Comparison of N-Acetyl Aspartate and Polyethylene Glycol as Chemical Shift Reference Standards for Proton Magnetic Resonance Spectroscopic Thermometry

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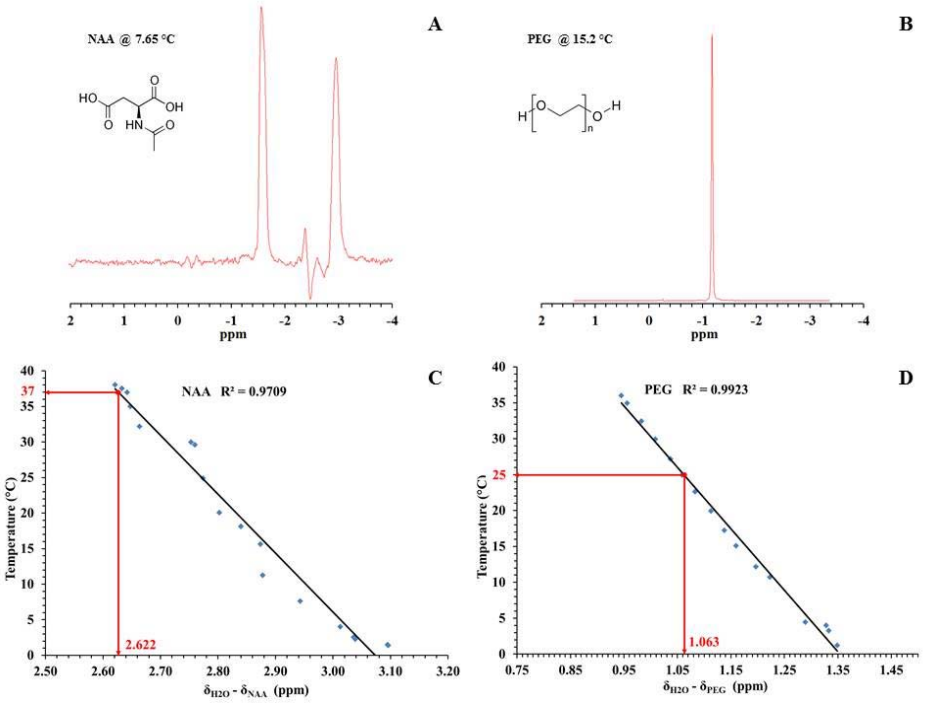
TARGET AUDIENCE: Research and clinical medical physicists, radiologists, and technicians.

PURPOSE. Polyethylene glycol (PEG) has been extensively studied for its medical and industrial uses. Recently ethylene glycol [1] and PEG [2] have been proposed as apparent diffusion coefficient standards for quantitative MR imaging. This study will demonstrate PEG's utilization as a nuclear magnetic resonance thermometer for absolute temperature reporting in a diffusion calibration phantom. Knowledge of the phantom medium's temperature-dependent diffusion characteristics will enable correction of the medium's apparent diffusion coefficient and scanner gradient amplitudes. This potential usage will be contrasted with the endogenous brain metabolite, N-acetyl aspartate (NAA), which is widely used *in vivo* and *in vitro*.
METHODS. The experiment consisted of a deionized water and 100 mM polyethylene glycol phantom (SigmaUltra P4338, avg mw: 3,350 g/mol, avg n: 75.7) and a deionized water and 40 mM NAA (Fluka 00920, mw: 1.7514 g/mol) phantom buffered to a pH of approximately 7.4. The two phantoms consisted of PEG-water and NAA-water in 50 mL test tubes that were each placed inside of a larger saline-filled cylindrical container for coil loading purposes. The magnetic resonance spectroscopy (MRS) was performed on a Siemens Trio 3T scanner with a 12-channel head matrix coil using a single-voxel PRESS sequence with the following parameters: TR = 2000 ms, TE = 135 ms, BW = 1200 Hz, and 1024 data points. A nonwater-suppressed spectrum was acquired with 16 signal averages and the metabolite spectrum was acquired with a water-suppressed CHESS sequence at 50 Hz and 64 signal averages. The ^{1}H spectra of PEG and NAA were acquired at various temperatures between 0 and 38 °C using temperature controlled water circulation. The internal temperatures of the phantom(s) were recorded with a thermocouple sensor validated against a NIST calibrated digital thermometer. The Siemens raw spectra were post-processed in the time domain using the AMARES plugin in jMRUI v5 [3]. The water peaks in both phantom solutions were normalized and quantitated using AMARES to identify the temperature-dependent chemical shift. The residual water peaks in the NAA and PEG solutions was removed in a range of ± 0.5 ppm using the HLSVD algorithm, the spectra were normalized and then quantitated using AMARES. The water peak positions were determined from the nonwater-suppressed spectrum and the reference peak positions were obtained from the water-suppressed spectrum [4].
RESULTS AND DISCUSSION. The NAA spectrum (**A**) was acquired at a temperature of 7.65 °C with a (δ_{H2O}-δ_{NAA}) range of 0.475. The temperature dependence of the NAA-water phantom T(°C) = (-82.85 ± 3.58)(δ_{H2O}-δ_{NAA}) + (254.59 ± 10.19) (**C**) was obtained using linear regression. The PEG spectrum (**B**) was acquired at a temperature of 15.2 °C with a (δ_{H2O}-δ_{PEG}) range of 0.404. The ^{1}H spectra of the PEG-water phantom exhibited a slightly steeper slope and smaller chemical shift difference of the linear temperature dependence between the water OH and PEG CH_2 resonances. The regression analysis for PEG produced a temperature dependent model of T(°C) = (-85.44 ± 2.30)(δ_{H2O}-δ_{PEG}) + (115.70 ± 2.01) (**D**). The temperature dependence and predicted body temperature chemical shift (2.622 ppm @ 37 °C) of δ_{H2O}-δ_{NAA} compared well with studies [5][6] which indicated the NAA-water temperature-dependent chemical shift decreases with ionic concentration and increases with protein concentration. An advantage of using PEG is that the electrical conductivity of the phantom solution does not need to be matched to that of brain gray matter or white matter *in vitro*. Other advantages of PEG are its biocompatibility and the capability to modify its molecular structure depending on the experimental requirements. The density and viscosity of PEG can be increased proportionately by increasing its number average molecular weight. This is an important factor to consider since high viscosity reduces scanner systematic errors caused by thermally-mediated flow and convection effects and gradient vibrations [7].



The single PEG CH_2 resonance is well resolved at a wide sampling interval and there no spectral overlap with other moiety resonances. Conversely, the CH_2 and CH_3 peaks of NAA are only viable at a limited sampling range, which can lead to peak inversion and loss of resolution if performed at a low sampling rate. Another area for future research in quantitative MRI phantoms and materials is the stable structure and long relaxation time for PEG-water solutions which decay with PEG concentration. The solution forms an ordered, dehydrated structure in equilibrium with a more flexible hydrated structure which exhibits two very different T_1 components [8].
CONCLUSION. This study demonstrates that PEG has a prominent and reproducible spectroscopic chemical shift at 3T and can reliably report temperature in a clinical environment. PEG's high viscosity makes it resistant to many of the artifacts that plague lower viscosity solutions such as the NAA metabolite.
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