Fractal analysis of parametric images derived from dynamic contrast enhanced MRI data in-vivo

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Introduction: Existing methods of (DCE) MRI data analysis involve the fitting of models to DCE-MRI time-series data. The clinical applicability of such methodologies is now well established [1]. Parameters derived from model fitting are displayed as parametric maps, which show the distribution of parameters on the scale of individual pixels. Radiological judgements, however, are often based on changes over larger regions of interest (ROIs) [1], which neglects the tissue heterogeneity often found in tumours and may lack the sensitivity to detect small changes associated with treatment. Similarly, pixel-based approaches are difficult to characterise due to heterogeneity. We have investigated a methodology involving fractal analysis, which has been shown to characterise tumour vasculature at different length scales [2,3]. From this analysis we were able to determine a number of metrics, which have been used to characterise tumour morphology, using the area under the gadolinium concentration-time curve (AUC [Gd]), derived from DCE-MRI time series data. The AUC [Gd] is used due to its simplicity and its signal to noise advantage making it suitable for pixel-by-pixel analysis. It also avoids difficulties associated with model-fitting to DCE-MRI data, such as fit failures or large, erroneous parameter values.

Methods: DCE-MRI data were acquired from adult patients with brain tumours (1 high-grade glioma, 1 low-grade glioma and 1 meningioma) using a sliding-window dual-spoiled gradient echo sequence [4]. The sequence included the following parameters: TE=7/30ms, TR=31ms and nutation angle 5º for proton density and 30º for T1w. Single slice images were reconstructed with a temporal resolution of 1.1s and a total duration of 165s. Injection of the contrast medium (Magnevist, 0.2 mmol/kg body weight) at 5ml/s started 8s after the initiation of the sequence. Both T1w and T2*w images were provided by the measurement sequence, allowing evaluation of contrast agent kinetics. The T1w time series curves were converted into gadolinium concentrations using the method of Hittmair [5]. For the analysis, an ROI encompassing the whole tumour was identified using the regions of contrast agent uptake in brain tumours. The AUC [Gd] was calculated for each pixel, using a range of images from the mean time of gadolinium arrival within the tumour (defined as t=0) to 30s later (a total of 30 images). Regions of low permeability (and therefore low AUC [Gd] [6]), such as those corresponding to radiologically normal brain tissue or fat, were used as a reference value at which to threshold the AUC [Gd] map. Such regions were assigned a value of 0 and the remaining pixels, with AUC [Gd] values greater than zero, were set to 1 to form a binary two-dimensional cluster. The sandbox algorithm [7] was applied to evaluate the fractal dimension of the cluster. Following analysis involving the linear regression of data derived from the sandbox algorithm, a number of fractal-based metrics were estimated from the cluster: mass, perimeter, correlation distance ξ, fractal dimension d_f and the fractal dimension of the minimum path through the lattice d_{min}. Mass is the number of occupied pixels within the cluster (an individual occupied pixel has mass of 1). The perimeter is a measure of the circumference of the cluster and includes both the external and internal boundaries (i.e. internal regions showing no gadolinium enhancement are included). d_f is a measure of how well the cluster fills its embedding space.

Discussion: Figure 1 shows an example of a cluster used in the fractal analysis, derived from AUC [Gd], data is from a high-grade glioma. The original AUC [Gd] values have been overlaid onto occupied pixels. Table 1 shows examples of values derived from fractal analysis of this and two other clusters. Radiological response of tumours is measured by the RECIST criteria, which is based on changes in the major dimension of the tumour. We propose that metrics such as perimeter and mass derived from fractal analysis will provide additional quantitative measures of tumour prognosis or response. Additional insight into the complex morphology of tumours may be gained from metrics such as d_f, and d_{min}, as these describe statistical properties of the distribution of clusters. Changes in the numbers of pixels showing uptake of Gd are easily characterised. The fractal analysis described above can be applied to any DCE-MRI time series data set and is simply an additional post-processing step for existing DCE-MRI data.

Conclusion: Several new metrics have been obtained from fractal analysis-based analysis of DCE-MRI data. The strategy could lead to a novel morphological assessment of functional data in human tumours. It can also be used as an adjunct to normal radiological response criteria such as RECIST.

Acknowledgements: This work was supported by Cancer Research UK (C1060/A808/G7643)

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	Patient 1	Patient 2	Patient 3
d_f	1.796 ± 0.002	1.878 ± 0.002	1.919 ± 0.002
d_{min}	1.427	1.744	1.748
Perimeter	42.6 ± 0.2 cm	19.0 ± 0.2 cm	17.2 ± 0.2 cm
Mass / Perimeter	2.272	2.652	5.344

Table 1: Example values of metrics derived from the fractal analysis of three tumours.

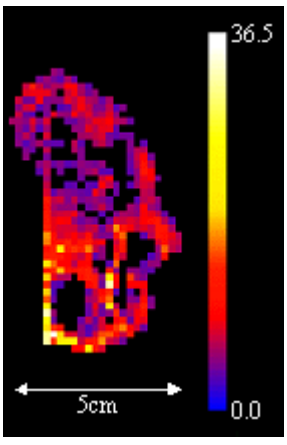

Figure 1: The binary cluster formed from patient 1 with a high-grade glioma. AUC [Gd] values have been overlaid on occupied pixels.