Assessment of liver fibrosis in rats by MRI with apparent diffusion coefficient and T1 relaxation time in the rotating frame

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Introduction

Early diagnosis and staging of liver fibrosis are vital clinical components[1]. Both apparent diffusion coefficients (ADC) and T1 relaxation time in the rotating frame (T1ρ) have been employed to evaluate liver fibrosis stages. Although reduced ADC is revealed to be associated with liver fibrosis and liver cirrhosis [2], the value of ADC in staging liver fibrosis is still controversial[3,4]. And recent studies, either in human or animal models, all uncovered higher mean liver T1ρ values in liver cirrhosis compared with those in normal health controls[5,6]. However, the relationship between T1ρ values and fibrotic stages was rarely reported. Here we exploit the characteristics of magnetic resonance imaging (MRI) with ADC and T1ρ in various stages of liver fibrosis, and expect to uncover their relationships with fibrotic stages in rats.

Methods

Various stages of liver fibrosis were induced[7] in 50 male Sprague Dawley rats by subcutaneous administration of different carbon tetrachloride (CCl_4) doses. Another fifteen untreated rats with normal livers were selected as controls. ADC (gradient factor b-values of 0 and 800 s/mm^2) and T1ρ MRI were performed on the rats with a 3.0-T clinical scanner (Achieva 3.0T TX, Philips Healthcare, Best, Netherlands), using an animal coil. T1ρ was performed using turbo field echo (TFE) sequence, scanning parameters were as follows: TR/TE= 4.9 ms/2.4 ms, FOV= 60mm × 60 mm; flip angle= 40°, matrix= 100×100; slice thickness= 2 mm; number of slices= 5; spinlock frequency= 500 Hz; spin lock time= 0, 10, 20, 40, 60 ms respectively. T1ρ relaxation map was generated by fitting different spin lock data with a mono-exponential decaying function. Stages of liver fibrosis were evaluated using METAVIR scores (stage F0-stage F4) of liver serial sections stained with hematoxylin and eosin and Masson's trichrome. Nonparametric methods and receiver operating characteristic (ROC) curve analyses were used to determine diagnostic accuracy.

Results and Discussion

All rats in the control group survived and underwent tests as stage F0=15. Five rats in the liver fibrosis model group died during the process of intervention, and 45 rats were pathologically diagnosed as liver fibrosis in varying degrees with the following distribution: stage F1=11, stage F2=12, stage F3=10, and stage F4=12 (Fig 1). The mean ADC decreased and T1ρ increased with increasing fibrosis stage (r=-0.732 P<0.001; r=0.863 P < 0.001) (Fig 1, 2). One-way analysis showed statistical differences among the different stages, except for stages F1 and F2 with T1ρ. There was no statistical difference among stages F2, F3, and F4 with ADC (Fig 2). ROC curves showed that the T1ρ was better than ADC in evaluating stages of fibrosis (AUC: 0.920-0.976 vs AUC: 0.781-0.924.) (Fig 3).

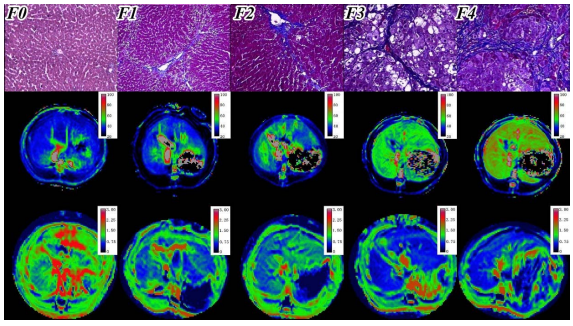

Figure 1: Liver fibrosis stages F0-F4, upper row: Masson's trichrome staining; middle row: T1ρ maps with mean T1ρ values 41.05, 48.44, 50.48, 55.58 and 59.44ms. Lower row: ADC maps with mean ADC values 1.29, 1.11, 0.93, 0.88 and 0.87× 10^{-3} mm^2/s.

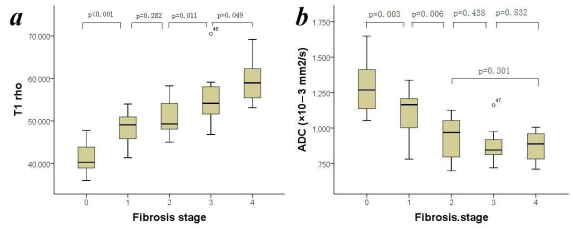

Figure 2: Box plots of (a) T1ρ values and (b) ADC values in liver parenchyma according to METAVIR fibrosis stages.

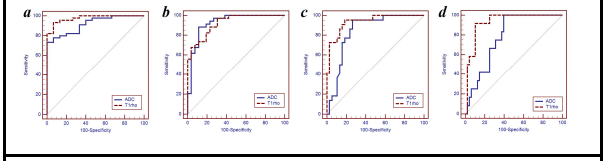

Figure 3: ROC curves for differentiation of fibrosis stages with ADC and T1ρ values. Area under ROC curve: (a) F0 vs F1-4, ADC=0.917, T1ρ=0.976; (b) F0–1 vs F2–4, ADC=0.924, T1ρ=0.920; (c) F0-2 vs F3-4, ADC=0.842, T1ρ=0.938; (d) F0-3 vs F4, ADC=0.781, T1ρ=0.931.

Conclusion

ADC and T1ρ showed significant correlations with stages of liver fibrosis in a rat model, where T1ρ is regarded to be superior to ADC in distinguishing the stages.

References

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