Development of a MRI Phantom to Emulate the Relaxation Times of the Neonatal Brain at 3 Tesla

T. N. Orr[1,2], N. Gelman[1,2], J. Winter[1,2], G. Campbell[2,3], and R. T. Thompson[1,2]

[1]Imaging Division, Lawson Health Research Institute, London, Ontario, Canada, [2]Department of Medical Biophysics, University of Western Ontario, London, Ontario, Canada, [3]Integrated Manufacturing Technologies Institute, National Research Council Canada, London, Ontario, Canada

Introduction: MRI assessment of brain morphology in the neonate is of great value for detecting impaired brain development. For this application, MRI techniques need to be adapted and optimized (at a given field strength) specifically for the neonate because the relaxation times of neonatal brain tissues differ greatly from those of adults and children (1). Experimental testing of these techniques would be useful, not only for optimizing contrast, but also for exploring the influence of imaging parameters on the efficacy of image processing techniques such as segmentation. However, performing tests on human neonates is not ethically appropriate. Also, animal models with appropriate relaxation times and morphology are not easily available. Thus, a realistic phantom to mimic both the MR parameters (T_1 and T_2) and morphological features of the neonatal brain would be a valuable tool. The first stage in the creation of a neonatal brain phantom involves the development of appropriate tissue-mimicking materials for neonatal white matter (WM) and grey matter (GM). Polyvinyl alcohol cryogel (PVA-C) has previously been investigated as a MRI phantom material (2) and has been used to create a homogenous adult brain phantom (3). Our previous work showed that the T_1 relaxation times of 6-15% PVA-C (T_1=1100-1900ms) (4) were substantially lower than those reported for neonatal WM (T_1~2800ms) at 3.0T (1). In the present study, we demonstrate that sufficiently long T_1 values to represent neonatal WM can be achieved by increasing the sample temperature above room temperature and further lowering the PVA concentration. In addition, we demonstrate that the T_1 and T_2 values for neonatal WM and GM can be approximately matched at this elevated sample temperature, by adjusting the PVA concentration and the concentration of an additive substance (agarose).

Methods: Sample Preparation: Samples of PVA-C for each concentration (3, 6, 10, 15%; [PVA]/[H_2O]; weight/weight) were prepared with 1 cycle of freezing/thawing using a standardized method (4). A second set of samples (3, 6, 11, 15%; [PVA]/[H_2O]; weight/weight) containing agarose (0, 0.2, 0.4, 0.6, 0.8, 1.0, 1.4, 1.8%; weight/weight) as an additive was also prepared. The samples were stored in water and refrigerated at 4°C for approximately 4 weeks before imaging. Sample Warming: The samples were heated in a water bath and held at a fixed temperature for 30 minutes. After heating, the samples were placed in an insulated container made of styrofoam, and then placed in the RF coil for MRI scans. Measurements were performed at 5 different temperatures (20, 25, 30, 35, 40°C) for the first set of samples and one temperature (40°C) for the second set. Imaging: MRI was carried out on a 3.0T MRI system. Image-based measurements of T_1 were obtained using the TOMROP pulse sequence (5), implemented as previously described (6). Image-based measurements of T_2 were obtained using a 16-segment spin-echo echo-planar imaging sequence as previously described (1). Regression Analysis: The measured relaxation times for the first set of samples were fit to the model:

$$T_i = a_0 + a_1[P] + a_2T + a_3[P]T \quad [1]$$

where T_i=T_1 or T_2, [P]=PVA%, T=temperature. Relaxation times for the second set of samples (all at 40°C) were fit to the models:

$$T_1 = c_0 + c_1[P] + c_2[A] + c_3[P][A] \quad [2] \qquad \& \qquad T_2 = (b_0 + b_1[P]) + (b_2 + b_3[P])\exp\{-[A](b_4 + b_5[P])\} \quad [3]$$

where [A]=agarose%. Optimal Values of all adjustable parameters (a_0 to a_3, b_0 to b_5, c_0 to c_3) were determined using the Gauss-Newton method.

Results: Figures 1 & 2 illustrate the measured relaxation times as a function of temperature, as well as the regression model (Eq. [1]). Error bars represent standard deviations. Horizontal lines on these figures represent mean T_1 and T_2 values previously obtained for neonatal WM and GM at 3.0T (1). From Fig. 1, it is evident that T_1 values sufficiently long to represent neonatal WM (mean T_1=2844ms) are obtained with [P]≈3% and T≈40°C. At this temperature, the T_1 of GM (mean T_1=2166ms) is obtained with [P]≈11%. The corresponding T_2 values (≈440ms and ≈270ms for 3% and 11% PVA, respectively) at 40°C are too long for neonatal WM (mean T_2=266ms) and GM (mean T_2=138ms). However, by adding agarose to PVA-C as measured at 40°C, it is possible to substantially shorten T_2 (Fig. 3) while only moderately affecting T_1 (Fig. 4). With the addition of agarose, T_2 values (Fig. 3) level off close to the mean T_2 value reported (1) for neonatal GM at 3.0T (bottom horizontal line). The regression models (Eq. [2] & [3]) are also shown in these figures. Using both regression models, it was determined that T_1 and T_2 of neonatal WM can be mimicked using [P]≈3% and [A]≈0.3%, and that T_1 and T_2 for neonatal GM can be approximately achieved (with T_2 slightly above the mean value (Fig. 3)) using [P]≈8% and [A]≈1.4%.

Conclusion: By adjusting the sample temperature, PVA concentration and agarose concentration, we can approximately mimic the relaxation times of neonatal WM and GM.

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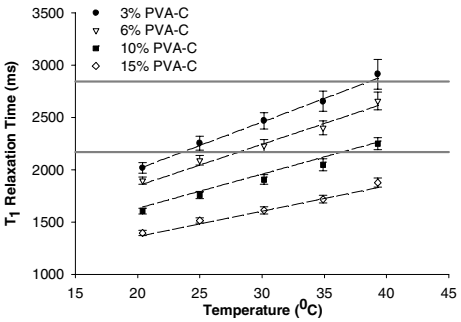

Fig 1. T_1 of PVA-C vs. temperature. Mean T_1 values (ref. 1) for neonatal WM (upper line) and GM (lower line) are shown.

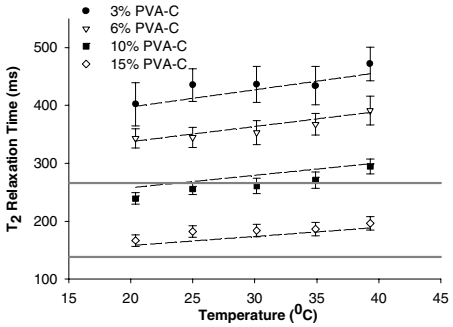

Fig 2. T_2 of PVA-C vs. temperature. Mean T_2 values (ref. 1) for neonatal WM (upper line) and GM (lower line) are shown.

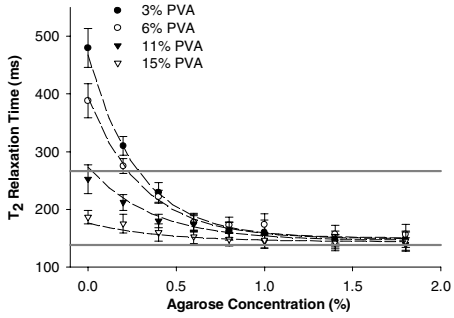

Fig 3. T_2 of PVA-C vs. agarose concentration at 40°C. Mean T_2 (ref. 1) for neonatal WM (upper line) and GM (bottom line) are shown.

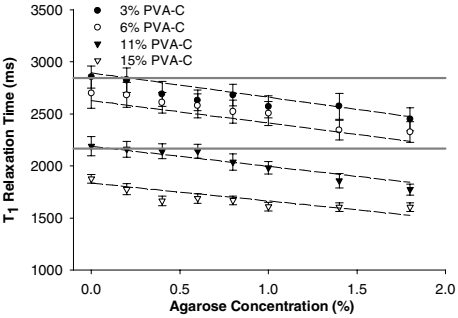

Fig 4. T_1 of PVA-C vs. agarose concentration at 40°C. Mean T_1 (ref. 1) for neonatal WM (upper line) and GM (bottom line) are shown.