## Comparison of Tumor Permeability/Perfusion Measured by Dynamic Contrast Enhanced CT and MRI Analyzed with a Novel Arterial Input Function Estimation Method

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**Introduction**: Unlike dynamic contrast enhanced CT (DCE-CT), accurate DCE-MRI based tumor permeability/perfusion measurements such as the rate constant  $k_{ep}$  are limited by difficulties in obtaining an accurate Arterial Input Function (AIF). We test if DCE-MRI can produce similar  $k_{ep}$  measurements as DCE-CT if a recently developed multiple reference tissue method (MRTM) (1) is used to estimate the AIF in DCE-MRI.

**Materials and Methods**: DCE-CT and DCE-MRI were performed on the same day through the tumors of 20 cervix cancer patients. Two axial slices of CT images were scanned at the rate of 1/s for 120s and then 1/15s for 120s after injection of iohexol 300 (1.5ml/kg, 4ml/s). Six axial slices of MRI images were scanned on a GE 1.5T MR scanner using 3D spoiled gradient echo sequence at the rate of 1/7.5s for 450s after injection of gadodiamide (0.1mmol/kg, 2ml/s). ROIs from the whole tumor, external iliac artery (**EIA**) and gluteus muscle were selected in 37 matched slices. In both CT and MRI data, the AIF was estimated by the MRTM using contrast agent (**CA**) uptake and washout data from muscle and tumor voxels (1). The AIF was also measured directly using the EIA signal; for CT it was calculated by subtracting the EIA signal by the mean baseline signals (2); for MRI, it was converted from the EIA signal using a previously described method (3). Using the Tofts model with the blood plasma term (4),  $k_{ep}$  of iohexol 300 was fit from CT data using the EIA measured AIF, and  $k_{ep}$  of gadodiamide was fit from MRI data using the MRTM estimated AIF.

**Results**: In CT data, the local AIFs determined by the MRTM matched well with the remote AIFs measured from the EIA, but as expected had more dispersion in the first pass peak (Fig. 1a). This suggests that the MRTM works in DCE-CT where the CA concentration can be measured and modeled quite easily. In MRI data, AIFs estimated by the MRTM matched well with the AIFs directly measured from the EIA in the washout phase, but had several-fold higher first pass peaks (Fig. 1b) and gave better fit to the data than the EIA measured AIF (Fig. 1c). It is known that in MRI the AIF in the washout phase directly measured from major arteries can be accurate under careful experiment setup, but often under-estimated during the initial uptake due to high CA concentration. The tumor  $k_{ep}$  maps from CT and MRI data had a similar morphology (Fig.1e-1f). The medians of  $k_{ep}$  in 37 matched tumor ROIs are strongly correlated between CT and MRI (r=0.87), but the MRI-based  $k_{ep}$  is 24% lower on average (Fig. 1d).

**Discussions and Conclusions**: Iohexol 300 and gadodiamide are both low molecular weight CA with similar molecular weight, thus their mainly perfusion weighted  $k_{ep}$  measured on the same day should be similar as well. The good linear relationship between the CT-based and MRI-based  $k_{ep}$  suggest that DCE-CT and DCE-MRI provide similar measurements of permeability / perfusion, likely because the MRTM is able to provide an

accurate estimate of the AIF as suggested by the data above. The systematically lower  $k_{ep}$  in MRI may reflect differences in the CA used, and/or systematic errors in measurements of CA concentration caused, for example, by the deviation from the fast exchange limit in clinical DCE-MRI (5). Importantly, many applications of DCE-MRI are concerned with relative changes in tumor perfusion / permeability. In those cases any absolute differences in kinetic parameters with different imaging modalities and contrast agents is less important than other clinical issues such as the intra-patient variability.





**Fig. 1.** (a-b) compare the AIF estimated by the MRTM (solid lines) with the AIF directly measured from the EIA (dashed lines). (c) shows the fit to the MRI data from muscle (dots) by the MRTM AIF (solid line) is much better than the AIF directly measured from arteries (dashed line) with 4 times less sum of squared errors. (d) shows the strong correlation between the medians of  $k_{ep}$  in 37 matched tumor ROIs measured by CT and by MRI (r=0.87). (e-f) show the  $k_{ep}$  maps measured by CT and MRI in one patient.