OSCILLATING GRADIENT DIFFUSION MRI IN THE EX-VIVO PROSTATE TO ASSESS ADC BEHAVIOR AT SMALL DIFFUSION TIMES

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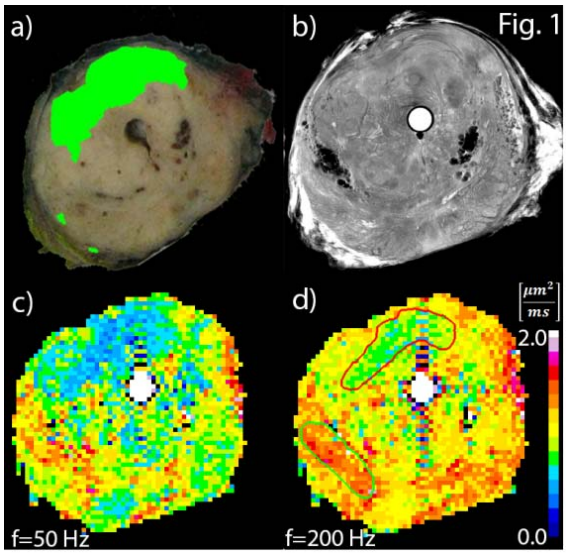
Target audience: Researchers interested in the biophysical basis of diffusion contrast and optimization of DWI for cancer detection

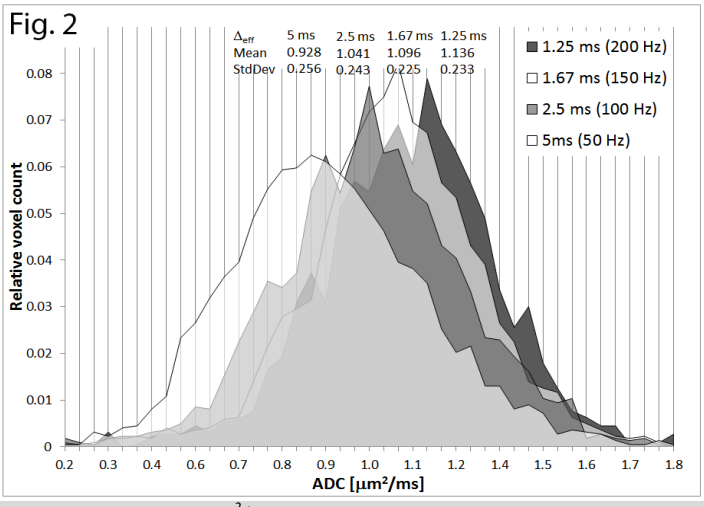
Purpose: To investigate regional ADC variation at short diffusion times using OGSE DWI in fresh and fixed prostate tissue.

Introduction: ADCs as measured by pulsed gradient (PGSE) DWI methods have been shown to be sensitive to cellular changes occurring in prostate cancer[1]. However, the exact nature of restrictions causing these changes and the corresponding non-mono-exponential diffusion decay is still unclear. As standard PGSE methods have limited capability to sample short diffusion times these methods are sensitive to multiple scales of restrictions, including internal cell structures and boundaries. The aim of this study was to explore the ability of OGSE to detect subcellular changes in prostate tissue.

Methods: A cos-OGSE sequence as described in [2] (OGSE-C1) was implemented on a BioSpec Avance III 94/20 system equipped with BGA-12S HP gradients (G_{max}=660mT/m, dG/dt_{max}=4570Tm/s) and 72-mm quad-RF-coil. A radical prostatectomy specimen histologically diagnosed with prostate cancer Gleason Score (3+4) was prepared as described in [3] and imaged in unfixed state and again after 48hr formalin fixation. OGSE DWI was performed at oscillation frequencies f = 50, 100, 150 and 200 Hz (corresponding to effective diffusion times Δ_{eff} = 5, 2.5, 1.66, 1.25 ms) and *b*-values 200, 400, 600, 800 s/mm^2 + "b0"-image for each frequency. Imaging parameters: FoV: 5.12x5.12cm, Matrix: 64x64, Resolution: 800x800 µm, Slice Thickness: 2mm + 2mm gap, 6 slices, TE = 90.2ms, TR= 2500ms, δ = 40ms, Δ = 44ms, Avg = 3, time per freq = 40 min. ADC maps were calculated for each oscillation frequency by mono-exponential fitting $S = S_o \times \exp(-ADC \times b)$. Distinct regions in cancer tissue and peripheral zone were delineated on H&E stained slices and co-registered to the DWI images by anatomical landmark matching. Dependency of apparent mean square displacement $\langle r_{app}^2 \rangle = 6 \times ADC \times \Delta_{eff}$ on sampled diffusion time was investigated in ROIs from histology.



Results: In the diffusion time range Δ_{eff} = 1.25—5 ms prostate tissue exhibits a systematic increase in ADC with decreasing diffusion time. Overall mean increase ΔADC 200Hz/50Hz was 23% for unfixed and 29% for fixed tissue (Fig. 2). ADC mapping revealed substantial dependence of ADC-diffusion-time-relation on prostate region and tissue type (Figs. 1& 3). Histologically defined cancer (Gleason 3+4) correlated well with regions of lowest ADC and showed substantially different ADC-diffusion-time dependence from normal peripheral zone tissue (Fig 3).



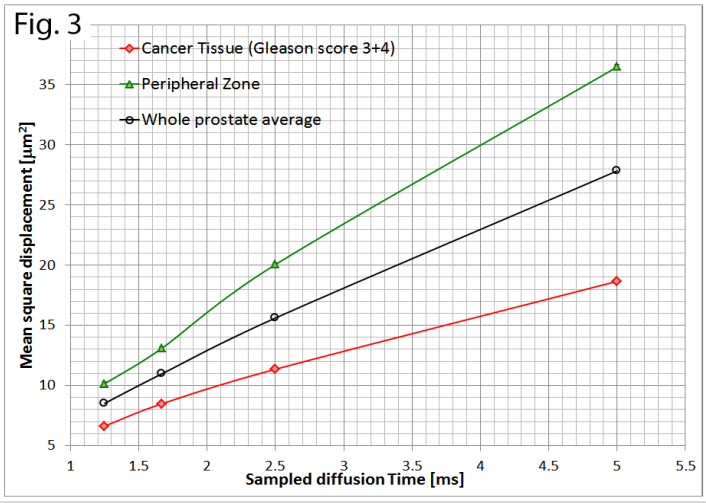


Fig 1: OGSE ADC maps [µm^2/ms], corresponding cancer delineation from histology, and T2w anatomy of unfixed prostate: a) Prostate section with cancer Gleason Score (3+4) region (green), b) TurboRARE T2w anatomical slice, c) OGSE ADC map 50Hz, d) OGSE ADC map f=200Hz (including ROIs). **Fig2:** Histograms of ADC values of complete prostectomy sample for Δ_{eff} = 5, 2.5, 1.66, 1.25 ms **Fig 3:** ROI analysis of apparent mean square displacement for distinct prostate regions/tissue types.

Conclusion: For the short diffusion times assessed in this study substantial tissue-specific ADC-diffusion time dependencies have been found. Apparent mean displacements for short diffusion times are less than cell dimensions and significantly smaller for cancer than for normal tissue, suggesting that cancer induces intracellular structure changes. Modeling of OGSE DWI can provide useful information about internal cell restrictions and help to elucidate the basis of non-mono-exponential behavior found in DWI signal decays of prostate cancer.

References: [1]Gibbs et al. MRM 46 (2001) ; [2]Does et al.: MRM 49 (2003) ; [3]Bourne et al. MRM 70 (2012)