Diffusion-weighted magnetic resonance imaging (DW-MRI) at 3.0 Tesla in evaluating water diffusion pattern in cirrhotic livers: preliminary results

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Purpose

Background

Over the last years, Diffusion-weighted Imaging (DWI) has been largely investigated as a tool to provide noninvasive detection [1] and quantification of liver fibrosis [2-3]. Fibrosis results from the accumulation of extracellular matrix components, which cause distortion of the parenchymal architecture [4], and theoretical restriction of water diffusion in the affected liver [5]. As expected, hepatic apparent diffusion coefficient (ADC), measured by means of DWI, has been shown to decrease proportionally to the degree of fibrosis and/or inflammation [6-9].

Nonetheless, major concerns still limit DWI clinical applications for liver fibrosis. Among them, technical issues like the choice of b-values, sequence optimization and methods of ADC measurement are those mainly affecting the reproducibility of results [4]. In this uncertain scenario, most appropriate direction of DWI motion probing-gradients is still undetermined. In previous studies, gradients have been applied multi- [1,7,9,10], or mono-directionally, based on the assumption that the liver shows isotropic water diffusion [5-6,11]. To our knowledge, this assumption has been investigated on humans only by Taouli et al. on a 1.5 T system [12], but no previous results are available at 3.0T.

Purpose

The purpose of this study was to investigate the pattern of water diffusion (isotropic vs. non-isotropic) in normal and fibrotic livers with as assessed by a DWI sequence at 3.0T. Cirrhotic patients were enrolled to form a homogeneous population of patients with end-stage liver fibrosis.
Methods and Materials

Patients

Over the period June-December 2010 we prospectively enrolled twenty-four subjects. Of these, twelve were patients with clinically and histologically proven hepatic cirrhosis (7 male, 5 female; age range 45-71, mean 54.1 y-o), addressed to Magnetic Resonance Imaging (MRI) surveillance for regenerative nodules (n=11) and hepatocellular carcinoma treated with radiofrequency ablation (n=1). All patients showed a Child-Pugh grade A. Median time between hepatic biopsy and MRI examination was of 7.2 months. Remaining twelve subjects (8 male, 4 female; age range 26-53, mean 31.4 years-old) were enrolled to form a control group without history of chronic liver disease. The group included nine healthy volunteers and 3 patients addressed to upper abdomen MRI for the following indications: suspected intrapancreatic accessory spleen, suspected liver haemangiomas, assessment of multiple renal cysts. Excluded were cirrhotic patients with known or suspected newly diagnosed hepatocellular carcinoma, ascitic patients, oncologic patients, subjects showing history of chronic liver disease without clinical and/or histological confirmation of cirrhosis. It was stated to exclude also patients or controls in whom artefacts substantially degraded image quality.

Institutional review board approval was obtained for this study.

**DWI protocol**

Examinations were performed on a 3.0T magnet (Achieva; Philips Medical Systems, Best, The Netherlands), equipped with a 16-elements phased-array surface coil. All patients underwent a routine upper-abdomen MRI protocol, including dynamic imaging after gadolinium injection in fifteen of them (no post-contrast study was performed in healthy volunteers).

Before contrast administration, DWI was performed by using a respiratory-triggered, single shot spin-echo echoplanar imaging sequence characterized by sequential, independent motion probing gradients that were applied - within the same acquisition - along the frequency-encoding (x), phase-encoding (y), and section-select (z) directions. B-values of 0, 400 and 800 sec/mm$^2$ were used. Remaining acquisition parameters are represented in Tab. 1 on page 5. Parallel imaging technique was not used, to avoid any additional signal loss in ADC determination [13].

A preliminary phantom study was performed to validate our system (not shown).

**Image analysis and ADC determination**
DWI acquisition determined 3 sets of images, corresponding to the x, y and z gradient directions. Each set included images obtained at different b-values (0, 400 and 800 sec/mm$^2$). For each set, two abdominal radiologists in consensus (R.G., D.B.) positioned 3 regions of interest (ROI) on a slice obtained with b=0 sec/mm$^2$, at two different hepatic sites: a) 1 cm above the portal plane (plane 1) (ROIs on the hepatic segments IVa, VII and VIII, respectively); b) 1 cm below the portal plane (ROIs on the hepatic segments IVb, V and VI, respectively) (Fig. 1 on page 5). Positioning carefully avoided inclusion of vascular structures, bile ducts or focal liver lesions. No measurements were performed on the left lateral lobe, to avoid artefacts from standing-wave effect [14] or respiratory motion. After this preliminary operation, ROIs were copied and pasted on same slices obtained at b=400 and 800 sec/mm$^2$. Signal intensity of each slice was calculated as the average of the three measurements. On this basis, liver ADC was calculated according to the following equation [15]:

$$ADC = \frac{1}{b_i} \times \ln \left( \frac{S_0}{S_i} \right)$$

where $S_0$ is the averaged signal sampled without diffusion probing gradients ($b_i = 0$ s/mm$^2$), and $S_i$ the averaged signal sampled with $b_i = 400$ and 800 sec/mm$^2$, respectively. Thus, in each patient we obtained two sets of liver ADC (0-400 and 0-800 sec/mm$^2$), at two different anatomic sites (planes 1 and 2), along x, y and z gradients direction.

According to the theory of intravoxel incoherent motion (IVIM), b-values greater than 200 sec/mm$^2$ make the influence of perfusion (D*) negligible in determining the ADC. Thus, liver ADC obtained at b=800 sec/mm$^2$ was considered as approximated to the pure diffusion coefficient (D) [16].

**Data analysis**

Isotropy (or not) of the liver was assessed by comparing the differences of ADC values obtained along x, y and z gradient directions within controls and cirrhotic patients, at both planes 1 and 2. After checking for data normality with the Levene’s test, we achieved this goal by using the analysis of variance (ANOVA) for repeated measures. Furthermore, we estimated the significance of the difference in ADC values as follows: a) within controls and cirrhotic, by comparing ADC values between planes 1 and 2; b) between cirrhotic patients and controls; c) within cirrhotic patients and controls between the 0-400 and 0-800 sec/mm$^2$ b-values set. Paired- or unpaired t-test were used accordingly.

Statistical significance was assumed for a p less than 0.01.
**Fig. 0:** Tab. 1 - Acquisition parameters of the single-shot spin-echo echo-planar diffusion-weighted sequence used in the study.

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Fig. 0: In each study subject, liver ADC was calculated at two different anamotic sites, i.e. planes 1 and 2 as illustrated. At each plane, signal was averaged. ADC was finally obtained by proper calculation (see text). Example images in the figure refer to $b=400$ sec/mm$^2$, and were obtained along phase-direction of the diffusion gradient.

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Results

*Image quality and homogeneity of measurements*

Overall, susceptibility or motion artefacts affected image quality in all study subjects, regardless of the plane of measurement and the set of b-value that was used. Nonetheless, artefacts were mild or minimal, and determined neither problems in ROIs positioning or subjects exclusion from ADC measurements (Fig. 2 on page 9).

Despite the presence of outliers, no significant difference was observed by comparing liver ADC of the plane 1 vs. that of the plane 2, both in controls and cirrhotics (p>0.01; unpaired t-test). This result was similar regardless of the motion-probing gradient direction that has been applied (Tab 2 on page 9).

*Patterns of water diffusion within the liver*

No significant differences were found in comparing liver ADC obtained along x (frequency-encoding), y (phase-encoding) and z (section-select) directions, both in controls and cirrhotic patients (p>0.01). This result was shown regardless of the plane of measurement and the maximum b-value (400 or 800 sec/mm²), suggesting that water diffusion is isotropic within the liver, even in case of advanced liver fibrosis. Data are summarized in Tab. 3 on page 10-4 on page 11.

Along each gradient direction, liver ADC significantly decreased by increasing the maximum b-value from 400 to 800 sec/mm² (p<0.01; paired t-test), both in controls and cirrhotic patients. Exceptions occurred in cirrhotic patients, along the y direction, both at planes 1 and 2, with a nearly statistical significant difference (p=0.0288 and 0.0111, respectively). However, ADC decrease was larger in controls than in cirrhotics, showing a mean of 0.57 (at the plane 1) and 0.54 (at the plane 2) x 10^{-3} mm²/sec vs. 0.17 (at the plane 1) and 0.26 (at the plane 2) x 10^{-3} mm²/sec. Data are summarized in Tab. 3 on page 10-4 on page 11.

*Diagnosis of cirrhosis*

As expected, liver ADC was found lower in cirrhotic patients as compared to controls, regardless of the maximum b-value, gradient direction and plane of measurement. The difference in ADC was significant in all cases (p<0.01; unpaired t-test), except along the x (p=0.0139) and y (p=0.0174) directions at the plane 1, by using the maximum b = 800 sec/mm². Data are summarized in Tab. 5 on page 12.
**Fig. 0:** Fig. 2 - No significant signal degradation was observed as b-values increased. Nonetheless, as commented in the text, overall image quality was affected by mild artefacts. It is unlikely that these findings might have substantially influenced the consistency of ADC measurements. Images in the figure were obtained along phase-encoding direction of the diffusion gradient.

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**Fig. 0:** Tab. 2 - Along each gradient direction, reported are p values of the ADC differences within controls and cirrhotics at two different anatomic planes (1 vs. 2). It is arguable that ADC measurements are consistent in our model. ADC values are reported in Tab. 3-4. X=frequency-encoding direction of the diffusion gradient; y=phase-encoding direction; z=select-section direction.

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Tab. 3 - Liver ADC values in study subjects as measured at the plane 1, along three different directions of the diffusion gradient (x=frequency-encoding direction; y=phase-encoding direction; z=select-section direction). No significant differences among ADCs were found in controls and cirrhotics, regardless of the b-values set employed. Along each gradient direction, liver ADC decreased by increasing the maximum b-value from 400 to 800 sec/mm², both in controls and cirrhotic patients. Statistical significance is reported across table cells.

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<table>
<thead>
<tr>
<th>Gradient direction</th>
<th>PLANE 1</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>p*</th>
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<tr>
<td><strong>Controls</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>ADC</td>
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<td>1.96±0.34</td>
<td>1.97±0.53</td>
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<tr>
<td>0-400 sec/mm²</td>
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<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
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<td></td>
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<tr>
<td>ADC (D)</td>
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<td>1.33±0.24</td>
<td>1.40±0.20</td>
<td>0.597</td>
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<tr>
<td>0-800 sec/mm²</td>
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<td></td>
<td></td>
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<tr>
<td><strong>Cirrhotics</strong></td>
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<tr>
<td>ADC</td>
<td>1.35±0.25</td>
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<td>0-400 sec/mm²</td>
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<td>p=0.0288</td>
<td>p=0.0008</td>
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<tr>
<td>ADC (D)</td>
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<td>1.08±0.23</td>
<td>1.01±0.19</td>
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<tr>
<td>0-800 sec/mm²</td>
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</table>

*repeated measures ANOVA **paired t-test

ADCs are expressed in x10⁻³ mm²/sec
**Fig. 0:** Tab. 4 - Liver ADC values in study subjects as measured at the plane 2, along three different directions of the diffusion gradient (x=frequency-encoding direction; y=phase-encoding direction; z=select-section direction). No significant differences among ADCs were found in controls and cirrhotics, regardless of the b-values set employed. Along each gradient direction, liver ADC decreased by increasing the maximum b-value from 400 to 800 sec/mm², both in controls and cirrhotic patients. Statistical significance is reported across table cells.

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**Fig. 0:** Tab. 5 - Differences between ADC values of controls and cirrhotics are reported, together with statistical significance.

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Conclusion

1. Water diffusion in the liver is isotropic at 3.0T

Like Taouli et al. [12], we found that liver ADC shows not significantly different values (p<0.01) if measured along different spatial directions, corresponding to that of frequency-encoding, phase-encoding and section-select gradients. However, differently from them we used a 3.0T magnet to image the liver. According to recent results, increasing the field strength would degrade image quality of the upper abdomen [17]. We actually found susceptibility or motion artefacts to affect image quality, although they were not so relevant to determine the exclusion of study subjects from measurements or reasonably impact on the signal within the ROIs. On the other hand, no differences within controls or cirrhotics were found, at different anatomic planes, by performing a comparison of the ADCs between each gradient direction (Tab. 2 on page ). It is arguable that, despite suboptimal image quality, the methodology of ADC measurement and the use of ultra-high field strength provided consistent results throughout the liver in our model. Even in the absence of a direct comparison with lower field strength, this suggests that image degradation at 3.0T is limited, and in any case has no substantial influence when determining parenchymal ADC. It remains questionable whether 1.5 or 3.0T provide more precise estimation of liver ADC, considering that many other confounding equipment-related, patients-related and DWI protocol-related factors currently limit its reproducibility [4]. Independently from ADC variability, our study shows that water diffusion results isotropic even at 3.0T. This finding matches with the previous observation that liver ADCs at a similar field strength show no difference by using diffusion encoding techniques with or without correction for anisotropy [18].

2. Why liver isotropy in cirrhotic patients?

Isotropy is not a surprising finding in healthy livers [12]. On the contrary, isotropy in cirrhotic livers is somewhat unexpected (Tab. 3 on page - 4 on page ). As known, the accumulation of extracellular matrix component characterizing fibrosis theoretically reduces water diffusion within the liver, i.e. parenchymal ADC [5]. One could argue that isotropy is lost under this condition. Despite other Authors [10,12] already reported isotropy in fibrotic livers, no studies investigated why this finding persists even when architectural changes are able to modify the ADC. It is difficult to provide a definite explanation. Fibrotic changes within the voxel could not directly affect tissue properties determining the ADC. Some results of ours support this hypothesis. First, differences in ADC between cirrhotics and controls were mainly related to perfusion rather than diffusion, as previously demonstrated [5,16], and as reported in our complementary study shown in the EPOS 2011 poster #3723. This is arguable by the fact that, by using higher b value set (b=0-800 sec/mm$^2$), DWI was shown unreliable in differentiating
between healthy and cirrhotic livers, because the ADC lowering in cirrhotics resulted not statistically significant at one of two planes of measurements, and along two of three gradient directions (y and z). Accordingly, ADC decreased as the maximum b-value increased from 400 to 800 sec/mm$^2$ (in most cases with a p<0.01), but at a lesser degree in cirrhotic patients than in controls (Tab. 3 on page -4 on page ). Thus, cirrhosis reduces predominantly the fraction of perfusion within the liver rather than diffusion. Consequently, isotropy would not supposed to change, because of preserved random-like perfusive motion within the reduced capillary net. This mechanism could be predominant at lower b-values. Unfortunately, previous hypothesis fails in explaining why isotropy occurs also at higher b-value (b= 800 sec/mm$^2$) in our series, i.e. under negligible effect of perfusion component of the signal.

3. Technical considerations

According to our results, DWI assessment of liver fibrosis is feasible with multi- or mono-directional diffusion gradients indifferently, as already arguable from previous studies [12,18]. The use of monodirectional gradient might be preferable because of a reduction in the acquisition time. Nevertheless, in our opinion, rather than represent a step towards DWI protocol standardization, our findings further emphasize the need for a still lacking, reliable radio-pathological correlation between fibrotic or cirrhotic changes and parenchymal ADC. At the state-of-the-art situation, DWI is probably technically immature to provide reliable information on liver fibrosis and cirrhosis. Targeted studies are needed to this purpose, possibly by using diffusion tensor imaging (DTI) [19]. Liver DTI is at an experimental stage, and has been poorly investigated [1,19].

Limitations

First, sample size is small. However, we performed ADC measurements at two different anatomic sites in each subject, in order to provide doubled sampling and take into account the variability in cirrhosis distribution.

Second, similarly to previous Authors [17-18], we used a maximum b of 800 sec/mm$^2$, i.e. lower than feasible at 3.0T. This choice was based on the assumption that, irrespective of the field strength, influence of perfusion D* should be minimal in determining the ADC at the b-value set of 0-800 sec/mm$^2$ [16]. Even if the approximation to the true diffusion coefficient D would have been inaccurate, the general trend of our results is not affected. Besides, we tried to avoid image degradation inherent to larger b-values.
References


14. Merkle EM, Dale BM. Abdomen MRI at 3.0T: the basic revisited. AJR 2006;186:1524-1532


18. Dale BD, Braithwaite AC, Boll DT, merkle EM. Field strength and diffusion encoding technique affect the apparent diffusion coefficient measurements in diffusion-weighted imaging of the abdomen. Invest Radiol 2010;45:104-108

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Thank you