Assessment of the Hepatocyte Fraction for estimation of liver function

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Target Audience Researchers and clinicians interested in body/liver imaging and disease

Introduction Gadoxetic acid (Gd-EOB-DTPA) is a hepatobiliary-specific contrast agent and has been proposed to evaluate liver function, fibrosis[1-4] and to quantify differences in hepatic uptake[5]. Most of these studies use the liver-spleen contrast ratio, T1 value changes of liver parenchyma and the volume of the liver as markers. The purpose of this study is to assess quantification of the hepatocyte fraction and ability of hepatic uptake using Gd-EOB-DTPA for evaluation of liver function.

Material and Methods

First, R1 values of liver and spleen are measured pre and post contrast administration, the latter in the hepatobiliary phase about twenty minutes after injection. In this paper, we propose a new method to calculate the hepatocyte fraction and the uptake function based on a pharmacokinetic model [5](Fig.1) and the ΔR1 values, as derived on the right.

$$\text{Hepatocyte Fraction} = \frac{\Delta R1Hepatobiliary}{\Delta R1Hepatobiliary + \Delta R1BloodEES}$$

Additionally, the k_{Hep} value was calculated as uptake function.

$$k_{Hep} = \left(\frac{\Delta R1Hepatobiliary}{\Delta R1BloodEES}\right) / t \quad \text{t: time after contrast injection(min)}$$

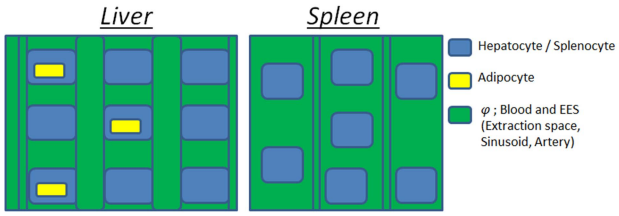
Seventy five patients underwent 99mTc-GSA scintigraphy and were classified in four severity levels as Normal (n=19), Mild (n=42), Moderate (n=8) and Severe (n=6)> Subsequently they were scanned on a 3T clinical scanner (Achieva TX, Philips Healthcare) using a multi transmit RF system and a 32 channel phased-array receiver coil. The R1map was calculated from the Look-Locker sequence with scan parameters: T1-TFE, TE/TR=1.7 / 7ms, 1.37×1.37×8mm, FA=7, single-slice, shot interval=5sec, SENSE factor=2, scan time was 15sec with breath holding.

The Hepatocyte fraction and k_{Hep} values of Normal, Mild, Moderate and Severe patients were compared statistically using the Kruskal-Wallis method. A p-value < 0.01 was considered significant.

Results The median values of hepatocyte fraction of Normal, Mild, Moderate and Severe were 76.7%, 72.5%, 50.4% and 44.8% respectively. The hepatocyte fractions were significantly different among groups classified according to 99mTc-GSA between Normal and Moderate,Normal and Severe, Mild and Moderate, and between Mild and Severe (Kruskal-Wallis method, p value < 0.01) (Fig.2). The median k_{Hep} values of Normal, Mild, Moderate and Severe were 0.18, 0.14, 0.06 and 0.04, respectively. The k_{Hep} were significantly different between Normal and Moderate, Normal and Severe, Mild and Moderate, and between Mild and Severe (Kruskal-Wallis method, p value < 0.01) (Fig.2). Typical hepatocyte fraction maps and k_{Hep} maps are shown in Fig.3. The hepatocyte fraction and k_{Hep} decreased with liver function deterioration.

Conclusion We have demonstrated quantification of hepatocyte fraction and k_{Hep} using R1 values pre and post Gd-EOB-DTPA administration. The results indicate that the hepatocyte fraction quantification is useful for a robust evaluation of liver function and that k_{Hep} provides information on hepatic uptake.

References [1] T. Katsube et al. Investigative Radiology, 2011;46:277-283 [2] N. Tusda et al. Eur J Radiol.,2010;73:137-142 [3]U.Motosugi et al. JMRI, 2009;30:1042-1046 [4] S.Nakamura et al. Jpn J Radiol., 2012;30:25-33 [5] O. Dahlqvst et al. Eur Radiol., 2012;22:642-653



R1 change after EOB

$$\begin{cases} \Delta R1_{Liver} = (1 - \varphi Liver) * \Delta R1_{Hepatobiliary} + \varphi Liver * \Delta R1_{BloodEES} \\ \Delta R1_{spleen} = \varphi spleen * \Delta R1_{BloodEES} \end{cases}$$

$$F_{Hep} = \frac{\Delta R1_{Hepatobiliary}}{\Delta R1_{BloodEES}} = 0.39 * \left(\frac{\Delta R1_{Liver}}{\Delta R1_{spleen}} - 0.77\right) \qquad \varphi Liver = 0.23, \varphi spleen = 0.3$$

Levitt DG ,BMC Clin Pharmacol, (2003)

$$k_{Hep} = F_{Hep} / t \qquad \text{t: time of after contrast (min)}$$

$$\text{Hepatocyte Fraction} = \frac{\Delta R1_{Hepatobiliary}}{\Delta R1_{Hepatobiliary} + \Delta R1_{BloodEES}}$$

Fig.1 Schematic drawing of the model and calculations used to derive the formulae for the hepatocyte fraction and k_{Hep}

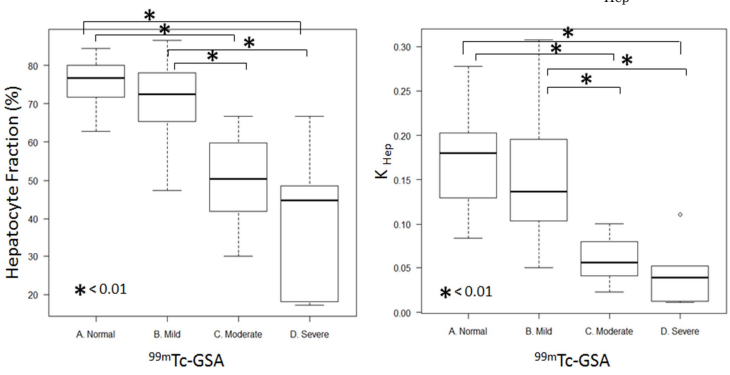


Fig.2 The value of Hepatocyte fraction and k_{Hep} for each severity class based on 99mTc-GSA

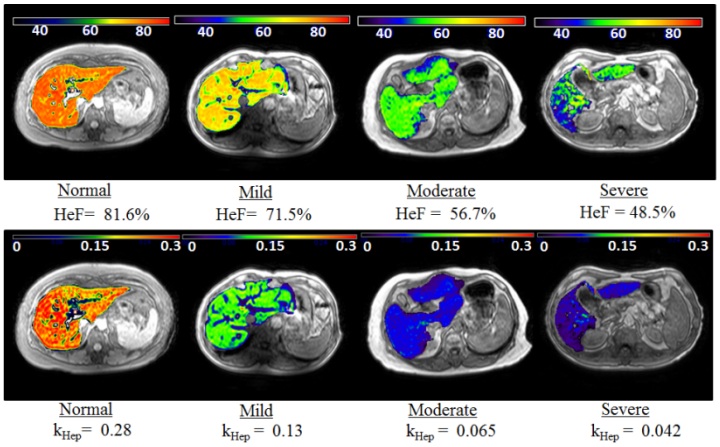


Fig.3 Hepatocyte fraction map(upper low) and k_{Hep} map(bottom raw) for each of severity class based on 99mTc-GSA