# Does the protein content influence on DWI-thermometry?: Artificial CSF phantom study

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## INTRODUCTION

Several different ways of assessing brain temperature have been proposed, including noninvasive methods that use magnetic resonance (MR) imaging [1, 2, 3, 4, 5]. Among these MR methods, the most clinically applicable may be the post processing of diffusion-weighted images (DWI) [5, 6]. Although only applicable to non-restricted water, e.g., cerebrospinal fluid (CSF), it is potentially useful in assessing the thermal pathophysiology of the brain in both patients [6] and healthy subjects [5]. However, this DWI-based method might be influenced by the composition of the CSF, which can strongly affect its viscosity and diffusivity [7]. We have also experienced temperature decline with DWI thermometry in the case of head trauma [8]. In normal adults, the CSF protein concentration is the range of 0.18 to 0.58 mg/ml [9]. The purpose of this study was to investigate the influence of protein content on DWI thermometry by using artificial CSF (ACSF) with variable protein concentrations.

## METHODS

***Artificial CSF phantom***: Diffusion-weighted and MR spectroscopy images of ACSF phantoms (six different albumin concentrations) were acquired to investigate the influence of protein content on DWI thermometry. The ACSF phantoms consisted of 37 ml ARTCEREB® irrigation and perfusion solution for cerebrospinal surgery ($Na^+$: 145mEq/l, $K^+$: 2.8mEq/l, $Mg^{2+}$: 2.2mEq/l, $Ca^{2+}$: 2.3mEq/l, $Cl^-$: 129mEq/l, $HCO_3^-$: 23.1mEq/l, P: 1.1mmol/l, glucose: 0.61 g/l, pH 7.3, Otsuka Pharmaceutical Factory, Inc., Naruto, Japan) and 0 – 40.7mg albumin from bovine serum (pH 7, Wako Pure Chemical Industries, Ltd., Tokyo, Japan). ***Data acquisition*:** Images were acquired five times using a 1.5T MR scanner (Sonata, Siemens, Erlangen, Germany) equipped with a receive-only CP head array coil. DWI were taken in the axial plane using a spin-echo echo planar imaging diffusion-weighted sequence (TR: 3500ms, TE: 79ms, flip angle: 90°, bandwidth: 1955Hz/pixel, slice thickness: 5.0mm, matrix size: 128 × 128, FOV: 230 × 230mm, NEX: 3, three slices, b value: 800s/mm$^2$, MPG: six directions, zero filling interpolation). Due to the difficulty of maintaining the consistent temperature of samples in the MR magnet, we acquired the images at room temperature (23.0ºC). ***Temperature calculation***: Temperature was calculated using the following equation: T (ºC) = 2256.74 / ln(4.39221 / D) − 273.15 [4], where D [mm$^2$/s] is the diffusion coefficient. The mean temperature was calculated by histogram curve-fitting method [10]. The region of interest was manually segmented on the b0 image. An optical fiber thermometer (Anritsu Meter Co., Ltd. FL-2400, Tokyo, Japan) was used as a reference. ***Viscosity measurement***: The viscosity of ACSF was measured at room temperature (24.0ºC) using an Ubbelohde viscometer (#0, Sibata Scientific Technology Ltd., Saimata, Japan) and the method was based on the Japan Industrial Standard K2283-2000. The mean kinematic viscosity (five times measured) of ACSF was calculated as $Ct$, where $C$ is the viscometer constant (0.003539mm$^2$/s$^2$) and $t$ is the ACSF migration time in the viscometer. ***Statistics***: Comparisons were performed using paired t tests (Matlab; The Mathworks, Natick, MA, USA). The correlation was evaluated as significant for P values <0.05.

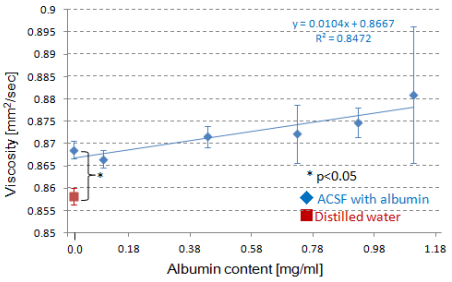


**Figure 1.** The relation between albumin concentration and viscosity (at 24.0°C). * indicates a significant

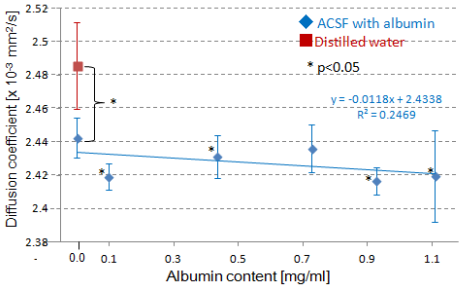


**Figure 2.** The relation between albumin concentration and diffusion coefficient (at 23.0ºC). * indicates a significant difference ($p < 0.05$).

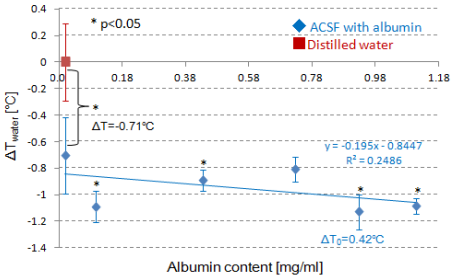


**Figure 3.** The relation between albumin concentration and temperature relative to distilled water (23.0ºC). * indicates a significant difference ($p < 0.05$).

## RESULTS AND DISCUSSION

***Albumin concentration vs. viscosity***: Figure 1 shows the relation between albumin concentration and kinetic viscosity. The difference in kinetic viscosity between distilled water and ACSF was significant ($p = 0.003$). Kinetic viscosity linearly increased with ACSF solution albumin concentration ($R^2 = 0.85$). Nevertheless, the relation between albumin concentration and kinetic viscosity was not significant. The difference between distilled water and ACSF without albumin was 2.46%, which was near two times of difference between ACSF with maximum albumin content (40.7mg/37ml) and without albumin (1.35%). ***Albumin concentration vs. diffusion coefficient***: Figure 2 shows the relation between albumin concentration and the diffusion coefficient obtained from DWI. The diffusion coefficient of ACSF was significantly lower than that of distilled water ($p < 0.001$). There was a significant negative relation between ACSF solution albumin concentration and diffusion coefficient ($p < 0.05$), but the linearity between albumin concentration and diffusion coefficient was low ($R^2 = 0.25$). The difference between distilled water and ACSF without albumin was 1.76%, which was 2.38 times of difference between ACSF with and without albumin (0.73%). ***Albumin concentration vs. DWI thermometry***: Figure 3 shows the relation between albumin concentration and the results of DWI thermometry. $\Delta T_{water}$ represents the temperature relative to distilled water. The temperature of ACSF was significantly lower than that of distilled water ($p < 0.001$, $\Delta T_{water} = -0.71$ºC). There was a significant negative relation between ACSF solution albumin concentration and $\Delta T_{water}$ ($p < 0.05$), but the linearity between albumin concentration and $\Delta T_{water}$ was low ($R^2 = 0.25$). The maximum temperature difference between the ACSF with and without albumin was 0.42ºC.

## CONCLUSION

The protein content of ACSF increased viscosity and decreased the diffusion coefficient. Consequently, the results of DWI thermometry were influenced by the protein content in the range of 0.10 to 1.11 mg/ml (0.10 ºC – 0.42ºC).

**References** [1]Kuroda S et al., Lancet Neurol., 2008; 7: 1056-1066, [2] Corbett RJ et al., AJNR Am J Neuroradiol., 1999; 20: 1851-1857, [3] Le Bihan D et al., Radiology 1989; 171: 853–857, [4] Kozak LR et al., Acta Paediatrica, 2010; 99: 237-243, [5] Sakai K et al., NMR Biomed, 2011; in press, [6]Yamada K et al., NeuroReport, 2010; 21: 851-855, [7]Reiber H, Restorative Neurology and Neuroscience, 2003; 21: 79-96, [8] Tazoe J et al, ISMRM, 2012; 3708, [9] Seehusen DA et al., American Family Physician, 2003; 68(6): 1103-1108, [10] Sakai K et al., NMR Biomed, 2012; 25(2): 340-346.