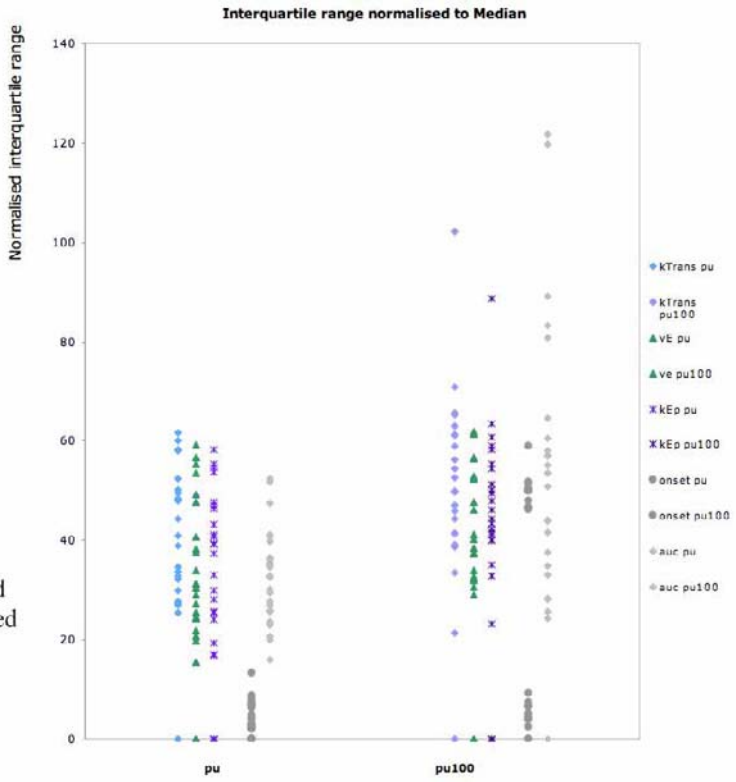
RADIOLOGIST SELECTION OF TUMOR REGIONS OF INTEREST FOR DYNAMIC CONTRAST ENHANCED MRI ANALYSIS: EFFECT ON REPRODUCIBILITY AND SPREAD OF MODELLED AND NON-MODELLED PARAMETERS

A. Tang[1], D. Collins[2], J. d'Arcy[1], M. Leach[1], S. Walker-Samuel[1], T. Wallace[2], N. deSouza[1]

[1]Section of Clinical Magnetic Resonance, Institute of Cancer Research, Sutton, Surrey, United Kingdom, [2]Section of Clinical Magnetic Resonance, Royal Marsden NHS Foundation Trust, Sutton, Surrey, United Kingdom

INTRODUCTION: Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI) is increasingly being applied to monitor treatment response to novel vascular targeted agents. It offers the potential advantages of being quantitative and demonstrating functional changes early before a change in lesion size. However, baseline variability in these studies can be as high 40% (1) which compromises sensitivity. Variability may be due to physiology, tumour heterogeneity within the region of interest (ROI), ROI selection, movement or measurement error. The default position for this type of analysis is to draw the ROI around the entire enhancing area of tumor. This study investigates how the selection of ROIs by a clinical radiologist affects modelled and non-modelled DCE-MRI parameters.

METHODS: 13 out of 23 patients taking part in a Phase I study of an anti-VEGF compound had 2 pre-treatment baseline DCE-MRI studies and were included in the study. DCE-MRI was performed on a 1.5T Vision (Siemens, Erlangen, Germany) using spoiled gradient-recalled echo sequences to acquire proton density (TE 4.7ms, TR 20.1ms, α 3°) and DCE-MR images (TE 4.7 ms, TR 11 ms, α 35°) with a temporal resolution of 7 seconds. Gd-DTPA was injected at 4ml/s at a dose of 0.1mMol/kg (Magnevist(R), Schering Health Care Ltd., Burgess Hill, UK). 3 x 8mm slices were acquired and the one with the largest tumor area was analysed. Post processing was performed on in-house software (MRIW, ICR UK) using the Tofts pharmaco-kinetic model (2) with an assumed arterial input function according to Fritz-Hansen (3). An experienced oncological radiologist drew an ROI around the entire tumor on the morphological images (pu100), and around a visually selected focal homogenously enhancing region of tumor (pu). Voxel-wise model fitting produced modelled (transfer constant (K^{trans}), rate constant (k_{ep}), leakage space (V_e)) and non-modelled (initial area under [Gd] curve at 60s (IAUGC), onset time) parameters. These data were non-parametric and analysed with a Wilcoxon Signed Rank test.



ROI selection significantly reduces spread in both modelled and non-modelled parameters.

Fig. 1

RESULTS: 26 paired studies from 13 patients were analysed. Mean ROI areas (cm^2) and ranges were: pu100=55.6 (1.74-136.4), pu=7.3 (0.75-29.8) For all modelled parameters of radiologist selected ROIs (pu), median values were significantly larger than for pu100 ROIs: K^{trans} 0.47 vs. 0.29, $p<0.001$; k_{ep} 1.25 vs. 0.89, $p<0.001$; V_e 0.47 vs. 0.40, $p=0.001$. A significant difference also was evident for non-modelled parameters: IAUGC 14.95 vs. 9.1, $p<0.001$; Onset Time 46.4s vs. 48.8s, $p=0.004$. Analysis of spread showed that the median-normalised interquartile range (IQR) was significantly lower in radiologist-selected voxels for both modelled and non-modelled parameters (Fig 1). Despite this, ROI selection did not significantly change the reproducibility for any parameter as defined by (difference in parameter values for 2 pre-treatment studies/ mean of parameter values for 2 pre-treatment studies).

DISCUSSION AND CONCLUSION: Radiologist selection can isolate regions within a tumor, which have significantly higher modelled and non-modelled measures of perfusion and permeability with significantly lower variation. However, ROI selection does not improve reproducibility of either modelled or non-modelled DCE-MRI parameters, suggesting that tumor heterogeneity is not the major factor contributing to reproducibility.

References:

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