The hepatic uptake of Gd-EOB-DTPA is strongly affected by the hepatobiliary function

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Introduction:

In hepatobiliary disease, liver function can be affected by several mechanisms, which can partially or wholly be compensated for by the regenerative capacity of the liver. New surgical and image-guided techniques lead to a growing need for non-invasive imaging methods for morphological and functional assessment of the liver and biliary system. Ideally these methods should provide quantification of remaining liver function and enable estimation of the regional distribution of liver function.

We have developed a liver function test [1] based on quantitative analysis of the hepatic extraction of the liver-specific MRI contrast agent Gd-EOB-DTPA (Primovist®, Bayer Schering Pharma AG, Berlin, Germany). The test has been integrated into a clinical liver MR protocol. In the present study, the purpose was to compare patients with hepatobiliary disease and healthy volunteers using this test and to relate the test result to clinical liver status scoring parameters.

Materials and Methods: After approval by the local ethics committee, ten healthy volunteers underwent contrast-enhanced liver MRI using Gd-EOB-DTPA (0.025 mmol/kg). Also, 21 consecutive patients with suspected hepatobiliary disease examined using a clinical Gd-EOB-DTPA-enhanced liver MR protocol were included retrospectively. Imaging was performed in an Achieva 1.5T (Philips Medical, Best, The Netherlands). A single breath-hold fat saturated T1W 3D FFE sequence (THRIVE), TR 5.2 ms, α 10°, scan time 23 s, was acquired prior to, in the arterial and venous phase, and 5, 10 and 20 minutes after bolus injection.

Signal intensity (SI) curves were averaged from seven regions of interest (ROIs) regionally distributed in the liver and from three ROIs in the spleen. The SI time series were recalculated into *R1* time series for each organ using the sequence-specific signal equation, assuming equal initial *T1* in the different organs for all subjects. The contrast agent concentrations, C_{liver} and C_{spleen}, were then estimated as

$C = (R1 - R1(t=0))/R$, where R is the relaxivity of the contrast agent.

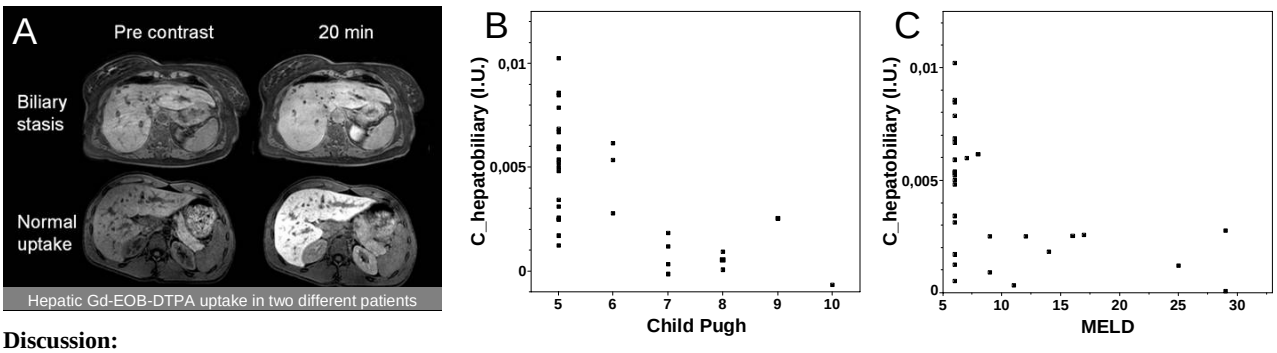
The dynamics of the contrast agent liver uptake was analyzed using a simplified model assuming two compartments in the liver – blood and hepatobiliary tissue – and two in the spleen – blood and splenic tissue, the latter inaccessible to the contrast agent. The hepatobiliary compartment comprises hepatocyte intracellular water, bile canaliculi and ductules. The model attempts to estimate the contrast concentration in the hepatobiliary compartment, $C_{hepatobiliary,}$ without influence from C_{blood}, the latter determined by measurements in the spleen:

$C_{hepatobiliary} = (C_{liver} - C_{spleen})/\varphi_{blood}$, where φ_{blood} denotes the volume fraction of blood, assumed to be 0.5 in both spleen and liver.

From laboratory tests and clinical data the Child-Pugh and Model For End-Stage Liver Disease (MELD) scores were determined for all subjects. The plasma bilirubin level at the time of the MR examination was noted. The clinically estimated hepatobiliary function of every patient was also classified by a liver surgeon into three groups: 1. Manifest biliary stasis 2. Other hepatic or biliary disease processes such as portal venous thrombosis or moderate primary sclerosing cholangitis 3. Only mild manifestations of or no hepatobiliary disease (i.e. "normal patients").

Results:

The mean of the 10- and 20-minute values of the contrast concentration in the hepatobiliary compartment, $C_{hepatobiliary}$, was 65% lower in the patient group compared to the healthy subjects ($p<0.001$; Wilcoxon rank sum test). A significant difference was found between the three patient groups ($p<0.05$; one way ANOVA). The contrast concentration was 81% lower ($p<0.02$; Tukey-Kramer post hoc test; fig. A) in the biliary stasis group (N=5) than in the normal patient group (N=11). The intermediate group (N=5) had 42% lower contrast concentration compared to the normal patient group (n.s.). A strong negative Spearman correlation was found between contrast concentration and Child-Pugh score, $\rho = -0.64$ (95% confidence interval, CI, from -0.82 to -0.40; fig. B). The correlation with the MELD score was similar, $\rho = -0.62$ (CI -0.80 to -0.34; (fig. C). Finally a significant negative correlation was found with bilirubin, $\rho = -0.55$ (CI of -0.23 to -0.76).



Discussion:

The results clearly show a strong effect of the hepatobiliary function on the late hepatic uptake of Gd-EOB-DTPA. The function test, which is estimated without *a priori* information about other clinical parameters, shows strong correlation with clinically assessed liver status scores and seems to be sensitive to hepatobiliary disease. Due to the limited number of subjects and the heterogeneous composition of the patient groups, the results must be interpreted with caution. The estimated uptake is a local measure, and should therefore not be influenced by differences in liver volume. Thus, the test rather reflects local hepatobiliary function than total liver function. The calculations in the test are entirely based on images acquired in the standard clinical liver imaging protocol using Gd-EOB-DTPA and they are therefore easy to implement within a clinical workflow.

Conclusion:

The hepatic uptake of Gd-EOB-DTPA correlates strongly with clinically assessed liver status scores. The test is a potential candidate to evaluate hepatobiliary specific liver function.

References:

[1] Dahlqvist Leinhard O, et al. Prog. no. 88, ISMRM 2008, Toronto, Canada.