In Vivo Human Brain Q-maps by Means of Dynamic Contrast-Enhanced Echo Planar Imaging

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Introduction

The number density of microvessels is a commonly used histopathogical measure of vascularity. In particular, the microvessel density is important for quantifying angiogenesis in solid tumors. Conventional MRI techniques can provide an estimate of regional blood volume, but this may not correlate with the microvessel density due to variations in vessel diameter. In order to provide an MRI index that reflects microvessel density more closely, a relaxation rate shift ratio, referred to as *Q*, has been introduced [1]. A recent animal study strongly supports the hypothesis that the measurement of *Q* can be used to obtain absolute estimates of microvessel densities in the brain [2]. This animal study, however, used a high dose of an iron oxide contrast agent that would not be feasible for human studies. Here we show that parametric maps of *Q* can be obtained in human brain by means of dynamic contrast-enhanced echo planar imaging (EPI). From the *Q*-maps, we find estimates for the microvessel density in the cerebral cortex and the putamen that are consistent with histological data.

Theory

The quantity *Q* is defined as the ratio $\Delta R2/(\Delta R2^*)^{2/3}$, where ΔR2 and ΔR2* are the shifts caused by a blood pool contrast agent in the relaxation rates R2 and R2* [1]. Provided the contrast agent concentration is sufficiently high, then the microvessel density in gray matter is approximately [2]

$$N \approx Q^3 \times 329 \text{ s/mm}^2 . \quad (1)$$

If Gd-DTPA is utilized as the contrast agent and ΔR2 and ΔR2* are measured in steady state, then a dose much larger than the standard dose of 0.1 mmol/kg is required for Eq. (1) to hold [1]. However, if ΔR2 and ΔR2* are measured during the first passage of an intravascular contrast agent bolus then a dose 2 or 3 times the standard dose may be adequate [2]. A key property of *Q* is that it is insensitive to the contrast agent dose provided the dose exceeds a threshold [1].

Methods

One subject was imaged at 1.5 T on a Siemens Avanto scanner using an interleaved spin echo/gradient echo EPI sequence following the injection of a triple dose of Gd-DTPA at a rate of 5 ml/s. One image was acquired each second with echo times of 53 ms for the spin echo images and 29 ms for the gradient echo images. A total of 60 images were acquired with a slice thickness of 5 mm, an acquisition matrix of 128 × 128, a field of view of 222 mm × 222 mm, and 3/4 phase space encoding. The set of 30 spin echo images with a temporal separation of 2 s were interpolated into a set of 60 images with a temporal separation of 1 s; a similar interpolation was performed for the gradient echo images. This allowed the construction of a time series of parametric maps for ΔR2, ΔR2* and *Q* with an interval of 1 s.

Results

Figure 1 shows the temporal variation of ΔR2 and ΔR2* for regions of interest within the cerebral cortex and the putamen. As ΔR2* is roughly proportional to the contrast agent concentration, the data in Fig. 1 indicate the peak concentration to be 3 to 5 times the steady state value. Because a triple dose was used, we then infer the peak concentration to be 9 to 15 times above the reference level (i.e., that produced by a single dose in steady state), which should be sufficient for the approximation of Eq. (1) to be valid. A typical gradient echo image acquired before the passage of the bolus is shown in Fig. 2, and the corresponding *Q*-map computed at the time of peak concentration is shown in Fig. 3. In the cerebral cortex, we obtain $Q = 1.18 \pm 0.15$ $s^{-1/3}$, and in the putamen, $Q = 0.72 \pm 0.04$ $s^{-1/3}$. From Eq. (1), we estimate microvessel densities of $N = 540 \pm 206$ mm^{-2} and $N = 123 \pm 21$ mm^{-2}, for the cerebral cortex and putamen respectively. These are comparable to the histological estimates of $N = 371 \pm 63$ mm^{-2}, for the cerebral cortex, and $N = 208 \pm 56$ mm^{-2}, for the putamen, that may be deduced from the data of Meier-Ruge and co-workers (3).

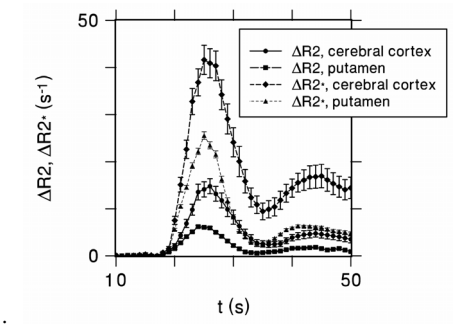

Figure 1. ΔR2 and ΔR2* as a function of time during the passage of a contrast agent bolus.

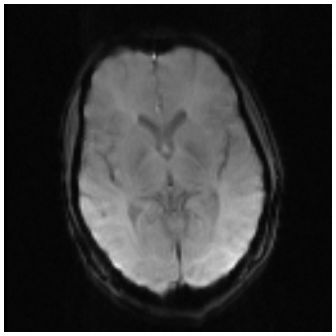

Figure 2. Gradient echo image obtained prior to the passage of the bolus.

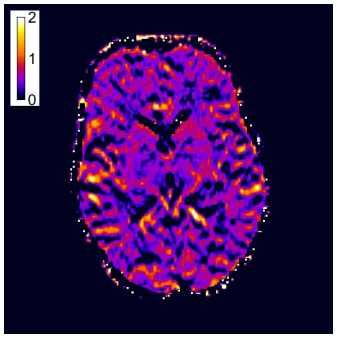

Figure 3. *Q*-map at the time of the peak contrast agent concentration. The scale bar gives *Q* in $1/s^{1/3}$.

Conclusions

In vivo *Q*-maps of the human brain can be obtained with dynamic contrast-enhanced EPI and a triple dose of Gd-DTPA. The resulting microvessel density estimates are in rough accord with histologically derived values.

References

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3. Meier-Ruge W, et al. *Mech Aging Dev*; **14**:233 (1980).