Advanced cervix cancer: Can simple DCE-MRI derived parameters predict treatment response?

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Introduction

Cancer of the cervix is the second most common female malignancy worldwide and its epidemiology is changing, with patients presenting at an earlier age with more advanced stage disease. Radiotherapy is the treatment of choice for locally advanced cervix cancer, with concurrent chemotherapy significantly improving survival, although such treatment has potentially serious side effects that are dose related. Even after careful stratification using standard staging and clinical parameters there is a large unpredictable variation in treatment response. An early predictor of response would allow individualisation of treatment avoiding "over" treatment in good responders and inappropriate treatment in non or poor responders. DCE-MRI is a non-invasive MR technique that can be implemented easily on most commercial whole body MRI systems. Parameters that can be estimated from DCE-MRI techniques include tumour vascularity and permeability which are likely to influence the sensitivity of a tumour to treatment [1,2,3]. At our institution a study in patients with advanced cancer of the cervix is underway to correlate DCE-MRI measurements with histopathological parameters and tumour molecular profiles in order to identify markers that might be used to predict treatment response. In this preliminary study of the initial cases the correlation between the DCE-MRI measurements and the volumetric tumour regression rate during treatment is investigated.

Materials / Methods

This pilot study recruited patients with locally advanced cervix cancer (FIGO stage Ib2-IVa) being treated with concurrent radiotherapy and weekly cisplatin: it was approved by the local research ethics committee and informed consent was taken from each patient. Examinations were performed on a 1.5T whole body MRI (Excite, GEHT, Milwaukee) with an 8-channel cardiac array. DCE-MRI examinations were conducted at three time points: prior to the start of external beam radiotherapy (EBRT), and after 2 and 5 weeks of treatment. Each examination included pre-contrast, high spatial resolution FRFSE sequences for optimal tumour localisation and delineation using T2 axial and sagittal, and T1 axial scans. A pre-contrast baseline T1 image was obtained using a multiple flip angle spoiled gradient echo technique [4]. The dynamic sequence consisted of T1w fast spoiled gradient echo (TR/TE = 4.8/1.5 ms, FA = 18°, bandwidth = 31 kHz, FOV = 24 cm) of 4 contiguous sagittal sections, section thickness 10 mm and positioned to maximally sample the tumour. The T1-weighted sequence is repeated every 3 seconds for a total of 180 seconds. A bolus of 0.1mmol/kg Gd-DTPA is machine-injected at 9mls/s 30 seconds after the start of imaging, followed by a 25ml flush of normal saline at the same rate. Tumour volumes were obtained by an experienced radiologist outlining the tumour on sagittal T2w images, calculating the in-plane area and multiplying by the slice thickness. The DCE-MRI parameters were obtained using Cinetools software (GE-HT, version 3.11.4). These consisted of the relative signal intensity (rSI), maximum slope for the signal intensity-time curve (Slope), transfer constant between the vascular space and extracellular compartments (K_{trans}) and the quantification of the low enhancement regions (10th percentile rSI). K_{trans} was calculated using a model arterial input function and the T1 baseline map [5]. The correlation between the DCE-MRI parameters and their temporal changes with the tumour regression rate was investigated using Spearman's correlation coefficient: statistical analyses were performed using SPSS (version 12.0.1). Full histological characterisation of the tumours will be available in the future.

Results

A total of 18 examinations were carried out on 6 patients. The initial tumour volume ranged from 11.5 cm^3 to 197 cm^3 (mean 79 cm^3, s.d. 66 cm^3). The percentage volume regression ranged from 50-85% (mean 68%, s.d. 13%). The percentage volume regression showed a positive correlation with with rSI of the first examination ($\kappa = 0.95$, $p = 0.004$), the slope of the uptake at the first examination ($\kappa = 0.87$, $p = 0.02$), and the maximum slope of the uptake ($\kappa = 0.91$, $p = 0.04$). While there was a correlation between the K_{trans} measured at the first examination and the percentage volume regression this failed to reach significance with this number of patients ($\kappa = 0.70$, $p = 0.12$). There was no correlation between the initial tumour volume and any of the kinetic parameters measured at the first examination. While there were strong correlations between the rSI, Slope and K_{trans} of the second examination and the % volume regression (κ = 0.76,0.77,0.81 respectively), these failed to reach significance with this number of patients (p = 0.08, 0.07 and 0.06 respectively). Likewise the 10th percentile of rSI at the second exam is correlated with the regression but not significantly ($\kappa = 0.79$, $p = 0.06$). Despite the non-linear relationship between signal intensity and gadolinium concentration on which the semi-quantitative parameters (rSI, slope) are based, they appear to be useful measures of tumour perfusion.

Table 1: Selected DCE-MRI estimated parameters from the first examination (pre-radiation therapy) and the tumour volumes (estimated from the T2w imaging) from all three examinations.

Patient	rSI (exam 1)	Slope (exam 1)	K_{trans} (x 10^{-4}) (exam 1)	Initial volume (cm3)	Final volume (cm3)	% Volume regression (-)
1	1.63	3.17	3.56	37.2	8.83	76
2	1.76	3.91	7.33	44.6	6.91	85
3	1.82	2.62	12.2	83.1	19.4	77
4	1.23	1.72	3.32	11.5	4.92	57
5	1.02	1.94	1.13	197	98.5	50
6	1.5	1.62	2.27	99	36.7	63

Conclusions :

The simple DCE-MRI parameters derived in this study of advanced cancer of the cervix appear independent of the initial tumour volume. Radiation response appears to be related to the relative signal intensity, which we speculate is an indication of the blood supply and oxygenation status of the tumour. This study provides preliminary evidence that DCE-MRI parameters measured before treatment may predict the extent of tumour regression. Larger patient numbers and full histological characterization of the tumours will allow further evaluation of the data, including any relationship between the heterogeneity of gadolinium uptake and its significance for treatment outcome.

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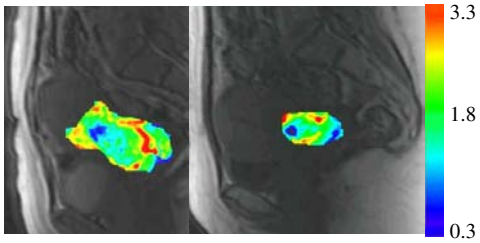

Figure 1: The rSI of the tumor (outlined originally on a matching T2w image) mapped onto one of the perfusion images from the first and third study in one of the patients. The tumor heterogeneity and volume regression are demonstrated.

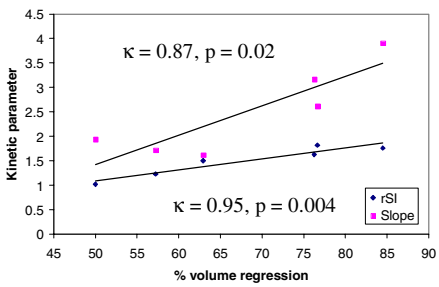

Figure 2: Correlations between the rSI and slope at the first examination and the % volume regression

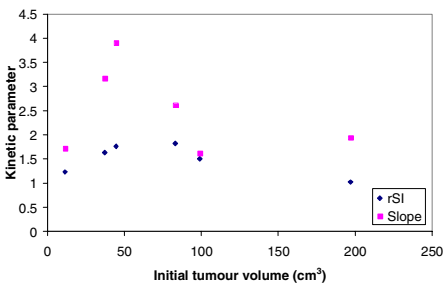

Figure 3: The rSI and slope at the first examination plotted against the initial tumour volume. There is no significant correlation