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### MR relaxometry in chronic liver diseases: Comparison of T1 mapping, T2 mapping, and diffusion-weighted imaging for assessing cirrhosis diagnosis and severity

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#### Abstract

Background: MR relaxometry has been extensively studied in the field of cardiac diseases, but its contribution to liver imaging is unclear. We aimed to compare liver and spleen T1 mapping, T2 mapping, and diffusion-weighted MR imaging (DWI) for assessing the diagnosis and severity of cirrhosis.

*Methods:* We prospectively included 129 patients with normal (n = 40) and cirrhotic livers (n = 89) from May to September 2014. Non-enhanced liver T1 mapping, splenic T2 mapping, and liver and splenic DWI were measured and compared for assessing cirrhosis severity using Child-Pugh score, MELD score, and presence or not of large esophageal varices (EVs) and liver stiffness measurements using Fibroscan<sup>®</sup> as reference.

Results: Liver T1 mapping was the only variable demonstrating significant differences between normal patients (500 ± 79 ms), Child-Pugh A patients (574  $\pm$  84 ms) and Child-Pugh B/C patients (690  $\pm$  147 ms; all *p*-values <0.00001). Liver T1 mapping had a significant correlation with Child-Pugh score (Pearson's correlation coefficient of 0.46), MEDL score (0.30), and liver stiffness measurement (0.52). Areas under the receiver operating characteristic curves of liver T1 mapping for the diagnosis of cirrhosis (O.85; 95% confidence intervals (CI), 0.77–0.91), Child-Pugh B/C cirrhosis (0.87; 95%CI, 0.76–0.93), and large EVs (0.75; 95%CI, 0.63–0.83) were greater than that of spleen T2 mapping, liver and spleen DWI (all p-values < 0.01).

Conclusion: Liver T1 mapping is a promising new diagnostic tool for assessing cirrhosis diagnosis and severity, showing higher diagnostic accuracy than liver and spleen DWI, while T2 mapping is not reliable.

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Keywords: Magnetic resonance imaging; MR relaxometry; T1 mapping; Diffusion-weighted imaging; Cirrhosis; Liver diseases

Abbreviations: Child-Pugh, Child-Pugh-Turcotte score; MELD, Model for End-Stage Liver Disease score; MR, magnetic resonance; ADC, apparent diffusion coefficient; LSM, liver stiffness measurement; BMI, body mass index; GGT, gamma-glutamyl transpeptidase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; PDFF, proton density fat fraction; TR, repetition time; TE, echo time; MOLLI, Modified Look-Locker Inversion Recovery; TI, inversion time. Corresponding author at: Department of Diagnostic and Interventional Imaging, Hôpital Haut-Lévêque, CHU and University of Bordeaux 1,

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# ARTICLE IN PRESS

#### 1. Introduction

Noninvasive diagnostic tests allowing assessing the severity of cirrhosis are relatively scarce. The Child-Pugh-Turcotte (Child-Pugh) and Model for End-Stage Liver Disease (MELD) scores, based on clinical and biological data, are widely used to assess the hepatic dysfunction, mainly for patients with advanced liver disease, but are less relevant to assess prognosis and outcomes of patients with compensated cirrhosis [1–3].

In recent years, liver magnetic resonance (MR) imaging has been increasingly used for diagnosing and staging chronic liver diseases. MR imaging methods are ideally suited for liver examination as they represent the best available diagnostic tool either for the detection and characterization of liver nodules or the tissue characterization. MR imaging can sample the entire liver quickly for quantifying objectively liver steatosis and iron overload [4,5].

Furthermore, several studies have recently addressed the ability of new MR sequences for assessing liver function and quantifying liver fibrosis. First, some authors have suggested that portal hypertension secondary to cirrhosis could be associated with a decrease of liver quantitative apparent diffusion coefficient (ADC), possibly due to fibrotic distortion, which restricts water molecule motion, and with an increase of splenic quantitative ADC (elevated portal blood pressure may lead to vasogenic edema) in cirrhosis [6-8]. More recently, several studies have assessed new MR sequences issued from cardiac MR relaxometry such as T1 mapping [9], in the field of chronic liver diseases [10–12]. Banerjee et al. [10] have shown that T1 mapping values (corrected for iron overload) correlated strongly with liver fibrosis in a population of 79 patients with liver biopsy, whereas other studies focused on the diagnostic impact of liver T1 mapping relaxation rate after Gd-EOB-DTPA injection to assess liver function [11,12]. Moreover, T2 mapping has been shown to accurately and reliably detect regions of oedematous myocardial tissue without the limitations of qualitative T2weighted imaging [13]. Owing to the capability of T2 mapping for reflecting regions of edema or congestion, we hypothesized in current study that T2 mapping splenic values could be related to splenic congestion secondary to portal hypertension.

Therefore, the purpose of this study was to compare the ability of liver and spleen T1 mapping, T2 mapping, and diffusionweighted MR imaging to assess the diagnosis and severity of cirrhosis.

### 2. Methods

#### 2.1. Patients

An ethics committee approved the study design and written informed consent was obtained for all patients. We prospectively included from May to September 2014 all consecutive patients with cirrhosis referred for liver MR examination at our radiology department (cirrhotic group). Inclusion criterion was cirrhosis either biopsy-proven (i.e. cirrhosis proved on histological analysis performed by pathologists specialized in chronic liver diseases within 2 years before inclusion if patients received no treatment of the liver disease's aetiology and within 6 months if patients had started treatment of the liver disease's aetiology)or diagnosed on combined physical, biological, and radiological evidence (i.e. association of chronic increased liver enzyme levels with either clinical/endoscopic signs of cirrhosis or radiological features of cirrhosis: surface nodularity, segmental hypertrophy/atrophy, signs of portal hypertension). Exclusion criteria were as follows: idiopathic portal vein thrombosis, presence of trans-jugular intra-hepatic porto-cave shunt, cardiac congestive liver, regenerative nodular hyperplasia, hepatocellular carcinoma (HCC). As a control group, we included during the same period of inclusion a total of 40 patients referred for abdominal MR examination without any history of liver diseases, cirrhosis or portal hypertension. All patients underwent upper abdominal examination including T1 mapping, T2 mapping, diffusion-weighted MR imaging, and multiecho T1 gradient-recalled echo. Cirrhotic group patients also underwent biological analysis and liver stiffness measurement (LSM) within the same week as MR examination.

## 2.2. Morphological, biological and liver stiffness parameters

For cirrhotic group patients, the following parameters were recorded at the time of MR imaging examination. Clinical parameters included age, gender, body mass index (BMI), history of diabetes or hypertension, presence and grading of esophageal varices (EV) on upper endoscopy examination. Biological parameters included platelet count, prothrombin time, total bilirubin levels, gamma-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, albumin, hyaluronic acid levels, creatinin, and haematocrit. Child-Pugh and MELD scores were calculated according to the published formulae [14,15]. LSM was performed with FibroScan® M probe (Echosens, Paris, France) by two trained nurses with more than 5000 LSM experience who were blinded to clinical, biological and MRI results. The objective was to obtain a total of 10 valid measurements (defining a successful liver stiffness measurement examination), with the maximum number of attempts set at 20.

#### 2.3. Magnetic resonance imaging methods

Imaging was performed at 1.5 T (Magnetom Avanto, Syngo VB17A, Siemens Medical Solutions, Erlangen, Germany), using a 16-channel body coil. The following non-contrast enhanced sequences were performed in all patients: (i) A multiecho chemical shift MR imaging with a 2D spoiled gradient T1 sequence allowing simultaneous proton density fat fraction and T2\* measurements based on previously published strategies [16,17]. Six echoes were obtained at consecutive opposed-phase and in-phase TEs (2.3, 4.6, 6.9; 9.2, 11.5, and 13.8 ms) after a single radiofrequency excitation (TR, 120 ms; field of view, 380 mm; matrix, 192 mm; slice thickness, 10 mm; parallel acquisition technique factor of 1). (ii) Diffusion-weighted MR imaging using a respiratory-triggered echo-planar imaging in the axial plane (repetition time (TR), 1600 ms; echo time

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