DCE-MRI at 3T in Patients with Advanced Prostate Cancer Undergoing Androgen Deprivation Therapy

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Introduction

Prostate cancer is the most common malignancy in men in the UK. Androgen deprivation (AD) by surgical or chemical castration remains a very important treatment modality for this disease and 60% of patients over 70 years old undergo AD therapy (1). However, 51% of these patients will develop resistance to AD within 5 years of starting treatment: therefore, there is a real need to identify quantitative biomarkers that can predict response to AD therapy. Dynamic Contrast-Enhanced (DCE) MRI is a technique that can generate parameters thought to reflect the tumour micro-environment such as perfusion and permeability indices (2). The local tumour environment is known to influence treatment response: tumours with reduced perfusion are more likely to be hypoxic with compromised delivery of therapy (3). The aim of this study is to evaluate DCE-MRI parameters before and after the initiation of AD therapy to see if they can be used to predict response to AD therapy in patients with advanced prostate cancer.

Materials/Methods

Patient selection: The study protocol was approved by the Ethics Committee. High risk patients who would be unsuitable for primary surgery due to co-morbidity were pre-selected on the basis of an abnormal DRE, or persistently elevated PSA level. In 16 patients, DCE imaging was performed prior to biopsy and then, if prostate cancer was confirmed (in 14 of 16 patients), DCE-MRI was repeated after 3 months of AD therapy.

Imaging protocol: MRI examinations were performed on a 3.0T whole body scanner (HDx, GE Healthcare, Waukesha, WI) using an 8-channel cardiac array coil and a dielectric pad. High resolution axial T2W FRFSE in axial, coronal and sagittal planes were used to evaluate the extent of the disease and confirm the position of the marker lesions. T_1 mapping was performed using a modified 3D IR-FGRE sequence with multiple inversion times. The dynamic sequence consisted of an axial 3D fast spoiled gradient echo (TR/TE = 2.9/1.3 ms, FA = 18°, FOV = 40×30 cm, matrix 176×132, 20 slices (interpolated to 5 mm thickness), 0.75 NEX, ASSET factor 2) for a total of 7 minutes with a temporal resolution of 1.6 sec. In some larger patients the PE FOV and matrix were increased leading to a slightly reduced temporal resolution. A bolus injection of Gadobutrol (Gadovist, Schering AG) was given (dose 0.1 mmol/kg at 4 ml/s) followed by a 25 ml saline flush.

DCE-MRI analysis: Areas suspicious for presence of tumour were outlined in the 16 patients by an experienced radiologist on the dynamic images using the T2W FRFSE images for guidance. Pharmacokinetic analysis of the DCE-MRI images was carried out using custom software written in Matlab (Mathworks, MA, USA). The [Gd] data were fitted with an extended Kety model (4) to allow investigation of the volume transfer constant (K^{trans}), the rate constant (k_{ep}), and the extracellular-extravascular tissue volume fraction (v_e), as well as the semi-quantitative measure integrated area under the [Gd] curve to 90 seconds (IAUGC90). The modelled arterial input function was based on data from Fritz-Hansen (5), concatenated with the Weinmann curve (6), with the arrival time varied to give the best fit. The Wilcoxon signed rank test was used for statistical analysis of pre and post AD therapy comparisons.

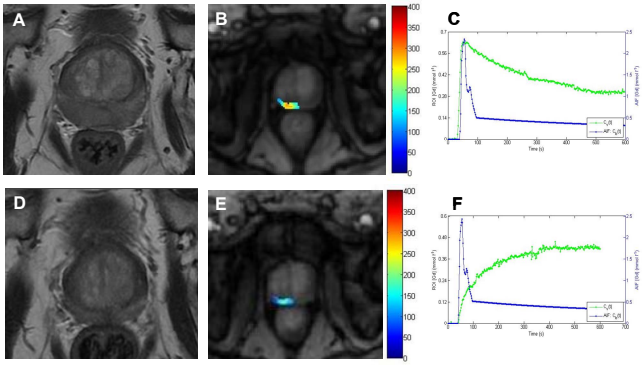

Figure 1: Baseline (a, b, c), and post-AD images (d, e, f). T2W (a, d); DCE-MRI K^{trans} maps (b, e); IAUGC curves (c, f) showing reduction in tumour wash-in (green) after treatment; arterial input in blue.

Results

DCE-MRI data were obtained from 16 patients before and 12 patients after AD therapy (2 patients were withdrawn as biopsy subsequently proved negative, 1 declined a second MRI study, and 1 failed for technical reasons). In total, biopsy identified 20 separate foci of prostate cancer in the 12 patients. Due to the often diffuse nature of tumours identified in the patient population studied, only 5 patients had sufficiently disease-free ('normal') areas of prostate available for comparison. Figure 1 shows example T2 images, K^{trans} maps and uptake curves before and after AD treatment. The k_{ep} value was found to decrease in all 20 areas of biopsy proven prostate cancer following 3 months of AD treatment; K^{trans} reduced in 19/20 cases, v_e in 19/20, and IAUGC-90 in 17/20. Overall, reductions in each quantitative and semi-quantitative parameter measured were all found to be significant, whereas there was no significant difference for any of these parameters derived from 'normal' tissue areas before and after AD therapy (Table 1).

Parameter	Tissue	N	Pre-AD Tx	Post-AD Tx	Change	p-value
K^{trans}	Tumour	12	0.260±0.101	0.133±0.042	-0.127±0.092	**0.002**
	Normal	5	0.124±0.110	0.080 ± 0.018	-0.044±0.122	0.892
k_{ep}	Tumour	12	0.436±0.125	0.204±0.058	-0.232±0.122	**0.002**
	Normal	5	0.321±0.200	0.136 ± 0.022	-0.185±0.201	0.08
v_e	Tumour	12	0.062±0.030	0.012±0.011	-0.049±0.038	**0.003**
	Normal	5	0.014±0.065	0.005 ± 0.005	-0.010±0.011	0.138
IAUGC-90	Tumour	12	36.00±13.36	17.50±5.47	-18.48±13.54	**0.002**
	Normal	5	15.00±10.55	10.20± 2.31	-4.78±12.55	0.5

Table 1: DCE parameters before and after AD therapy (mean ± SD)

Discussion & Conclusions

To our knowledge, this is the first study to assess changes in DCE-MRI parameters following AD therapy in patients with advanced prostate cancer. Our initial results in a small population demonstrate significant reductions in all quantitative and semi-quantitative parameters measured. These results are encouraging and suggest that DCE-MRI has the potential to monitor response to AD therapy and thus offers the potential to select out patients with AD resistance at early time-points, and in such cases allow the opportunity for other treatment options to be explored. Further work in this ongoing study will include correlation with biochemical response (PSA level) and genomic data from pre- and post-treatment biopsies.

References

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