Evaluation of v_e in a Rat Glioma Model with DCE-MRI and Quantitative SPECT

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Introduction

Dynamic contrast enhanced MRI (DCE-MRI) is used to characterize perfusion and extracellular volume in tumors through the tracer kinetic modeling of MRI contrast agents (typically Gd-DTPA). However, the parametric estimates resultant of DCE-MRI may be influenced by several confounding factors, including inter-compartmental water exchange [1]. In contrast to MRI contrast agents, radiotracer imaging with SPECT uses direct measures of tracer activity and is, therefore, insensitive to water dynamics. Here we compare extracellular volume, v_e, in a C6 glioma model in rat brain as measured by DCE-MRI and dual-isotope SPECT.

Methods

Female Sprague-Dawley rats were inoculated with C6 brain tumor cells approximately two weeks prior to imaging. MRI was performed at 9.4T on two prescribed slices, one through the linguofacial artery in the neck and the other through the brain tumor. A T_1 map was recorded using an inversion-recovery snapshot sequence (TR=12s, TI=0.250s-11.0s), and dynamic scans were acquired during and following a 200μL injection of Gd-DTPA (0.05mmol/kg) using a spoiled gradient echo sequence (TR=10ms, FA=15°, NEX=2). Using the vascular input function signal from the artery, the dynamic data from the tumor were analyzed on both an ROI and voxel-by-voxel basis using the Tofts pharmacokinetic model with the addition of a plasma term [2]. When possible, distinction was made between the tumor core and rim.

Upon completion of the DCE-MRI experiment, a dual-isotope SPECT protocol was implemented for radiotracer imaging. The animal was prepared for imaging by undergoing a full nephrectomy procedure to prevent radiotracer washout and to create a state of equilibrium between the vascular and interstitial space. An extracellular agent, ^{111}In-DTPA (~0.5 mCi), was injected first and allowed to equilibrate for approximately 30 minutes before an intravascular tracer, ^{99m}Tc-RBCs (~4.0 mCi), was injected. Images were collected shortly after injection of the second tracer and a blood sample was obtained for use in analysis. The SPECT images were co-registered to the dynamic MR images for data analysis. Assuming the concentration of ^{111}In-DTPA was approximately equal in the vascular and tissue space during imaging, a value for the extracellular-extravascular volume fraction was calculated using the known activities and volumes from the blood sample and tissue ROI.

Results

Fig. 1 shows an example fit to the DCE tumor data as well as the v_e maps for the DCE and SPECT data with corresponding ROIs. The value of v_e from the DCE-MRI analysis, on a voxel-by-voxel basis, overestimated the value of v_e found from the independent SPECT measurement (Table 1). Average values of K^{trans} ranged from 0.03-0.07 min^{-1} with v_p ranging from 0.03-0.09. Incorporation of water exchange in the kinetic modeling is being investigated as a means of evaluating the measure of v_e from DCE-MRI.

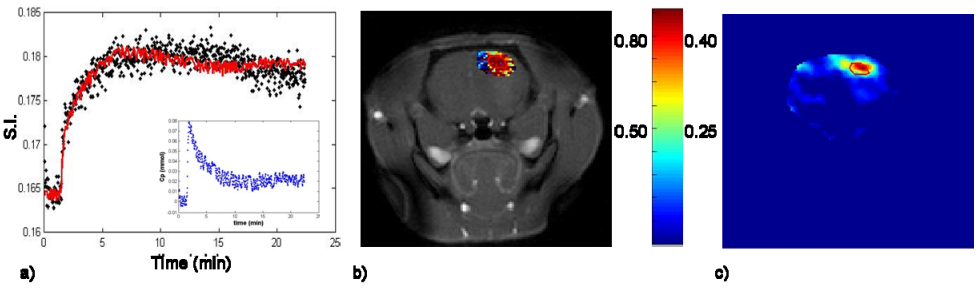

Figure 1. a) DCE time course from tumor ROI (inset: VIF) b) v_e parametric map from DCE-MRI c) Segmented SPECT v_e map.

Table 1. Value of v_e from tumor tissue ROI based on voxel-by-voxel analysis.

Animal #	DCE-MRI	SPECT
1 Rim	0.28±0.09	0.11±0.04
1 Core	0.41±0.09	0.20±0.04
2 Rim	0.69±0.34	0.18±0.07
2 Core	0.96±0.13	0.29±0.09
3 Rim	0.71±0.24	0.25±0.06

Mean ± SD.

Conclusion

The value of v_e in a rat brain tumor model was overestimated by standard DCE analysis methods when compared to a radiotracer method that is insensitive to compartmental exchange. This finding aids in the evaluation of v_e in conventional DCE-MRI analysis and might reveal a need for investigating the inclusion of other NMR and physiological parameters in the kinetic modeling.

References

1. TE Yankeelov et al. Magn Reson Med (2003) 50:1151-1169.
2. PS Tofts. J Magn Reson Imag (1999) 7:91-101.