Evaluation of area under curve [Gd] data derived from DCE-MRI time series in brain tumours

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Abstract

Area under the Gd concentration-time curve (a.u.c [Gd]) is used as an alternative to pharmacokinetic model based methods of dynamic contrast-enhanced (DCE) MRI data analysis [1]. DCE-MRI is widely used in the evaluation of response to therapy and the detection of malignant tumours [2]. We have investigated the relationship between data derived from a.u.c [Gd] and two pharmacokinetic model-based methods of DCE evaluation. The DCE-MRI data were obtained in-vivo from malignant tumours in brain. We show that a strong correlation exists between estimates of the extra-cellular extra-vascular space (Ve) derived from the standard Tofts model and the a.u.c [Gd] for specific ranges. We demonstrate there is an improved correlation between a.u.c [Gd] and transfer constants derived from the Tofts model only when arterial Gd concentration is reasonably constant after the initial first pass of Gd.

Introduction

a.u.c [Gd] is desirable for the analysis of T1w DCE-MRI due to its simplicity and signal to noise advantage making it suitable for pixel-by-pixel analysis. The a.u.c method is also reliable and reproducible. It has been argued that it is possible to normalise the a.u.c method to account for differences in cardiac output and variations in bolus delivery using an adjacent radiologically normal tissue a.u.c or using a measure of the arterial concentration [1]. A further advantage is that no kinetic model is required. The a.u.c is thought to relate to the tissue extraction fraction (K_{trans}) based on an analysis of the flow limited Kety equation [1]. We have compared data derived from a.u.c estimates with parameters derived from pharmacokinetic models. The a.u.c [Gd] was evaluated at three time intervals: 0-30s, 0-90s and 50-80s, where t=0 was defined as the mean time at which contrast agent arrived in the tumour (approximately 30s after the start of the sequence). These intervals were chosen with the following rationale: from 0-30s, the first pass of Gd is dominant; at 90s exchange between vascular and extra-cellular compartments has reached near equilibrium, and from 50-80s the concentration in the arteries is reasonably constant. These values are based on the blood kinetics following the bolus, which were obtained from a T2* time series obtained simultaneously, converted to $\Delta R2*$ [3] (figure 1a).

Methods

DCE-MRI data were acquired from patients with brain tumours using a Sliding-Window dual-spoiled gradient echo sequence [3]. The sequence includes the following parameters: TE=7/30ms, TR=31ms, nutation angle 5º for proton density and 30º for T1w. Single slice images were reconstructed, with a temporal resolution of 1.1s and total sequence duration of 165s. Contrast medium (Magnevist) was injected at 5ml/s starting 8s after the start of the sequence. Both T1w and T2*w images are provided by the sequence for the evaluation of contrast agent kinetics. T1w time series curves were converted into [Gd] using the method of Hittmair [4]. The [Gd] time series was then evaluated using the Tofts model and Weinmann [Gd] extraction coefficients [5]. Gamma-variates were fitted to the $\Delta R2*$ data to obtain relative estimates of blood volume and flow [3]. Parametric images were created from the a.u.c [Gd] at different time intervals and from the model parameters derived from fitting the time series data. In order to establish spatial correlation between parameters, the maps were then cross-correlated using the following expression:

$$P_{xy} = \frac{\sum_{k=0}^{N-1}(x_k - \bar{x})(y_k - \bar{y})}{\sqrt{\left[\sum_{k=0}^{N-1}(x_k - \bar{x})^2\right]\left[\sum_{k=0}^{N-1}(y_k - \bar{y})^2\right]}}$$

where x and y are vectors containing parameter values. P_{xy} can take a value between –1 and +1, where –1 indicates strong negative correlation and +1 indicates strong positive correlation; $P_{xy} = 0$ indicates no correlation. x and y were then plotted against one another and a linear regression was performed (figure 1b). The quality of this fit was given by an r^2 parameter. Parameters are considered strongly correlated if $r^2 > 0.64$ or strongly spatially correlated if $|P_{xy}| > 0.64$. The results of the most significant cross-correlations and linear regressions are shown in table 1.

Discussion

Parameters most significantly correlated according to P_{xy} and r^2, were Ve (derived from the Tofts model) and a.u.c. for 0-90s (figure 1b.). All patients show a stronger correlation between K_{trans} and a.u.c. [Gd] (50-80s) than a.u.c. [Gd] (0-30s) or a.u.c. [Gd] (0-90s), even though in some cases r^2 or $P_{xy} < 0.64$. This suggests that K_{trans} only correlates with a.u.c. [Gd] when arterial Gd concentration is reasonably constant. There was no significant correlation found between the a.u.c [Gd] and parameters derived from the fitting of gamma-variates to the T2*w data. Inconsistencies between P_{xy} and r^2 are likely to be due to poor SNR, which introduces scatter into plots of image vectors but does not affect the spatial correlation as significantly.

Conclusion

a.u.c [Gd] (0-30s, 0-90s) correlate well in these examples with Ve derived from the standard Tofts model in brain tumours. K_{trans} is not significantly correlated with either of the initial a.u.c [Gd] (0-30s, 0-90s) intervals. The a.u.c [Gd] (50-80s) has an improved correlation with K_{trans}.

Acknowledgements

References

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a.u.c [Gd] (s)	Patient 1		Patient 2		Patient 3	
	K_{trans}	Ve	K_{trans}	Ve	K_{trans}	Ve
0-30	$P_{xy}= 0.726$ $r^2= 0.527$	$P_{xy}= 0.954$ $r^2= 0.911$	$P_{xy}= 0.187$ $r^2= 0.131$	$P_{xy}= 0.630$ $r^2= 0.397$	$P_{xy}= 0.446$ $r^2= 0..475$	$P_{xy}= 0.816$ $r^2= 0.854$
0-90	$P_{xy}= 0.706$ $r^2= 0.487$	$P_{xy}= 0.975$ $r^2= 0.951$	$P_{xy}= 0.049$ $r^2= 0.046$	$P_{xy}= 0.762$ $r^2= 0.5802$	$P_{xy}= 0.452$ $r^2= 0.424$	$P_{xy}= 0.807$ $r^2= 0.843$
50-80	$P_{xy}= 0.750$ $r^2= 0.528$	$P_{xy}= 0.718$ $r^2= 0.516$	$P_{xy}= 0.486$ $r^2= 0.336$	$P_{xy}= 0.038$ $r^2= 0.001$	$P_{xy}= 0.659$ $r^2= 0.574$	$P_{xy}= -0.031$ $r^2= 0.037$

Table 1: Cross-correlation P_{xy} values and r^2 values for K_{trans} and Ve compared with a.u.c. [Gd] maps for various ranges.
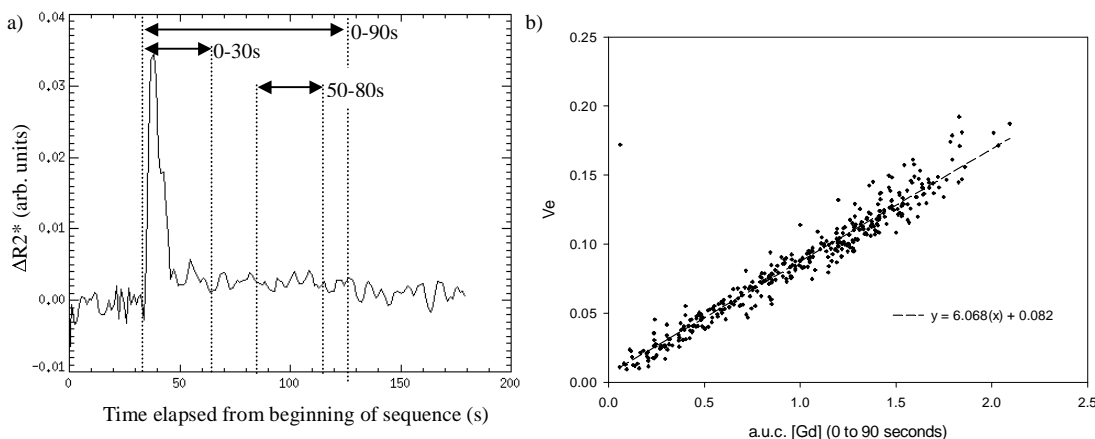

Figure 1: a) Example of $\Delta R2*$ with time. Arrival of Gd is identified by a large peak at ~40 seconds that then drops to a constant value by 30s after arrival. From 50s to 80s after arrival, ΔR_2* is constant, which indicates a constant Gd concentration. b) Relationship between a.u.c. [Gd] (0 to 90 seconds) and Ve for patient 3, with linear regression fit overlaid.