Dynamic Contrast Reagent Induced Differences in Transverse Relaxation and Susceptibility Shift Observed by Echo Planar Spectroscopic Imaging

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INTRODUCTION

A major assumption in dynamic contrast enhanced MRI is the existence of a linear relationship between signal enhancement and concentration of contrast reagent ([CR]). While this is often true, the relationship is demonstrably non-linear at [CR] > ca. 2 mM, thus reducing the effective dynamic range. Such limitations are especially critical when accurate [CR] are needed, such as for pharmacokinetic studies or for relaxometric determination of intra-tumoral pH. Therefore, the need exists for the development of a novel method for the determination of the [CR]. In this communication, we describe the detection of Dy-labeled CR Using Echo Planer Spectroscopic imaging (EPSI) as an alternative method for [CR] determination with high dynamic range. In these studies both Gd- and Dy-labeled CR can be used simultaneously; with Gd-providing spin-lattice relaxation contrast determined by T_1-weighted imaging, and by-providing transverse relaxation contrast determined as linewidths in EPSI spectra.

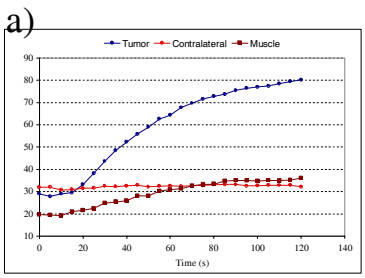

Figure 1. Relative enhancement (a) and the corresponding T_1-weighted images (b) tracking infusion of GdDTPA/DyDOTP over two hours.

To correlate these quantities and explore the best measure of [Dy], we performed a series of experiments to determine the dependence of the transverse relaxation rates R_2^* and Bulk Susceptibility Shift ($\Delta\delta$) of a mixture of Dy- and Gd-CRs in a pharmacokinetic time-series in an intracranial rat glioma. This is assumed to yield the [Gd] given that both the Gd-CR and the Dy-CR perfuse and extravasate in precisely the same manner. Knowledge of the [Dy] and hence the [Gd] will then yield the desired Spin Lattice Relaxivity (r_1).

The EPSI pulse sequence is a gradient echo version that allowed the observation of the intensity, shift, and linewidth of the in vivo water resonance with high spatial and temporal resolution [1]. These data showed that the EPSI-determined R_2^* from linewidths had a higher dynamic range, compared to T_2 weighted imaging, and that $\Delta\delta$ was uninformative, except in muscle, where structural anisotropy exists.

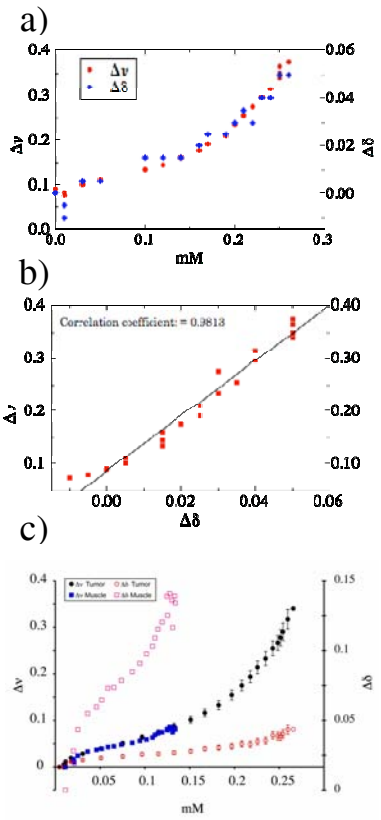

Figure 2. Correlation of $\Delta\delta$ versus $\Delta\nu$ (b) and infusion plot as a function of increasing concentration (time) (a, c) in the glioma. In (c), both tumor and muscle values are depicted where is a tissue dependent difference in $\Delta\delta$.

METHODS

Experiments were carried out on female Wistar rats implanted with glioma cells. Stereotaxic injection, in the right caudate nucleus, of 10^5 C6 cells was performed [2]. The cells were injected to a depth of 5.5 mm. After implantation, the tumors were allowed to grow and studied after two weeks, at which point they occupied up to 50% of the right hemisphere. The weight of rats (N = 3) was 200-250 g.

All experiments were carried out on a Bruker Biospec 4.7 T scanner. EPSI was performed with two spatial dimensions without the use of water- nor outer volume suppression. Trapezoidal gradients and a single 90° pulse RF excitation were used. Changes in the full width at half maximum linewidth, denoted as $\Delta\nu$, are plotted rather than changes in transverse relaxation ΔR_2^*.

RESULTS

DISCUSSION

The effect of the CR mixture infusion for two hours is observed in Figure 1. It is clear that [CR] is gradually increasing in the tumor. After reconstruction and post-processing, $\Delta\delta$ and $\Delta\nu$ were plotted versus the apparent concentration based upon the T_1-weighted values in the tumor - Figure 2(a). It is clear that $\Delta\delta$ and $\Delta\nu$ are both sensitive to- and proportional to the [CR] inside the tumor. In Figure 2(b), $\Delta\nu$ shows a linear dependence on $\Delta\delta$. However, it is interesting to note that there are tissue dependent differences in $\Delta\delta$ while $\Delta\nu$ curves overlay independently of whether ROIs are in muscle or tumor. These results imply that EPSI may be used to determine CR concentrations based on ΔR_2^* which is a more robust quantity than $\Delta\delta$ for this purpose.

REFERENCES

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