DCE and DWI functional parameters as indicators of response to radical chemoradiation in head and neck cancer

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Introduction

Dynamic Contrast-Enhanced (DCE) and Diffusion-Weighted (DWI) MRI have proved to be useful in the diagnosis and staging of head and neck carcinoma [1,2]. Head and neck primary lesions and lymph nodes are known to be heterogeneous; both DWI and DCE parametric maps show spatial variations within large lesions. In this work we investigate longitudinal variations of functional MRI parameters during the course of treatment in a cohort of patients with histologically proven head and neck carcinoma undergoing radical chemoradiotherapy. We evaluate the use of functional MRI parameters (Apparent Diffusion Coefficient (ADC) and Pharmaco-kinetic (PK) parameters) for treatment follow up of primary tumours (TU) and lymph nodes (LN), and their predictive value.

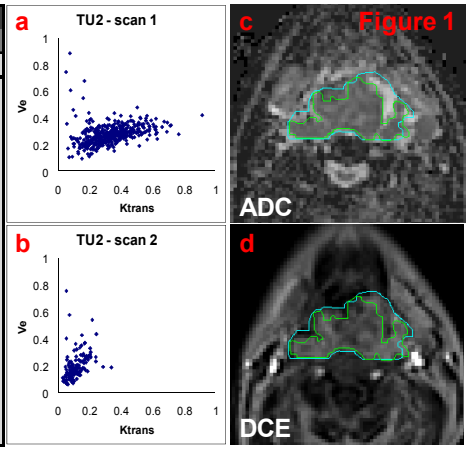
Materials and Methods

Clinical Examinations: Nine subjects were scanned following written consent - as approved by the Local Ethics Committee - at the following time points: baseline, following two cycles of induction chemotherapy (Cisplatin and 5-fluorouracil), after 40 Gy of chemoradiation, three and six months post-treatment. The MRI protocol at 1.5T includes: T2-Weighted Imaging, DCE (following gadolinium injection (0.2 mg/kg), 2x2x5 mm voxel, 1.5 s temporal resolution) and DWI (b = 0, 100, 500, 1000 s/mm^2, TE = 91 ms, TR = 2000 ms, 2x2x5 mm voxel, SPAIR used for fat suppression), aligned over the same volume.

Data Analysis: The slice with largest cross-section was identified in all primary lesions and malignant lymph nodes (> 1.5 cm in short axis diameter) by expert radiologists, and Regions Of Interest (ROIs) were drawn around the tumour and/or lymph node. ROI-DCE was drawn on DCE images, with reference to anatomical images, to encompass the lesion or lymph node. The following parameters were computed pixel-wise: the transfer constant (Ktrans) and the volume of extravascular extracellular space per unit volume of tissue (Ve) from PK modeling, and the initial (60s) area under the gadolinium curve (IAUGC60). In PK modeling we used a population-based Arterial Input Function described with a cosine model [3]. Similarly, ROI-DWI was drawn on the highest b-value (b = 1000 s/mm^2) DW image to encompass the high intensity portion of the tumour or lymph node, interpreted as an area of restricted diffusion. ADC was calculated pixel-wise using a mono-exponential model. The tumour and lymph node ROIs were then analyzed separately. Here we report an analysis of data sets for the first two time-points of the study: baseline (scan 1) and following two cycles of chemotherapy (scan 2), providing preliminary information on response to chemotherapy. Responders are preliminarily defined using DCE data as patients where the percentage of enhancing pixels in the ROI reduced by more than 10%.

Table 1

		ROI-DWI				ROI-DCE							
		scan 1		scan 2		scan 1				scan 2			
	Responder	*area*	*ADC*	*area*	*ADC*	*area*	*Ktrans*	*Ve*	*IAUG60*	*area*	*Ktrans*	*Ve*	*IAUG60*
TU1	YES	56	1.055	37	1.192	54	0.269	0.327	23.96	0	-	-	-
TU2	YES	342	0.924	48	1.325	462	0.337	0.277	26.06	155	0.117	0.197	8.64
TU3	NO	128	0.816	108	1.611	233	0.126	0.229	12.85	159	0.145	0.243	12.33
TU4	NO	197	0.651	17	1.096	212	0.270	0.320	23.96	115	0.331	0.394	27.67
TU5	NO	OV	OV	OV	OV	102	0.304	0.273	24.46	35	0.178	0.203	11.56
LN1	YES	41	0.678	38	0.889	54	0.382	0.397	22.79	27	0.087	0.318	4.50
LN2	YES	42	0.942	22	1.202	34	0.273	0.284	23.69	29	0.204	0.254	15.12
LN3	YES	47	0.649	22	1.113	37	0.396	0.301	30.39	17	0.174	0.187	6.74
LN4	YES	49	1.104	35	1.034	50	0.171	0.204	11.19	32	0.119	0.180	5.95
LN5	YES	63	0.944	14	1.303	68	0.323	0.224	21.91	20	0.162	0.240	13.75
LN6	YES	71	1.021	14	1.081	26	0.347	0.412	29.02	14	0.236	0.262	14.31
LN7	YES	73	1.134	62	0.924	90	0.181	0.242	13.81	53	0.126	0.235	8.82
LN8	YES	OV	OV	OV	OV	31	0.274	0.373	26.51	9	0.169	0.197	9.09
LN9	NO	37	0.827	34	0.872	31	0.238	0.316	21.92	37	0.287	0.229	20.12
LN10	NO	39	0.957	23	0.752	27	0.224	0.163	14.80	13	0.258	0.204	18.26
LN11	NO	170	1.025	93	0.899	187	0.174	0.155	8.54	106	0.118	0.172	8.87



Figures. *Table 1:* Functional parameters at scan 1 and 2 for primary tumours (TU#) and lymph nodes (LN#). Units: area (pixels), ADC is intended × 10^{-3} (mm^2/s), Ktrans (min^{-1}), Ve, IAUG60 (mmol·s). OV = out of volume. *Figure 1 - a* and *b:* pixel-wise correlation "Ve versus Ktrans" at scan 1 and 2 for TU2. *c:* ADC map and *d:* most enhanced frame from DCE, for TU2 at scan 1, with ROI-DWI (green) and ROI-DCE (blue) overlapped.

Results

In total 16 ROI (5 TU and 11 LN) were considered in this study (Table 1). In 14 cases (4 TU and 10 LN) it was possible to obtain a set of paired ROIs (ROI-DCE and ROI-DWI) contoured on DWI and DCE images independently. In one subject (TU5 + LN8) ROI-DWI could not be contoured due to a misalignment of the volume. The absence of an enhancing structure corresponding to TU1 on DCE at scan 2 was interpreted as a response, but at the same time point it was possible to contour a ROI on DWI.

Primary tumours: For large lesions ROI-DWI is always smaller than ROI-DCE and generally contained within it, suggesting that the area of enhancement extend further than the core of restricted diffusion. All TU were found to reduce in size after chemotherapy, but only 2 of them are classified as responders by the criterion used. In Figure 1a and b the response is characterized by a significant reduction in Ktrans and Ve - the two graphs show the pattern of response, for the region (ROI-DCE, blue) shown in Figure 1c and d. ADC at baseline is noticeably lower for non-responders, but increases at scan 2 for all TU, and therefore does not characterize our preliminary definition of response.

Lymph nodes: There is no evidence of a difference in size between ROI-DCE and ROI-DWI associable with a difference in characteristics of the tissue. This might be in part due to the smaller size of the structures. ADC values at baseline and changes in ADC after the first two cycles of chemotherapy are not associated with response as preliminarily defined above.

Discussion and Conclusions

In most cases the main outcome of the first two cycles of chemotherapy appears to be a significant reduction in size both primary tumour and nodal volumes. Considerably lower Ktrans, Ve and IAUG60 are found at scan 2 for responders. In general, we cannot find evidence of ADC reflecting response as defined here, but for TU low ADC at baseline might suggest a predisposition to non-response. Functional MRI has provided useful information on treatment response at an early time point, and merits further investigation as an additional tool in patient management. These MR functional parameters will be assessed at the subsequent time-points defined in the study protocol along with clinical outcomes to further investigate their value in predicting response to treatment.

Acknowledgement: CRUK and EPSRC Cancer Imaging Centre in association with the MRC and Department of Health (England) grant C1060/A10334, also NHS funding to the NIHR Biomedical Research Centre.

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