Effect of Formalin Fixation on Biexponential Modeling of T1 and T2 Decay in Prostate Tissue

Tryggve Holck Storås[1], Andre Bongers[2], Carl Power[2], and Roger Bourne[3]
[1]*Interventional Centre, Oslo University Hospital, Oslo, Norway,* [2]*Biomedical Resource Imaging Laboratory, University of New South Wales, Sidney, Australia,* [3]*Discipline of Medical Radiation Sciences,Faculty of Health Sciences, The University of Sidney, Sidney, Australia*

Purpose: T2 relaxation has been demonstrated to be non-monoexponential in prostate tissue imaged in vivo[1]. The pilot study presented here investigated T1 and T2 relaxation behavior at 9.4 T with high spatial resolution in fresh and fixed whole prostate specimens.

Methods: The intact organ was sent with ethics approval to the pathology department immediately upon surgical resection and without immersion in a fixative solution. After conclusion of imaging of the fresh unfixed specimen (total time of ischemia at 20-22^{o}C was 7-10 hr) the whole organ was immersed ~72 h in 400 mL 10% neutral buffered formalin then imaged again without removal of formalin. For imaging the organ was suspended on a salin-filled 5-mm NMR tube inserted through the urethra[2]. Imaging was performed at room temperature (22^{o}C) on a 9.4 T Bruker (Germany) BioSpec . A rapid acquisition with relaxation enhancement (RARE) sequence with variable repetition time (VTR) was used for T1 measurements. T2 measurements were based on a multi-slice multi-echo (MSME) sequence for the fixed tissue acquisition and the faster RARE sequence with multi echo for the fresh tissue. Scan parameters are given in Table 1. TE and TR were equally and logarithmically spaced respectively

Table 1. Acquisition parameters

Scope	Sequence	# TR (TR ms)	# TE (TE ms)	Matrix	Voxel size (mm^3)
T1 in fresh tissue	RARE VTR	6 (322 – 7500)	1 (14)	128x128	0.31x0.31x2.2
T1 in fixed tissue	RARE VTR	22 (430 – 20000)	1 (14)	128x128	0.48x0.48x1.0
T2 in fresh tissue	RARE	1 (2086)	8 (14 – 210)	128x128	0.31x0.31x2.2
T2 in fixed tissue	MSME	1 (15000)	32 (11 - 342)	256x192	0.24x0.32x1.0

Postprocessing was performed in IDL (Exelis VIS, Boulder, Col, USA). A region of interest (ROI) was drawn in the central slice to include the whole prostate excluding the NMR tube and periprostatic fat. Within the ROI, decay curves were extracted pixel by pixel and fitted to both mono- and bi-exponential models using MPFIT, a freely available IDL program based on a Levenberg-Marquardt algorithm. Residues from mono- and biexponential fits were compared by an F-test, and a decay curve was considered biexponential if the residuals of this fit were significantly lower than that for the monoexponential fit ($p<0.05$). Mean and standard deviation were calculated for the regression parameters. Mean relaxation times and signal fractions of the smaller component were based on only pixels deemed biexponential.

Results: Regression results are summarized in Table 2. Example parameter maps are shown in Fig. 1.

Table 2. Summary of results

	% of voxels with biexponential T2	T2 (ms) major component	Signal fraction major T2 component	% of voxels with biexponential T1	T1 (ms) major component	Signal fraction major T1 component
Fresh	2	63 ± 10	80 ± 16	7	2148 ± 237	84 ± 17
Fixed	80	27 ± 3	97 ± 1	0	1665 ± 138	-

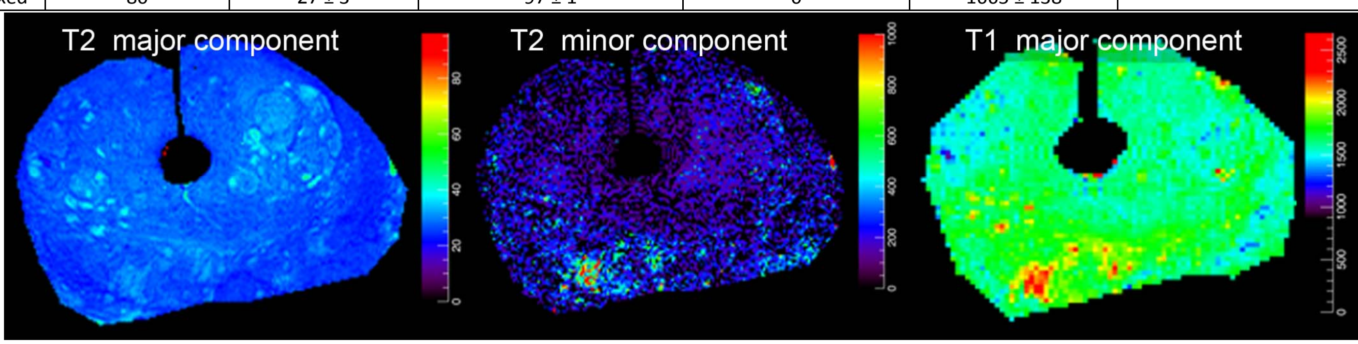

Fig. 1. Representative parametric maps from a central slice of fixed prostate tissue.

Discussion: The signal fractions in fresh tissue were comparable with those reported for biexponential T2[1] and diffusion[2] in vivo. In fixed tissue the signal fraction of the slowly decaying T2 component was smaller, and in T1, only one component was found. This is in contrast to diffusion studies where relaxation rates changed while signal fractions were barely affected by tissue fixation.

Conclusion: T1 and T2 decay curves are biexponential in fresh tissue and fractions are comparable with findings invivo. After fixation with formalin, relaxation properties are changed and signal fractions are not preserved.

References:

1. Storås, T. H., Gjesdal, K. I., Gadmar, Ø. B., Geitung, J. T. & Kløw, N. E. Prostate magnetic resonance imaging: Multiexponential T2 decay in prostate tissue. *Journal of Magnetic Resonance Imaging* **28**, 1166–1172 (2008).

2. Bourne, R. *et al.* Effect of Formalin Fixation on Biexponential Modeling of Diffusion Decay in Prostate Tissue. *Magnetic Resonance in Medicine* doi:10.1002/mrm.24549