Change in ADC values in the prostate during radiotherapy.

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Introduction
The effects of ionising radiation on cells are complex and include cell apoptosis, cell swelling and cell lysis, all of which affect the cellular density. The aim of this study was to investigate if the apparent diffusion coefficient (ADC) changed before and after external beam radiotherapy (EBRT) in response to these effects using similar acquisition techniques to studies that have (a) demonstrated a significant difference in ADC between normal prostatic peripheral zone and prostate cancer (1, 2) and (b) demonstrated a significant change in ADC during chemotherapy (3).

Methods.
17 patients who were undergoing radical EBRT (55 Gy in 20 fractions) for prostate cancer participated in this study. The inclusion criteria for the study were patients with localised prostate cancer who had had no previous radiotherapy treatment and had been on hormone therapy prior to EBRT commencing. Patients were excluded if they had contraindications to MRI scanning. MRI scans were performed on a 1.5T Siemens Avanto scanner with SQ gradients. All patients had T2W-TSE and diffusion MRI scans of their prostate before the first EBRT fraction and immediately after their last fraction of EBRT. The diffusion MRI scans used a single-shot diffusion weighted echo-planar imaging (DW-EPI) sequence with b-values of 0, 50, 300, 500 and 800 s/mm². The scanning software automatically produced ADC values from these b-values. The slice positions of T2W-TSE and DW-EPI scans were matched.

Regions of interest were drawn on the T2W images pre-radiotherapy corresponding to areas of low signal intensity (cancerous regions) and areas of high signal intensity (normal peripheral zone). These regions were transferred onto scanner calculated ADC maps of the prostate. The regions were shifted in the phase encoding direction (anterior-posterior) if the prostate centre of gravity had moved between the T2W and ADC maps.

The T2W images acquired post-radiotherapy were registered to the pre-radiotherapy T2W images using specialised registration software (Slicer Version 2.6, www.slicer.org). This was done using a combination of automatic mutual information algorithms and manual registration. The transformation matrix was then used to register the post-radiotherapy diffusion trace images and ADC images to the pre-treatment diffusion scans. The regions of interest used pre-radiotherapy were transferred to the registered post-radiotherapy images and manual adjustments of positions were allowed. ADC values for malignant and normal prostate were measured from the scanner calculated ADC maps. The pre- and post-treatment ADC values were compared using the paired t-test.

Results
Two patients were excluded from the analysis due to technical problems. In 14 patients normal peripheral zone was identified whereas malignant tissue was identified in all 15 patients. The ADC values pre- and post-treatment are shown in figure 1 for malignant and normal regions.

The mean ADC value post-treatment was significantly reduced compared to the pre-treatment value for both malignant regions (0.772 mm²s⁻¹ vs 0.883 mm²s⁻¹ respectively, p<0.05) and normal peripheral zone (0.960 mm²s⁻¹ vs 1.244 mm²s⁻¹ respectively, p<0.01).

Discussion
These preliminary results have demonstrated that the ADC of both suspicious and normal areas of the prostate change as a result of EBRT. Problems that still need addressing are (i) investigation of the most appropriate calculation of the ADC, particularly in the choice of which b-values to use, (ii) inter-scan registration which is challenging because the prostate may change shape and move relative to other pelvic structures due to differences in bladder and rectal filling and (iii) improved identification of malignant areas within the prostate using biopsy information as the T2W scans can be non-specific.

Conclusion
EBRT leads to decreases in ADC values that are apparent by the end of treatment in both healthy and cancerous tissue. Further work is needed to fully characterise the time course and magnitude of this change and to establish the inter-scan reproducibility.

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References

Figure 1

Table 1

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<thead>
<tr>
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<th>Pre EBRT</th>
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<tbody>
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</tr>
<tr>
<td>Normal ROIs</td>
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