Observation of anomalous perfusion effects in the rat liver using temporal diffusion spectroscopy

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Introduction and purpose: In classical diffusion-weighted imaging (DWI), the evolution time Δ separating the 2 motion-encoding gradients dictates the potential observable spatial scale of displacement of the water molecules [1]. Because of usually long evolution times (Δ >> 10 ms [2]) leading to mean displacements of approximately 30 µm, structural information about objects of less than 10 µm in diameter will be lost. The oscillating gradient spin-echo (OGSE) technique [1] aims to fill this gap, replacing classical DWI gradients by oscillating gradients within a spin-echo sequence. With oscillation frequency of 100-1000 Hz (and corresponding evolution times of 1-10 ms), small spatial scales of the order of the micron can be probed. OGSE has therefore the potential to assess microstructural changes at the subcellular level. This has the potential to better understand pathological processes or therapy-induced early cellular changes. This technique has so far only been applied to measure subcellular diffusion coefficients in cells (in vitro) [3] or rat brains (in vivo) [1, 2]. The present study focuses on the feasibility of OGSE in the rat liver.

Material & methods: In vivo experiments were conducted in rats presenting different hepatic lesions: i) grade 2 liver fibrosis obtained using CCl_4 induction (i.p. injections of 0.1ml/100g CCl_4 twice a week for 3 weeks), ii) liver metastases of 3-5 mm in diameter 2 weeks after injection of 0.5×10^6 colorectal tumor cells in the left liver lobe, and iii) healthy control rats. MR experiments were conducted on a small animal 7T MRI system (Pharmascan, Bruker). Animals were anesthetized with isoflurane (1.5% - 1 L/min) and imaged in prone position. For OGSE experiments, TE 30 ms, TR 2500 ms, 6 averages, no gating, FOV 6×6 cm^2, matrix 64×64, 9 slices, Δ = 3/7/11ms (333/145/90 Hz, resp.), b = 0/15/30/45 s/mm^2 (max gradient strength 413 mT/m) were used. In addition, morphological T2-weighted and classical EPI-DWI scans (same imaging parameters as OGSE but Δ fixed at 11ms) were acquired.

Results: OGSE image quality was good, with SNR values between 10 and 50 (Fig. 1). A TE of 30 ms was considered as optimal, guarantying enough signal but also enough time to insert oscillating gradients rendering b values of up to 45 s/mm^2. The short evolution times (3 and 7 ms) allowed to probe on a theoretical spatial scale of ~5 µm. For a long evolution time (11 ms) and identical b values, EPI-DWI and OGSE had similar ADC values (in healthy parenchyma, 19.3×10^{-3} mm^2/s and 18.3×10^{-3} mm^2/s, resp.). By contrast, ADC increased when the evolution time shortened, whether in healthy tissue, fibrosis or metastases (from 18.3×10^{-3} mm^2/s to 37.1×10^{-3} mm^2/s for healthy parenchyma, for Δ = 11 and 3 ms, resp. (Fig. 2), or from 3×10^{-3} mm^2/s to 7.6×10^{-3} mm^2/s for metastasis, for Δ = 11 and 3 ms, resp.). Differences in ADC between healthy and diseased tissues were also more pronounced with shortened evolution times (Fig. 3).

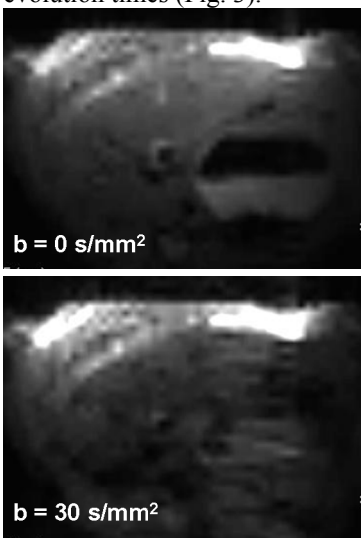

Fig. 1: OGSE images of healthy rat liver

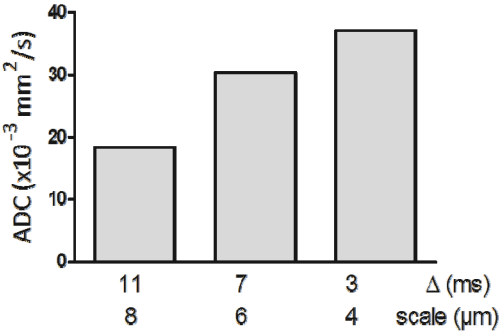

Fig. 2: OGSE - ADC ($\times10^{-3}$ mm^2/s) of healthy liver, for different evolution times and spatial scales

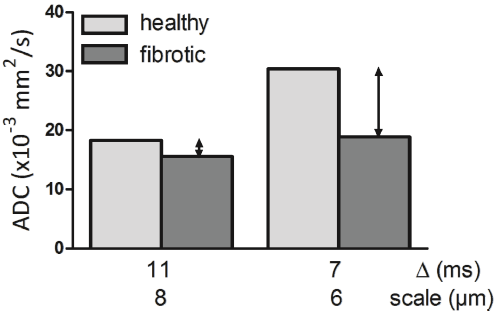

Fig. 3: OGSE - ADC ($\times10^{-3}$ mm^2/s) of healthy and fibrotic liver for different evolution times and spatial scales

Conclusion: We showed here for the first time the feasibility of acquiring OGSE data in the rat liver in vivo, with sufficient SNR and relatively short TE (30 ms). The need for a short TE (due to the short T2 of liver at 7T) and technical gradient limitations restricts the b values which can be applied (here, up to 45 s/mm^2). The ADC thus determined were perfusion-related diffusion coefficients, since microperfusion is the predominant phenomenon in diffusion experiments with b values below 100 s/mm^2 [4]. OGSE experiments showed that liver ADC increased when the probed spatial scale shortened. This would suggest that the perfusion is sensitive to the size and distribution of obstacles in the tissue. This ADC evolution over the spatial scale was different according to the nature of the tissue, for instance more pronounced for healthy parenchyma than for fibrotic liver. The proposed method allows to quantify micro-circulatory effects with a larger dynamic range, and could be envisaged as a novel technique for obtaining a new dimension of functional information in hepatic lesion characterization and follow-up of antivascular treatment.

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