# Multiparametric MRI imaging in patients undergoing ultra-hypofractionated radiotherapy for localised prostate cancer

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**Introduction.** Radiotherapy (RT) plays an important role in the treatment of prostate cancer. Technological advances have enabled radiation to be delivered to the tumour target with increasing conformality. This in turn has allowed radiation oncologists to increase safely the dose given per fraction of treatment, a practice termed hypo-fractionation. In the extreme case of stereotactic body radiotherapy (SBRT), doses far higher than the conventional 2 Gy/fraction are used, and the whole course of treatment can be completed in a few days rather than weeks. SBRT is increasingly being used to treat localised prostate cancer.

In common with other tumour sites, hypoxia can adversely influence the clinical outcome following RT for prostate cancer. One theoretical disadvantage with hypofractionated RT schedules is that there is insufficient time for the tumours to undergo re-oxygenation during the much shortened course of treatment. This may compromise the effectiveness of SBRT. In this feasibility study, we assess the vascular & blood oxygenation changes in the prostate gland during a course of SBRT using multiparametric MRI imaging.

**Methods & Materials.** Five patients with localised prostate cancer undergoing SBRT were recruited. Two of them had been treated with androgen deprivation therapy prior to their RT. Each patient received five fractions of 7.25 Gy (total dose = 36.25 gray) over 10 days using a cyberknife RT delivery system. Serial multi-parameter MRI scans consisting of intrinsic susceptibility-weighted MRI (ISW-MRI: TE 4.76-62ms, TR 100ms, flip angle 90°, acquisition matrix 128x128, 16 slices of 5mm, FOV 260mm), dynamic contrast-enhanced MRI (DCE-MRI: 3D VIBE, TE 1.24ms TR 6.6ms, flip angles 3° and 21°, acquisition matrix 256 ×174, 20 slices of 5mm, field of view (FOV) 260mm) and dynamic susceptibility-contrast MRI (DSC-MRI; TE 30ms TR 1481ms, flip angle 90°, acquisition matrix $128^2$ , 20 slices of 5 mm), were performed at six time-points: baseline (<7 days of commencement of RT), immediately after the first, third, fifth fractions of RT, 10 days after the end of treatment and 3-6 months after the end of treatment.

The whole prostate was outlined as the region of interest by a single radiation oncologist. Voxel-based calculations were performed using two bespoke software analysis packages: Magnetic Resonance Imaging Workbench for DCE-MRI ($K^{trans}$ – transfer constant ($min^{-1}$), $IAUGC_{60}$ – initial area under gadolinium curve over 60 seconds (mmol.s) & DSC-MRI (rBV/rBF – relative blood volume/flow (arbitrary units) & DiffusionView for ISW-MRI ($R_2$*, $s^{-1}$) analysis (both © Institute of Cancer Research, London).

**Results.** Percentage changes compared with the baseline values among all the MRI parameters assessed are shown in Table 1. Mean $R_2$* decreased immediately after the 1st RT fraction, continued to fall during the course of RT and remained lower than before the start of RT for three to six months post-treatment. At the same time, both the $K^{trans}$ and $IAUGC_{60}$ rose sharply immediately after the 1st fraction, continued to rise during treatment, but then decreased 10 days after completing RT (Figure 1). The $T_2$*-weighted dynamic parameters (rBF & rBV) also showed a similar time course pattern of change (Figure 2).

**Conclusions.** Prostate gland hypervascularity induced by ultra-hypofractionated RT suggests that re-oxygenation occurs immediately after the 1st fraction and that the process of re-oxygenation continues during the rest of the course of treatment. Whilst the blood supply normalises back to the pre-treatment level very quickly after the completion of radiotherapy, the prostate $R_2$* signal decrease remains for 3 to 6 months after the end of treatment. A larger patient cohort study undergoing SBRT for prostate cancer is needed to confirm these findings. These findings need to be compared with patients receiving conventionally fractionated RT in order to study the specific effects of RT ultra-hypofractionation.

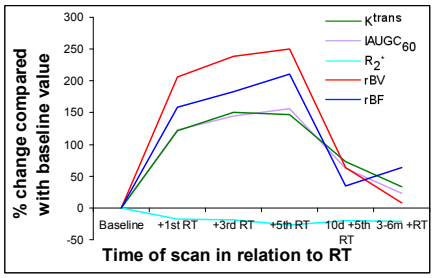


*Figure 2: parametric changes with radiotherapy*

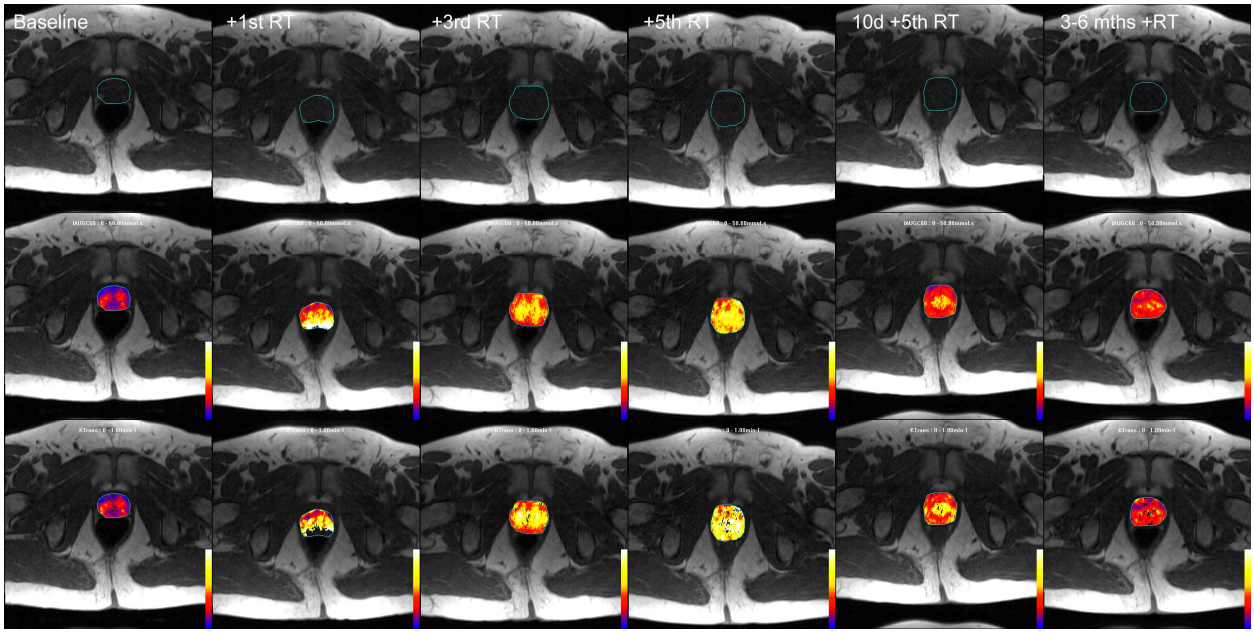


Table 1: Percentage change in kinetic parameters compared with baseline values

| Time | +1st RT | +3rd RT | +5th RT | 10 d +5th RT | 3-6 mths +RT |
|---|---|---|---|---|---|
| **$R_2$*** | -17% | -18% | -26% | -20% | -21% |
| **$K^{trans}$** | 123% | 145% | 156% | 62% | 24% |
| **$IAUGC_{60}$** | 122% | 150% | 147% | 73% | 34% |
| **rBV** | 206% | 238% | 251% | 63% | 8% |
| **rBF** | 159% | 183% | 211% | 35% | 63% |

*Figure 1: DCE-MRI images for 6 scans.*
*Row 1: T1W imaging showing ROI placements*
*Row 2: $IAUGC_{60}$*
*Row 3: $K^{trans}$*