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Original Article

Diffusion Phantom Assessment in 3 Tesla MRI Scanner

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ABSTRACT

Purpose- Diffusion imaging is widely used for an early diagnosis of cerebral ischemia. Tissue equivalent diffusivity phantoms can play a major role in quality control of MRI scanners. The purpose of this study is to construct diffusion phantom equivalents to body tissues and to assess the function of such phantoms in the 3 Tesla MRI scanner.

Methods- We designed a diffusion phantom, analyzed it in 3 Tesla Siemens Prisma MRI scanner, and then calculated T_1, T_2 and ADC values.

Result- T_2 gel values, 84.8, 80.77, 79, 77.77, 86.8 (ms), were respectively obtained for BT, P2, P2 in air, P2 in oil, P1. Also, their corresponding T_1 measurements were 1090.92, 1742.75, 1284.75, 1400, 1358.23 (ms) respectively. For the sake of comparison, the typical T_2 value of white matter was 82 ms, of grey matter was 92 ms, of cerebrospinal fluid was 2280 ms, and of tumor was 98 ms. The T_1 values of white matter, grey matter and cerebrospinal fluid were 1374 ms, 914ms, and 80 ms, respectively. This suggests that this phantom might be useful for diffusion imaging.

Conclusion- According to the results, this phantom can be employed to examine diffusion imaging. Therefore, the phantom constructed by Lavdas *et al*., which was tested on 1.5 Tesla device, can also be used for 3 Tesla machine. Considering the results of Lavdas *et al*., as expected, there was only an elevation in T_1 value which was due to the increase in the magnetic field strength of the device; however, the T_2 value did not change significantly.

Key words:
Diffusion - Weighted MRI,
Tissue-Equivalent Diffusivity,
Materials,
Diffusion Phantom,
Apparent Diffusion Coefficient.

1. Introduction

Physiologically realistic diffusion phantoms can be employed to evaluate the accuracy and reproducibility of ADC measurements in clinical systems or compare ADC measurements among vendors, field strengths, and imaging centers [1]. The ice water phantom delivers a low-cost and consistent method for measuring diffusion, but the ADC value of ice water is well above the ones found in malignant tissues in the body. Moreover, the actual device needs to be reassembled every time it is used and it is unfeasible to store and transport [2, 3]. Tofts *et al*. have described the use of alkane's hydrocarbons as reference materials for diffusion measurements. Nonetheless, these materials are potentially perilous to handle and expensive to obtain [4, 5]. Laubach *et al*. recommended the use of aqueous sucrose solutions to control the ADC. Increasing the concentration of sucrose in these solutions not only lowers the ADC, but also reduces the T_2 relaxation time [1]. Adopting the approach taken by Lavdas *et al*., we prepared a phantom and examined it in the MRI scanner. The T_1, T_2, and

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ADC values were measured and compared to the ones obtained by Lavdas *et al*.

2. Materials and Methods

2.1. Nickel-Doped Agarose/Sucrose Gels

To assess the quality control, we prepared Nickel-doped agarose/sucrose gels, according to the literature [6], in which the concentration of one of these three chemical components was changed, while the concentration of the two other chemical constituents was kept constant. Firstly, agarose (Ultrapure Agarose, Invitrogen Life Technologies, UK), sucrose (Improve Sucrose, Merck ,Germany) and 9g/L of sodium chloride (Improve Sucrose, Merck ,Germany), were mixed in a glass beaker with deionized water and stirred well at room temperature. Then, the mixture was placed in the microwave until the agarose was completely dissolved and a clear solution was formed (approximately 7 min/500 mL of solution). Subsequently, the hot mixture was placed on a stirring plate (Radleys Discovery Technology, UK) where it was kept with continuous stirring at 1000 rpm and the temperature was checked by an immersed thermometer. As soon as the temperature fell below 80 °C, the nickel salt (Emsure Nickel II nitrate hexahydrate, Merck, Germany) and 6 g/L of diazolidinyl urea (ACS Urea, Merk, Germany) (Sigma-Aldrich, UK) were added to the mixture and this was left stirring until all the components were fully dissolved and the temperature dropped to 60°C. Finally, the gels, which were still in liquid form, were emptied into 50mL centrifuge tubes (Corning, USA) and left in room temperature to settle. Sodium chloride was added to the gels to mimic the electric conductivity of biological tissues, and diazolidinyl urea was utilized as an anti-bacterial, anti-fungal agent. Diazolidinyl urea is the active component of the commercial product German Plus. Besides this substance is an effective preservative for tissue mimicking gels and has been used as an alternative to Thimerosal, which contains mercury and is potentially toxic.

It has been known that the concentration of agarose alters the transverse relaxation time in agarose gels [6] and nickel doping can be employed to control the longitudinal relaxation time of agarose gels independently [6]. The ADC of aqueous sucrose solutions can be controlled by modifying the sucrose concentration. T_2 and ADC can be controlled independently by changing the concentration of agarose and sucrose, individually [5].

Twelve gels were prepared via the method described above. In four of these gels, the nickel concentration varied from 0.5 to 2 mM, whereas the agarose and sucrose concentrations were kept constant (agarose 2% w/v and sucrose 15% w/v). In four other gels, the agarose concentration ranged from 0.5% to 3% w/v, while the sucrose and nickel concentrations were kept unchanged (sucrose 15% w/v and nickel 1 mM) and in the final four gels the sucrose concentration ranged from 5% to 30% w/v, while the agarose and nickel concentrations were kept unchanged (agarose 2% w/v and nickel 1 mM). The relaxation and diffusion properties of the 12 gels were measured on a 3 T clinical system using the methods described in the appropriate section.

2.2. Diffusion Phantom

In order to perform a quality control on MRI protocols, we designed a spherical phantom by solid software work in accordance to lecture [6]. The main compartment's diameter was 195mm. Two smaller spherical components with 60mm diameter were designed within the main phantom compartment. Two more even smaller spherical components with 40mm diameter surrounded by bigger spherical compartments with 60mm diameter were also devised in the main compartment. Following that, the designed phantom was manufactured by a 3D printer and was made of plastic (Figure 1). Finally, the main compartment was filled with gels showing relatively free diffusivity like healthy tissues, cysts, or benign lesions. The two smaller spherical components with 60mm diameter were filled with gels displaying various degrees of reduced diffusivities to resemble malignant tissues ("P1" and "P2" compartments). The two more even smaller spherical compartments with 40mm diameter, filled with gels showing the reduced diffusivities, were surrounded by fat and air-filled spaces with 20mm diameter in order to mimic the conditions normally found in biological tissues in the body (e.g., breast or neck imaging).

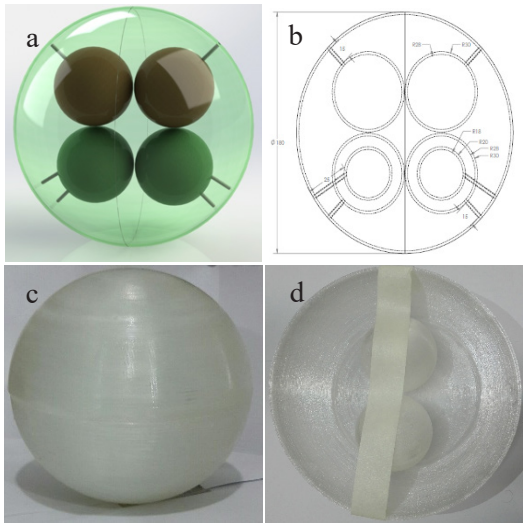

Figure 1. a) The designed phantom by solid work software. b) Internal pattern of phantom. c) The external pattern of phantom manufactured by 3D printer. d) The internal pattern of phantom manufactured by 3D printer.

Before the two parts of each sphere were glued together, a hole was drilled in and a 15mm plastic tube was glued to it. Through this tube, the spheres were filled with the liquid gels before these were set. Finally, the tubes were glued to the main sphere and the entire internal structure was held in the main compartment. The plastic parts were attached together using Tensol 12 adhesive (Bostic Ltd, UK). After all the phantom compartments were filled with gels, the tubes were sealed air-tightly with acrylic rods and the phantom was stored in the MRI scanner suite at a controlled temperature of 21°C.

The nickel, agarose, and sucrose concentrations that were used to prepare the gels, with which the corresponding phantom compartments were filled, are shown in Table 1.

Table 1. Nickel, agarose, and sucrose concentrations used for the phantom gels.

Compartment	Agarose concentration (% w/v)	Sucrose concentration (% w/v)	Nickel concentration (mM)
BT	1.2	-	1.8
P1	0.8	14	0.6
P2	0.8	38	-

2.3. MRI and Quantitative Image Analysis

The quality control protocol was applied on a 3 T clinical MRI system (Siemens Prisma), by means of a circularly polarized 64 channel head coil in receive mode. The test-object was placed within the 64 channel head coil and left in the magnet bore a few minutes prior to scanning to keep the test-object temperature at 21°C. Subsequently, the relaxation and diffusion properties (T_1, T_2, and ADC) of the gels were measured in a whole-body. The employed measurement methods have been described here. A Spin Echo (SE) pulse sequence with the following parameters was used for T_1 and T_2 measurements:

The field of view was (FOV) ¼ 185 _ 185 mm, the matrix size was ¼256 _ 256, the number of averages was NA ¼ 1, the image bandwidth was ¼ 320 Hz/pixel, the slice thickness was ¼ 5.5 mm, and the number of slices was ¼ 16. For the T_1 measurements, seven Repetition Time (TR)

values were used (500 , 1000 , 1500 , 2500 , 3500 , 5000 (ms)) with an Echo Time (TE) of 6.4 ms and for the T_2 measurements, 16 TE values were used (15- 240 ms in steps of 15 ms) with a TR of 3000 ms. DW-MRI was performed using a single-shot EPI pulse sequence with the following parameters: FOV ¼ 250* 250 mm, matrix size ¼ 130* 130, TR ¼ 7600 ms, TE ¼ 72 ms, NA ¼ 1, image bandwidth ¼ 2100 Hz/pixel, GRAPPA factor 2, reference lines ¼ 46, SPAIR fat suppression, slice thickness ¼ 4 mm, number of slices ¼ 26, zero slice gap and distance factor. Three b-values were used: 0, 150, 400, and 1000 s/mm^2. It is essential to state that the b values used in the diffusion pulse sequence did not allow the diffusion-weighted signal to approach the background noise intensity level. The ADC parameter was obtained by measuring the MRI signal at least twice [7].

T_1, T_2, and ADC maps were generated in EXCEL and MIPAV image processing software (Medical Image Processing, Analysis and Visualization, National Institutes of Health, Bethesda, MD). Regions of interest (ROIs) were drawn on the center of each phantom compartment to calculate the average T_1, T_2, and ADC values.

3. RESULTS

3.1. Dependence of Relaxation and Diffusion Properties on the Nickel, Agarose, and Sucrose

Figure (2a) shows that the longitudinal relaxation time of the gels, T_1, depends on the concentration of nickel-doping and also on the sucrose concentration. Figure (2b) demonstrates that the transverse relaxation time, T_2, of the gels depends only on the agarose concentration. This can be combined with Figure (2c), which shows that the ADC of the gels depends only on the sucrose concentration. Following the measurement of the dependence of relaxation time and diffusion properties on gel concentrations, the appropriate nickel, and agarose and sucrose concentrations were determined for the desired relaxation and diffusion properties.

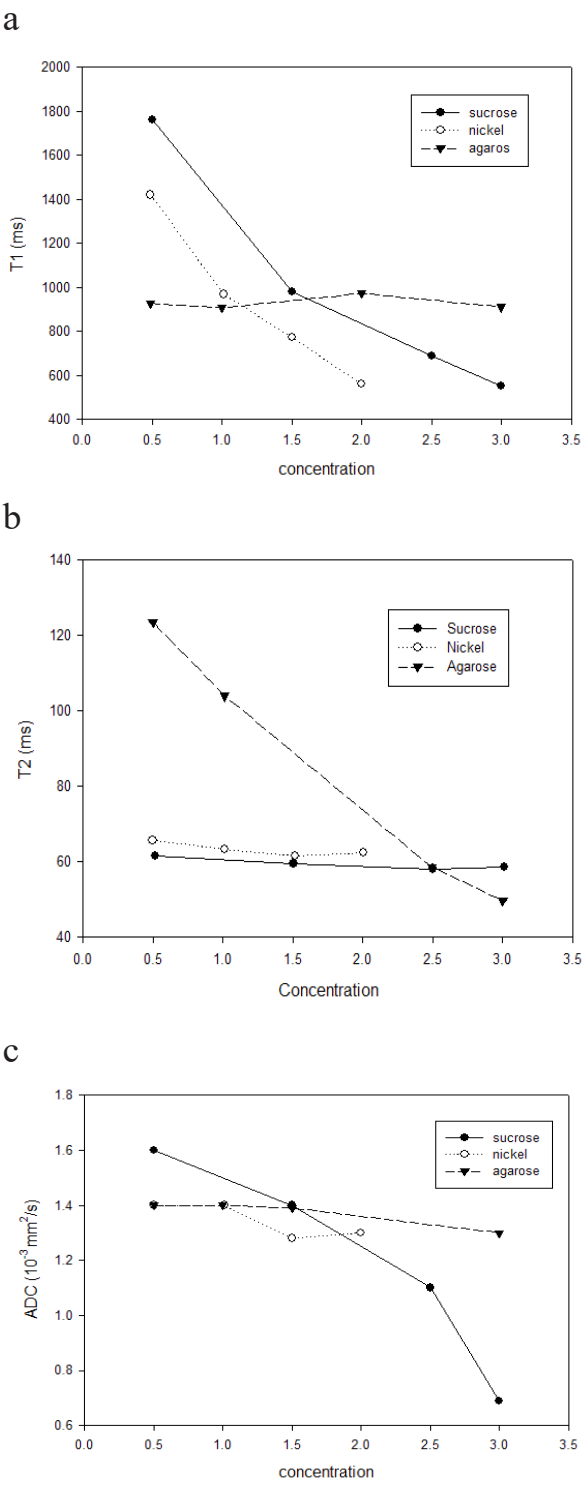

Figure 2. (a) T_1 dependence on nickel, agarose, and sucrose concentration.(b) T_2 dependence on nickel , and sucrose concentration and (c) ADC dependence on nickel, agarose, and sucrose concentration. Horizontal axis shows concentration in w/v for agarose, in ×10 w/v for sucrose and in mM nickel.

3.2. Relaxation and Diffusion Properties of the Gels within the Spherical Phantom

To calculate the average T_1, T_2, and ADC values, ROIs were placed in the center of each compartment, avoiding artifacts regions. For the "BT" compartment, five ROIs were drawn throughout the whole compartment and were grouped before the calculating the average T_1, T_2, and ADC values.

T_1, T_2, and ADC maps were generated for the spherical phantom using the methods described in the relevant section and are shown in the Figure 3.

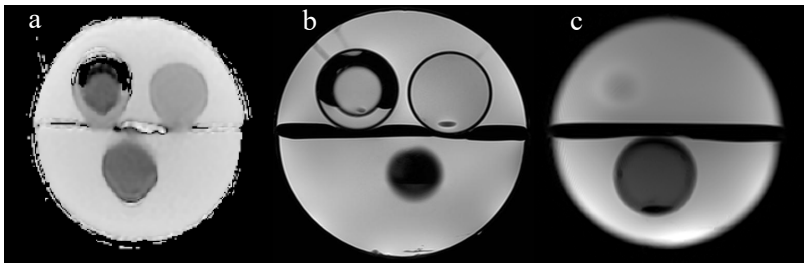

Figure 3. a) T_1. b) T_2. c) ADC map.

Table 2. The T_1 and T_2 results from different signal intensity in comparison with different repetition time (TR) and the ADC of the test-object solutions employed in the quality control programmed at 21°C.

Compartment	T_1 (ms)	T_2 (ms)	ADC ($\times 10^{-3}$ mm^2/s)
BT	1090.92	84.8	1.91
P2	1742.75	80.77	0.93
P2 IN AIR	1284.75	79	0.74
P2 IN OIL	1400	77.77	0.79
P1	1358.23	86.8	1.74

Table 3. The T_1, T_2 and ADC results from measurement in the beginning of 8 weeks.

Compartment	T_1 (ms)	T_2 (ms)	ADC ($\times 10^{-3}$ mm^2/s)
BT	1090.92	84.8	1.91
P2	1742.75	80.77	0.93
P2 IN AIR	1284.75	79	0.74
P2 IN OIL	1400	77.77	0.79
P1	1358.23	86.8	1.74

Table 4. The T_1, T_2 and ADC results from measurement in the end of 8 weeks.

Compartment	T_1 (ms)	T_2 (ms)	ADC ($\times 10^{-3}$ mm^2/s)
BT	1090.92	77.6	1.91
P2	1742.75	73	0.93
P2 IN AIR	1284.75	72	0.74
P2 IN OIL	1400	70	0.79
P1	1358.23	79.3	1.74

4. Discussion

As Figure (2) shows, the relaxation time and diffusion properties depend on the nickel, agarose, and sucrose concentrations. The longitudinal relaxation time of the gels depends on the concentration of the nickel-doping and sucrose concentration [1, 8]. Therefore, the T_1 relaxation time of the gels can only be controlled by using one of them. For example, if a gel with very low ADC value is required, then nickel-doping can be omitted from the gel preparation and T_1 can be controlled by the sucrose concentration, in a similar way we have done in the ''P2'' compartments of our phantom. The agarose concentration does not affect the T_1 time of the gels. Figure 2b displays that the transverse relaxation time, T_2, of the gels depends only on the agarose concentration. This can be combined with Figure 2c, which shows that the ADC of the gels hangs only on the sucrose concentration. This finding is very significant because it displays that very low ADC values can be obtained without lowering the T_2 relaxation time of the gels and thus compromising the SNR of the imaging experiments. This is in contrast to the aqueous sucrose solutions that have been normally described to control the ADC in which the T_2 time is shortened with increasing concentrations of sucrose [5].

The T_1, T_2 and ADC maps in Figure 3 show the relaxation and diffusion properties of this phantom are similar to the ones found in biological tissues especially in fat tissue and air tissue boundaries (Table 2). The T_2 of the gels was assessed to be 84.8 ms, 80.77 ms, 79 ms, 77.77 ms, and 86.8 ms for BT, P2, P2 in air, P2 in oil, and P1, respectively, with the measurement accuracy of 5%. Their T_1 measurements were 1090.92 ms, 1742.75 ms, 1284.75 ms, 1400 ms, and 1358.23 ms respectively. For the sake of comparison, typical T_2 value of white matter is 82 ms, of grey matter is 92 ms, of cerebrospinal fluid is 2280 ms [6, 9], and of tumor is 98 ms. The T_1 values of white matter, grey matter, and cerebrospinal fluid are 1374 ms, 914ms, and 80 ms, respectively. The value of the ADC is characteristic of tissue structure and ranges between 60 and $105\times10^{-5}mm^2s^{-1}$ in white matter, between 60 and 83 $\times10^{-5}mm^2s^{-1}$ in grey matter and between 240 and 440 $\times10^{-5}mm^2s^{-1}$ in cerebrospinal fluid [10]. This means that using this phantom DW-MRI experiments can be performed under very realistic conditions. Temporal stability of the gels was assessed twice by imaging over 8 weeks. Once in the beginning, and once again at the end of 8 weeks. There was no change on T_1 and ADC during the 8-week period. However, T_2 decreased approximately 1 ms per week. This drop in T_2 had been described before [1] and could be the result of water evaporation from the gels. Thus the specific imaging object can be of valuable assistance for optimizing diffusion protocols, exploring the effectiveness of novel pulse sequences for DW-MRI and comparing ADC values between field strengths, vendors and imaging centers. In conclusion, we manufactured nickel-doped agarose/sucrose gels used as reference materials for DW-MRI experiments. The gels are made of readily available, cost-effective, and nontoxic materials. The relaxation and diffusion properties of these gels are similar to the ones found in healthy or malignant biological tissues. We used this phantom for the quality control of the whole-body diffusion protocol in 1.5 Tesla MRI system at Imam Khomeini Hospital; the reproducibility of ADC measurement was assessed using Delakis method which indicated a problem with diffusion gradients of the device.

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