Could we accurately measure in vivo diffusion coefficients of brain metabolites using single-voxel MR spectroscopy?

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Introduction

Diffusion-weighted magnetic resonance imaging is an accepted tool for the early detection of ischemia or other disorders in human. For multi-shot diffusion weighted imaging, motion artifacts have been well known to cause phase changes in both read-out and phase-encoding directions and intensity dropout in the slice direction. Throwing away the interleaves with intensity lower than 70% of the maximum intensity of all measured interleaves has been used to eliminate the images with most severe motion artifacts and ensure accurate apparent diffusion coefficients (ADC) [1]. Recent animal studies have shown that diffusion-weighted MR spectroscopy is valuable for the evaluation of intracellular environments since most metabolites, unlike water, are located predominantly in the intracellular compartments. While head constrain and phase corrections on each free induction decays (FID) have been proposed to minimize the motion artifacts, no explicit experiments were carried out to estimate the motion contributions to the measured ADCs using single voxel MR spectroscopy. In this abstract, we reported an unexpected result: the measured ADCs of the brain metabolites obtained from single-voxel diffusion weighted MR spectroscopy depend on the voxel size.

Methods

The data were acquired on a Siemens Magnetom Trio 3T system with a birdcage head coil. The diffusion measurements were performed using the reported single-voxel, diffusion-weighted stimulated echo acquisition mode (STEAM) method [3]. The diffusion gradient length was 20 ms. Sequence parameters were 4096 data points, spectral width 2 kHz, TE = 180 ms. TM = 30 ms, TR = 3.0 s. 1 average and 128 averages for each b-value were applied for water and NAA respectively. Sixteen b-values ranging from 300 s/mm^2 to 1400 s/mm^2 were used for water diffusion measurement. Four b-values ranging from 300 s/mm^2 to 3000 s/mm^2 were used for NAA diffusion measurement. In addition, water suppression pulses were applied during the NAA diffusion measurements. To minimize subject motion, the volunteer was constrained using head tapes and was told to keep as still as possible. To further eliminate the phase error induced from patient motion, raw data of every FID was acquired and averages were carried out using magnitude spectrum. The summed spectra were then baseline corrected and fitted using mono-exponential decay to obtain the apparent diffusion coefficients.

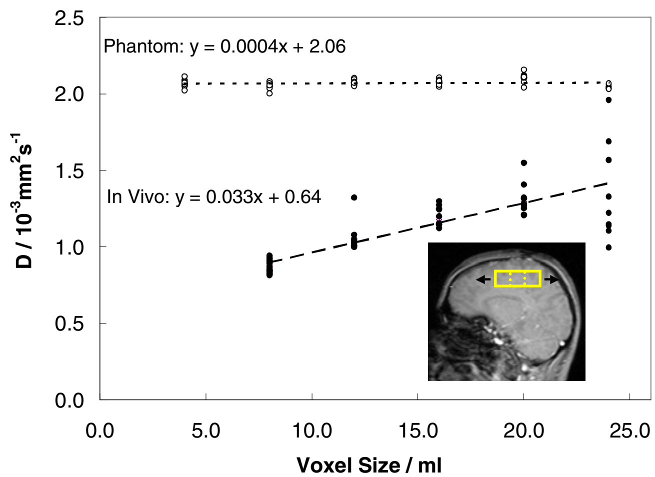

Fig. 1 Measured ADCs of water with different voxel size, (○) in phantom and (●) *in vivo*. For each voxel size, 10 measurements were carried out. The lines are the least-square fitting of the data.

Results and Discussion

Fig. 1 shows the ADCs of water in phantom and *in vivo,* respectively. With the voxel size of the other two dimensions kept at 20 mm, the length of the voxel in Fig.1 was varied from 10 mm to 60 mm in the posterior-anterior directions with the center remained at the same location. For each voxel size, 10 measurements were carried out. As in Fig.1, the ADCs of water in the phantom do not depend on the voxel size. In contrast, *in vivo* water ADCs varied strongly with the voxel size. Fig.2 illustrates that the ADCs of *in vivo* NAA in the same locations showing similar voxel size dependence. For voxel size less than 10 ml, the measured diffusion coefficients of water in phantom, water *in vivo*, and NAA *in vivo* were 2.04×10^{-3} mm^2/s, 0.85×10^{-3} mm^2/s and 0.17×10^{-3} mm^2/s respectively, which agree with the reported values using similar voxel size [2]. However, the *in vivo* ADCs of water and NAA are several folds higher for the large voxel (e.g., 24 ml in Figs 1and 2). Since the ADCs of water depends on tissue types, six $20 \times 20 \times 10$ mm^3 voxels were placed uniformly in the brain and their ADCs were determined to be $(0.85 \pm 0.20) \times 10^{-3}$ mm^2/s. This variation of water diffusion coefficients in the selected tissues is therefore much smaller than those demonstrated in Fig. 1 and hence cannot explain the voxel dependence of measured ADCs. Further, the standard deviation of 10 measured *in vivo* ADCs of water increase significantly with voxel size, which contradicts the expectation that larger voxel, thus higher signal to noise ratio, shall lead to less variation of the measured diffusion coefficients. In our opinion, this observation is due to motion. Anderson and Gore [3] have shown that rigid-body motion of the scanned subject during the diffusion sensitizing gradients is equivalent to a residual gradient. This indicates that signal drop linearly depending on the voxel size and could lead to an apparent larger diffusion coefficient as we observed in this study. Certainly, further experiments are required to clarify the origin of voxel dependence of the measured ADCs.

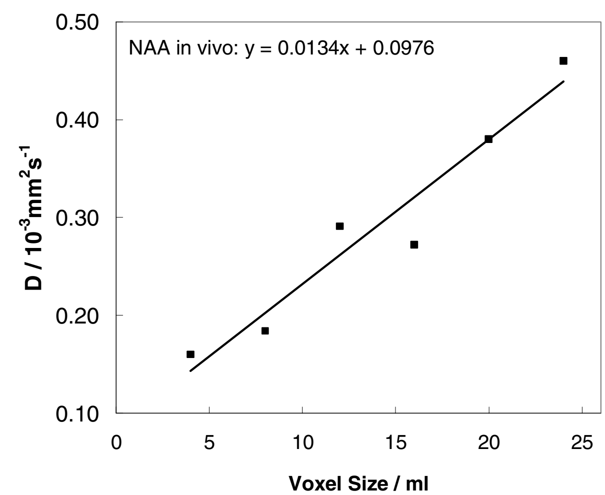

Fig. 2 Measured *in vivo* diffusion coefficients of NAA with different voxel size. The lines are the least-square fitting of the data.

Conclusions

The measured *in vivo* diffusion coefficients of water and NAA demonstrate a strong dependence on the corresponding voxel size. For voxel size less than 10 ml, the measured diffusion coefficients of water in phantom, water *in vivo*, and NAA *in vivo* were 2.04×10^{-3} mm^2/s, 0.85×10^{-3} mm^2/s and 0.17×10^{-3} mm^2/s respectively, which agrees with early reported value using similar voxel size. However, for 24 ml voxel, the measured *in vivo* ADCs of water and NAA were about 1.5 ~ 3.0 time higher than those of small voxels.

References

[1] (a) Liu C., *et al.*, Magn Reson Med 2004; **52**:1388-1396. (b) Atkinson D., *et al.*, Magn Reson Med 2000; **44**:101-109.
[2] Ellegood J., *et al.*, Magn Reson Med 2005; **53**:1025-1032. [3] Anderson AW., et al., Magn Reson Med 2004; **32**:379-387.