Diffuse liver and kidney disease: value of Diffusion-weighted imaging (DWI)

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In this presentation, we will review:

1. How to optimize DWI parameters for assessment of the liver and kidneys
2. Current applications and results of DWI for assessment of diffuse liver and renal diseases.
3. Limitations and future directions of DWI for these particular applications

Diffusion acquisition parameters for imaging the upper abdomen

Breath-hold or free breathing or respiratory triggered (using a navigator echo) SS EPI DWI sequence can be acquired before contrast injection, with the suggested following parameters: axial or coronal acquisition, fat suppression, tridirectional gradients using the following b-values: 0 (used as reference), 50 (black-blood sequence-useful for lesion detection in the liver)-400 to 500 (intermediate) and 800 to 1000 (high) sec/mm^2. Lower b-values will generate higher ADC values, owing to the contribution of intravoxel incoherent motion effects other than diffusion (eg, perfusion or flow phenomena), as opposed to higher b-values, which will enable "pure" diffusion-weighting, at the expense of lower residual signal. To reduce the effects of intravoxel incoherent motion, maximum b-values ≥ 800 sec/mm^2 are suggested whenever possible. We suggest a baseline b=0 sec/mm^2 image (used as a reference), and intermediate b-value (for example, 400-500 sec/mm^2) which provides intermediate diffusion-weighting with acceptable image quality, and a higher b-value (for example, b=800-1000 sec/mm^2) which provides higher diffusion-weighting, free from perfusion and flow contamination. In addition, the use of 3 b-values provides a more precise ADC fit. The other parameters used in our protocol are as follows: TR 1800-2300 msec., TE min., matrix 180x192, slice thickness/gap 7/1.4 mm, number of averages 2 (breath-hold) or 4 (respiratory triggered acquisition), parallel imaging (acceleration factor 2), EPI factor 144-192, bandwidth 1302 Hz/pixel, acquisition time approximately 2 x 20 sec. to cover the whole kidneys (for the breath-hold acquisition), and at least 2 min. for the respiratory triggered acquisition. We obtain pixel-based ADC maps (integrating the 3 b-values) using a commercial workstation, ADC is calculated with a linear regression analysis of the function $S = S_0 \times \exp(-b \times ADC)$, where S is the SI after application of the diffusion gradient, and S_0 is the SI at b = 0 sec/mm^2.

DWI applications in diffuse liver disease

The early detection of liver fibrosis and inflammation in patients with chronic viral hepatitis has important clinical and therapeutic implications. Antiviral treatment of chronic hepatitis B and C can eradicate the infection, increase patient survival and reduce the need for liver transplantation (1). Liver biopsy is not risk free (4,5), and is prone to inter-observer variability and sampling errors (6-8). DWI provides non invasive quantification of water diffusion by calculating the ADC, and can be used for in vivo quantification of the combined effects of capillary perfusion and diffusion (43). There is data suggesting a decrease in liver ADC in liver fibrosis and cirrhosis (9-14). Restricted diffusion in liver fibrosis relies on the hypothesis that architectural distortion due to the tightly bound and

proton-poor collagen fibers restricts water Brownian motion within fibrotic liver, as well as changes in perfusion associated with fibrosis (15). Lewin et al. (20) investigated the role of DWI compared to FibroScan and serum markers in patients with HCV, and demonstrated an excellent performance of ADC for prediction of fibrosis, with sensivity and specificity of 87% for prediction of severe fibrosis. In a recent study, we showed that ADC was a significant predictor of fibrosis stage $\geq$ 2 and fibrosis stage $\geq$ 3 with AUCs of 0.896 and 0.896, respectively. A recent study showed significant differences between normal and cirrhotic livers using perfusion fraction calculated with DWI (16). However, validation in larger studies is needed. In addition, better diffusion quantification is necessary before using DWI as a possible marker of response in anti-fibrotic and antiviral drug trials.

DWI applications in diffuse renal disease

There are several published studies that have investigated the use of DWI in normal kidneys (17-24), for the assessment of diffuse renal disease (20,25,26), renal artery stenosis (27) and renal transplants (28). The reported ADC values of renal cortex and medulla vary considerably from study to study depending on the equipment and the sequence parameters, particularly the b-value (17,19,20,25).

Several studies have shown the potential use of ADC as a marker of renal function, most studies showing lower ADC in kidney dysfunction. For example, Namimoto et al (25) demonstrated that the ADC values in both the cortex and were significantly lower than those of normal kidneys. Thoeny et al (24) have shown that ADC of cortex was higher than medulla in normal kidneys. In addition, the ADC values using all b-values were lower in chronic renal disease compared with normal kidneys, as well as in patients with pyelonephritis compared with the contralateral side, whereas patients with ureteral obstruction showed varying degrees of difference in all ADC values compared with the contralateral side. Xu et al (26) reported a positive correlation between ADC (measured with b-values of 0 and 500 sec/mm^2) and the split GFR in 55 patients (r = 0.709). The ADCs were significantly lower in impaired kidneys than in normal kidneys. Yildririm et al (27) compared the ADC values of 13 kidneys with RAS and 26 with normal renal arteries using multiple b-values, and found significant differences in mean ADC of kidneys using lower, average, and high b-values between two groups (average ADC 1.7 x10^{-3} mm²/sec for RAS vs. 1.9x10^{-3} mm²/sec for normal kidneys).

There is extremely limited data on the use of DWI in renal transplant. The study by Thoeny et al (24) was performed in normal functioning kidney transplants and normal native kidneys. In their study, the ADCs of native kidneys were significantly higher in the cortex than in the medulla, whereas the ADCs of the transplant kidneys were almost identical in the medulla and the cortex, while the perfusion fraction (measured with smaller b-values) showed greater variation. The perfusion fraction reflects microcirculation of blood and movement in predefined structures, such as tubular flow and glomerular filtration in the kidneys. The corticomedullary difference was relatively small and was not significantly different in the transplanted kidneys. This suggests that perfusion fracture is influenced predominantly by factors other than blood perfusion, such as tubular flow. There are no reports on the utility of DWI for the diagnosis of post-transplant complications, such as vascular complications (stenosis, thrombosis, and infarction), acute tubular necrosis, and rejection. Validation of DWI is needed in renal transplants with histopathologic correlation, given the non invasive nature of diffusion measurement, performed without gadolinium injection.

Conclusion

DWI is a promising technique for the assessment of focal and diffuse renal disease. The ability to perform DWI without intravenous gadolinium is also a major advantage of DWI. However, more supporting histopathologic correlation and better diffusion quantification tools are needed.

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