Treatment effects one year after radiotherapy of the prostate: a quantitative MRI study

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Introduction.
Quantitative estimates of the physiology and MR characteristics of the prostate before and after radiotherapy may help to predict the response of the gland to treatment. The purpose of this study was to assess these characteristics in the pathological prostate gland before and one year after treatment with external beam radiotherapy using T_1 and T_2 mapping, dynamic contrast-enhanced MRI and a distributed parameter tracer kinetic model. The hypothesis to be tested is that these characteristics will serve as sensitive indicators of tissue response to treatment and thereby provide a useful prognostic tool.

Methods.
Twenty-two men aged between 57 and 76 years old (mean, 67 years) with histologically proven adenocarcinoma of the prostate were recruited into the study [1]. The Local Research Ethics Committee gave approval and written consent was obtained from all men. Imaging was performed before and 13.6 ± 1.4 months after treatment with neoadjuvant hormonal therapy and 3D conformal radiotherapy (50 Gy given in 16 fractions). The patients were scanned on a 1.5 T Philips MR system using a pelvic phased-array coil. T_2-weighted fast spin echo images of the entire gland were acquired using a TR of 4.75 s at echo times of 7, 45, 100 and 240 ms to estimate baseline T_2 [2]. A 3D T1-weighted gradient echo pulse sequence was used at flip angles of 2º, 10º, 20º and 30º to estimate baseline T_1 [3]. This was followed by a dynamic series in which volumes (flip angle 30º) were acquired every 2.3 s for approximately 4 minutes. Early in this series 0.1 mmol/kg Gd-DTPA-BMA was injected at 3 ml/s using a power injector.

For each patient regions of interest were drawn in the external iliac arteries (to provide an arterial input function). With the aid of T_2-weighted images a radiologist (CEH) drew further regions in prostate tumour, muscle (internal obturator) and, where possible, normal contralateral peripheral zone. Regions were mapped onto the post-treatment images to match the pre-treatment regions as closely as possible. For each region estimates of T_1 and T_2 were made, signal intensity variations were converted to temporal changes in Gd-DTPA-BMA concentration and a distributed parameter model was fitted to the data [1, 4].

Results.
Twenty-one patients underwent both imaging studies (one patient was unable to complete the study). With the limited follow-up time on many of these patients a full outcomes analysis is not possible. However, significant changes in both relaxation times and vascular characteristics were observed following radiotherapy. The table indicates median values of parameters showing significant change following treatment:

Tissue	T_1 (ms)	T_2 (ms)	Flow (ml/100 ml/min)	PS-product (ml/100 ml/min)	Interstitial volume (ml/100 ml)
Tumour (n = 21)	922 → 1071 *(p = 0.010)*			19.2 →10.4 *(p = 0.023)*	
Normal (n = 20)		126 → 106 *(p = 0.009)*			25.0 → 49.8 *(p = 0.002)*
Muscle (n = 21)		50 → 56 *(p = 0.001)*	7.4 → 16.0 *(p = 0.007)*		6.2 → 14.4 *(p = 0.010)*

Comparisons made using the non-parametric Wilcoxon Signed Ranks test.

Discussion.
To our knowledge, these results represent the first such quantitative measures made in the prostate gland before and after radiotherapy. Our estimates of the relaxation times compare well with previous results and underscore the reduced T_2 seen in cancer pre-treatment [2]. The treatment-related decrease in normal prostate T_2 is consistent with the loss of contrast seen in the gland following radiotherapy [5]. The vascular changes measured in the gland were less consistent though several patients have already relapsed while others have responded well. Conversely, the consistent results in nearby muscle located within the treatment field may reflect direct endothelial cell damage caused by radiation and subsequent oedema.

Previous studies have employed dynamic contrast-enhanced CT to evaluate the vascular characteristics of the prostate [6]. However, the associated radiation burden prevents the examination of more than one or two sections and these must be chosen with little prior knowledge of the location of cancer. MRI may be used repeatedly and our 3D protocol provides complete coverage of the gland providing a promising tool for the assessment of treatment response and prognosis.

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