Magnetic Resonance Imaging 34 (2016) 1220–1225

Contents lists available at ScienceDirect

Magnetic Resonance Imaging

journal homepage: www.mrijournal.com

Original contribution

MRI-based estimation of liver function by intravoxel incoherent motion diffusion-weighted imaging

Jing Zhang [a], Yihao Guo [b], Xiangliang Tan [a], Zeyu Zheng [a], Mengqi He [a], Jun Xu [c], Yingjie Mei [d], Jiajun Zhang [a], Xixi Zhao [a], Chunhong Wang [a], Yanqiu Feng [b], Queenie Chan [e], Yuankui Wu [a], Yikai Xu [a,*]

[a] Department of Medical Imaging Center, Nanfang Hospital, Southern Medical University, Guangzhou, China
[b] Guangdong Provincial Key Laboratory of Medical Image Processing, School of Biomedical Engineering, Southern Medical University, Guangzhou, China
[c] Department of Hematology, Nanfang Hospital, Southern Medical University, Guangzhou, China
[d] Philips Healthcare, Guangzhou 18F, Tower B, CIC No.33 Zhongshan san Road, YueXiu District, Guangzhou, China
[e] Philips Healthcare, Science Park East Avenue, Hong Kong Science Park, New Territories, Hong Kong

ARTICLE INFO

Article history:
Received 5 July 2015
Revised 30 May 2016
Accepted 30 May 2016

Keywords:
Intravoxel incoherent motion
DWI
Liver function
Child–Pugh class

ABSTRACT

Purpose: To explore the usefulness of intravoxel incoherent motion (IVIM) to evaluate the hepatic functional reserve as expressed by the model for Child–Pugh class.
Materials and methods: IVIM diffusion-weighted imaging (DWI) using 10 different b values were performed on a Philips 3.0 T MR scanner in 70 patients with liver cirrhosis and 60 healthy volunteers as the control group. Patients with liver cirrhosis were subdivided into three groups: Child–Pugh class A: 29 cases; Child–Pugh class B: 19 cases; Child–Pugh class C: 22 cases. Pure molecular diffusion (D), pseudo-diffusion (D*), perfusion fraction (*f*) and apparent diffusion coefficient (ADC) values were calculated, and used to determine liver function, as indicated by the Child–Pugh class.
Results: The ICC values of D, D*, *f* and ADC between two radiologists were 0.997, 0.986, 0.985 and 0.995, respectively. D*, *f* and ADC values of liver cirrhosis group were significantly lower than control group ($P < 0.001$, $P = 0.016$, $P = 0.042$, respectively). D*, *f* and ADC values significantly decreased with increasing Child–Pugh scores ($p < 0.05$). Child–Pugh scores were inversely correlated with D* and *f* values ($r = -0.423$, $r = -0.620$, respectively). The areas under the curve (AUCs) of D* and *f* for evaluating liver function were 0.67–0.90 and 0.78–0.89, respectively.
Conclusion: IVIM DWI may be a useful image-based method for assessing liver function.

1. Introduction

The quantitative evaluation of hepatic function is important not only for monitoring patients but also for preoperative assessment of the hepatic reserve [1]. In clinical practice, the severity of liver disease is often assessed on the basis of clinical signs and biochemical blood parameters. Scoring systems, such as the Child–Pugh class, combined with biochemical values to determine liver function in the setting of liver cirrhosis, play a crucial role in the management of patients with liver disease [2]. The indocyanine green clearance test [3] and elastography [4] are useful methods for evaluating liver function. However, tests that assess global liver function may fail to detect regional liver dysfunction. Thus, liver function may be estimated more accurately by using imaging-based tests, which can detect both regional and global liver function.

Single photon-emission computed tomography with 99mTc-iminodiacetic acid (IDA) can be used to assess regional hepatic function [5]. Recent advances in the evaluation of liver disease by means of magnetic resonance imaging (MRI) with the hepatocyte-specific contrast agent gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid have enabled the assessment of the liver parenchyma in patients with liver impairment [6–8]. However, a reliable method for the quantitative evaluation of liver function has not yet been established.

Intravoxel incoherent motion (IVIM) diffusion-weighted imaging (DWI) is a promising method for the assessment of diffuse liver disease, given its potential for providing multi-parametric information and combinations of diffusion and perfusion effects. IVIM, which was initially described by Le Bihan et al. [9–12] in brain imaging, has the potential to measure both true molecular diffusion and the incoherent motion of water molecules in the capillary network. Chronic liver diseases are associated with extracellular matrix accumulation, which may affect both true diffusion and microcirculation. Therefore, IVIM DWI must be sensitive to these changes in

* Corresponding author at: Department of Medical Imaging Center, Nanfang Hospital, Southern Medical University, 1838 Guangzhou Ave. N., 510515, P.R. China. Tel.: +86 20 61642086.
E-mail address: yikai.xu@163.com (Y. Xu).

http://dx.doi.org/10.1016/j.mri.2016.05.013
0730-725X/

both these parameters to be a useful tool for evaluating liver function in patients with chronic liver diseases.

The purpose of our study was to determine whether hepatic IVIM measurements are affected by the severity of liver disease, as determined using the commonly applied Child–Pugh class.

2. Materials and methods

2.1. Patients

Our institutional review board approved this prospective study, and written informed consent was obtained from all participants before enrolment.

The patients were enrolled in our study according to the following inclusion criteria: (1) the diagnosis of cirrhosis in patients with hepatitis B was based on laboratory investigations, physical findings, laboratory investigations, imaging findings and histopathological findings [13]; (2) The patients underwent IVIM DWI of the liver and Child–Pugh score calculation according to 5 parameters, including albumin, bilirubin, prothrombin activity, ascites and encephalopathy; (3) The patients lacked hepatic carcinoma and portal vein emboli. From January 2014 to December 2014, 158 consecutive patients with cirrhosis resulting from hepatitis B were recruited for this study. Patients were excluded from the study in the following cases: they were unable to complete the full MRI sequences, or their images showed severe motion artifacts due to poor breath rhythm (n = 7); Susceptibility Weighted Imaging (SWI) and T1-weighted dual gradient-echo sequence showed iron or fat load clearly (n = 12); their clinical data were incomplete (n = 31); and they had previously received local treatment for liver disease (n = 38). Thus, a total of 70 patients with liver cirrhosis (49 men, 21 women; range, 20–75; mean age, 46.4 years) were included in this study. A biochemical test was performed to determine the Child–Pugh scores, and no more than a one-week delay was allowed between the biochemical test and the MR scans. As a result, 29, 19, 22 patients were classified as having Child–Pugh A, B or C, respectively. A control group of 60 random consecutive healthy volunteers (32 men, 28 women; range, 22–58; mean age, 45.2 years) who underwent IVIM DWI of the liver served as the reference group. The inclusion criteria for the controls included no history of liver disease (hepatocellular carcinoma or fatty liver) and normal serum liver enzyme levels; Hepatitis B and C surface antigen tests revealed negative findings.

2.2. MRI protocols

All imaging was performed with a 3.0-T MRI system (Achieva, Philips Healthcare, The Netherlands). A 16-channel body matrix coil was used. The imaging sequences used to evaluate the whole liver were as follows: (1) transverse breath-hold T1-weighted dual gradient-echo sequence, (2) transverse T2-weighted turbo spin-echo sequence with fat suppression, (3) transverse breath-hold SWI sequence and (4) transverse IVIM DWI sequence. The protocols used for the above sequences were as follows: (1) T1-weighted imaging, repetition time (TR), 3.3 ms; echo time (TE), 1.18/2.1 ms; matrix, 384; field of view (FOV), 375 mm × 304 mm × 212 mm; slice thickness, 2.5 mm; slices, 80; and number of signal average (NSA), 1; (2) T2-weighted imaging, TR, 1699 ms; TE, 80 ms; matrix, 512; FOV, 375 mm × 302 mm × 198 mm; slice thickness, 5 mm; slice gap, 0 mm; slices, 36; and NSA, 2; (3) SWI, TR/TE, shortest; matrix, 256; FOV, 375 mm × 302 mm; slice thickness, 2 mm; slice gap, 0 mm; slices, 20; SENSE, 1.5; and NEX, 1; and (4) IVIM DWI, TR, 1642 ms; TE, 62 ms; matrix, 256; FOV, 375 mm × 302 mm × 176 mm; slice thickness, 5 mm; slice gap, 0.5 mm; slices, 32; and NSA, 2. In addition, IVIM DWI employed a respiratory triggered single-shot echo planar imaging (EPI factor, 53) sequence with a parallel sampling technique (Sensitivity Encoding, SENSE 2). Axial DWI was performed with the following 10 b values: 0, 10, 30, 60, 100, 150, 200, 400, 600 and 1000 s/mm^2.

2.3. Image analysis

The biexponential model was used to calculate the signal attenuation in IVIM sequences as follows:

$$S_b/S_0 = (1-f)\exp(-bD) + f\exp[-b(D*+D)]$$

where S_b and S_0 represent the signal intensities acquired with the b-values of b and 0, respectively; D is the true diffusion coefficient representing the pure molecular diffusion (slow component of diffusion); D* is the pseudo-diffusion coefficient representing the incoherent microcirculation within the voxel (fast component of diffusion or perfusion-related diffusion); and f is the perfusion fraction related to the microcirculation.

All curve-fitting algorithms were created using a home-developed program based on MATLAB (MathWorks, Natick, MA) and developed by the Guangdong Provincial Key Laboratory of Medical Imaging Processing, School of Biological Engineering, Southern Medical University. This software allowed the abstraction of the parametric maps of f, D, D* and apparent diffusion coefficient (ADC). All regions of interest (ROIs) were positioned on DW images with b-values of 0 by two radiologists, each with 10 years of experience in reading abdominal MR images. The specific methods used were as follows: (1) the liver was outlined using its contour, and this was repeated seven times to obtain a three-dimensional

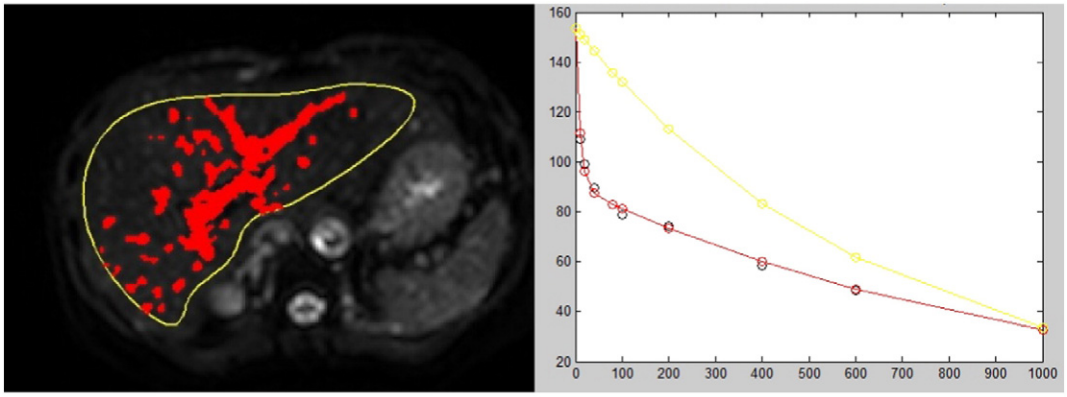

Fig. 1. (a) The region of interest (ROI) was placed over the whole liver for diffusion-weighted MRI with b = 0, and vascular data were removed by means of the threshold method. (b) The intravoxel incoherent motion (IVIM) fitting curve of measured signals showed a biexponential decay.