Effect of Superparamagnetic Iron Oxides on Hepatic Apparent Diffusion Coefficient at 3T in Human Subjects with Chronic Liver Disease

M. Shiehmorteza[1], C. A. Kohl[1], S. M. Mazhar[1], T. Yokoo[1], N. Pinto[1], R. Znamirowski[1], L. O. Pacheco[1], M. S. Middleton[1], and C. B. Sirlin[1]

[1]Radiology, University of California, San Diego, Liver Imaging Group, San Diego, CA, United States

Introduction: Diffusion-weighted (DW) MR imaging permits quantitative measurement of the apparent diffusion coefficient (ADC) of water molecules in tissues. Recently, the application of DW imaging for in vivo quantification of liver fibrosis has been evaluated and a negative correlation between hepatic ADC values and severity of liver fibrosis has been shown by some investigators [1-2]. In addition to fibrosis, there are other tissue alterations that may occur in chronic liver disease and many of these alterations may modify the observed ADC. To accurately interpret ADC measurements in chronic liver disease, an understanding of such modifying factors is critical. Iron accumulation may occur in chronic liver disease [3] and by shortening T2* may alter tissue ADC values [4]. To our knowledge, no prior study has investigated the effect of iron accumulation on hepatic ADC measurements. To assess the effect of intrahepatic iron on ADC measurements in cirrhotic liver, we compared the ADC values at 3T in human subjects with chronic liver disease before and after superparamagnetic iron oxide (SPIO) administration.

Methods: This investigation was a retrospective, HIPAA compliant, single center study which was approved by the local IRB. Fifteen consecutive patients (8 men, 7 women; mean age, 54 years; range, 39–71 years) with chronic liver disease who underwent transverse breath-hold single-shot echo-planar DW MR imaging before and after SPIO administration (ferumoxides, Feridex®; Advanced Magnetics, Cambridge MA, USA, for Berlex Laboratories) were included. The etiology of liver disease in the study group was hepatitis C (n=9 patients), hepatitis B (n=1), primary biliary cirrhosis (n=1), and cryptogenic cirrhosis (n=4). 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. Fat-saturated DW images were acquired with b-values of 0 and 500 sec/mm^2; TR/TE 3500/50 msec; 128×160 matrix; 300-480 mm field of view; 8-mm slice thickness without gaps; two signals averaged; and parallel imaging acceleration factor 2. A trained observer placed 10 co-localized oval regions of interest (ROIs) (400-600 mm^2) in representative areas of each liver, while excluding intrahepatic vessels, focal liver lesions and artifacts. The ADC in each ROI was calculated according to the following formula: $ADC = -(\ln S_{500} - \ln S_0)/500$, where S_{500} and S_0 were the mean signal intensities on images acquired with b-values of 500 and 0 sec/mm^2, respectively. The per-patient ADC was the average of the 10 individual ROIs. Per-patient ADC values were log transformed to normalize their distribution. A paired t-test was used to compare the log-transformed values before and after SPIO administration.

Table 1 Hepatic Apparent Diffusion Coefficient (ADC) in 15 Human Subjects with Chronic Liver Disease at 3T Pre and Post SPIO (b-value=500 sec/mm^2)

	Pre SPIO	Post SPIO	p_1
ADC($\times 10^{-3}$ sec /mm^2)			
Mean Signal ±SD	1.39± 0.19	1.50± 0.24	0.02
Range	1.09-1.77	1.08- 2.07	

1 Paired t-test, two-tailed, alpha level=0.05

Results: Fig. 1 shows the ADC value for each patient pre and post SPIO. Prior to SPIO administration, mean ADC was 1.39± 0.19 sec /mm^2 (Table 1). After SPIO administration, ADC increased to 1.50±0.24 sec /mm^2 (p=0.02). Fig. 2 shows a representative set of images.

Conclusion: Administration of exogenous iron causes a mild but statistically significant elevation in hepatic ADC. Based on this observation, we speculate that endogenous iron may have a similar effect and may modify the relation between ADC and fibrosis stage in chronic liver disease.

References: (1) Koinuma M, Ohashi I, Hanafusa K, Shibuya H. J Magn Reson Imaging 2005; 22:80–8. **(2)** Taouli B, Toli A, Losada M, et al. AJR 2007;189:799806. **(3)** Zhang J, Krinsky GA. NMR Biomed. 2004 Nov;17(7):459-64**. (4)** Zhong J, Kennan RP, Gore JC. J Magn Reson 1991;95:267–280

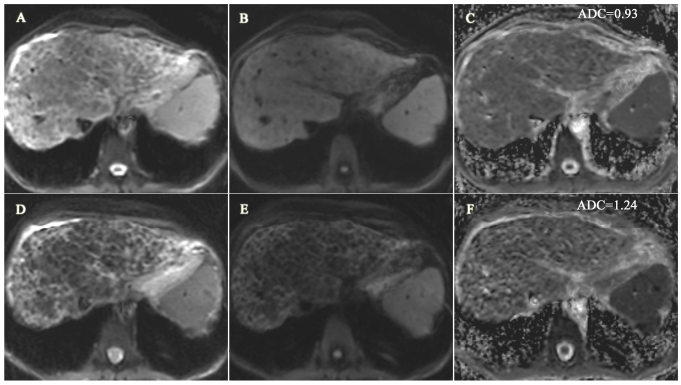

Fig. 2–42-year-old womam with chronic hepatitis C cirrhosis. Diffusion-weighted MR images obtained pre SPIO with b-values 0 sec/mm^2 (**A**) and 500 sec/mm^2 (**B**). and corresponding ADC map (**C**). **D**-**F**. Diffusion-weighted MR images obtained post SPIO at b value with b-values of 0 sec/mm^2 (**D**) and 500 sec/mm^2 (**E**). and corresponding ADC map (**F**). The ADC value is higher post SPIO