Fractal parameters derived from analysis of DCE-MRI data correlates with response to therapy in rectal carcinoma

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Introduction: It is recognised that MR can probe various physiological parameters in vivo. This is likely to impact on the implementation of personalised treatment. Examples include measures of tissue vascularity such as capillary permeability and blood volume. In the field of oncology, tissue vascularity is a particularly important parameter since it is known to influence features such as an aggressive phenotype, metastatic potential and is currently a focus of novel drug development. Although the MR methodologies available to probe vascularity are rapidly evolving and substantial bodies of data are accumulating, there is currently no optimal method for analysing these complex physiological data. Simple measures such as means and medians are likely to have limited sensitivity to the considerable structural and functional heterogeneity characteristic of tumours. Fractal analysis has been applied to many fields including biology and medicine, exploiting characteristic size invariance. We have applied fractal analysis to functional MR data in order to identify potentially useful clinical associations.

Methods: 15 patients were studied (4 women, 11 men; mean age 65 years, SD 11.2) all with clinically and pathologically verified locally advanced rectal adenocarcinoma. All studies were performed on a 1.5 T Magneton-Vision system (Siemens, Erlangen, Germany) using a four-element pelvic phased array coil. Diagnostic T2 scans were performed prior to and immediately following the end of chemotherapy (8 week course) and chemoradiotherapy (12 week course) in order to assess response. We used a dual-echo gradient-echo FLASH sequence [1] to acquire single slice T1 and T2* data (T1w images: TR/TE/α = 11.5ms/5ms/20°, T2*w images: TR/TE/α = 26.5ms/20ms/20°) through the greatest diameter of a tumour in its axial plane. All functional data reported here pertain to the pre-treatment scan. The temporal resolution of the sequence was one T1w image every 12s and one pair of T2*w images every 12s with a 4s interval between T2*w images. T1w and T2*w data were converted to [Gd] and ΔR2*, respectively. ROIs were defined for each patient corresponding to the tumour area. AUC [Gd](0-90s) and AUC ΔR2*(0-30s) were calculated within the ROI on a pixel-by-pixel basis. The maximum values within the ROIs of the AUC maps were used to create binary masks, such that pixels were assigned a value of 0 below a given threshold value and 1 if above or equal to the threshold value. Threshold levels of 0, 10 and 20% of the maximum AUC values were created, producing three binary masks for each AUC map (see Figure 1). These binary masks and the distributions of AUC values were evaluated using fractal analyses, from which a number of parameters were derived, including the box-counting dimension d_f, relative dispersion dimension D, lattice concentration (the ratio of occupied pixels in the binary mask to total number of pixels in the ROI) and perimeter P (internal and external circumference of the binary mask) [2,3]. Tumour response was assessed on diagnostic T2 images and expressed as the % regression in tumour size after chemotherapy and chemoradiation. The associations between the % regression in tumour size and fractal parameters were determined using Pearson correlation statistics.

Results: The results are summarised in Table 1. A significant positive correlation was found between the parameters d_f and lattice concentration derived from AUC ΔR2*(0-30s) at 20% threshold and response post-chemotherapy. A significant negative correlation was also identified between D from AUC ΔR2*(0-30s) at 10% threshold and response post-chemotherapy. d_f was positively correlated with post-chemoradiotherapy response at 10% and 20% threshold for the AUC ΔR2*(0-30s) data. Lattice concentration also correlated positively with post-chemoradiotherapy response at 20% threshold. No associations were found for any parameters derived from AUC [Gd] data. As AUC ΔR2*(0-30 s) is believed to correspond to relative blood volume, we propose that lattice concentration is a parameter characterizing drug delivery to the tumour. According to this hypothesis, therefore, tumours with a low lattice concentration are poorly perfused with chemotherapeutic agents, resulting in poor therapeutic response

Conclusion: Fractal analysis of DCE-MRI data has provided potentially useful predictive parameters in a clinical study. The method of analysis can be readily applied as an additional post-processing step to suitably acquired DCE-MRI data.

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References: [1] Baustert IC et al., ISMRM 1998:1655 [2] Bunde A., Havlin S., 'Percolation 1 and 2' in Fractals and Disordered Systems, 1991, Springer-Verlag, pp. 51-150 [3] Bassingthwaighte JB, Fractal Physiology, 1994, Oxford University Press.

Parameter (from AUC ΔR2*(0-30s))	Threshold	Regression in tumour size after chemotherapy	Regression in tumour size after chemotherapy and chemoradiation
df	0%	*nc*	p = 0.08, r = 0.46
Lattice concentration		*nc*	*nc*
D		*nc*	*nc*
df	10%	*nc*	*nc*
Lattice concentration		*nc*	*nc*
D		p = 0.06, r = -0.68	*nc*
df	20%	p = 0.01, r = 0.64	p = 0.03, r = 0.56
Lattice concentration		p < 0.01, r = 0.82	p = 0.02, r = 0.60
D		*nc*	*nc*

Table 1: r and p values for each parameter derived from fractal analysis of AUC ΔR2*(0-30s), when correlated against % regression in tumour size following chemotherapy and following all therapies. *nc* signifies no correlation, i.e. r < 0.4 and p > 0.1.

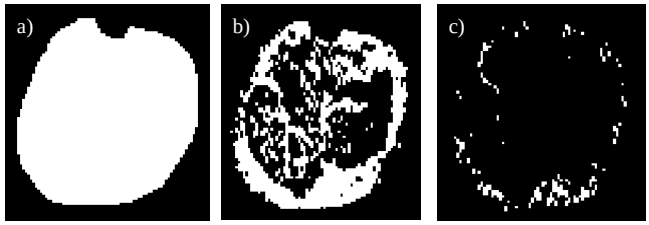

Figure 1: Binary clusters derived from AUC [Gd](0-90), at thresholds of a) 0, b) 10 and c) 20% of the maximum value.

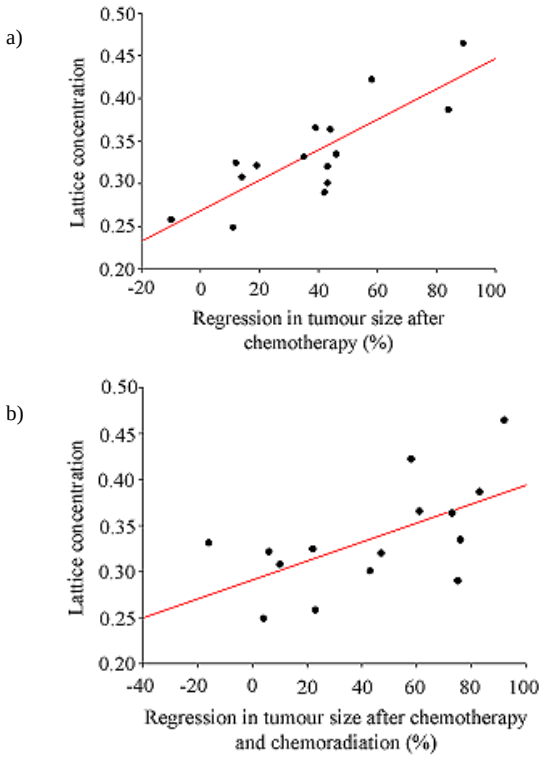

Figure 2: Graphs of a) lattice concentration against regression in tumour size following chemotherapy and b) lattice concentration against regression in tumour size following chemoradiotherapy.