DCE and intrinsic susceptibility-MRI investigations of prostate gland physiological changes with androgen deprivation

R. Alonzi[1], N. J. Taylor[2], P. J. Hoskin[1], J. J. Stirling[2], J. A. d'Arcy[3], D. J. Collins[3], M. I. Saunders[1], and A. R. Padhani[2]

[1]Marie Curie Research Wing, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, United Kingdom, [2]Paul Strickland Scanner Centre, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, United Kingdom, [3]CRUK Clinical MR Research Group, Royal Marsden NHS Foundation Trust, Sutton, Surrey SM2 5PT, United Kingdom

Introduction: Hypoxia is a known cause of radioresistance and is known to be a poor prognostic factor in prostate cancer[1]. There are no simple, non-invasive methods by which tumour hypoxia can be assessed *in-vivo* and recently, intrinsic susceptibility-weighted MRI has been suggested as a suitable biomarker in prostate cancers[2] (when used with blood volume information). It is known that androgen deprivation has a potent antiangiogenic effect on prostatic vasculature and thus potentially may induce tumour hypoxia[3]. Androgen suppression also reduces tumour proliferation rates and induces cell cycle arrest in animal models which may additionally inhibit the effects of radiotherapy. The purpose of this study was to document the antiangiogenic effects of neoadjuvant androgen deprivation on the human prostate gland using dynamic contrast enhanced MRI (DCE-MRI) and concomitant effects on blood oxygenation levels using intrinsic susceptibility weighted MRI.

Methods:13 patients with prostate cancer (age 57-78, Gleason 6-9, PSA 3.7-29.8ng/ml) that were due to be treated with neo-adjuvant androgen deprivation (Goserelin, 10.8mg every 3 months, administered subcutaneously) prior to radical radiotherapy underwent 5 MRI investigations; two prior to the commencement of androgen suppression to define the baseline values and measurement variability, one after a month of hormone treatment and two scans after 3 months of therapy, to measure the final effect of androgen deprivation and to reassess reproducibility whilst on hormones: Patients were imaged on a Siemens Symphony 1.5T MRI scanner using phased array pelvic coils. T_2-weighted images were used to identify tumour slice locations. Multiple gradient echo images were acquired with varying TE (5-60ms), TR=100ms, α=40°, FOV=200mm, 256^2 matrix, & three slices from which R_2* maps were calculated. T_1W spoiled GRE [FLASH] sequences (TE 5ms, TR 74ms, α=70°, 3 slices) were acquired before and after the bolus administration of 0.1 mmol/kg b.w. of Gd-DTPA with 40 time points over 8 min, through the prostate. ROI were placed around the whole gland to calculate pixel-by-pixel values of transfer constant (K^{trans}), rate constant (k_{ep}) and the initial area under the gadolinium curve over the first 60 seconds ($IAUC_{60}$) using the methods of Tofts[4] on MRIW software[5].

Results: After 3 months of therapy there was a marked increase in R_2*, from 15.1 to 21.5 s^{-1} ($p<0.0001$), accompanied by marked decreases in K^{trans}, from 0.61 to 0.27 min^{-1} ($p=0.0003$) (Figs 1& 2). The rate constant and $IAUC_{60}$ decreased significantly with androgen suppression ($p=0.0002$ and $p=0.0004$ respectively). Both R_2* and K^{trans} experiments became more reproducible following 3 months of androgen deprivation; the coefficient of variance (wCV) changed from 29.8% to 16.1% and from 39% to 30.3% respectively.

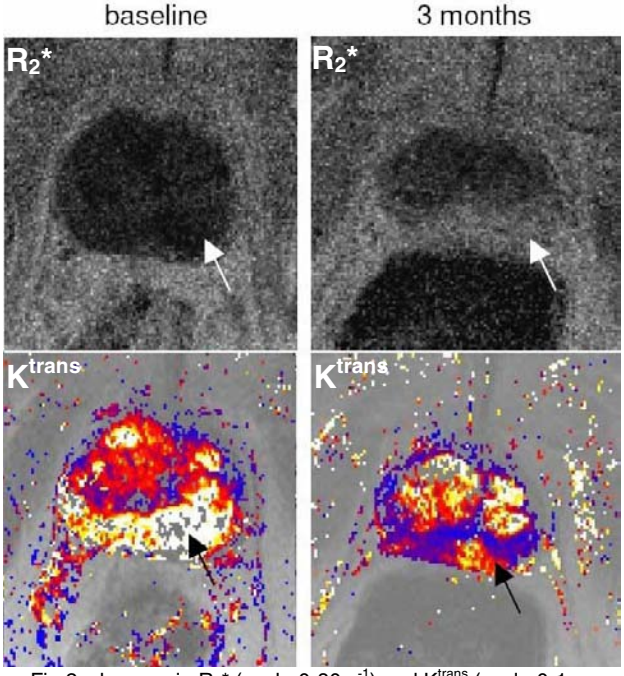

Fig 2: changes in R_2* (scale 0-80 s^{-1}) and K^{trans} (scale 0-1 min^{-1}) in a single patient with prostate cancer (arrow).

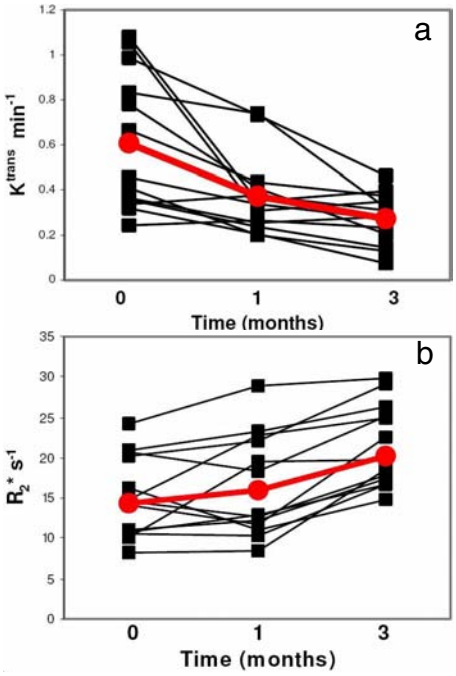

Fig 1: changes in a) K^{trans} and b) R_2* with androgen deprivation

Discussion: Reductions of K^{trans} are compatible with decreases in blood flow and vascular permeability caused by the apoptosis of vascular endothelial cells initiated by androgen deprivation. An increasing R_2* probably indicates an increase in blood deoxyhaemoglobin concentration (or possibly may reflect the development of prostate gland fibrosis) and independent verification of intraprostatic pO_2 levels is required to clarify the cause of R_2* increases. These results have implications for the design of clinical trials that will evaluate the timing of androgen deprivation in relation to radiotherapy administration for prostate cancer patients.

References

[1]*Movsas B. Cancer 2000; 89:2018-2024*
[2]*Carnell D. ISMRM 2005; 270*
3Shabsigh A. Prostate 1998; 36:201-206
[4]*Tofts PS and Kermode AG. Magn. Reson. Med. 1991; 17: 357-367*
[5]*d'Arcy JA. RadioGraphics 2006; 26: 621-632*