Diethylenetriaminetriacetic acid 유도체와 Gd-DTPA와의 영상비교

Image Comparisons using a Diethylenetriaminetriacetic Acid Derivative and Gd-DTPA

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요약

본 연구는 상자성이며 중성자를 흡수하는 힘이 큰 gadolinium(Ⅲ) 전이금속과 polyaminocarboxylic ligand를 합성하여 제조한 MRI 조영제와 현재 임상에서 널리 사용되고 있는 Gd-DTPA의 영상을 비교하였다. 1.0T(Harmony, SIEMENS) MR 장비를 이용하여 Saline 100cc에 Diethylenetriaminetriacetic acid 유도체와 Gd-DTPA를 각각 0.05mmol/L, 0.1mmol/L, 0.15mmol/L, 0.2mmol/L, 0.3mmol/L, 0.5mmol/L, 1mmol/L, 2mmol/L, 3mmol/L, 4 mmol/L로 희석한 팬텀을 영상화하였다. Head Coil을 사용하였으며, SE Pulse sequence와 영상변수는 TE를 14ms, 1NEX, matrix는 256×201로 고정하고, TR을 300ms, 400ms, 500ms, 600ms, 700ms, 800ms, 900ms, 1000ms, 1200ms, 1400ms, 1600ms로 변화하여 각 조영제의 농도와 TR의 변화에 따른 신호강도와 단순대조도비를 비교하였다. 측정된 자료는 통계패키지 프로그램인 SAS v8.1(GLM procedeur)을 사용하여 분석하였다. 조영제의 농도와 TR의 변화에 따른 영상의 신호강도를 비교한 결과 최대신호강도를 보인 1~2mmol/L에서 두 조영제간의 차이는 크지 않은 것으로 나타났다. 하지만 1mmol/L 이하의 낮은 농도에서는 Diethylenetriaminetriacetic acid 유도체의 신호강도가 현저히 높은 것을 알 수 있다. 단순대조도비를 비교한 결과에서도 신호강도와 같은 양상을 보였으며, 대체로 1mmol/L 이하의 낮은 농도에서는 Diethylenetriaminetriacetic acid 유도체가 Gd-DTPA에 비해 높은 대조도비를 보이고 그 이상의 농도에서는 Gd-DTPA의 대조도비가 높은 것으로 나타났다. 또한 TR에 따라 각각의 조영제 농도별 신호강도의 차이가 현저한 것으로 나타났다. 따라서 Gd-DTPA에 비해 Diethylenetriaminetriacetic acid 유도체의 효능이 뛰어나며, 조영제의 농도에 맞추어 적절한 TR을 사용하여 최적의 영상을 얻어야 할 것으로 사료된다.

■ 중심어 : | 과학기술 | 조영제 | 가돌리늄 | 신호강도 |

Abstract

In this study, image comparisons were carried out using a MRI contrast medium which was derived by mixing a polyaminocarboxylic ligand and a gadolinium (III) transition metal which is paramagnetic and has good neutron absorbing capabilities with Gd-DTPA which is currently being used widely in the clinical setting. By using a 1.0T (Harmony, SIEMENS) MR equipment, phantoms of which 100cc of saline was diluted with a diethylenetriaminetriacetic acid derivative and Gd-DTPA were imaged. The amount of diethylenetriaminetriacetic acid and Gd-DTPA which was diluted into the 100cc of saline was 0.05mmol/L, 0.1mmol/L, 0.15mmol/L, 0.2mmol/L, 0.3mmol/L, 0.5mmol/L, 1.0mmol/L, 2.0mmol/L, 3.0mmol/L and 4.9mmol/L respectively. Head coils were used and while fixing the SE pulse sequence and image variable (as TE is 14ms, 1NEX with a 256x201 matrix), the signal intensity and simple contrast ratios according to changing concentrations and TR were compared with various TR at 300ms, 400ms, 500ms, 600ms, 700ms, 800ms, 900ms, 1000ms, 1200ms, 1400ms and 1600ms. According to the comparison results of the signal intensity of the image based on changes in contrast medium concentrations and TR, the differences in signal intensity between the two contrast mediums were found to be small at 1.0~2.0mmol/L when the highest signal intensity was achieved. However, at concentrations of 1.0mmol/L or less, the signal intensity was markedly higher in the Diethylenetriaminetriacetic acid derivative than in the Gd-DTPA complex. It was also found that the differences in the signal intensities demonstrated by the concentrations of the contrast mediums were affected by the TR. Accordingly, the efficacy of the Diethylenetriaminetriacetic acid derivative was shown to be better than the Gd-DTPA and also possible to get the optimum image quality by the use of an appropriate TR with appropriate concentrations of contrast medium.

■ keyword : | Science Technology | Contrast Media | Gadolinium | Signal Intensity |

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I. Introduction

Magnetic Resonance Imaging (MRI) is a powerful and non-invasive diagnostic technique useful in providing images of the inside of the human body. Gadolinium (III) complexes are used as magnetic resonance imaging contrast agents [1]. Contrast agents using paramagnetic metals such as gadolinium are routinely used in MRI to shorten longitudinal relaxation times (T1) of water protons and enhance image contrast. Because gadolinium allows up to nine coordinate sites, chelating moieties are typically octadentate with either acyclic or macrocyclic polyaminopolycarboxylate ligands that form kinetically and thermodynamically stable complexes with gadolinium. However, the gadolinium (III) ion is too toxic at the levels which are required in MRI and therefore cannot be injected intravenously. The currently used gadolinium (III) chelates are based on polyaminocarboxylate ligands [2]. The ligands for gadolinium complexes are polyaminepolycarboxylic acids such as diethylenetriaminepentacetic acid, 1, 4, 7, 10-tetraazacyclododecane-N,N',N",N'"-tetra acetic acid and diethylenediaminetetra acid are among the chelating agents which have been used in such studies [3][4].

The use of intravenous contrast media for MRI procedures is a well-established clinical practice and investigations have been performed to assess the safety aspects of MRI contrast media. Numerous MRI contrast agents were developed in attempts to obtain higher quality images with resultant lowered toxicity by improving the characteristics and sensitivities of the contrast mediums [5-11].

In this study, image comparisons were carried out using MRI contrast mediums derived from mixing gadolinium (III) transition metals which is paramagnetic and has good neutron absorbing capabilities with Gd-DTPA which is currently being used in the clinical setting.

II. Material & Method

1. Synthesis of Diethylenetriaminetri-acetic acids

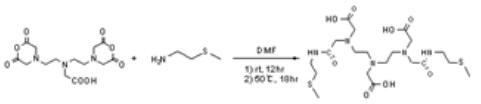


Fig. 1. Synthesis of Diethylenetriamine-*N,N″*-bis(N-benzylethylenediamide)-*N,N′,N″*- triacetic acid

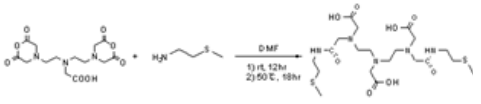


Fig. 2. Synthesis of Diethylene-triaminee *N,N″*-bis[(2-methylthio)ethylamide]-*N′,N″*-triacetic acid

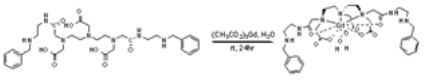


Fig. 3. Synthesis of [Diethylene-triamine -N,N"-bis(N-benzylethylenediamide) -N,N',N"-triacetato]gadolinium(Ⅲ)

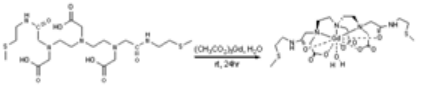


Fig. 4. Synthesis of [Diethylenetriamine -*N,N″*-bis[(2-methylthio)ethylamide] -*N,N′,N″*-triacetato]gadolinium(Ⅲ)

In formulating new ligands for gadolinium (III) complexes for potential MRI reagents, diethylenetriaminepentaacetic dianhydride and amine, N-benzylethylenediamine and 2-(methylthio) ethylamine were used to set the starting materials.

2. Image comparison between Diethylene-triaminetriacetic acid derivative and Gd-DTPA

By using a 1.0T (Harmony, SIEMENS) MR equipment, phantoms of which 100cc of saline was diluted using diethlyenetriaminetriacetic acid and Gd-DTPA were imaged.

The amount of diethylenetriaminetriacetic acid and Gd-DTPA which was diluted into the 100cc of saline was 0.05mmol/L, 0.1mmol/L, 0.15mmol/L, 0.2mmol/L, 0.3mmol/L, 0.5mmol/L, 1.0mmol/L, 2.0mmol/L, 3.0mmol/L and 4.9mmol/L, respectively. Head coils were used and while fixing the SE pulse sequence and image variable (as TE is 14ms, 1NEX with a 256x201 matrix), the signal intensity and simple contrast ratios according to changing concentrations and TR were compared with various TR at 300ms, 400ms, 500ms, 600ms, 700ms, 800ms, 900ms, 1000ms, 1200ms, 1400ms and 1600ms.

Fig. 5. Image of GD-DTPA according to density

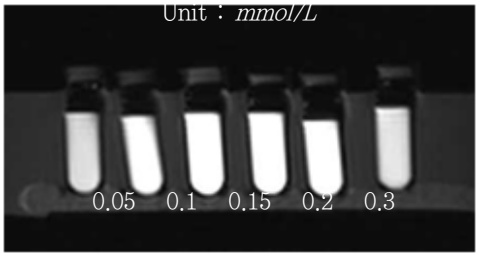


Fig. 6. Image of Diethylenetriaminetriacetic acid derivative according to density

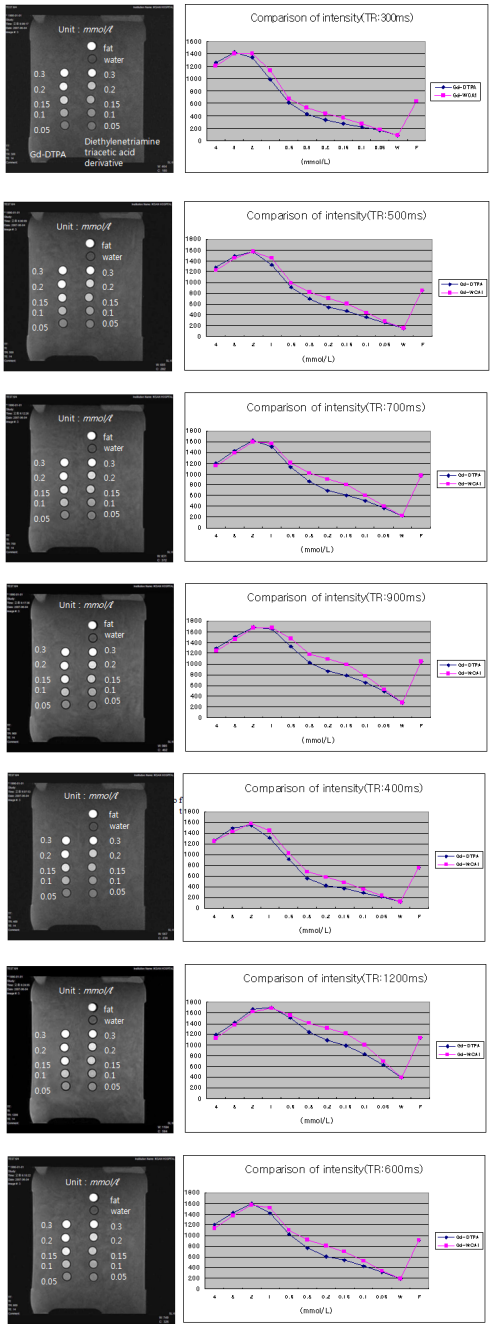
Ⅲ. Results

The reaction of diethylenetriaminepentaacetic dianhydride with amine gave triacetic acid, diethylenetriamine-N,N"-bis(N-benzylethylenediamide)-N,N',N"-triacetic acid (Fig.1) and diethylenetriamine-N,N"-bis[(2-methylthio)ethylamide]-N-N'N"-triacetic acid [Fig. 2] with a 82~87% yield. The resultant ligand was reacted with gadolinium acetate in water at room temperature to give gadolinium complexes, [diethylenetriamine-N,N"-bis(N-benzylethylenediamide)-N,N",N"-triacetato] gadolinium (Ⅲ) [Fig. 3] and [diethylenetriamine-N,N"-bis[(2-methylthio)ethylamide]-N,N',N"-triacetao] gadolinium (Ⅲ) [Fig. 4] with a 82~87% yield.

According to the signal intensity comparison results [Fig. 5][Fig. 6], at the low concentrations of lower than 1.0mmol/L the signal intensity of the diethylenetriaminetriacetic acid was higher than that of the Gd-DTPA. However, at higher than 1.0mmol/L concentrations, the signal intensity of the Gd-DTPA was higher than that of the diethylenetriaminetriacetic acid derivative. The highest signal intensity was demonstrated at 3.0mmol/L with TR set at 300ms, 2.0mmol/L with TR set at 400 to 800ms and at 1.0mmol/L with TR set at 900 to 1600ms for the diethylenetriaminetriacetic acid. When Gd-DTPA was used, the highest signal intensity was achieved at 3.0mmol/L with TR set at 300ms, 2.0mmol/L with TR set at 400 to 1000ms and at 1.0mmol/L with TR set at 1200 to 1600ms [Fig. 7].

The simple contrast ratio comparison results also demonstrated similarities with the signal intensity comparison results. The simple contrast ratio was shown to be higher in the diethylenetriaminetriacetic acid derivative than in the Gd-DTPA at concentrations of lower than 1.0mmol/L while it was higher in the Gd-DTPA at concentrations greater

than 1.0mmol/L.



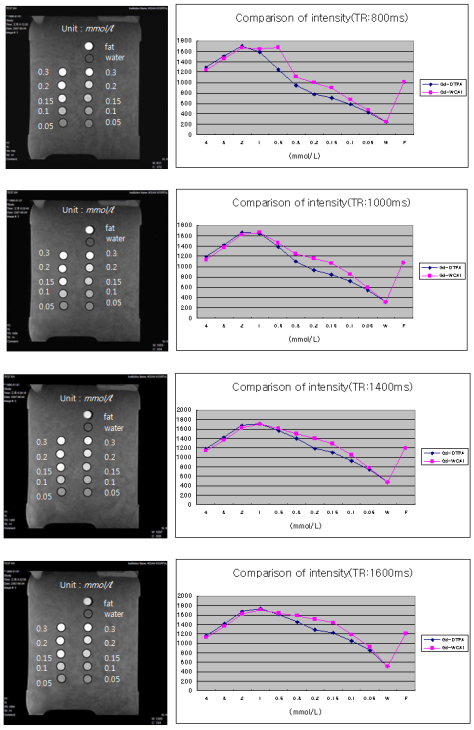


Fig. 7. Images and graphs of signal intensity according to repetition time(TR)

Ⅳ. Conclusion

According to comparison results of the signal intensities of the images based on the changes in the concentrations of the contrast medium and TR, the signal intensity differences between the contrast mediums was found to be relatively small at contrast medium concentrations of 1~2mmol/L where the highest signal intensities were demonstrated. However, at concentrations of lower than 1.0mmol/L, the signal intensity was markedly higher in the diethylenetriaminetriacetic acid derivative than in the Gd-DTPA. It was also found that the differences in signal intensities achieved using varying concentrations of contrast medium were also affected by the TR. By referring to the study which was

undertaken, it can be concluded that the efficacy of the diethylenetriaminetriacetic acid derivative is better than Gd-DTPA and it is also possible to obtain optimum image qualities by using an appropriate TR in relations to the varying concentrations of contrast medium diluted in saline solution.

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