DCE-MRI Summary and Heterogeneity Statistics Predict Response to Combined Chemo- and anti-VEGF Therapy

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INTRODUCTION Clinical trials of cancer therapies increasingly use dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) and tracer kinetic modelling. Typically, a model is fitted to the contrast agent concentration time series of each tumour voxel; the tumour is then summarised by the average value of each parameter over the tumour voxels. There is limited evidence that DCE-MRI parameters predict response to novel or cytotoxic therapies. While useful, this approach neglects intratumoural structure and spatial heterogeneity—see Fig. 1—that may carry important diagnostic and prognostic information. Recently, methods based on fractal measures have been proposed to capture this aspect of DCE-MRI data. In this abstract we investigate the ability of one of these fractal measures, the correlation dimension (CD), to predict treatment response.

THEROY We now provide a very coarse overview of CD; the interested reader is referred to Ref. 4. Given a 3-D parameter map, CD is computed by normalising the parameter values such that they sum to one. The resulting map is recursively subsampled, creating versions of the original at a number of scales; at each step the sum of squared normalised parameter values is computed. CD is calculated as follows: the log of these sums is plotted against the log of the corresponding scales; CD is equal to the slope of the line of best fit to these points. In this abstract we investigate whether CD and summary statistics of DCE-MRI parameter maps are able to predict response to treatment.

METHOD Ten patients with 26 analysable liver metastases from histologically-confirmed colorectal cancer underwent DCE-MR imaging on a 1.5T Philips Intera system following Research Ethics Committee approval and written informed consent. Scanning was performed twice at baseline to allow repeatability to be assessed. The DCE-MRI time series were modelled using the extended Tofts model, providing estimates of $K_{trans}$, $v_e$, and $v_p$ at each voxel. All DCE-MRI data underwent a thorough quality assurance procedure. The patients received a combination of VEGF antibody and conventional chemotherapy over five two week cycles. The patients were clinically evaluated using RECIST criteria, providing one-dimensional measurements of tumour size at baseline and after treatment. At each baseline visit, median $K_{trans}$, mean $v_p$, median $v_e$ and correlation dimension for all three model parameters were computed. We assessed the repeatability of each biomarker by computing the within-subject coefficient of variation.

Multiple linear regression was performed to investigate the relationship between the baseline DCE-MRI biomarkers and the change in tumour size. This study suggests that median $K_{trans}$ and the spatial heterogeneity of $v_p$ maps, assessed by CD, both appear to predict response to the combined therapy (see Fig. 2). The parameter $v_p$—possibly related to cellular density—should be particularly useful in cancer applications, but median $v_p$ is rarely a useful summary statistic. Our results suggest that this parameter may be of more use in analyses of spatial heterogeneity and that its repeatability is within the range reported for summary DCE-MRI parameters. Tumours with baseline median $K_{trans}$ greater than about 0.25 min$^{-1}$ or with baseline CD computed for $v_p$ greater than about 2.0 may be expected to reduce in size following combined chemo- and anti-VEGF therapy.

REFERENCES