

Early quantitative T1 and T2 response of the prostate gland during radiotherapy

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Introduction: Quantitative MRI biomarkers, including apparent diffusion coefficient and quantitative perfusion metrics, are demonstrating promising predictive value when measuring early response to radiation therapy (1,2). Monitoring of T1 and T2 MRI relaxation times over time may augment a comprehensive evaluation of early radiation response. T2 relaxation provides intrinsic sensitivity to changes in water and protein volume fractions, plus to the density and denaturation state of hemoglobin, while direct T1 relaxation may improve the conversion between signal and contrast agent concentration in dynamic contrast-enhanced studies (3,4). This study evaluates T2 and T1 changes in benign and tumor-dense regions of the prostate gland in patients with localized prostate cancer at two week intervals throughout an 8-week time-course of definitive radiation therapy.

Methods: Studies were based on parallel adaptations of a magnetization-prepared spiral imaging technique for prostate MRI at 1.5 Tesla, termed T2prep for T2 quantification (5) and T1prep for T1 quantification (the method developments are submitted as individual abstracts). Both methods share the same basic structure, including a variable duration contrast generation interval, imaging interval, and final magnetization-nulling pulse prior to a constant duration longitudinal recovery interval. T2 contrast preparation utilizes a MLEV pattern of composite 90x180y90x refocusing pulses of duration TE, followed by a tip-up pulse for longitudinal storage of the magnetization. T1 contrast preparation uses an adiabatic inversion pulse followed by a delay TI. For both designs, imaging proceeds with a spectral-spatial pulse and spiral imaging gradient, plus trailing spoiler gradient. This imaging interval is repeated at approximately 20ms temporal resolution for multi-slice imaging. The final imaging interval is followed by a BIR-4 pulse to null all remnant longitudinal and transverse magnetization. The delay between the final imaging interval and BIR-4 pulse is varied to preserve a constant longitudinal recovery interval for variable TE or TI. Finally, RF cycling is common to both methods, by toggling on of an adiabatic inversion pulse prior to the first imaging interval of every even-numbered acquisition. Subtraction of even- and odd-numbered data pairs enables T2prep and T1prep signal modeling as monoexponential decays (6).

Scanning proceeded on 16 patients with low or intermediate-risk localized prostate cancer at baseline and at 2-week intervals through to week 8. For each session, patients were oriented in supine position within a 1.5T GE Signa, using a torso-phased array (MEDRAD) placed anterior and posterior to their pelvis. Sessions included FSE images as a stack of axial 3-mm slices with whole-gland coverage (TE/TR = 98/5000ms), diffusion-weighted EPI (TE/TR=64/5575ms, b=0 and 600s/mm²), T2prep, and T1prep acquisitions with matched longitudinal coverage in 6-mm sections in separate 5-minute acquisitions. Scan parameters included 2 TEs (3, 88ms) or 2 TIs (14, 1014ms) respectively, with 1.1mm in-plane resolution, 20-cm field-of-view, and 125 kHz readout.

Data analysis used MIPAV (NIH, Bethesda, MD) for manual segmentation and histogram analysis of mean and standard deviation signals. Origin software (OriginLab, Northampton, MA) provided regression algorithms. Central gland (CG), uninvolved peripheral zone (PZ), and tumor-dense (T) ROIs were delineated on FSE and/or ADC images by an experienced radiation oncologist, copied onto T2prep and T1prep images, and manually adjusted to account for motion-related mis-registration. Both FSE and DWI images guided tumor delineation. Significance testing used the Student's two-tailed t-test at p of 0.05.

Results: T2 presented with differential significant responses between prostate zones and tumor regions. Relative to a mean baseline value of 78±7ms, central gland T2 elevated modestly but significantly at weeks 2 and 4 before returning to baseline equivalence (Wk2: 84±9ms, p=0.008; Wk4: 81±7ms, p=0.005; Wk6: 79±8ms, p=0.192; Wk8: 77±5ms, p=0.257; p<0.008). Relative to a mean baseline value of 109±25ms, uninvolved peripheral zone T2 demonstrated a variability at Wks 2 and 4, but reduced through Wk 6 to a significant level by Wk8 (Wk2: 110±19ms, p=0.321; Wk4: 102±16ms, p=0.253; Wk6: 95±14ms, p=0.067; Wk8: 91±12ms, p=0.0261). Relative to a mean baseline value of 84±11ms, tumor presented with Wk2 equivalence before reducing to a significant level from Wk 4 through 8 (Wk2: 83±8ms, p=0.79; Wk4: 75±6ms, p=0.022; Wk6: 73±7ms, p=0.04; Wk8: 73±4ms, p=0.020). Trends were not observed in T1 response to radiation. CG T1 varied from 1312±78 at Wk2, 1348±70 at Wk4, 1310±71 at Wk6, to 1291±45 at Wk8 (p-values between 0.23 and 0.53 compared to baseline). Pz T1 varied from 1336±133 at Wk2, 1434±191 at Wk4, 1289±84 at Wk6, to 1276±69 at Wk8 (p-values between 0.14 and 0.62 compared to baseline). Tumor T1 varied from 1253±80 at Wk2, 1280±98 at Wk4, 1212±107 at Wk6, to 1283±118 at Wk8 (p-values between 0.23 and 0.50 for Wk2-Wk6, but reducing to 0.07 at Wk 8). In contrast to the considerable inter-patient T1 heterogeneity, the percentage standard deviation of intra-patient T1 measurements across treatment weeks was 3.0±1.5% for CG, 6.6±3.9% for PZ, and 4.3±2.2% for tumor.

Summary and Conclusions: Quantitative evaluation identifies changes of T2 in the prostate gland of patients with low and intermediate risk localized cancer during a course of external beam radiation therapy, which are apparent as early as Wk 2 in the central gland, Wk 4 in tumor-dense regions, and by Wk 8 in the uninvolved peripheral zone. These changes support an overall loss of intra-prostatic contrast in diagnostic images following radiation therapy. T2 information may prove to have some independence in biologic origin to ADC and perfusion metric fluctuations during external beam irradiation, to complement a multi-parametric comprehensive evaluation of radiation response. T1 values of prostate regions-of-interest appeared insensitive to treatment, and inter-patient heterogeneity was considerably greater than intra-patient variability across time-points. These findings support an adequacy of baseline T1 values for serial quantitative analysis of DCE within 8 weeks of the start of treatment, though with minor cost to the repeatability confidence limits.

References: (1) Hamstra et al, *PNAS*, 2005; (2) Franiel et al. *Radiother Oncol*, 2009; (3) Foltz et al. *Magn Reson Med*, 2006; (4) Dale et al *J Magn Reson Imaging*, 2003; (5) Foltz et al. *Magn Reson Med*, 1997; (6) Hsu et al. *Magn Reson Med*, 2006.

Figure (a) Representative images including a tumor demarcated in red: (i) ADC and (ii) FSE for tumor contouring; (iii) T1map and (iv) T2map in matched slices. (b) T2 response to radiation in CG (square), PZ (circle), and tumor (triangle); (c) T1 response to radiation (shared legend with (b)).

