A novel phantom for quantitative diffusion MRI based on acetone and deuterium oxide

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Target audience: Researchers and clinical scientists working on quantitative diffusion MRI

Purpose: Quantitative diffusion weighted MRI (q-DMRI) techniques have tremendous potential for various imaging applications, including tumor characterization and treatment monitoring. However, in order for q-DMRI to become a valid biomarker, validation of its accuracy and robustness is needed. Phantoms exhibiting desired diffusion behavior could provide a controlled setting for the development and validation of q-DMRI techniques. Ideally, such phantoms should possess a single-peak MR spectrum, single exponential diffusion decay profile, and ADC values over the entire physiological range (eg. 0.62-2.6 $\cdot 10^{-3}mm^2/s$)[1]. Recently proposed phantoms for q-DMRI, including water solution phantoms such as sucrose solution and polyvinylpyrrolidone (PVP) solution do not meet all of these requirements. ***The purpose of this study*** is to investigate the spectral diffusion behavior of sucrose and PVP phantoms, and propose a mixture of acetone and deuterium oxide (D_2O) as an alternative for phantoms that have a single spectral peak and ADC values that span the entire physiological range.

Methods: *Previously proposed phantoms:* Four agar-based sucrose phantoms were built, with sucrose concentration of 10%, 20%, 30%, 40% as described by Lavdas et al[2]. Four PVP phantoms[3] were built as aqueous solution of PVP in concentration 0%, 20%, 40%, 60%.

Proposed phantom: The proposed phantom is based on the principle that increasing concentrations of water (H_2O) decrease the ADC of acetone due to hydrogen-bond strengthening[4]. Pure acetone has higher ADC than water[5], such that increasing the concentration of water enables a wide range of ADC values at 0°C. The NMR spectrum of this phantom can be reduced to a single peak (acetone) by replacing H_2O with D_2O. For the proposed acetone-D_2O phantoms, D_2O concentrations of 0%, 5%, 10%, 20%, 40% were used. Acetone-H_2O phantoms were built for comparison in identical concentrations.

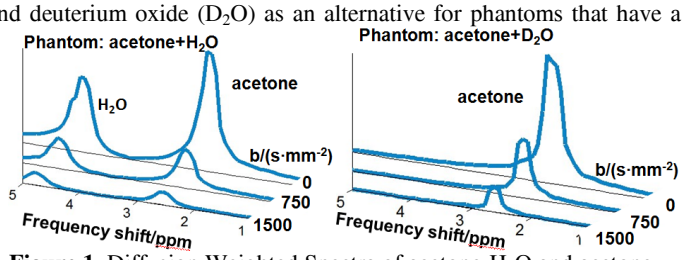

Figure 1. Diffusion Weighted Spectra of acetone-H_2O and acetone-D_2O phantoms show that using D_2O instead of H_2O eliminates the H_2O peak while maintaining its effect on acetone diffusion.

Imaging and data processing: All phantoms were scanned in a GE HDxt 1.5T system with a spin-echo single-shot DW-EPI sequence. Acquisition parameters included b=100, 250, 500, 750, 1000, 1500s/mm^2, TE=80ms, TR=6000ms (TR=16s for acetone-D2O phantom due to long T1). Phantoms were scanned at room temperature and in an ice-water bath. Signals were averaged in an ROI chosen in each phantom before calculating ADC with single exponential fitting. Diffusion weighted MR spectroscopy (DW-MRS)[6] was also performed in each phantom with the same b-values as DW-EPI, TE=147ms, TR=2000. At each b-value, the DW-MRS spectrum was separated into the solvent and the solute signal using prior spectral knowledge[7], and fit into a single exponential curve to measure ADC.

Results: D_2O affects the diffusion of acetone similarly to H_2O, but has no NMR peak like H_2O (**Figure 1**). Sucrose peaks were observable near the water peak at 17°C. At 0°C, sucrose peaks overlapped with water peak, therefore its individual ADC could not be separated using DW-MRS at 0°C. As shown in **figure 2**, very low ADCs were measured for sucrose signal compared with water in the same phantoms. Both PVP phantom and acetone-D_2O phantom exhibited a single NMR peak in DW-MRS and excellent agreement was observed between ADC measured using DW-MRS and DW-EPI. At 0°C, the PVP phantom ADC does not exceed 1.2, while the acetone-D_2O phantom ranged between 0.57 - 3.16 $\cdot 10^{-3}mm^2/s$.

Discussion and Conclusions: In the sucrose phantoms, a slow diffusing signal generated by sucrose confounds the ADC measured in DW-EPI. In the PVP phantom, only water peak was observed, likely due to short T2 of PVP. However, in ice-water bath, the PVP phantom exhibits a relatively narrow range of ADC values compared to physiological ADC values. Compared with alternative phantoms for q-DMRI, the proposed acetone-D_2O phantom has a single spectral peak with a wide range of ADC values covering the entire physiological range. Therefore , this novel phantom may prove useful for the development and validation of q-DMRI techniques.

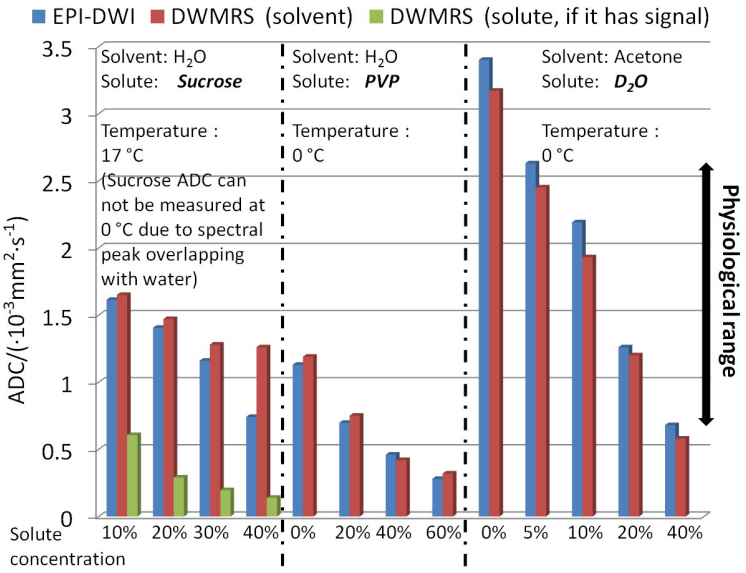

Figure 2.The ADC measurements obtained from DW-EPI and DW-MRS demonstrate the confounding effects of multiple spectral peaks with sucrose and the limited ADC range for PVP, while the acetone-D2O phantom has a simple spectrum and a broad range of ADC values. Sucrose phantoms were measured at 17°C because at 0°C, a sucrose peak overlaps with water. DW-EPI and DW-MRS showed close agreement in PVP and acetone-D_2O phantoms due to their single peak MR spectral profile. PVP phantoms showed a limited ADC range, while acetone-D_2O phantoms ranged from 0.57 to 3.17 $\cdot 10^{-3}mm^2/s$ (DW-MRS).

References: [1] Hara et al. Onco Lett 2014;8:819-824. [2] Lavdas et al. JMRI 2013;38:173-179. [3] Pierpaoli et al. ISMRM 2009 p.1414. [4] Toryanik et al. J Struct Chem 1988;28:714-719. [5] Guo et al. JMRI 2002;16:172-178. [6] Taviani et al. ISMRM 2013 p.0597. [7] Bock et al. Carbonhydr Res 1982;100:63-74.

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