detecting mild steatosis. Moreover, because CT relies on ionizing radiation, it is not suitable for use in children, or for longitudinal monitoring of adults with liver fat.

Magnetic resonance (MR) techniques provide for a noninvasive means of estimating fat content in vivo. It is widely accepted that single-voxel proton magnetic resonance spectroscopy (MRS) allows for MR fat quantification in the liver with superior sensitivity and dynamic range over that of conventional MR imaging [9]. However, MRS is prone to liver inhomogeneity, although this can be compensated for by using data acquisition from multiple voxels but with the disadvantage of an increased scan time. To fully profit from the larger spatial coverage with MR imaging, a variety of fat quantification methods have been proposed. Among the MR imaging methods to date, chemical shift-based multipoint water-fat separation methods (to be referred to as multipoint water-fat separation) have been most widely used, which may be represented by the two-point Dixon method, the 3, 4, 6-point Dixon method with phase correction, and the iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) method [9–14]. The two-point Dixon methods utilizing only magnitude data are insensitive to phase errors, but they are limited in

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water-fat ambiguity and lack of T2* relaxation correction. In the situation of co-occurrence of hepatic steatosis and iron deposition, the shortened T2* relaxation time of the liver tissues reduces the signal intensity, resulting in inaccurate fat quantification if T2* correction is not implemented [9,11,15]. The hybrid magnitude and phase data method has been used in the clinical setting to quantify the fat content with NAFLD, with significant correlation with the grade of steatosis assessed by liver biopsy [11,12,16–18]. Recently, a promising method based on a 3D T1-weighted gradient-echo (GRE) acquisition with six-point Dixon (6-p Dixon) reconstruction has been described. This algorithm, which is performed during image reconstruction, automatically calculates signal intensity ratios from five sets of images with whole liver: fat-only, water-only, % fat fraction (FF), R2* and T2* (related to iron content) [19]. The main idea behind this 6-p Dixon technique thereby is to have a fast liver classification method which can be used to quickly screen for hepatic iron overload or fatty liver disease. In some of the previous studies, the techniques used were similar to those used in the present study, and a significant correlation between proton density fat fraction (PDFF) MR imaging and MRS determined hepatic fat fraction was observed [9,12,13,16,17,20,21]. However in these previous studies, the reference technique for quantification of liver fat was MRS or biopsy, and the correlation of PDFF techniques with liver CT attenuation value was not well evaluated.

The purpose of this study was to evaluate the automated 6-p Dixon fat quantification method screening for the detection of hepatic FF on a 3.0-T MR imaging system. We compared this method with conventional dual-echo GRE chemical shift imaging (CSI) methods in a phantom validation study and in clinical study with CT.

2. Materials and methods

2.1. MR protocol

MRI was performed by using a 3.0 T unit (Ingenia CX, Philips Medical Systems, Best, the Netherlands) with a ds torso coil. The liver MR imaging protocol included the following sequences: transverse 3D T1-weighted 6-p Dixon GRE; Six-echo gradient-echo images were acquired with the following imaging parameters: TR 120 ms; TE 1.1, 1.9, 2.7, 3.5, 4.3 and 5.1 ms, corresponding to consecutive in-phase and opposed-phase TE; matrix 115 × 192; breath hold acquisition time 16 s.; flip angle 3° to reduce the T1-weighting with 6-p Dixon reconstruction and dual-ratio signal discrimination algorithm (Philips Medical Systems). Following image acquisition, MR datasets were processed by using a reconstruction algorithm to estimate imaging FF and T2* maps on a pixel-by-pixel basis with correction for known confounders that included T1 bias, noise bias, and eddy currents. In clinical studies, whole liver slices were acquired during one breath-hold. 2D transverse T1-weighted dual-echo (opposed- and in-phase) GRE CSI was performed with TR 144 ms, TE 1.2/2.3 ms, flip angle 55°, matrix 256 × 192, field of view (FOV) 300 × 400 mm, slice thickness 5 mm, breath hold acquisition time 19 s × 2 times. For gadoxetic acid (Primovist; Bayer Schering Pharma, Berlin, Germany) enhanced MR imaging unenhanced, arterial phase (30–45 s), portal phase (80 s), late phase (240 s), and 20-min delayed hepatobiliary phase images were obtained using a T1-weighted 3D turbo-field-echo sequence (T1-weighted high-resolution isotropic volume examination; THRIVE, Philips Healthcare) with TR 3.1 ms, TE 1.5 ms, flip angle 10°, matrix size 304 × 243, FOV 350 × 400 mm, slice thickness 4 mm. Fat suppressed T2-weighted sequence was performed with TR 750 ms, TE 80 ms, flip angle, 90°; matrix size, 288 × 174, FOV 350 × 400 mm, slice thickness 7 mm. Diffusion-weighted single-shot echo-planar imaging with simultaneous respiratory triggering was performed with TR 2100 ms, TE 60 ms. The TR was matched to each patient's length of the respiratory cycle. The scanning parameters were a b-value of 0 and 800 s/mm^2, spectral presaturation with inversion recovery for fat suppression, matrix size 128 × 112, FOV 380 × 380 mm, slice thickness 7 mm.

2.2. MR data analysis

The averaged signal intensities within each region of interest (ROI) acquired at in-phase/opposed-phase image, fat and water images were used for fat fraction (Fig. 1). In 6-p Dixon, the fat image and water image signals (SIF and SIW) were used to calculate the fat fraction as WF index = SIF / (SIW + SIF) × 100 (%) [22]. In dual-echo GRE, the in-phase and opposed-phase signals (SII and SIO) were used to calculate the fat fraction as SI index = (SII − SIO) / SII × 100 (%) [23].

2.3. Lipid emulsion-based phantom study

A phantom study was performed to validate the accuracy of the MR imaging for fat fraction measurement. The various fat concentrations in the phantoms consisted of nine vials that contained saline with 0% fat, emulsifying of mayonnaise (Kewpie, Tokyo, Japan) with 14.7–80.7% fat on a weight-to-weight basis, rape seed oil (J oilmills Tokyo, Japan) with 100% fat [24]. The main ingredients of mayonnaise were oil, egg yolk, vinegar, and salt. The resultant chemical fat concentrations were 0.0%, 14.7%, 24.0%, 34.7%, 57.3%, 66.7%, 74.7%, 80.7% and 100.0%.

Two acquisitions were obtained for phantom study, one with a T1-weighted opposed- and in-phase GRE, and the other with a 6-p Dixon in the FF measurement. Data were analyzed by using ROI of 2 cm^2 on each in- and opposed-phase, water and fat image, and automated imaging FF. Data acquisition was repeated three times, and the average value of three measurements was appropriated to a calibration reference for fat quantification. All measurements were made by two investigators. Averaged measurements with both readers were used for analysis. Quantitative measurements were calculated as SI index with dual-echo CSI, WF index and imaging FF of 6-p Dixon in this phantom study.

2.4. Clinical study

This retrospective study was approved by the institutional review board, and the requirement for informed consent was waived. Between July 2015 and March 2016, fifty-nine patients were examined both MR imaging and CT in the same day. Of these 59 patients, 49 were men, and 10 were women (mean age, 67.7 ± 9.5 years; range, 44–82 years). These patients had the following underlying liver diseases: hepatitis C (n = 34), hepatitis B (n = 9), alcohol-induced hepatitis (n = 9) and liver metastases (n = 7). Prior to the administration of contrast, two acquisitions were obtained, one with a T1-weighted dual-echo CSI, and the other with 6-p Dixon in the FF measurement. In addition, T2* values were also measured from T2* maps to assess the effects of hepatic iron deposition. ROIs were drawn in right lobe of the liver, avoiding larger vessels. The average value of three measurements was appropriated to a calibration reference for fat quantification and T2* measurement. All measurements were made by two investigators. Averaged measurements with both readers were used for analysis. Quantitative measurements were calculated as SI index with dual-echo CSI, WF index, imaging FF and T2* value of 6-p Dixon in this study.

CT was performed by using a 64-detector row helical CT instrument (Brilliance-64, Philips Healthcare). The imaging parameters of unenhanced helical scans were as follows: detector collimation, 64 × 0.625 mm; helical pitch, 0.798; gantry rotation time, 0.5 s; reconstructed section thickness, 5.0 mm; reconstruction interval, 5.0 mm; tube voltage, 120 kV; and planned tube current-time product, 300 mAs. Liver attenuation index (LAI), derived from the difference between mean hepatic attenuation and mean splenic attenuation, was used as a CT imaging parameter for the degree of steatosis [25]. The following threshold values for were used: LAI >5.0 HU, no steatosis; LAI between 5.0 HU and −10 HU, mild-to-moderate steatosis; LAI less than −10 HU, severe steatosis.