Assessing the effects of water exchange on quantitative dynamic contrast enhanced MRI (DCE-MRI) by comparison with DCE-CT

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Introduction Dynamic contrast-enhanced MRI (DCE-MRI) is a valuable tool for the quantitative assessment of tumour microvascular function by tracer kinetic analysis. However, the tracer is measured indirectly via its effect on local water molecules and therefore the rate of water exchange between tissue compartments can have a significant impact upon the resultant parameters [1]. Quantifying water exchange is challenging, but one option to assess the magnitude of its effect is to reference DCE-MRI measurements to those made using DCE-CT. DCE-CT is unaffected by water exchange, but the technique and tracer size are very similar to those used in MRI. In this study, data were acquired using both techniques in the same patients and the results of tracer kinetic analysis compared.

Methods Ten male patients aged between 53 and 80 years old (mean, 68 years) with primary bladder cancer (stage T2 to T4) underwent DCE-CT followed by DCE-MRI within 1 week. The homogenous nature of these tumours minimizes the impact of a difference in CT/MR volume coverage. DCE-CT was performed on a GE Lightspeed Plus scanner at 1 s temporal resolution for the first 60 s, followed by scans every 30 s for a further 4 min (5 min total scan time). 100 ml of iohexol (Omnipaque 300) was injected immediately before the start of scanning at 5 ml/s. Four 5-mm slices were reconstructed at each time point with a 512 × 512 matrix. DCE-MRI was performed on a Philips Intera 1.5 T system using a 3D T1-weighted RF spoiled gradient echo sequence (flip/TR/TE = 20°/4 ms/0.8 ms, FOV 375 × 375 × 100 mm, matrix 128 × 128 × 25) at 5 s temporal resolution for a duration of 6 minutes. Baseline tissue T1 was determined using acquisitions at flip angles of 2°, 10° and 30° (5 averages). 0.1 mmol/kg Gd-DTPA-BMA (Omniscan) was injected shortly after the start of scanning using a power injector at 2 ml/s.

Analysis Tracer kinetic analysis was performed using a two compartment exchange model (2CXM) [2]. This was fitted directly to the baseline subtracted CT data while 2 variants, representing the limiting effects of water exchange, were fitted to the MR signal-time data. The first assumed water exchange between 3 tissue compartments (cell, interstitium and blood) was at the fast limit (FXL) and the second assumed no water exchange at all (NXL) [3]. Thus 3 estimates (1 CT, 2 MR) of each of the following parameters were obtained: tissue perfusion (F_p), plasma volume (v_p), interstitial volume (v_e) and permeability-surface area product (PS). A t-test was used for hypothesis testing; as there were four independent parameters a Bonferroni correction was applied ($p < 0.0063$ was considered significant).

Results Seven of the datasets were best fit by the 2CXM (3 were unsuitable for water exchange analyses) [4], and only these patients were included in the comparisons. In several cases the DCE-CT data had clear first pass peaks that weren't seen in the DCE-MRI data despite their sharper AIFs (Fig. 1); a symptom of limited vascular-interstitial water exchange. The 2CXM produced excellent fits to each data set (see Fig. 1); however, in 3 CT data sets it wasn't possible to estimate v_e due to slow tracer uptake. NXL estimates of v_p were significantly higher ($p = 0.0002$) and FXL estimates of F_p were lower (but not significantly, $p = 0.017$) than the corresponding CT estimates (Fig. 2). There was no evidence for systematic bias in the remaining parameters.

Discussion DCE-CT provides a useful reference standard for assessing the influence of water exchange on DCE-MRI. The technique and contrast agent employed are similar, but CT images reflect the tracer directly. Our preliminary findings suggest that the effects of water exchange on tracer kinetic analysis are measurable but variable. If we assume, as is conventional, that water is in the FXL then perfusion is likely to be underestimated, while assuming NXL results in blood volume overestimates. Preliminary attempts to estimate water exchange rates using these data alone proved unsuccessful (estimates were so imprecise that no conclusions could be drawn) and highlight the need for additional exchange-sensitive data to quantify the impact of water exchange on MRI data [3].
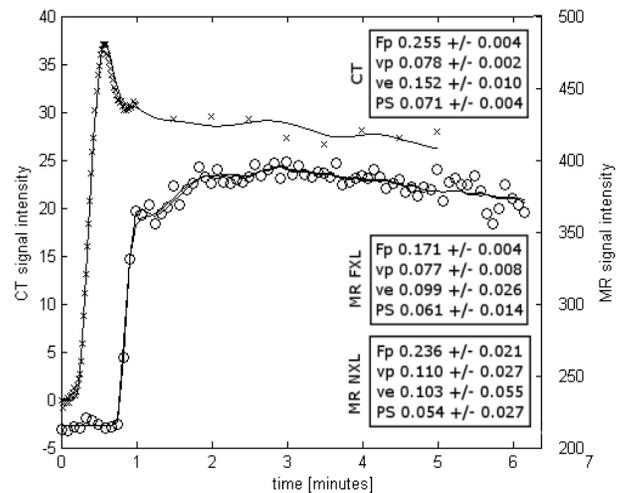
Figure 1. CT (crosses) & MR (circles) DCE data and 2CXM fits (solid lines) from an example tumour. Parameter estimates and their precision (+/- 1 SD) for each fit are shown.
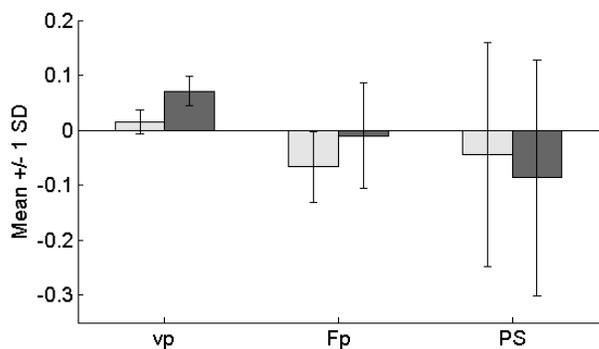

Figure 2 Mean difference between MR and CT parameter estimates. The mean FXL (light) and NXL (dark) results are both shown +/- 1 SD. Units: v_p [unitless], F_p [ml/min/ml], PS [ml/min/ml].

References [1] Donahue et al., *J Magn Reson Imaging.* 1997;**7**:102; [2] Brix et al., *Radiology,* 1999;**210**:269; [3] Buckley et al., *Magn Reson Med.* 2008;**60**:1011; [4] Ewing et al., *J Cereb Blood Flow Metab.* 2006;**26**:310.