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Evaluation Study of T1 Relaxation Time via Contrast Agent Molarity and Magnet Field Strength in MR

Jeongmin Seo*

Department of Radiologic Science, Catholic University of Pusan, Busan 46252, Republic of Korea

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The purpose of this study was to evaluate the T1 relaxation times to distinguish between media with different contrast agent molarities (0.5 mmol/mL and 1.0 mmol/mL) for different magnetic field strengths (1.5 T and 3.0 T) in magnetic resonance imaging. Herein, we used the T1 mapping technique instead of signal intensities for evaluation. The T1 times were shorter for higher molarities at the same magnetic field strength ($p = 0.043$); however, there were no significant distinctions for the same molarity at different magnetic field strengths. The rate of change of the T1 duration for half the molarity of the phantom concentration was higher at low concentrations of the contrast agent. Therefore, the results indicate that higher concentrations of the contrast agent may not be necessary to obtain better imaging contrast.

Keywords : MRI, MRA, magnet resonance, magnet relaxation time, magnetization

1. Introduction

Magnetic resonance imaging (MRI) is the preferred mode of evaluation to assess the behavior of a hydrogen nucleus in a magnetic field [1]. MRI is a well-established imaging method capable of providing high resolution structural and functional images of tissues of in the human body ; further, MRI is relatively safer than some of the other imaging modalities such as X-ray, CT and PET with respect to ionization [2, 3]. Contrast media (or medium) (CM) are used in imaging techniques to enhance the differences between the various bodily tissues by producing areas with different contrast on the acquired images. The diagnosis of disease and treatment planning are thus highly dependent on such contrast media [4]. The CM for MRI constitute an important parameter to clearly distinguish between normal tissue and lesions [5]. Hence, the ideal contrast agent should achieve a sufficiently high concentration of accumulation in the target tissues without producing any adverse effects [6].

The two types of CM have been developed for medical imaging exam such as MRI and radiography [7]. The agents for electromagnetic radiation such as those in radiography, CT and fluoroscopy are kinds of high-density (high atomic number) materials that attenuate the radiation through the human body; however, CM for MRI are based on the kinds of paramagnetic substances which have small local magnetic fields that shorten the relaxation times of their surrounding protons [8, 9]. This effect is termed proton relaxation enhancement. The human body generally contains paramagnetic substances under normal circumstances. Gadolinium, a paramagnetic substance, is the most commonly used agent in MRI. The CM typically change the signal intensities by shortening the T1 and T2 relaxation times of their surroundings [8]. The T1 relaxation time called spin-lattice relaxation is a measure of how quickly the net magnetization vector recovers 63% from excitation to ground state.

Magnetic resonance angiography (MRA) is a type of noninvasive medical procedure to study blood vessels. The contrast between the blood vessels and surrounding tissues in MRI and MRA depend on the T1 relaxation effects; in general, the T1 relaxation effects depend on the molarities of gadolinium in the CM [10]. It has been observed that low gadolinium content (0.5 mmol/mL) in the contrast agent has a low T1 shortening effect, and owing to its short residence time in the blood, the contrast-enhanced image has low signal intensity, low signal to noise ratio (SNR), and low contrast to noise ratio (CNR). Therefore, recent trends in MRA lean toward using a high molarity of gadolinium (1.0 mmol/mL) in the contrast

*Corresponding author: Tel: +82-51-510-0581
Fax: +82-51-510-0588, e-mail: prayersjm@gmail.com

agent to obtain high SNR and high CNR [10]; however, other fields in MRA still use low gadolinium CM to avoid adverse effects from high viscosity of the agent.

In previous studies, comparisons based on only the differences in molarity or magnetic field strengths at the same molarity have been performed. In the present study, we aim to provide a comprehensive evaluation of the distinction in T1 relaxation effects using the molarity of the CM and magnetic field strength in MR, that is, for CM diluted to the same concentrations, two variables based on the molarity of the contrast agent and magnetic field strength of the MR were simultaneously applied to assess the differences in the T1 relaxation times.

2. Materials and Methods

2.1. Phantom

Complexes of the element gadolinium are the most widely used of all MR contrast agents. Because of its unique electronic structure, gadolinium is strongly paramagnetic [12] and facilitates proton magnetic relaxation with strong contrast enhancement; hence, it is generally used as CM or MRI [13].

When CM with high Gadolinium content are injected into the blood vessels of the human body, their mole concentrations change through dilution by blood, thereby causing changes in the MR signal intensities and T1 time [14].

In the present study, phantoms were made using CM of two different molarities, namely Dotarem (0.05 mmol/mL) and Gadovist (1.0 mmol/mL), for evaluations based on the concentrations. The samples were prepared by diluting each agent with purified water to obtain five different concentrations. To create the phantoms for the evaluations, plastic tubes of 50 mL capacity (polypropylene, conical shape, 115 mm length, 30 mm outside diameter, BD Falcon Conical-Bottom Disposable Plastic Tubes, BD Falcon) were used. To enable standing the phantoms in the MR coil, five tubes were affixed to a foam board, as shown in Fig. 1.

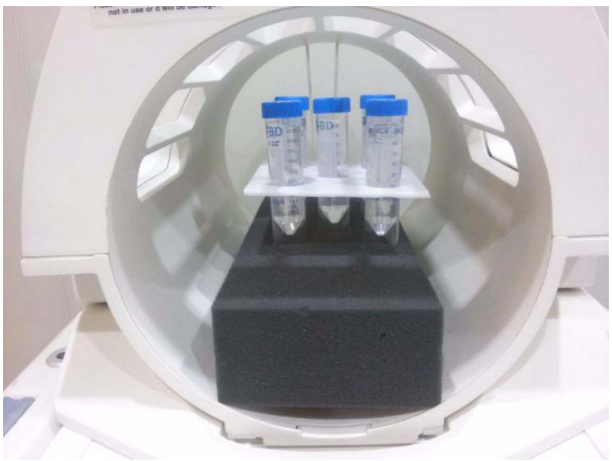

Fig. 1. (Color online) Phantoms placed in the head coil of the MR machine.

The phantom samples prepared were as follows. Samples of volume 0.25 mL, 0.5 mL, 1.0 mL, and 2.0 mL of the agent with molarity 0.5 mmol/mL were diluted in 1000 mL of purified water; further, samples of volume 0.125 mL, 0.25 mL, 0.5 mL, and 1.0 mL of the agent with molarity 1.0 mmol/mL were diluted in 1000 mL of purified water. Thus, five different samples with dilution ratios 0.125 mmol/L, 0.25 mmol/L, 0.5 mmol/L, 1.0 mmol/L, and purified water only were configured for each contrast agent.

2.2. Experiments

MR imaging studies were performed with two different magnet strength, namely 1.5 T (Tesla) and 3.0 T. In this study, evaluations were performed using the SIGNA HDxt 1.5 T (GE Healthcare, US) and SIGNA HDxt 3.0 T (GE Healthcare, US) MR machines to compare the reactions of the CM diluted to the same concentrations to different magnetic fields; the head coil was used in each case considering the sizes of the phantoms.

To evaluate the effects of each of the phantoms, the T1 time mapping strategy was used rather than simply comparing the signal intensities of the images. In MRI, the T1 and T2 relaxation times represent the characteristic tissue properties that can be quantified by specific imaging strategies [15]. Owing to the composite nature of the MR signal, it is not possible to acquire raw images with pure, quantifiable T1 or T2 properties directly. In fact, to obtain the pure T1 or T2 information, it is necessary to acquire a set of raw images with varying acquisition parameters and to perform multiparameter curve fitting analysis of this raw data based on mathematical functions that describe the underlying physical processes [18]. If this analysis is performed on a pixel-by-pixel basis, parametric “maps” can be created; these maps allow visualization of the T1 or T2 properties quantitatively because the signal intensity of each pixel in a map directly reflects the calculated relaxation time (typically of the order of milliseconds) [15].

T1 maps can be generated from sets of inversion recovery images (multiple series with each containing one image) with varying inversion times (TI) [15, 16, 17]. Therefore, the inversion recovery (IR) pulse sequence was used in this study, and TI was set to 150 ms, 300 ms, 700 ms, 1100 ms, and 2500 ms to acquire images that were later

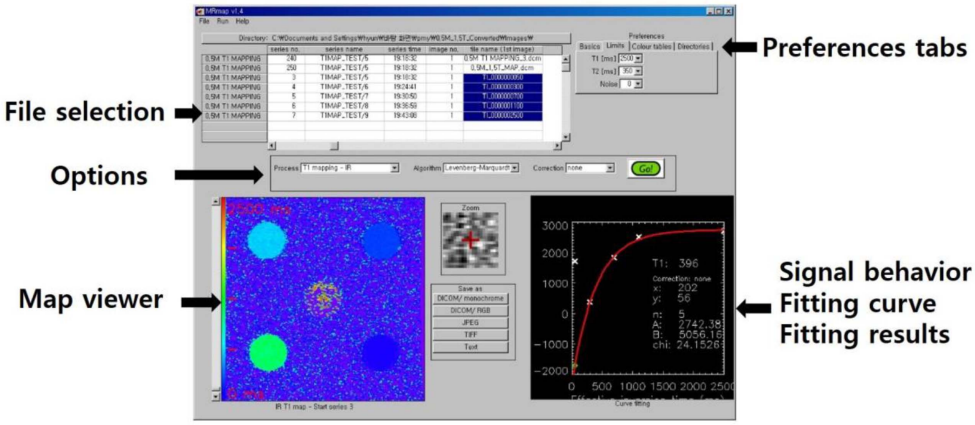

Fig. 2. (Color online) User interface of MRmap used in this study.

fused and analyzed to obtain the T1 mapping. The scan parameter settings used were repetition time (TR) of 2550 ms, echo time (TE) of 10 ms, field of view (FOV) of 149 × 149 mm^2, and slice thickness of 3 mm. MRmap (1.4, Project MRmap, Germany) (Fig. 2) was used as the T1 mapping tool to evaluate the acquired data . MRmap is a flexible open-source software tool for creating parametric maps of the MR relaxation times [15].

2.3. Analysis

The data obtained by T1 time mapping were compared by molarity and by magnet strength, and nonparametric statistical tests as Wilcoxon's signed rank test, Friedman's test, and Spearman's correlation analysis were performed by SPSS (SPSS 24, IBM, US).

3. Results and Discussion

The results of T1 mapping according to the magnetic field strengths and molarities of the CM are shown in Table 1. For higher concentrations, shorter T1 times were observed. There were significant differences between the samples prepared with the 0.5 mmol/mL and 1.0 mmol/mL CM for a given magnetic field strength ($p = 0.043$). The contrast agent with high molarity (1.0 mmol/mL) showed significantly shorter T1 times than the low-molarity agent. Friedman's test also showed a significant difference ($p = 0.044$) for these two agents. The distinctions based on molarity for the same magnetic field strengths are shown in Fig. 3 and Fig. 4. It is observed that the contrast agent with high intrinsic molarity shows shorter

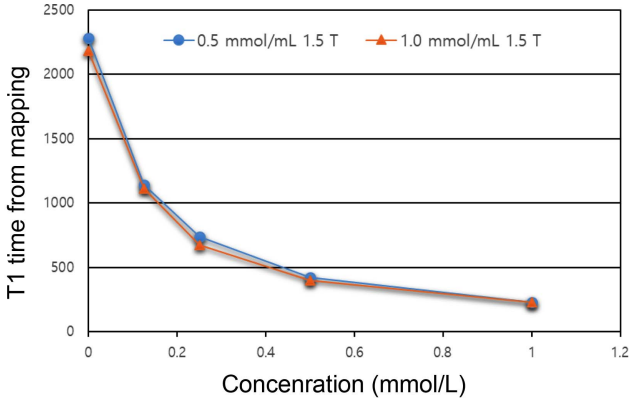

Fig. 3. (Color online) T1 times of the CM for each molarity by mapping with the 1.5 T MR machine.

Table 1. Results of T1 times from mapping according to CM molarities and magnetic field strengths.

MRI field strength	CM molarity (mmol/mL)	Phantom concentration (mmol/L)					p-value	
		1.0	0.5	0.25	0.125	None[1)]		
1.5T	0.5	228.99	420.56	739.19	1138.67	2284.97	0.043[2)]	0.044[3)]
	1.0	226.71	398.13	674.52	1112.53	2180.72		
3.0T	0.5	176.70	426.22	746.71	1169.17	2363.66	0.043[2)]	
	1.0	123.76	400.34	681.89	1139.47	2286.46		

[1)]Purified water only without the contrast agent
[2)]Wilcoxon's signed rank test
[3)]Friedman' test

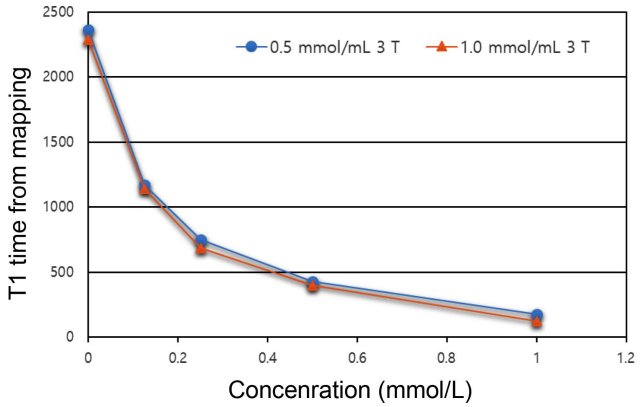

Fig. 4. (Color online) T1 times of the CM for each molarity by mapping with the 3.0 T MR machine.

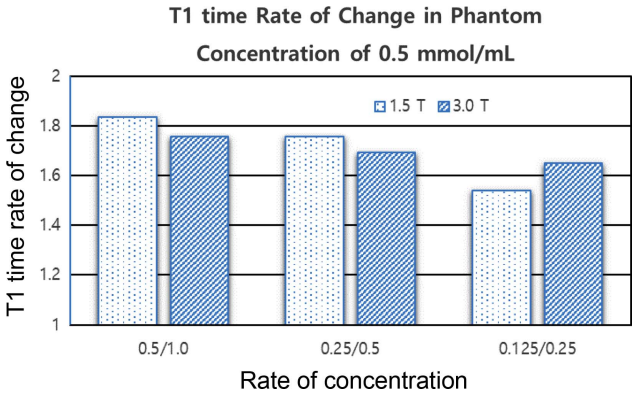

Fig. 5. (Color online) Rate of change in phantom concentration of 0.5 mmol/mL of CM (here, '0.5/1.0' indicates the rate of T1 time of 0.5 mmol/L over 1.0 mmol/L in the phantom concentration).

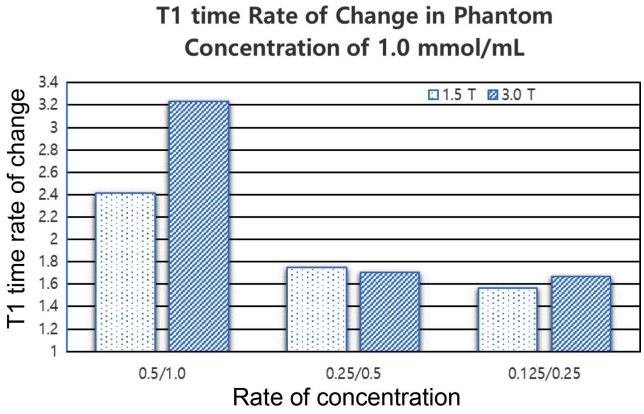

Fig. 6. (Color online) Rate of change in the phantom concentration of 1.0 mmol/mL of CM (here, '0.5/1.0' indicates the rate of T1 time of 0.5 mmol/L over 1.0 mmol/L in the phantom concentration).

to identical concentrations.

Manthis [19] and Haneder [20] suggested that high-contrast images could be obtained using CM with high gadolinium concentrations. Lee studied the differences between CM with 0.5 mmol/mL and 1.0 mmol/mL concentrations using the SNR and CNR [5]. The results of the present study confirm those of Manthis, Haneder, as well as Lee. In previous studies, comparisons were performed for the arrival times of the CM after injection or only for the signal intensities and not the T1 time mapping.

In the study of Jeong *et al.*, the CM agents which 0.5 mmol/mL Gadoteridol and 1.0 mmol/mL Gadobutrol were scanned by T1 and FLASH test only at 1.5 T with several different dilution ratio. This study shows that the signal reaction time of 1.0 mol CM is slower than the one of 0.5 mol CT in contrast-enhanced MRI. However, owing to the fact that there are not any signal intensity differences between 1.0 mol and 0.5 mol contrast, it is not true that the high concentration gadolinium MR contrast agent does not always mean high signal intensity in MRI [11]. This study results highlight T1 time evaluation is more effective than obtaining signal intensity. These studies have not been able to show a quantitative difference by molarity and magnet strength all.

The results of Spearman's correlation analysis for all groups showed significant correlations ($p = 0.01$, $r = 1.0$). Therefore, the changes in T1 times according to the concentrations are all similar. To distinguish the CM reactions in MR according to the concentrations of the phantoms, it is seen that as the concentrations increase, the T1 times reduce exponentially (Figs. 3, 4, 7, and 8).

In the study by Lee, only the 0.25 mmol/mL contrast agent was evaluated in 11 concentration steps from 0.0 mmol/L to 7.0 mmol/L, and the signal intensity according to the concentration was obtained by measuring the T1 relaxation time for the 3.0 T magnetic field strength. Lee found that although there was a difference in signal intensity according to the concentration, its pattern was different according to the type of pulse sequence used [21]. In Seo's study, the 3.0 T device was used with a 1.0 mmol/mL contrast agent diluted to 36 different concentrations from 0.0125 mmol to 1000 mmol. The signal intensities increased rapidly from 0.0125 mmol and peaked at 20 mmol; thereafter, above 20 mmol, the signal decreased to a very low value gently and achieved equilibrium from around 200 mmol [22].

In Han's study, the contrast agent Primovist with a molarity of 0.25 mmol/mL was diluted with saline and divided into 32 sample concentrations from 0.05 mmol/mL to 250 mmol/mL; in this study, the parameters of the readout segment and the GeneRalized Auto calibration

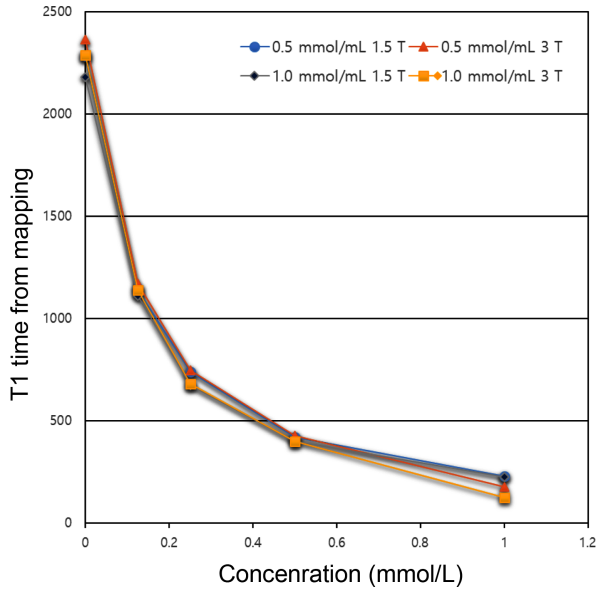

Fig. 7. (Color online) T1 times for the two magnetic field strengths when mapping with CM of 0.5 and 1.0 mmol/mL molarity.

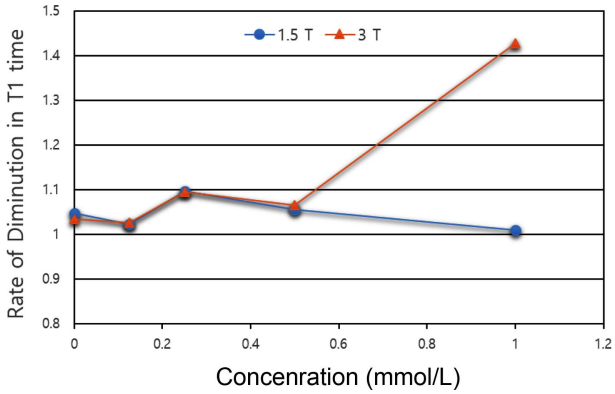

Fig. 8. (Color online) Rates of change in T1 times for each magnetic field strength (each point in the graph represents the rate of T1 time of 0.5 mmol/L over 1.0 mmol/L of the phantom concentration).

Partial Parallel Acquisition (GRAPPA) acceleration factor in Readout segmentation of long variable echo-trains (RESOLVE) diffusion weighted image were obtained. The signal was measured from less than 50 mmol/mL, showing a maximum signal intensity at 0.5 mmol/mL, and rapidly decreased to a lower concentration, so that they suggested selecting the optimal test parameter by applying the difference in signal intensity according to differences in the molar concentrations [23].

According to prior studies, the patterns for signal intensity may be diverse depending on various circumstances, but the present study shows appropriate comparison by T1 mapping and not signal intensity, with certain patterns based on concentrations. For a given molarity, there was no significant distinction in the T1 time mapping result for differences in the magnetic field strength ($p = 0.345$). Moreover, there were no significant differences between the two different molarities and various magnetic field strengths. Note that the 1.5 T and 0.5 mmol/mL as well as the 3.0 T and 1.0 mmol/mL had p-values of 0.225, whereas the 1.5 T and 1.0 mmol/mL as well as 3.0 T and 0.5 mmol/mL had p-values of 0.138.

In the study by Burnhard, myocardial delayed enhancement MR imaging at 3 T was shown to be a robust procedure yielding superior tissue contrast at 3 T compared with 1.5 T; however, this is not reflected by increased image quality as no significant differences were observed [24]. It is known that the 3.0 T field has a greater effect than the 1.5 T field in clinical applications and produces insignificant effects even with different signals, depending on the molarities of the CM.

Table 2 shows the rate of change of T1 time as the molarity of the phantom concentration is reduced by half. This rate of change according to the magnetic field strength for the same molarity is shown in Fig. 5 and Fig. 6. At 0.5 mmol/mL of molarity, the rate of change of the 3.0 T results is relatively lower than those of the 1.5 T results, but not at 1.0 mmol/mL.

Characteristically, in the low concentration region, CM of both molarities show high rates of change at 3.0 T. At the same molarity, the T1 time for most concentrations is shorter at 1.5 T than 3.0 T, but at the highest concentration, 1.0 mmol/L, the T1 time is shorter at 3.0 T. This is

Table 2. Rate of change of phantom concentrations for each contrast medium (here, '0.5/1.0' indicates the rate of T1 time of 0.5 mmol/L over 1.0 mmol/L in the phantom concentration).

MRI field strength	CM molarity (mmol/mL)	Rate of change in phantom concentration				
		0.5/1.0	0.25/0.5	0.125/0.25	Mean	SD
1.5T	0.5	1.837	1.758	1.540	1.712	0.125
	1.0	2.412	1.752	1.566	1.910	0.363
3.0T	0.5	1.756	1.694	1.649	1.699	0.044
	1.0	3.235	1.703	1.671	2.203	0.730

Table 3. Rates of change of T1 times for each magnetic field strength.

MRI field strength	CM molarity (mmol/mL) rate	Phantom concentration (mmol/L)					Average
		1.0	0.5	0.25	0.125	None[1)]	
1.5T	0.5/1.0	1.010	1.056	1.096	1.023	1.048	1.047
3.0T	0.5/1.0	1.428	1.065	1.095	1.026	1.034	1.129

[1)]Purified water only without contrast agent

shown in Fig. 7. Table 3 and Fig. 8 show the rate of change of T1 time based on molarity of the CM for each magnetic field strength. At high molarities of the CM, the T1 times decrease by about 4–5 %, even at 3.0 T, and the T1 time of the highest concentration (at 1.0 mmol/L) decreased to 43 %.

4. Conclusions

In this study, it is clearly confirmed that CM of higher molarities cause more effective reduction in T1 times than CM with low molarities for a given magnetic field strength or concentration. The results of experiments in this study show that the T1 times are shortened to a greater extent in low magnetic fields for molarities exceeding 1 mmol/mL, but these effects cannot always be duplicated for other conditions. Thus, T1 times are shorter when the initial molar concentrations are higher.

The findings of this study also indicate that low concentrations of the CM are more effective than high concentrations for obtaining greater contrast in MR applications, even with slight changes in the concentration of the contrast agent because of dilution in the human body. Therefore, the present study demonstrates that lower molarity CM have longer T1 relaxation times for a given concentration and magnetic field strength than higher molarity substances; this implies that high initial concentrations are not necessary for obtaining images with better contrast from the human body.

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