Rotating Frame Relaxation Measurements in Prostate Cancer Model

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Introduction

Rotating frame relaxations ($T_{1p}$ and Relaxation Along a Fictitious Field (RAFF) $T_{RAFF}$)²,³,⁴ have shown to be quantitative MRI markers to follow up disease progression, including brain and myocardial ischemia³,⁴ and to follow up response to therapy⁵. $T_{RAFF}$² has been shown excellent correlation with cell density in rat glioma model, which makes it potential biomarker to follow up cancer therapy outcome. In this study, rotating frame relaxation times $T_{RAFF}$², $T_{RAFF}$⁴, $T_{1p,CW}$, $T_{1p,adiab}$ and $T_{2p,adiab}$ were measured in subcutaneous prostate cancer (PC3-RFP) tumors in several time points.

Materials and Methods

Prostate cancer cells expressing red fluorescence protein (PC3-RFP, Anticancer Inc., USA) were implanted in right hind limbs of 11 nude mice. The tumor growth was monitored for three weeks using optical imaging and MRI. The mice were anesthetized with 1.5% isoflurane in (70%N₂:30%O₂) and imaged once a week up to 3 weeks after the implantation first at IVIS Illumina and then during two following days at 7T Bruker Pharmascan using volume transmitter and surface receiver coil. The parameters for fluorescence based optical imaging were the following: Exposure time: auto / 1 s, Binning: medium, F/Stop: 2, Excitation filter: 535 and 465 (background) and Emission filter: DsRed. The MRI scans consisted of $T_{RAFF}$² and $T_{RAFF}$⁴ (RAFF2 or 4-pulses¹ pulse train length of 0-36 ms, $\gamma B_1/(2\pi) = 1250$ Hz for RAFF2 and 648 Hz for RAFF4), $T_{1p,CW}$ (spin-lock time=0 - 45.4 ms, $\gamma B_1/(2\pi)=1250$ Hz), $T_{1p,adiab}$ (train of AFP pulses, train length 18 -72 ms), $T_{2p,adiab}$ (3 ms AHP excitation pulse before AFP pulse trains as with $T_{1p,adiab}$, then 3 ms AHP back pulse), and for comparison $T_2$ (adiabatic Hahn double echo preparation with TE = 8 - 22 ms), and $T_1$ (saturation recovery with TR = 200 - 5000 ms). We monitored also $B_1$ (altering hard pulse lengths between 0.2 and 1.6 ms). All data were acquired from one axial slice placed on the largest tumor cross section. Fast spin echo sequence (TR = 4 s, effective TE = 8 ms, ETL = 8, FOV = 30x15 mm², matrix size 256x128, and slice thickness of 1 mm) with fat suppression was used as readout imaging sequence. In addition, $T_2$ weighted anatomical images covering the whole tumor were obtained for assessing tumor volumes (TR = 2500 ms, effTE = 33 ms, ETL = 8, matrix size 256x256, FOV = 30x30 cm², 15 slices). ROIs representing the tumor and skeletal muscle were hand drawn for further analysis based on $T_2$ weighted images.

Results and Discussion

Table 1. Relaxation times for tumor and skeletal muscle in three time points (mean± SD [ms]).

Tumor growth from week 1 to 3 is well visualized on the $T_2$ weighted images (Fig. 1). The averages of relaxation times over the tumor area in single slice was significantly longer compared to the muscle area with all methods used, except with $T_{1p,adiab}$ (Fig. 2, Table 1). There was a significant decrease from week 1 to weeks 2 and 3 in $T_{1p,CW}$ and $T_{RAFF}$ values (1-way ANOVA, p<0.05). Other relaxation times did not change significantly during tumor growth. Most likely decrease is related to lower cell density of the tumors in the first time point, especially in small tumors. The present data serve as baseline measurements of MRI relaxation time constants for upcoming therapy follow up study. Anticancer therapy induced cell death in the tumors is assumed to be shown as longer relaxation times, opposite to found decrease in $T_{1p,CW}$ and $T_{RAFF}$.

References


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