Characterization of Liver Fibrosis Using Fat-Suppressed Ultrashort TE (FUTE) Imaging and Multipoint Water-Fat Separation MRI in Patients with Hepatitis C Virus (HCV)-Induced Liver Fibrosis

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INTRODUCTION

Liver fibrosis is a pathologic change caused by chronic liver damage, and its end-stage, cirrhosis, is one of the leading causes of morbidity and mortality in the world [1]. Given that the accumulation of an excess amount of macromolecules such as extracellular matrix proteins (ECM) in response to liver injury is one of the most widely accepted pathobiological manifestations of liver fibrosis [1], magnetization transfer techniques (MT) [2] have been explored as a means of assessing liver fibrosis [3, 4, 5]. However, due to the sensitivity of MT contrast (MTC) to many biological changes, the results have been somewhat disappointing [3, 4, 5]. To this end, ultrashort echo time (UTE) imaging [6, 7] may be an alternative to quantifying the amount of short T2 components in the diseased liver, which may be associated with severity of the disease. In this report, we explore the feasibility of UTE imaging in assessing liver fibrosis in patients with different stages of hepatitis C virus (HCV)-induced liver fibrosis. As hepatic steatosis and concomitant iron overload are common features in many chronic liver diseases, the quantification of hepatic fat content and T2* mapping are also performed and their effect on the quantification of short T2 components is addressed.

METHODS

Human Subjects: The human research protocol was approved by the Human Investigation Committee. A total of 16 HCV patients with different stages of liver fibrosis entered the study (Metavir scores; F0 (absent; n = 1), F1 (mild; n = 3), F2 (moderate; n = 5), F3 (severe; n = 4) and F4 (cirrhotic; n = 3)). To account for the small number of subjects, the patients were regrouped into F0-1, F2 and F3-4.

MRI: All MRI studies were conducted on a 1.5T Siemens Sonata scanner with a phased-array torso coil (USA Instruments, Inc., Aurora, USA).

Fat-Suppressed Ultrashort TE (FUTE): An UTE sequence with half excitations and radial acquisitions were used with a preparation period for fat saturation [6, 7]. The sequence parameters are: TEs = 0.08 ms (ultrashort) and 4.4 ms (water and fat in-phase at 1.5T), TR = 28 ms, matrix size = 256x256, flip angle = 30^{o}, 5 slices with the thickness of 10 mm (1 slice/breath-hold), 4 averages.

Multipoint Water-Fat Separation MRI: three-point IDEAL (3PI) data [8] were collected from the abdominal region of the subjects using trueFISP (Siemens). The imaging parameters are: TEs = 1.49/2.69/3.89 ms (thus, sampling interval Δt = 1.2 ms), TR = 5.38 ms (therefore, the second TE = TR/2), matrix size = 144x256, flip angle = 55^{o}, 14 slices with the thickness of 10 mm (single breath-hold), 1 average.

Data Analysis: Regions of interest (ROIs) were defined including as much liver parenchyma tissue as possible while avoiding blood vessels. For the quantification of short T2 components, the in-phase images were subtracted from the images acquired at the ultrashort TE [7]. For each slice, T2* was estimated from the ultrashort and in-phase images assuming a mono-exponential decay [7]. For the 3PI data, images were reconstructed from raw data according to the original IDEAL algorithm for multicoil data acquisition [8] using MATLAB™ (MathWorks Inc.). From the calculated water-only and fat-only images hepatic fat fraction (HFF) images were obtained (HFF = fat/(water+fat)x100) and mean HFF was calculated over the predefined ROIs.

RESULTS

All results are expressed as mean±SEM (standard error of the mean).

Fat-Suppressed Ultrashort TE (FUTE): The changes in the amount of short T2 components are shown in Fig.1(a) as a function of the severity of liver fibrosis where the values for the F0-1 and F3-4 groups were normalized to that of the F2 group which has the highest value (F0-1 = 97.8±11.5%, F2 = 100.0±12.4% and F3-4 = 73.5±16.3%). The smallest amount of short T2 components in the F3-4 group results from the drastic decrease of the MRI measure in F4 patients (only 60% of the mean of the rest of the patients; $p < 0.001$). For the T2* measurement (Fig.1(b)), there is a trend that it is slightly increased in the F2 group with respect to the F0-1 group and appears to be maintained thereafter (F0-1 = 17.0±1.6 ms, F2 = 19.0±1.3 ms and F3-4 =19.2±1.7 ms).

Multipoint Water-Fat Separation MRI: The estimated HFFs for the patient groups are shown in Fig.1(c). There is a trend that initially HFF drastically increases (HFF of F0-1 being ~ 40% higher than that of control) but appears to be reducing thereafter (control = 10.3±0.5%, F0-1 = 14.3±2.8%, F2 = 12.2±0.9% and F3-4 = 11.9±0.7%).

DISCUSSION

The substantial decrease in the amount of short T2 components observed in the F3-4 group is in accordance with previous findings [6, 7]. That is, less endoplasmic reticulum may be present in cirrhotic livers thereby resulting in a reduction in the concentration of short T2 components (e.g., those membrane-bound protons) [6, 7]. Thus, using UTE imaging, liver fibrosis with and without cirrhosis may be differentiated. The increased HFFs (particularly in the F0-1 group) relative to the baseline and the shorter T2* values (T2* in normal liver ~ 25 ms at 1.5T [9]) in the HCV patients suggest that there may be (mild) iron deposition concomitant with steatosis. The higher T2* values in the F2 and F3-4 groups relative to the F0-1 group is most likely a consequence of the loss of the short T2 components [6, 7] rather than due to a reduction in the amount of iron deposit. It should be noted that the presence of steatosis may influence the measurement precision of T2* [9]. However, the preparation period for fat suppression in our UTE sequence in combination with the use of the in-phase images (4.4 ms at 1.5T) excludes such a potential source of error in the estimation of T2*. Likewise, changes in T2* (due to iron overload) are known to hinder accurate determination of HFF [10]. However, given the spin echo-like signal behavior of trueFISP [11], the actual temporal interval that permits T2* decay herein is only ~ 1.2 ms which corresponds to the sampling interval (Δt) for the 3PI data collection. Thus, the effect of the short and varying T2* component observed in our study on the HFF estimation should be minimal.

In conclusion, FUTE imaging may potentially provide a means of non-invasively discriminating the end stage of liver fibrosis from its milder forms in the presence of steatosis and/or iron overload.

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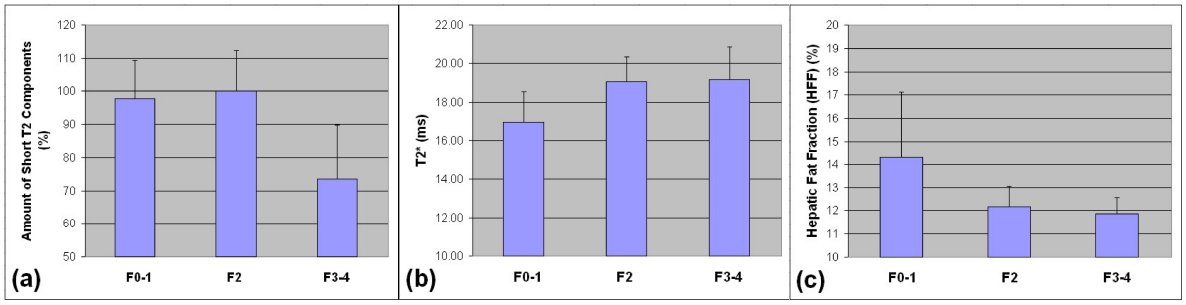

Fig.1 *Changes in (a) the amount of short T2 component, (b) T2*, (c) hepatic fat fraction (HFF) in patients with different stages of liver fibrosis.*