MRI measures of tumor perfusion and T_2 relaxation in response to radiotherapy for prostate cancer

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Introduction.

Quantitative estimates of the vascular 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 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 hypofractionated 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. A 3D T1-weighted gradient echo pulse sequence was used at flip angles of 2º, 10º, 20º and 30º to estimate baseline T_1. 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 tumor, 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, 2].

Results.

For this preliminary analysis 6 patients were classified as non-responders (biochemical failure, ASTRO definition) and have been treated with further hormone therapy. 16 patients were classified as responders (mean follow-up time 29 ± 7 months). Significant changes in both relaxation times and vascular characteristics were observed across the sample following treatment. Increases were measured in tumor T_1, muscle T_2, normal gland interstitial volume and muscle PS-product. Decreases were observed in normal gland T_2 and tumor perfusion, an effect that was response-specific. Responders showed a smaller decrease in perfusion ($p = 0.018$, repeated measures ANOVA). Relative tumor perfusion (rTP), the ratio of tumor to normal prostate perfusion, was also calculated. There was a significant difference pre-treatment in both rTP and tumor T_2 between responders and non-responders ($p = 0.004$ in each case).

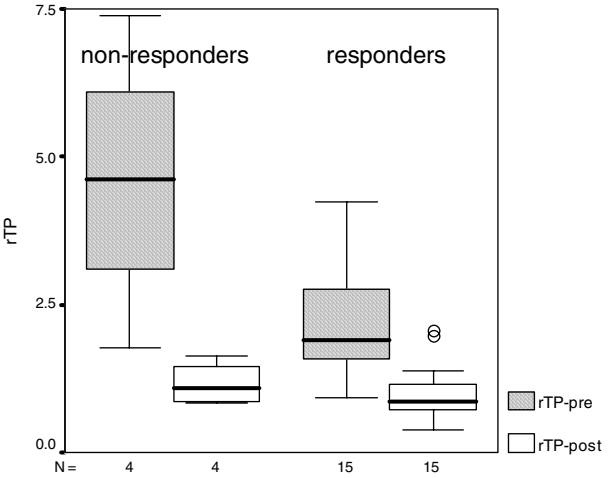

Figure 1 rTP as a function of treatment. rTP is higher pre-treatment in non-responders (1st column) than in responders (3rd column). The reduction in perfusion seen post-treatment is bigger in non-responders.

Discussion.

Prognosis Prostate tumors with low pre-treatment T_2 and high rTP responded poorly to treatment. The use of a relative measure helps to correct for inter-patient variations in whole gland perfusion (under hormonal control) but requires normal tissue for comparison (none visible in 2 non-responders). While these preliminary results are promising, they need to be tested in a larger patient cohort.

Treatment response The decrease in prostate T_2 is consistent with the loss of contrast seen in the gland following radiotherapy [3] while the vascular changes observed may represent the first such quantitative data reported. Changes seen in nearby muscle located within the treatment field probably reflect direct radiation-induced endothelial cell damage (increase in PS-product) and subsequent edema (increased T_2), data important for the assessment of radiation toxicity. Previous studies have employed dynamic contrast-enhanced CT to evaluate the vascular characteristics of the prostate [4]. However, the associated radiation burden prevents the examination of more than a few sections and these must be chosen with little prior knowledge of the location of cancer. MRI offers additional information (e.g. T_2), may be used repeatedly and our 3D protocol covers the whole prostate gland. Further studies are required to assess the reproducibility our techniques that provide a promising tool for the assessment of treatment response.

References.

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