Comparison of Endothelial Permeability Surface Area Product, ktrans, Derived by Steady-State T1 and First-Pass T2* Methods for Brain Tumors

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Introduction

Endothelial permeability of vessels within brain tumors provides important information about the nature of neovascularization and blood-brain barrier (BBB) integrity [1]. The widely accepted MR imaging method to determine the endothelial permeability surface area product, k^{trans}, utilizes steady-state contrast-enhanced T1-weighted 3D spoiled gradient-recalled acquisition sequence following the intravenous administration of gadopentetate dimeglumine (Gd-DTPA) using analysis methods described by Tofts and Kermode [2]. Although this approach affords high spatial resolution, it requires long scanning times, complex post-processing algorithm, and may over- or underestimate k^{trans} [3,4]. A newer approach for quantifying k^{trans} utilizes T2*-weighted gradient-echo echo-planar images during the first pass of a tracer bolus [5]. In this approach, the dynamic data is converted to tracer concentration values in two compartments acquired during this first pass. By comparison to the conventional method, this newer technique affords higher temporal resolution and broader slice coverage in addition to allowing simultaneous determination of vascular volume. The utility of this first-pass T2* k^{trans} measurement is compared with steady-state T1 values in two types of brain tumors with different degrees of permeability: gliomas and meningiomas.

Methods

Twenty-seven patients with treatment-naive brain tumors who underwent MR imaging prior to resection were included in our study. There were 20 gliomas (10 grade IV, 4 grade III, 5 grade II, and 1 grade I) and 7 meningiomas. MR examinations were performed on a 1.5T unit. Gd-DTPA enhanced (0.1mmole/kg) dynamic MRI permeability sequence was acquired by obtaining T1-weighted axial 3D spoiled gradient-recalled acquisition in the steady state with the following parameters: 6.5/1.24/1 (TR/TE/excitations); flip angle, 30°; matrix, 128x128; section thickness, 3mm; field of view, 26cm; acquisition time, 3 minutes and 48sec. A total of 12 dynamic acquisitions were obtained with a 40 second injection delay. A second injection of Gd-DTPA was performed 30 minutes after the 3D SPGR sequence, and dynamic contrast-enhanced T2*-weighted dynamic MRI perfusion sequence was performed using the following parameters: 2000/54.0/1 (TR/TE/excitations); flip angle, 35°; matrix, 128x128**;** section thickness, 4.5mm with spacing of 0 mm; field of view, 26cm; acquisition time, 1 minute and 18 seconds. A total of 60 dynamic acquisitions were obtained before, during, and after a bolus injection of Gd-DTPA at 4 ml/sec followed by saline flush at the same rate.

Signal intensity values measured over time in regions of interests in blood (typically superior sagittal sinus) and tumor tissue (the enhancing portion of the tumor) were analyzed using MRVision software (The MRVision Co, Menlo Park, CA) on a UNIX Workstation. In nonenhancing tumors, the most solid appearing portion was used for analysis. Uniform sized (5mm diameter) regions of interest (ROIs) within tumors were drawn and saved on the post-contrast 3D SPGR image. Two investigators independently and separately measured k^{trans} from the steady-state T1 using a unidirectional model (assumes flow only from blood into tissue and not in reverse) and the first-pass T2* technique based on the ROIs defined on post-contrast 3D SPGR images. The first-pass T2* algorithm assumed that contrast exists in two interchanging compartments (plasma and extravascular extracellular space) and used an exact expression for the contrast concentration in the tissue [5]. k^{trans} was derived by estimating vascular contrast concentration from normal white matter and fitting it to the expression for the tissue concentration.

Results

All meningiomas (n=7) and grade IV gliomas (n=10) showed conventional contrast enhancement on post-contrast 3D SPGR images. Three of 10 grade I-III gliomas did not demonstrate enhancement. As shown in Figure 1, there was good linear correlation between k^{trans} for gliomas calculated using the steady-state T1 and the first-pass T2* techniques (R^2=0.91). The first-pass T2* k^{trans} values were consistently higher than those calculated using the steady-state T1 method. Figure 2 shows the lack of a linear correlation for k^{trans} in meningiomas calculated using the steady-state T1 and the first-pass T2* methods.

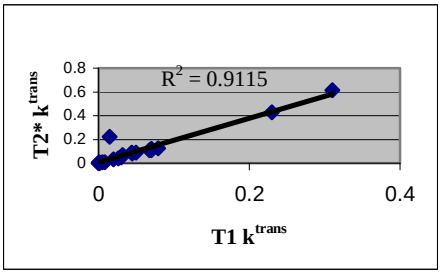

Figure 1. k^{trans} for gliomas

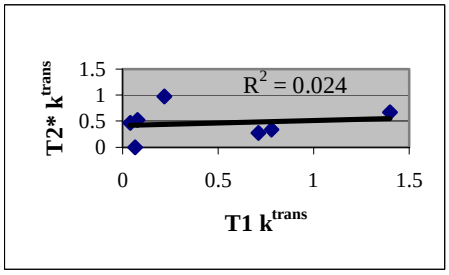

Figure 2. k^{trans} for meningiomas

Discussion

The goals of our study were (a) to measure k^{trans} using steady-state T1 and dynamic susceptibility first-pass T2* methods in brain tumors and (b) to assess correlation between the two methods. Our study suggests that k^{trans} derived by the steady-state T1 and the first-pass T2* methods are linearly correlated for gliomas but not for meningiomas. We postulate that the poor correlation of k^{trans} in meningiomas may, in part, be due to their high capillary permeability and vascularity as well as their complete lack of a BBB. The discrepancy may be due to marked decrease in Gd-DTPA T2* relaxivities in meningiomas where the Gd-DTPA is relatively uniformly distributed. Since the steady-state T1 method ignores the first-pass behavior of the contrast agent bolus, this method would lead to an underestimation of k^{trans} in highly and uniformly vascular tumors such as meningiomas. On the other hand, the susceptibility effect Gd-DTPA during the first-pass in meningiomas may be exaggerated and can lead to over-estimation of k^{trans}. The higher vascularity and permeability of higher grade gliomas (vs lower grade gliomas) could possibly explain our observation that the correlation is poorer in grade IV gliomas (R^2=0.8764) than in all other gliomas combined (R^2=0.9934) or grade II (R^2=0.9926) and grade III (R^2=0.9908) gliomas individually (data not shown). To date, we are unaware of any published reports that systematically compare k^{trans} derived from steady-state T1 and first-pass T2* methods. Although our sample size and range are limited, the good correlation we have found for gliomas suggests that the first pass T2* method may prove to be a valuable technique for estimating capillary permeability in gliomas (and potentially other intraaxial brain tumors) as it may be more useful from a standpoint of image acquisition and computational speed. However, further investigations to directly correlate imaging with histologic standards may strengthen the validity of the T2* derived k^{trans} as a noninvasive imaging marker of microvascular permeability.

References

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This work was supported by grant NIH NS045013.