Comparison of DCE-MRI and DCE-CT in bladder cancer

J. H. Naish[1], D. M. McGrath[2], L. J. Baines[1], K. Passera[3], C. Roberts[1], S. Cheung[1], M. B. Taylor[4], J. P. Logue[4], D. L. Buckley[1], J. Tessier[5], H. Young[5], J. C. Waterton[1,5], and G. J. Parker[1]

[1]Imaging Science and Biomedical Engineering, School of Cancer and Imaging Sciences, University of Manchester, Manchester, United Kingdom, [2]Radiation Medicine Program, Princess Margaret Hospital, Toronto, Ontario, Canada, [3]Dipartimento di Ingegneria Biomedica, Politecnico di Milano, Milan, Italy, [4]Christie Hospital, Manchester, United Kingdom, [5]AstraZeneca, Macclesfield, Cheshire, United Kingdom

INTRODUCTION • DCE-MRI biomarkers are used increasingly in cancer clinical trials to monitor the effects of anti-angiogenic or vascular targeting agents [1]. However the quantitative physiologic accuracy of derived parameters is difficult to prove. DCE-CT provides independent measurement of closely related biomarkers and in addition while MRI does not use ionising radiation, CT is more widely available, cheaper, has higher resolution, is less confounded by motion artefact and is more robustly modelled because of the direct relationship between contrast agent concentration and signal intensity. To date there have been very few studies directly comparing the biomarkers obtained using DCE-MRI and DCE-CT [2,3]. Van den Berg *et al* [2] found good agreement between DCE-MRI and DCE-CT biomarkers in the prostate by using protocols closely matched in temporal and spatial resolution although this inevitably compromises one or both acquisition protocols. In this study we sought to compare DCE-MRI and DCE-CT using protocols typical for each modality and modelled using a standard DCE-MRI approach.

METHODS • Ten patients with confirmed diagnosis of primary bladder cancer (T2-T4) were recruited following local research ethics approval and patient informed consent. Patients were scanned once using DCE-CT then once using DCE-MRI within a one week period. DCE-CT was performed using a GE Lightspeed scanner. Contrast agent (Omnipaque 300, iohexol, GE Healthcare) was administered as a standard bolus at a rate of 5 ml/s, 5s prior to the start of imaging. Images were acquired at a temporal resolution of 1s for a 60s period followed by a 1s scan every 30s for a further 4min (5 min total scan time) and reconstructed to a 512x512x4 matrix with slice thickness 5mm. DCE-MRI was performed at 1.5T using a Philips Intera system using 3D T_1-weighted spoiled gradient echo axial acquisitions with temporal resolution 4.9s, TR=4ms, TE=0.8ms, 30° flip angle, matrix=128x128x25, slice thickness 4mm. Tissue T_1 was determined at baseline using the variable flip angle method with flip angles 2°, 10° and 20° (5 averages each, parameters as for dynamic scans). Contrast agent (0.1 mmol/kg Omniscan, gadodiamide, GE Healthcare) was administered after the 6th image using a power injector at a rate of 2 ml/s. Contrast agent concentration over time was calculated from the dynamic image set using the baseline T_1 measurement and the known relaxivity of gadodiamide. Anatomical scans were also performed for tumour ROI definition. For the DCE-CT data, the contrast agent concentration is directly proportional to the change in signal intensity. Baseline signal intensity was calculated as the average of the images prior to contrast agent being observed in the iliac arteries. An extended version of the Kety model [4] was fitted to both sets of data on a voxel-by-voxel basis to extract values for the volume transfer coefficient K^{trans}, the blood plasma volume fraction v_p, the extracellular extravascular space fraction v_e and an additional parameter ω to account for the time delay between the measured arterial input function (AIF) and the actual input function at the voxel of interest. The AIF was determined for the DCE-MRI data set using an automated extraction technique [4], and for the DCE-CT a manual ROI was placed in the iliac artery. The tumour ROI was manually delineated by an experienced radiographer using anatomical scans for the MRI data and the dynamic scans for the CT data. Median values for each of the parameter values were calculated across the tumour ROIs and were compared using Bland Altman plots. A disadvantage of DCE-CT is that due to the limited coverage, tumours are likely to extend beyond the CT imaging volume leading to errors in serial studies due to repositioning. In order to investigate the effect of sub-sampling and to compare corresponding regions, first the affine registration between the MR and CT data that maximised the normalised mutual information was found using routines from the ITK toolkit (Ixico Ltd., UK). The CT volume was then transformed into the MR space and the region intersecting with the MR ROI found (see figure 1). Median parameter values were calculated across this sub-region and compared with the CT median parameter values.

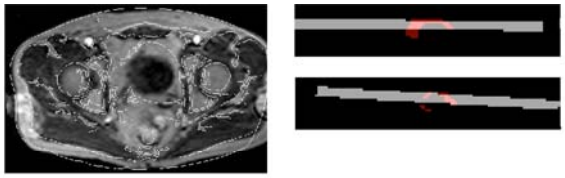

Figure 1: CT edges (Canny edge detector) overlaid onto MR data post-registration. The panels on the right are a visualization in the sagittal and coronal planes of the CT volume (gray) transformed into the MR volume (black) and intersecting the MR tumour ROI (red)

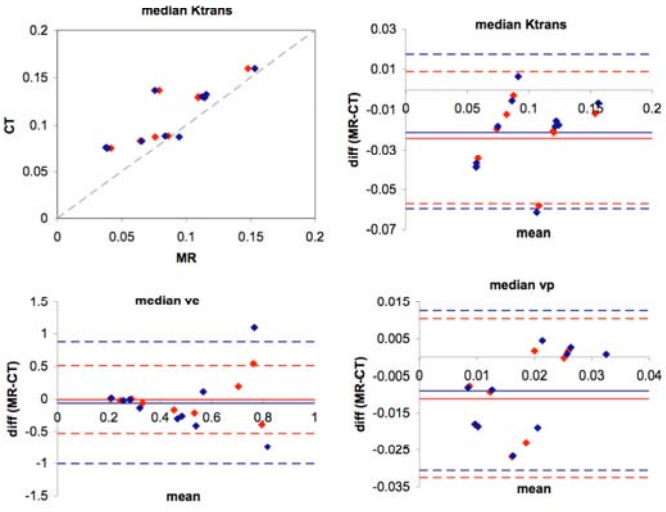

Figure 2: Median parameter values and Bland Altman plots showing the mean difference (solid lines) and limits of agreement (dashed lines) for the whole tumour ROIs (blue) and the matched regions (red)

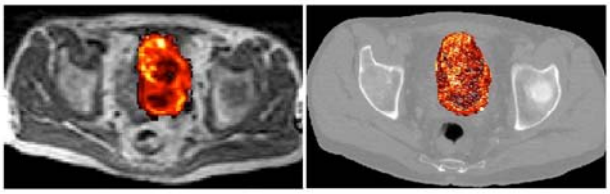

Figure 3: Example MR and CT K^{trans} maps (scale:0-0.5) transformed to CT space

RESULTS • Median values for K^{trans} showed good quantitative agreement between the modalities across a wide range of values (plotted in figure 2 in units min^{-1}). This is reflected in the Bland Altman plot and the calculated CoV (100% x within subject sd from ANOVA s_w/ mean difference) of 21%. The limits of agreement are improved only marginally by sub-sampling the MR ROI. The Bland Altman plot for v_e suggests that the difference scales with the mean such that the limits of agreement may be overestimated for small v_e in the data domain. Log transformation of the data results in a CoV ($\exp(s_w)$-1) of 15%. The limits of agreement are large for v_p and the corresponding CoV is 69% which is consistent with typically poor reproducibility of this parameter in DCE-MRI studies. Both K^{trans} and v_p are systematically lower in the DCE-MRI analysis compared to the DCE-CT (P=0.008 and P=0.014 respectively) while v_e shows no measurable bias (P=0.68).

DISCUSSION • The agreement between DCE-MRI and DCE-CT surpassed that often achieved in clinical trials for repeat DCE-MRI studies. This may be due to the particular tumour type investigated in this study as compared with the range of abdominal and pelvic lesions encountered in a phase I trial setting. Bladder tumours tend to be homogeneous and the pelvic location reduces the impact of physiological motion. To fully ascertain the utility of DCE-CT potentially alongside DCE-MRI in multi-centre trials, further studies in a wider range of tumour types and location are required.

DCE-MRI was observed to systematically underestimate both K^{trans} and v_p relative to DCE-CT. This may be due to trans-endothelial water exchange effects present in MRI but not in CT or may be a result of the differences in the contrast agent or acquisition protocols (particularly the temporal resolution over the first pass peak) and further work is underway to investigate this.

REFERENCES • [1] Jackson A *et al*, Clin Cancer Res. 2007; 13, 3449-59; [2] Van den Berg *et al*, Proc ISMRM 2007, p792; [3] Yang C *et al*, Proc ISMRM 2007, p974; [4] Parker GJM *et al*, Magn. Reson. Med. 2006; 56, 993.