Correlation Between Quantitative Autoradiography and the Reference Region Model of DCE-MRI

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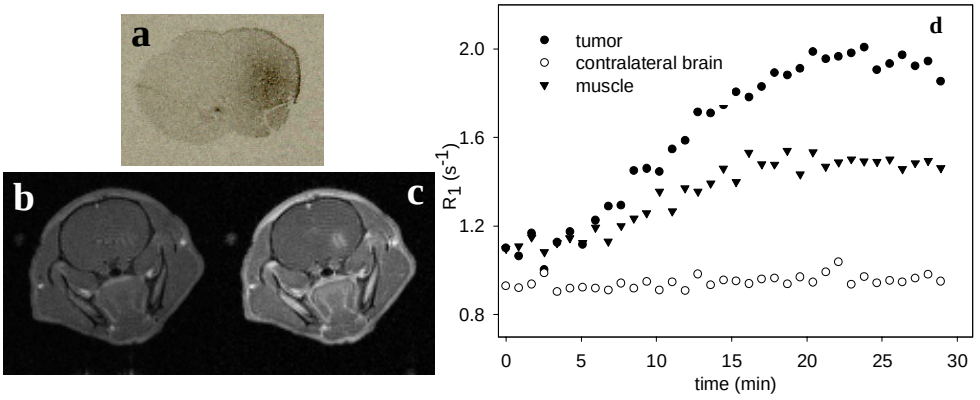
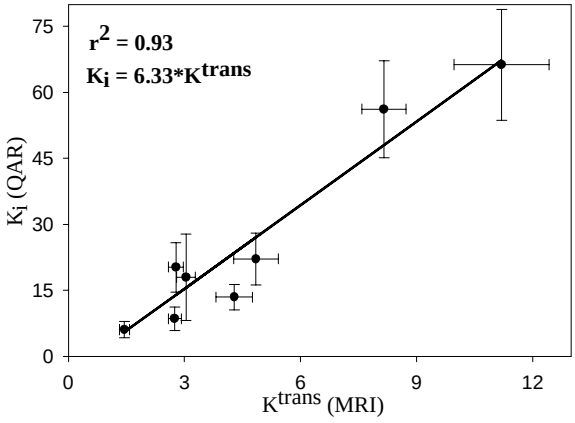
INTRODUCTION Dynamic contrast enhanced MRI (DCE-MRI) may be used to assess tumor perfusion, microvascular vessel wall permeability, and extravascular extracellular volume fraction (1). While there is much interest in the applications of this method to assess tumor growth and treatment response (2), there has been comparatively little correlation of this noninvasive technique with more accepted (i.e., "gold standard") measurements of tumor perfusion. Here we compare the measurement of the transfer constant K_i, as measured by quantitative autoradiography (QAR), to the transfer constant K^{trans}, as measured by DCE-MRI, in a C6 rat glioma model. Both transfer constants measure the initial rate for blood to brain transfer of a tracer.



METHODS Four female Wistar rats had 10^6 C6 glioma cells injected into the basal ganglia. Seven days later they were imaged using a Varian 4.7 T scanner equipped with a 63 mm quadrature birdcage coil one week post injection. A variable flip angle gradient echo approach was employed to produce a R_1 ($\equiv 1/T_1$) map. The DCE-MRI protocol employed a standard T_1-weighted, gradient echo sequence to obtain 35 serial images for each of 8 axial oriented planes in 45 min of imaging. The parameters were: TR = 200 ms, TE = 3.0 ms, flip angle = 30°, FOV = $(30\text{ mm})^2$,acquisition matrix = 128^2, slice thickness = 1.0 mm, and NEX = 2. A bolus of 0.2 mmol/kg Magnevist was delivered within 30 s *via* a tail vein catheter. DCE-MRI data analysis was done via the reference region model as previously described (3); this analysis returns K^{trans} and v_e, the extravascular extracellular volume fraction. QAR with the radiotracer [^{14}C] labeled sucrose was performed as previously described (4). K_i was determined for 35 voxels from the tumor core and for 35 voxels from the tumor periphery on each slice of five contiguous QAR slices. Averaging the results for all five slices determined the overall K_i for the tumor rim and tumor core. This process was repeated for each animal. For the K^{trans} measure, four voxels from the tumor rim and four voxels from the tumor core were selected from the most central imaging slice, corresponding to the region seen in QAR. These two measurements were then compared. The units for K_i and K^{trans} are both mL (blood)/[mL(tissue)·min].



RESULTS **Figure 1** displays typical results from this study: axial views of the tumor from a central slice of mouse 4. Panel a is a QAR image, b is the pre-contrast MR image, c is the ten minute post-contrast MR image, and panel d is a plot of several characteristic MR signal intensity time courses from the tumor core, jaw (masseter) muscle, and contralateral healthy appearing brain. Figure 2 displays the K_i versus K^{trans} scatter plots and the linear regression line. The coefficient coefficient is 0.93 ($P<0.05$), indicating a strong relationship between K_i and K^{trans}. The regression line has a slope of 6.19.

DISCUSSION We have shown that the noninvasive, clinically relevant DCE-MRI metric of tissue vessel perfusion-permeability (as assessed by the reference region model) correlates significantly with the invasive QAR technique. This represents a validation of the reference region model for the analysis of DCE-MRI data in, at least, the C6 glioma tumor model. One obvious limitation, however, of this study is the difficulty in co-registering the histological scale thickness (~10 microns) of the QAR images with that of the MR images (10^3 microns); we are working to address this problem more thoroughly. Another aspect which requires clarification is the slope of the regression line in Figure 2. It is reasonable to expect the smaller molecular weight QAR tracer (MW=342) to have a significantly higher transfer rate than the larger MRI tracer (MW=938), but the difference of a factor of >6 requires further investigation. We are currently increasing the number of animals in this study.

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ACKNOWLEDGEMENTS NCI 1R25 CA92043 and NCI 1P50 098131-01