

Effects of Extracellular Hepatobiliary Gadolinium Based Contrast Agents on Apparent Diffusion Coefficient

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Introduction: Diffusion-weighted (DW) imaging permits quantitative measurement of apparent diffusion coefficient (ADC) of tissues. The ADC value is inversely related to tissue cellularity and cellular membrane integrity [1]. Recently, the application of DW imaging for in-vivo quantification of liver fibrosis has been evaluated with a reported negative correlation between hepatic ADC values and severity of liver fibrosis [2-3]. In cirrhotic livers, various confounding tissue factors alter the observed ADC values; an understanding of these factors is critical. Iron is one of these factors that may alter tissue ADC values by shortening T2*. In the previous ISMRM annual meeting we showed that super paramagnetic iron oxides (SPIO) increase ADC values in hepatic tissues after SPIO administration[4]. From this, we postulated that since gadolinium based contrast agents (GBCA) also shorten T2*, GBCA will also increase ADC. However, recently investigators reported that an extracellular GBCA (gadopentetate dimeglumine) showed no significant difference between ADC values obtained before and after its administration [5], but this may not apply to mixed extracellular hepatobiliary agents used in our study, gadoxetate disodium (Gd-EOB-DTPA) and gadobenate dimeglumine (Gd-BOPTA). On delayed images extracellular GBCA have lower hepatic concentrations than do mixed extracellular hepatobiliary GBCA. Given that mixed extracellular hepatobiliary agent have higher concentration on delayed images and that it shortens T2*, we hypothesize that mixed extracellular hepatobiliary GBCA will increase ADC after its administration. The purpose of this study is to evaluate the effects of mixed extracellular hepatobiliary GBCA on DW imaging and ADC values in patients with focal hepatic lesions.

Methods: This investigation was a IRB-approved, HIPAA compliant, single center prospective study, conducted on twelve patients (7 men, 5 women; mean age, 53.5 years; range, 27–72 years) who underwent clinically indicated MR imaging for evaluation of liver disease. The etiology of liver disease in the study group was n=4 cirrhosis, n=1 HBV with HCC, n=1HCV with HCC, n=1 metastatic rectal carcinoma, n=1 intrahepatic cholangiocarcinoma, n=1FNH, n=1 hepatic cyst, n=1 biloma post adenoma resection, n=1 chronic lymphocytic leukemia. Imaging was performed sequentially after the intravenous injection of Gd-EOB-DTPA (0.025 mmol) in 5 patients and Gd-BOPTA (0.1 mmol/kg) in 7 patients. Subjects were scanned supine using an eight-element phased-array coil centered over the liver on a 3T GE Twin Speed (Milwaukee, WI) with 40 mT/m gradient strength. Transverse breath-hold single-shot echo-planar DWI were obtained before and after mixed extracellular hepatobiliary GBCA administration (Median 108 sec, range 77-167 sec). Fat-saturated diffusion-weighted images were acquired with two different protocols: (A) 2 *b*-values of 0 and 500 sec/mm² and (B) 6 *b*-values of 1000, 750, 500, 250, 100, and 0 sec/mm². Ten of the twelve patients underwent DW imaging using protocol (A) and of these ten patients 4 also underwent DW imaging using protocol (B). Two of the twelve patients underwent only DW imaging using protocol (B). A trained observer placed 3-6 co-localized oval regions of interest (ROIs) (300-400 mm²) in representative areas of each liver, while excluding intrahepatic vessels, focal liver lesions and artifacts. For protocol (A), ADC_{2b-values} in each ROI was calculated according to the following formula: $ADC_{2b-values} = (\ln(S_0/S_{500}))/500$, where S₅₀₀ and S₀ were the mean signal intensities on images acquired with protocol (A) 2 *b*-values of 500 and 0 sec/mm², respectively. For protocol (B) an ADC map, designed and verified in our lab by non-linear least squares fitting of the 6 *b*-values data to a mono-exponential decay function, was generated and the ADC_{6b-values} was collected. For both protocols, the per-patient ADC was the average of the 3-6 individual ROIs and a paired t-test was used to compare the per-patient ADC values before and after mixed extracellular hepatobiliary GBCA administration. Statistical significance was set at an alpha value of 0.05.

Results: Figure 1 shows the pre and post contrast ADC values of Gd-BOPTA and Gd-EOB-DTPA, calculated from 2 *b*-values (a) and 6 *b*-values (b). Prior to mixed extracellular hepatobiliary GBCA administration, mean ADC_{2b-values} was 1.30±0.23 sec /mm² and ADC_{6b-values} was .96±0.19 sec /mm²(Table 1). After its administration, ADC_{2b-value} increased to 1.44±0.27 sec /mm² (p=0.005) and ADC_{6b-value} increased to 1.06±0.21 sec /mm² (p=0.01). For protocol (A) the ADC values increased by 8.7% and 6.1% after administration of Gd-BOPTA and Gd-EOB-DTPA respectively. The difference between pre and post contrast ADC value was lower when 6 *b*-values data was used in protocol (B).

Conclusion: Administration of mixed extracellular hepatobiliary GBCA results in a mild but statistically significant elevation in hepatic ADC.

References

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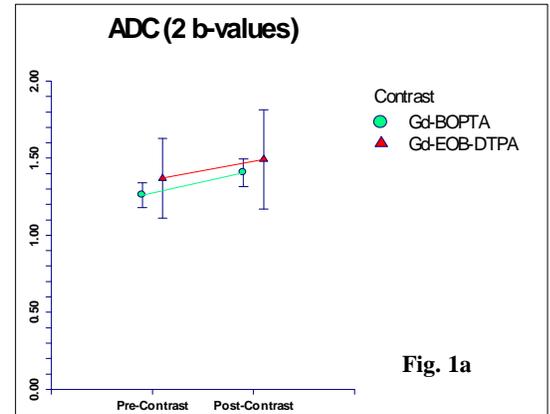


Fig. 1a

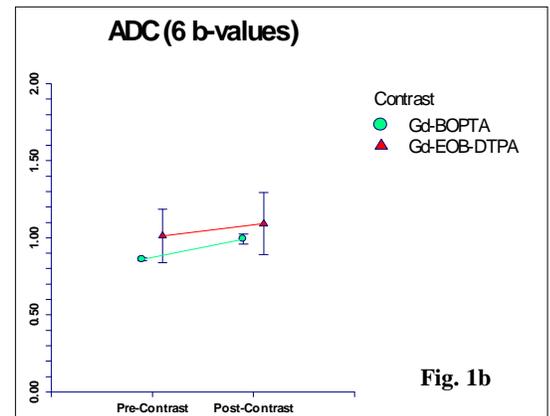


Fig. 1b

	ADC Pre Gd (sec /mm ²)	ADC Post Gd (sec /mm ²)	P
ADC _{2b-values}	1.30±0.23	1.44±0.27	0.005
ADC _{6b-values}	0.96±0.19	1.06±0.21	0.01