

Original Article

Effect of Echo Time on the Maximum Relationship between Contrast Agent Concentration and Signal Intensity Using FLAIR Sequence

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Abstract

Introduction

Contrast-enhanced fluid-attenuated inversion recovery (FLAIR) is one of the MRI sequences that can be used for detection and evaluation of pathological changes in the brain. In this work, we have studied the effect of different echo times (TE) on the maximum relationship between signal intensity and concentration of the contrast agent using the FLAIR sequence.

Materials and Methods

For assessment of the relationship between signal intensity (SI) and concentration, a water-filled phantom containing vials of different concentrations of Gd-DTPA (0 to 19.77 mmol/L) was used. The mean SI was obtained in the region of interest when T1-weighted images were implemented. The SI was corrected for coil non-uniformity.

Results

This study showed that an increase in TE is associated with a decrease in the maximum relationship between SI and concentration.

Conclusion

TE is an important parameter when the SI is measured in clinical FLAIR studies. The concentration leading to a maximum SI depends on this parameter, with the relevant concentration range decreasing at high TE.

Keywords: Concentration; Echo Time; FLAIR; Signal Intensity; T1-Weighted

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1. Introduction

Contrast agents such as gadopentetate dimeglumine act indirectly on the MR signal. This effect stems from the decreasing influence of these agents on the relaxation times of the surrounding nuclear spin [1].

Transport of the contrast material through a capillary produces local magnetic field inhomogeneities in the bulk tissue, and this field causes a decrease in the transverse relaxation time (T_2^*), and longitudinal relaxation time (T_1). A decrease in T_1 characteristically leads to an increase in signal intensity (SI), whereas a decrease in T_2^* causes a decrease in signal intensity. The net effect on the signal intensity of the MR depends on the type of imaging sequence adopted [2,3].

MRI enables distinction between soft tissues and other structures. It is well-suited for studies of nervous system diseases. Contrast-enhanced fluid-attenuated inversion recovery (FLAIR) is one of the MRI sequences that can be used for detection and evaluation of pathological changes in the brain [4,5]. FLAIR images allow distinction between lesions and normal brain tissue. T_1 and T_2 relaxation times have an influence on FLAIR images [6].

For example, FLAIR images obtained after intravenous injection of 0.1 mmol/kg of body weight of contrast agent can reveal different stages of multiple sclerosis (MS) lesions, early diagnosis of infectious meningitis, and earlier diagnosis of definite MS in the brain [7–10]. Kubota *et al.* [11], Essig *et al.* [12], and Zhou *et al.* [13] injected 0.1 mmol/kg of body weight of contrast agents for evaluation of the brain, intracranial tumors, and patients with high cerebrospinal fluid (CSF) blood or protein levels by means of FLAIR images.

Lavdas *et al.* [14] assessed the effect of chemical shift artifacts and fat suppression between contrast-enhanced T_1 -weighted fast spin echo (FSE) sequence with fat suppression and FLAIR sequence with fat suppression in MRI of the thoracic spine at 3.0 T with injection of 0.1 mmol/kg of body weight of gadopentetate dimeglumine.

Shah *et al.* [15] Compared gadolinium-enhanced fat-saturated T_1 -weighted FLAIR and FSE MRI of the spine at 3.0 T after injection of 0.1 mmol/kg of body weight for evaluation of extradural lesions.

In addition, Parmar *et al.* [16] and Oner *et al.* [17] compared contrast-enhanced FLAIR images with contrast-enhanced T_1 -weighted images after injection of 0.1 mmol/kg of body weight of gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) for diagnosing infectious leptomeningitis and in depicting meningiomas.

The aforementioned publications suggest that the contrast-enhanced FLAIR sequence may be used for studying of different parts of the brain. Although different image parameters were chosen for the FLAIR sequence, a common feature of these studies was that 0.1 mmol/kg of body weight of contrast agent was injected.

Previous studies have shown that the inversion time (TI), repetition time (TR), and different sequences (e.g., inversion recovery and saturation recovery) can have an effect on the relationship between changes in signal intensity and concentration for T_1 -weighted images [18–20]. In this work, we have studied the effect of different echo times (TE) on the maximum relationship between the SI and the concentration for the FLAIR sequence.

2. Materials and Methods

2.1. Theory

Many factors such as image sequences (e.g., T_1 -, T_2 -, T_2^* -, and PD-weighted) and image parameters may affect the SI. The magnetic susceptibility of contrast agent, the magnetic field strength, pulse sequence parameters, dose of the contrast agent, injection rate and bolus volume, cardiac output and blood volume, and tissue topology are factors that have a significant effect on the SI [21].

MR sequence can influence the relation between T_1 and the SI, which, in turn, is dependent on the concentration of contrast agent [22].

Equation (1) expresses the standard inversion recovery sequence in terms of TI and TR:

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$$S(t) = S_0 \left(1 - (1 - \cos \theta_{inv}) \exp \frac{-TI}{T_1} + \exp \frac{-TR}{T_1} \right), \quad (1)$$

where $S(t)$ is the SI after administration of the contrast agent and S_0 is the observed SI when no magnetization preparation pre-pulse is applied or there is no contrast agent. θ_{inv} denotes the flip angle of the inversion pulse. If $\theta_{inv} = 180^\circ$, in FLAIR sequences or at higher concentrations of the contrast agent, then Equation (1) can be written as follows [11, 23-25]:

$$S(t) = S_0 \left(1 - 2 \exp \left(-TI \left(\frac{C(t)}{K} + \frac{1}{T_{1Pre}} \right) \right) + \exp \left(-TR \left(\frac{C(t)}{K} + \frac{1}{T_{1Pre}} \right) \right) \right) \exp \left(-\frac{TE}{T_2} \right), \quad (3)$$

$$S(t) = S_0 \left(1 - 2 \exp \frac{-TI}{T_1} + \exp \frac{-TR}{T_1} \right) \exp \left(-\frac{TE}{T_2} \right), \quad (2)$$

where TE and T_2 denote the echo time and transverse relaxation time, respectively. Equation (2) contains concentration of contrast agent at time t ($C(t)$) and can be described as [25]:

Inversion recovery (spin echo)

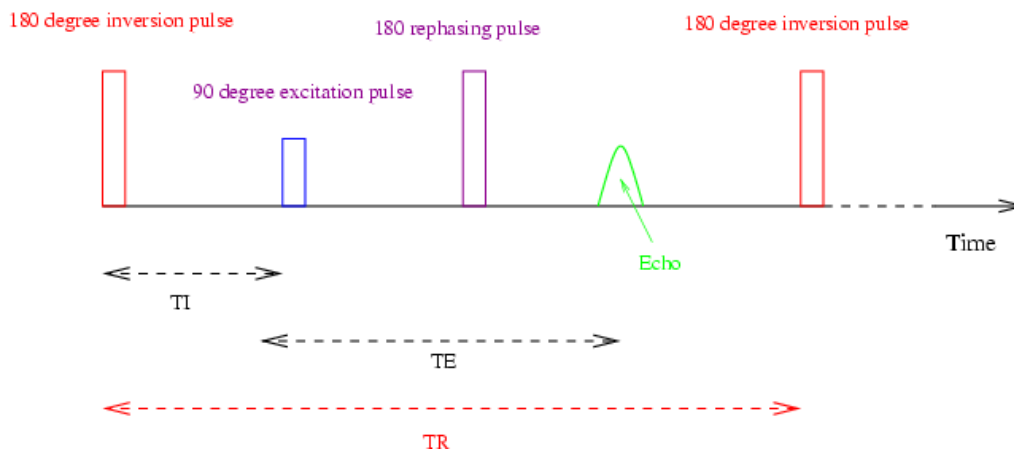


Figure 1. Inversion recovery spin echo sequence for one line of K space. TI is the time between the 180° inversion pulse and 90° excitation pulse. Imaging gradients are not shown in this diagram.

T_{1Pre} is the longitudinal relaxation times before contrast application. K is a constant that depends on the contrast medium [26].

Figure 1 shows inversion recovery spin echo sequence for one line of K space. TI is the time between the 180° inversion pulse and 90° excitation pulse. Imaging gradients are not shown in this diagram [27].

2. 2. Calculation of injection volume of contrast agent

The amount of the injected dose required to establish a known concentration of the contrast agent in the region of interest (ROI) of brain has been reported by Nazarpour et al. and Moody et al. [20, 28,29].

$$\text{Amount of injected volume (mL or CC) dose} = \frac{[(BSA \times 700 - 700) + (BSA \times 150)]}{0.6 \times 10^3} \times 2X \left(\frac{\text{mmol}}{\text{L}} \right). \quad (4)$$

X is the concentration of contrast agent (mmol/L) of the ROI. BSA (m^2) is body surface area. BSA can be described as [29-30]

$$BSA (\text{m}^2) = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (Kg)}}{3600}} \quad (5)$$

2. 3. Phantom

In order to investigate the relationship between concentration and the SI in stationary vials, a phantom was made to hold vials that could contain varied or constant concentrations of the contrast agent.

Radiofrequency (RF) coil non-uniformity is one of the significant sources of image non-uniformity in MR scanners [31]. Therefore, the uniformity of the response of the RF coils is an important factor in the measurement of the accurate SI of an image. Coil non-uniformity was assessed by use of vials (glass tubes, inner diameter approximately 15 mm) of constant concentration and then the vials were used with varied concentrations to measure the SI–concentration correlation.

The phantom holding various concentrations of the contrast agents with 22 vials filled with different concentrations of Gd-DTPA (Magnevist, Schering HealthCare Ltd., West Sussex, UK). The concentration was varied between 0 and 19.77 mmol/L (0.00, 0.30, 0.45, 0.60, 0.75, 0.90, 1.20, 1.50, 1.80, 2.10, 2.39, 2.69, 2.99, 3.28, 3.58, 3.98, 4.96, 5.95, 7.93, 9.90, 13.85, and 19.77 mmol/L).

A clinical head coil was used for this experiment with the phantom. The vials were arranged in vertical positions with their axes perpendicular to the image plane (coronal image). Two experiments were carried out, first with the varied concentrations and the second with a constant concentration of 1.20 mmol/L in the vials exactly in the same positions.

Vials with constant concentration were used to calculate the non-uniformity of the coil. This value was then normalized to give a correction factor. To calculate the corrected SI for the varied concentrations, we multiplied the SI of each individual vial by the correction factor (see our previous study for more information [27,28, 32-33]).

2. 4. Image acquisition and image analysis

The phantom was situated within the coil. All studies were performed in Shikholraies clinic (Tabriz - Iran) using an open 0.3 T clinical MR scanner (Hitachi Medical Corporation, Japan). Signal intensities in the vials with both

different and constant concentrations were assessed by means of FLAIR images.

The FLAIR imaging parameters were as follows:

Matrix size = 128×128, TR = 8500 ms, TI = 2100 ms, TE was varied between 30 and 120 ms, pixel size = 2×2 mm, slice thickness = 10 mm, and Echo Train Length = 11.

The images were processed by transferring the image data from the MR scanner to a personal computer and computerized them by image processing software in interactive data language (IDL, Research Systems, Inc).

Programs were written to find automatically:

1. The correction factor for the non-uniformity of the coil from the vials with constant concentration. The SI values of the vials with different concentrations were then multiplied by this factor,
2. The mean SI of the 9 innermost pixels of the total number of 44 pixels inside the vial, to avoid partial volume effects, and
3. The concentration at which the corrected SI is maximized. These programs can be run on either a UNIX workstation or a personal computer.

3. Results

Figures 2, 3, 4, and 5 show the mean corrected SI from the 9 innermost pixels of the vials versus the concentration of the contrast agent at TE values of 30, 60, 90, and 120 ms, respectively. The maximum corrected SI was obtained at different concentrations for the different values of TE. The figures show that the T₁-shortening effect is dominant at low concentrations of Gd-DTPA, based on Equation (1), whereas the T₂-shortening effect is dominant at high concentrations and leads to a decrease in the SI (see Equation (3)).

For example, 0.030 and 0.012 mmol/kg of body weight (for an average body, i.e., height = 175 cm, weight = 85 kg) of contrast agent should be injected for TE values of 30 and 120 ms, respectively, to give a maximum SI in the region of interest based on Equation (4). Injection of contrast agent in excess of the above values would lead to a net decrease in SI in the images.

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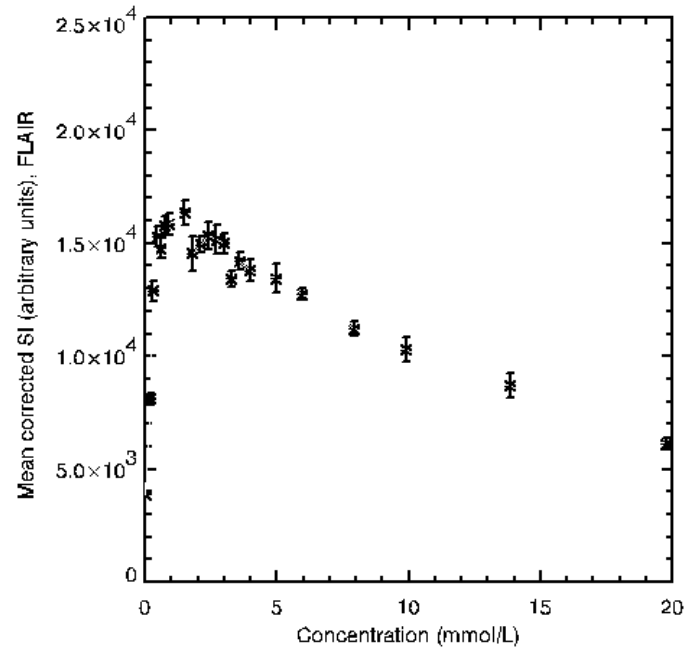


Figure 2. Mean corrected SI (for non-uniformity of the coil) from the 9 innermost pixels of the vials versus concentration of contrast agent at TE = 30 ms. The maximum corrected SI (16364 ± 520 , mean \pm standard deviation) can be obtained at a concentration of 1.5 mmol/L. The error bars show the standard deviation for each vial.

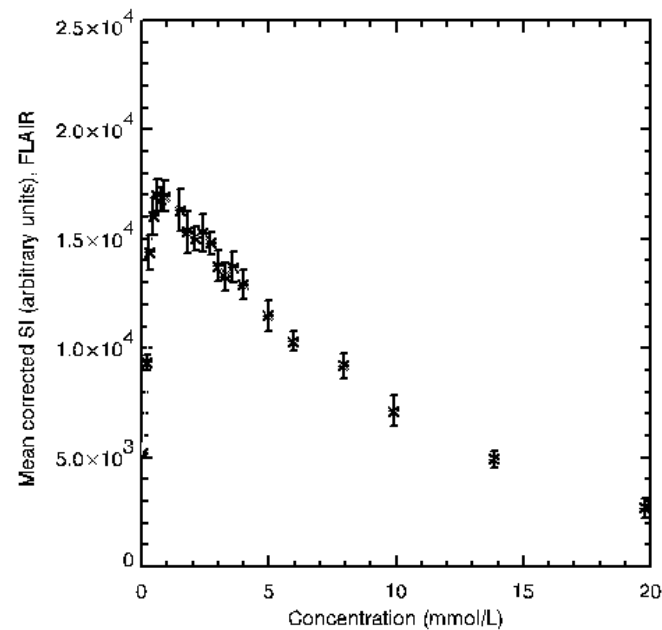


Figure 3. Mean corrected SI (for non-uniformity of the coil) from the 9 innermost pixels of the vials versus concentration of contrast agent at TE = 60 ms. The maximum corrected SI (16959 ± 707 , mean \pm standard deviation) can be obtained at a concentration of 0.9 mmol/L. The error bars show the standard deviation for each vial.

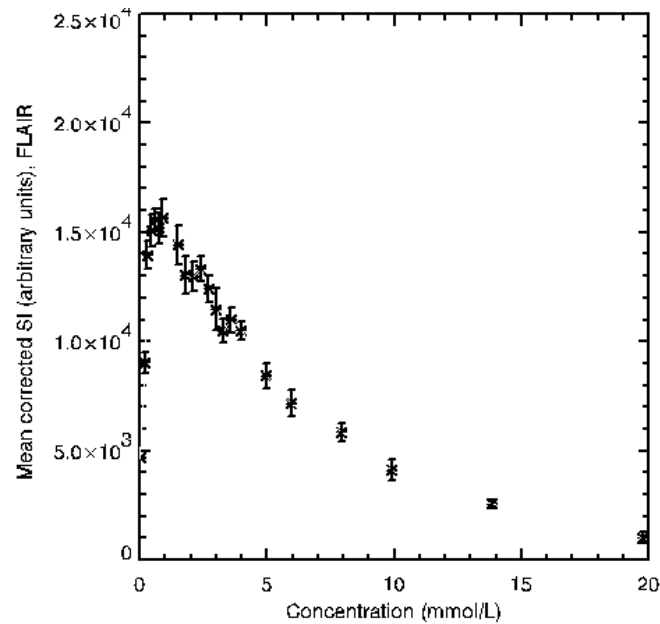


Figure 4. Mean corrected SI (for non-uniformity of the coil) from the 9 innermost pixels of the vials versus concentration of contrast agent at TE = 90 ms. The maximum corrected SI (15642 ± 847 , mean \pm standard deviation) can be obtained at a concentration of 0.9 mmol/L. The error bars show the standard deviation for each vial.

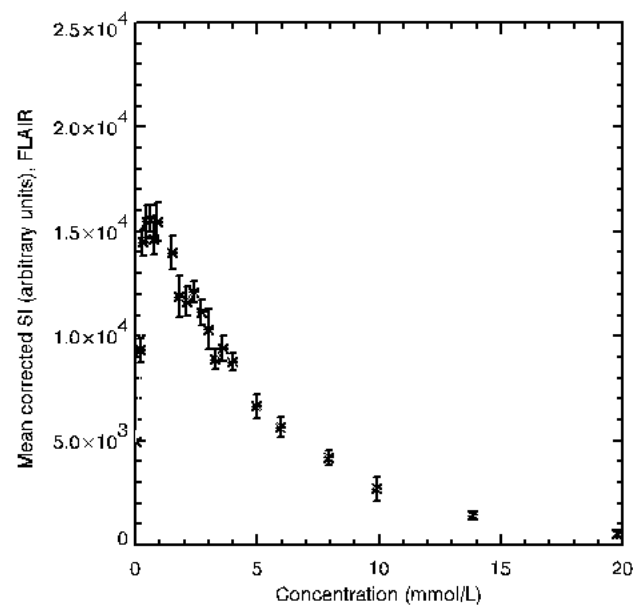


Figure 5. Mean corrected SI (for non-uniformity of the coil) from the 9 innermost pixels of the vials versus concentration of contrast agent at TE = 120 ms. The maximum corrected SI (15611 ± 631 , mean \pm standard deviation) can be obtained at a concentration of 0.6 mmol/L. The error bars show the standard deviation for each vial.

4. Discussion

Linearity permits the substitution of the signal strength by the concentration in equations describing the kinetics of the distribution of contrast media in CT or radioisotope

scintigraphy, but in MRI, the concentration of a contrast agent such as Gd-DTPA has essentially no linear correlation with the SI. Gd-DTPA induces both T_1 - and T_2 -shortening effects. Decreases in both T_1 and T_2 have opposing

effects, with T_1 -shortening increasing the SI and T_2 -shortening decreasing it.

As indicated by Equation (1), the effect of T_1 -shortening is significant when the concentration of Gd-DTPA is low, whereas the T_2 -shortening effect becomes dominant at high concentrations. Both T_1 and T_2 can be affected at high concentrations or in FLAIR sequences, as the SI response changes disproportionately with an unsteady plateau (see Equation (3)) [11, 23- 25].

Rovaris et al. [8] performed fast FLAIR after Gd injection (0.1 mmol/kg) to compare active MS lesions. After rapid intravenous injection of a standard dose of contrast medium (0.1 mmol of gadolinium per kilogram), Splendiani et al. [10] used FLAIR sequences at 1.5 T for the early diagnosis of infectious meningitis. Kubota et al. [11] also injected 0.1 mmol/kg of body weight of contrast agent for the evaluation of brain tumors by applying a FLAIR sequence. Essig et al. [12] used a FLAIR sequence following the intravenous injection of 0.1 mmol/kg of body weight of gadodiamide into patients with high CSF blood or protein levels. Zhou et al. [13] injected 0.1 mmol/kg of body weight of contrast agent for the evaluation of intracranial tumors by means of FLAIR images.

Lavdas et al. [14] compared T1-weighted FSE and fast T1-weighted FLAIR for assessing the effect of chemical shift artifacts and fat suppression at 3.0 T with injection of 0.1 mmol/kg of body weight of gadopentetate dimeglumine.

After injection of 0.1 mmol/kg of body weight, Shah et al. [15] compared gadolinium-enhanced fat-saturated T1-weighted FLAIR and FSE MRI of the spine at 3.0 T for evaluation of extradural lesions.

Parmar et al. [16] compared contrast-enhanced FLAIR images with contrast-enhanced T1-weighted images after injection of 0.1 mmol/kg of body weight of gadolinium-DTPA in studying infectious leptomeningitis. Oner et al. [17] compared post-contrast FLAIR imaging with post-contrast T1-weighted images in depicting meningiomas after

injection of 0.1 mmol/kg of gadopentetate dimeglumine.

To sum up briefly, in various investigations, 0.1 mmol/kg of body weight of contrast agent has been injected for FLAIR studies with different imaging parameters without consideration of the image parameters and strength of the MRI magnetic field [8, 10–17]. The effects of TI, TR, saturation time (T_S) and different sequences (e.g., inversion recovery and saturation recovery), and strengths of the MRI magnetic field on the maximum linearity on T1-weighted images were investigated in our previous studies [18–20, 25, 33,34]. The results of this study show that a change in TE also has an effect on the concentration that gives the maximum SI in FLAIR images.

Injection of a contrast agent leads to an increase in SI for T1-weighted images and a decrease in SI for T2-weighted images. Therefore, for obtaining the maximum SI for an image, the optimal concentration of contrast agent has been identified.

This study has shown that TE is an important parameter when the SI in a FLAIR sequence is measured, because it also affects the maximum relationship between SI and concentration.

The results of this study show that the maximum SI at lower TE is greater than the higher TE. In addition, the concentration which leads to maximum SI appears at lower TE than the higher TE. The results of this study may be used for clinical studies with similar image parameters [35]] which is one limitation of the current study.

5. Conclusion

In conclusion, an increase in TE leads to a decrease in the concentration range in which SI is maximized. The results of this study may be used for clinical studies with similar image parameters. The effect of the TE on the clinical studies should be further investigated.

Acknowledgements

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