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ORIGINAL ARTICLE

Optimisation of Gadolinium and Iodinated Contrast Ratio for 1.5T and 3T MR Arthrography: An In Vitro Study

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ABSTRACT

Objectives: *To determine the optimal ratio of gadolinium to iodine for 1.5T and 3T magnetic resonance (MR) arthrography.*

Methods: *An in vitro model with a mixture of six concentrations of gadolinium (0.02, 0.01, 0.005, 0.0025, 0.00125 and 0.000625 mmol/mL) and six concentrations of iodine (297, 225, 150, 112.5, 75 and 37.5 mg I/mL) were first scanned with fluoroscopy, then with 1.5T and 3T MR scanners, each acquiring a T1-weighted imaging sequence, a T2-weighted imaging sequence, and a proton density (PD) sequence. The concentrations of gadolinium and iodine were plotted against radiopacity and signal-to-noise ratio (SNR). Spearman's rank correlation coefficient test was used to investigate the correlation between radiopacity/SNR and concentrations of the two agents.*

Results: *At 1.5T, the optimal ratio was 0.0025 mmol/mL gadolinium and 37.5 mg I/mL. At 3T, the optimal ratio was 0.00125 mmol/mL gadolinium and 75 mg I/mL. When the optimal ratio for 1.5T was used for 3T, the results were comparable. There were significant correlations between iodine concentration and SNR in 3T MR T1-weighted imaging and iodine concentration and SNR in a 3T MR (PD) sequence.*

Conclusion: *The optimal ratio of gadolinium and iodine concentrations for 1.5T MR arthrography is 0.0025 mmol/mL gadolinium and 37.5 mg I/mL iodine, and that for 3T MR arthrography is 0.00125 mmol/mL gadolinium and 75 mg I/mL iodine, but the concentrations used for T1-weighted imaging at 1.5T also work well at 3T.*

Key Words: *Gadolinium; Iohexol*

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Contributors: CKMM and KYC designed the study. All authors acquired the data, analysed the data, and drafted the manuscript. KYC, AKYA, and CYC made critical revisions to the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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Data Availability: All data generated or analysed during the present study are available from the corresponding author on reasonable request.

Ethics Approval: The study was approved by the Hong Kong East Cluster research ethics committee (Ref: HKECREC-2020-021). All patients provided written informed consent.

中文摘要

體外實驗以確定1.5T及3T磁力共振關節造影術的最佳釓碘顯影劑濃度比例

巫冠文、曹君彥、區嘉殷、朱志揚

目的：確定在1.5T和3T磁力共振關節造影術的最佳釓碘顯影劑濃度比例。

方法：體外實驗模型來自六個濃度的釓顯影劑（0.02、0.01、0.005、0.0025、0.00125及0.000625 mmol/mL）及六個濃度的碘顯影劑（297、225、150、112.5、75及37.5 mg I/mL）的混合物。在螢光透視，1.5T及3T磁力共振的T1W、T2W及質子加權序列影像中，分別測量射線不透性及信雜比。釓碘濃度及射線不透性／信雜比進行作圖，並使用Spearman等級相關係數用作分析它們之間的關聯。

結果：於1.5T磁力共振關節造影術中，最佳釓碘顯影劑比例為0.0025 mmol/mL比37.5 mg I/mL。於3T磁力共振關節造影術中，最佳釓碘顯影劑比例為0.00125 mmol/mL比75 mg I/mL。於3T磁力共振中，1.5T的最佳釓碘顯影劑比例效果相若。於3T磁力共振T1加權像及質子密度序列影像中，碘濃度與信雜比有顯著相關。

結論：於1.5T磁力共振關節造影術中，最佳釓碘顯影劑比例為0.0025 mmol/mL比37.5 mg I/mL。於3T磁力共振關節造影術中，最佳釓碘顯影劑比例為0.00125 mmol/mL比75 mg I/mL。1.5T磁力共振下的最佳釓碘比例在3T磁力共振中效果相若。

INTRODUCTION

Magnetic resonance (MR) arthrography using a fixed concentration of gadolinium in the form of a contrast agent is an ideal diagnostic modality for assessment of the internal structure of joints.[1] It is a common practice to insert the needle under fluoroscopic guidance with a small iodinated contrast injection to confirm proper needle placement.[2]

There have been numerous suggested concentrations of gadolinium for this procedure.[2-7] A known effect of iodinated contrast is that it diminishes the signal intensity of gadolinium in T1-weighted images (T1WI).[5-8] It is crucial to optimise the ratio of gadolinium to iodine to achieve the best signal intensity and minimise signal loss from iodinated contrast.

We aimed to determine the optimal ratio of gadolinium to iodine concentration for 1.5T and 3T MR arthrography using an in vitro approach.

METHODS

Experimental Model

The study was performed using 0.5 mmol/mL gadoteric acid (Dotarem; Guerbet, France), a macrocyclic ionic gadolinium-based contrast agent, and with iohexol, 300 mg I/mL (Omnipaque; GE Healthcare, US), a nonionic, monometric, triiodinated, water-soluble contrast agent. These are used for MR arthrography and X-ray contrast media, respectively.

Gadoteric acid solutions were prepared at the following six concentrations diluted using normal saline (0.9% sodium chloride): 0.02 mmol/mL (1:25 dilution), 0.01 mmol/mL (1:50 dilution), 0.005 mmol/mL (1:100 dilution), 0.0025 mmol/mL (1:200 dilution), 0.00125 mmol/mL (1:400 dilution), and 0.000625 mmol/mL (1:800 dilution). Iohexol solutions were prepared at the six concentrations as follows: 297 mg I/mL (99% volume), 225 mg I/mL (75% volume), 150 mg I/mL (50% volume), 112.5 mg I/mL (37.5% volume), 75 mg I/mL (25% volume), and 37.5 mg I/mL (12.5% volume). A total of 36 mixtures of contrasts were obtained, and then placed into two rectangular-shaped tissue culture plates (24-well plate, 6 × 4, BKMAM). Each well could accommodate mixtures up to 4 mL. The plates were sealed with lids to prevent evaporation or spillage.

Fluoroscopy and Magnetic Resonance Imaging

The plates were placed on a fluoroscopy platform (Artis zee; Siemens, Germany) and spot images were

captured. Subsequently, they were placed in MR image gantries (1.5T Avanto and 3T Skyra; Siemens) systems and imaged with a head coil. The field of view was 160 × 160 mm with a matrix of 256 × 256 pixels for all sequences in both systems. All the sequences (T1WI with repetition time and echo time [TR/TE]: 400/13 ms, T2-weighted images with TR/TE: 4000/60-84 ms, and proton density [PD] with TR/TE: 2200-3500/24-30 ms) were acquired in the coronal plane with section thickness of 8 mm.

Image Analysis and Data Collection

The images were transferred to a picture archiving and communication systems server and were analysed on workstations with medical imaging software (Carestream, Rochester NY, US). A region of interest 1.0 cm in diameter was placed at the centre of each well to measure the radiopacities and signal intensities. In addition, six background radiopacity or signal intensity measurements were obtained. Each measurement was performed 5 times. Maximum and minimum measurements were discarded and means of the remaining three values were calculated. Radiopacity and signal-to-noise ratio (SNR) were determined using the following equations:

Radiopacity = Radiopacity mean / Radiopacity background

SNR = Signal intensity well / Signal intensity background

Radiopacity/SNR were plotted against concentrations of iodine/gadolinium mixtures. The optimal concentrations of gadolinium and iodine were determined.

Statistical Analysis

The Kruskal–Wallis test was used to identify any significant differences between radiopacities/SNRs and iodine/gadolinium concentrations; Spearman's rank correlation coefficients were used to determine correlations between the two mixtures. All statistical computations were performed in SPSS (Windows version 16.0; SPSS Inc, Chicago [IL], US). All p values <0.05 were considered significant.

RESULTS

Fluoroscopy

As expected, there were significant differences in the radiopacities among the different concentrations of iodine ($p < 0.001$), as well as a significant correlation between radiopacity and concentrations of iodine ($r = 0.977$, $p < 0.001$). No significant difference ($p = 0.999$) or correlation ($r = 0.052$, $p = 0.761$) in radiopacities among the six concentrations of gadolinium mixtures was found (Figure 1).

1.5T Magnetic Resonance Imaging

In T1WI, the SNRs generally increased with decreased concentrations of gadolinium (Figure 2). This trend was the same in T2-weighted images and PD sequences (Figures 3 and 4). At higher concentrations of iodine, the SNR reduced gradually. This effect was independent of the concentration of gadolinium and MR sequences. There was no significant correlation between iodine concentration and SNR in all three sequences ($r = -0.327$, $p = 0.051$; $r = -0.204$, $p = 0.233$; $r = -0.241$, $p = 0.157$ for T1, T2 and PD sequences, respectively). The maximal SNR in the T1 sequence was found in a mixture with gadolinium 0.0025 mmol/mL (1:200) and 37.5 mg I/mL (12.5% by volume).

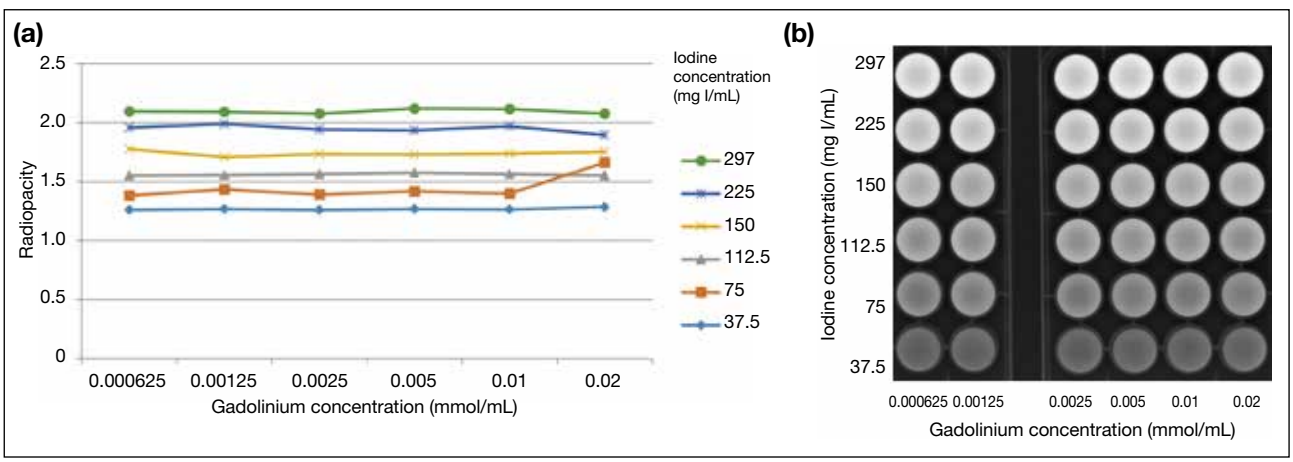

Figure 1. (a) Radiopacities against concentrations of gadolinium in the mixture at different concentrations of iodine. (b) Fluoroscopy image of the tissue culture plates.

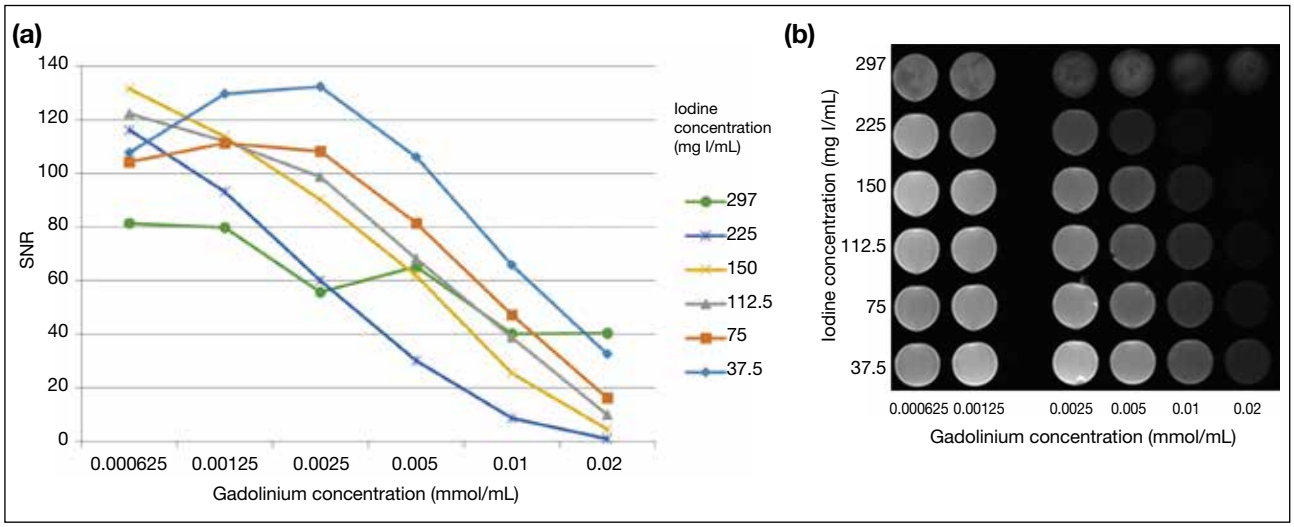

Figure 2. (a) Signal-to-noise ratios plotted against gadolinium concentrations at different concentrations of iodine in 1.5T magnetic resonance T1-weighted images. (b) 1.5T magnetic resonance imaging T1 sequence images of the tissue culture plates.

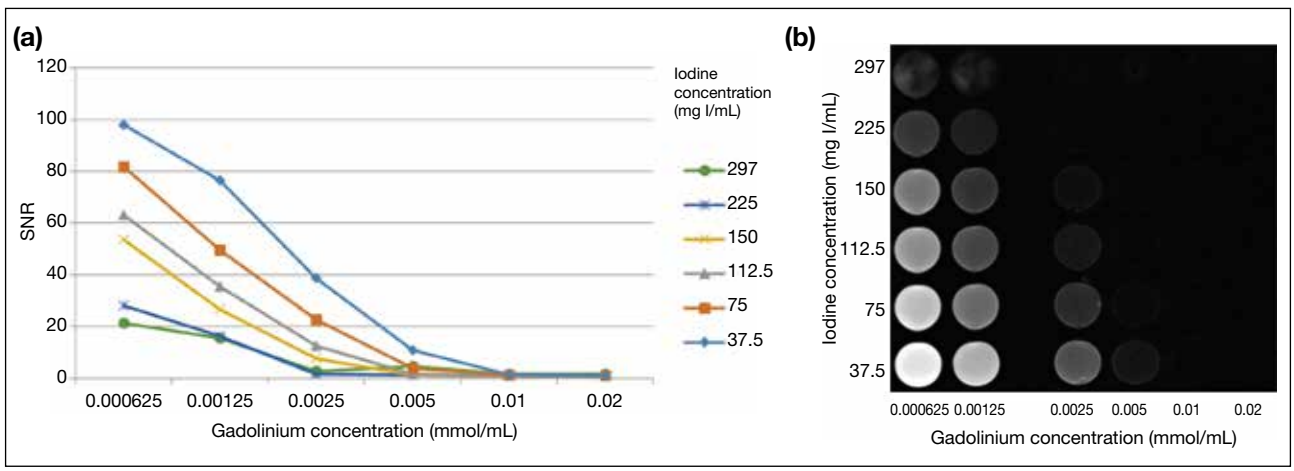

Figure 3. (a) Signal-to-noise ratios plotted against gadolinium concentrations at different concentrations of iodine in 1.5T magnetic resonance T2-weighted images. (b) 1.5T magnetic resonance imaging T2 sequence images of the tissue culture plates.

3T Magnetic Resonance Imaging

The results at 3T were roughly similar to those at 1.5T. SNR increased with decreasing gadolinium concentration in the T1 (Figure 5), T2 (Figure 6), and PD sequences (Figure 7). However, in the T1 sequence, SNR was maximised at 0.00125 mmol/mL gadolinium and 75 mg I/mL. There was a significant correlation between concentrations of iodine and SNRs in 3T MR T1WI and PD imaging (r = -0.947, p = 0.02; r = -0.354, p = 0.034 for T1 and PD sequences, respectively). No significant correlation was demonstrated between concentrations of iodine and SNRs in the T2 sequences (r = -0.294, p = 0.081).

DISCUSSION

Fluoroscopy-guided needle insertion into the joint space for MR arthrography is a common approach.[2] A test injection of iodinated contrast is helpful to confirm needle placement, but it may compromise the signal intensity derived from gadolinium contrast as shown in the present study. The reason for keeping a constant ratio of gadolinium to iodine is to avoid changing of the syringe and potentially introducing air bubbles.[2]

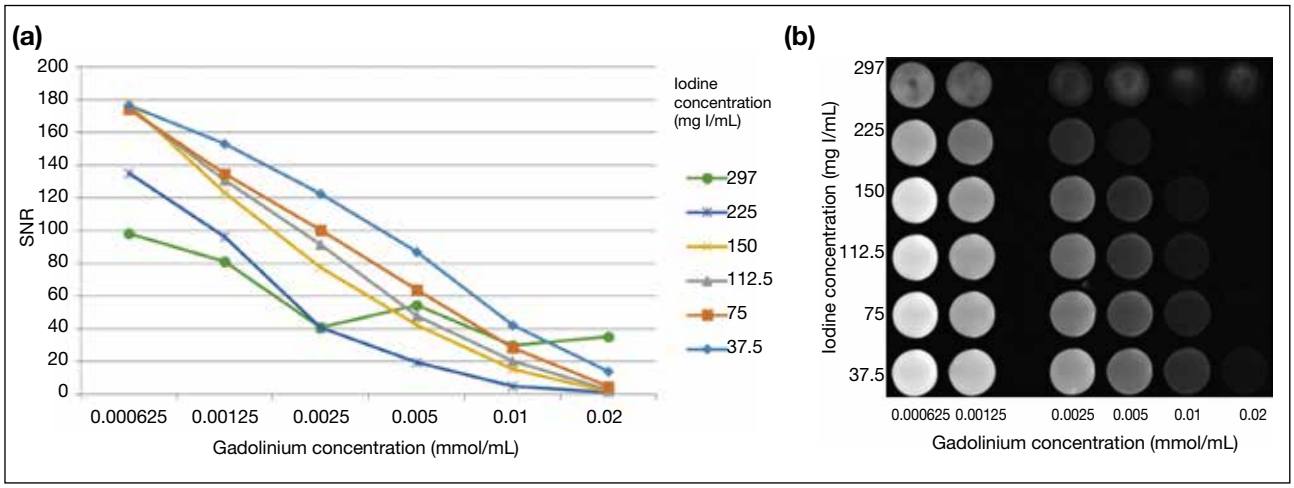

Figure 4. (a) Signal-to-noise ratios plotted against gadolinium concentrations at different concentrations of iodine in 1.5T magnetic resonance proton density images. (b) 1.5T magnetic resonance imaging proton density sequence images of the tissue culture plates.

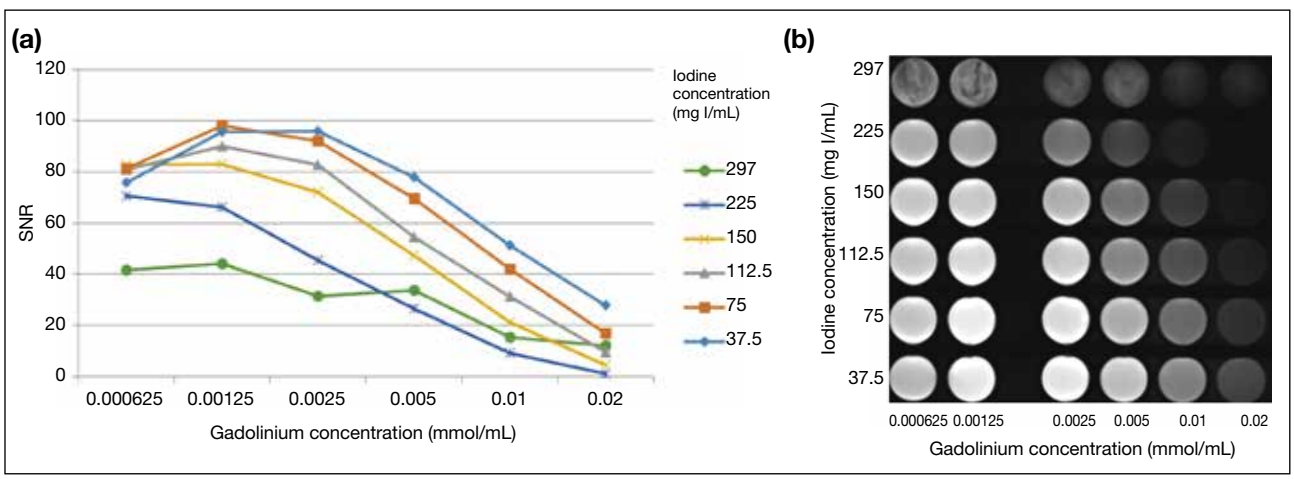

Figure 5. (a) Signal-to-noise ratios against gadolinium concentrations at different concentrations of iodine in 3T magnetic resonance T1 images. (b) 3T magnetic resonance imaging T1 sequence images of the tissue culture plates.

Although the SNR in 3T MR T1 sequences peaked at 0.00125 mmol/mL gadolinium and 75 mg I/mL, the resulting image was visually comparable to that of the mixture with the second-highest SNR, which was 0.0025 mmol/mL gadolinium and 37.5 mg I/mL. Diluting gadolinium contrast (1:200) is easier to achieve in the clinical setting. This ratio also gives maximal SNR at 1.5T, allowing the same concentrations to be used at 3T and 1.5T.

SNRs are generally reduced by increasing the concentration of iodine in all sequences at both 1.5T and 3T. This is compatible with many prior in vitro studies.[5-10] Montgomery et al[8] proposed that this effect could be related to an increase in the viscosity or reduction in the PD in the contrast mixtures. Masi et al[6] explained the reduction of signal intensity by iodinated contrast to be due to the magnetic susceptibility of iodine.

However, there is an exception to the trend mentioned above. For 1.5T and 3T MR T1 sequences, at the most diluted gadolinium concentration (0.000625 mmol/mL), SNRs were increased with associated iodine concentrations of 75 to 150 mg I/mL (Figure 2). The

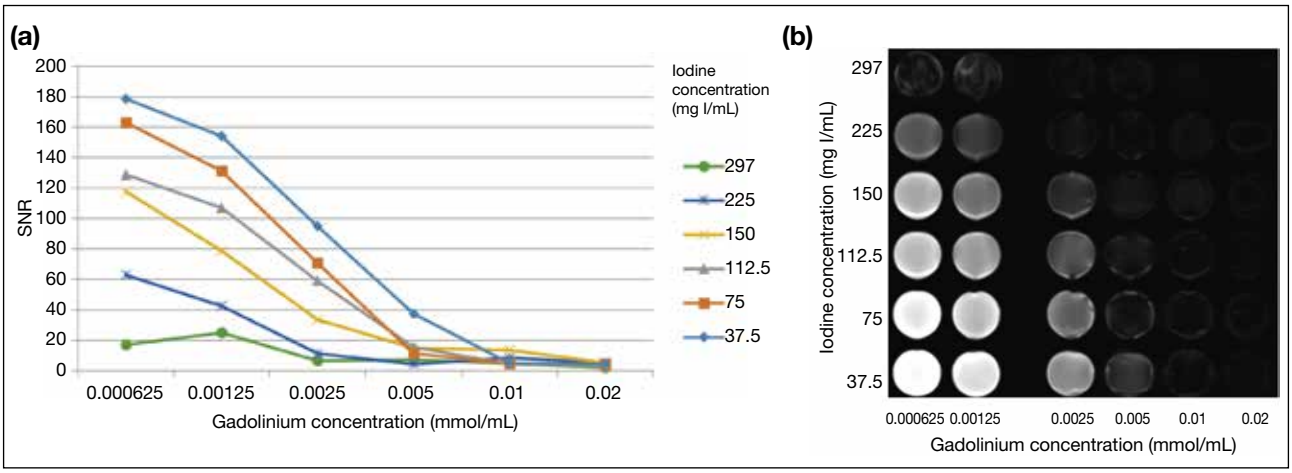

Figure 6. (a) Signal-to-noise ratios against gadolinium concentrations at different concentrations of iodine in 3T magnetic resonance T2 images. (b) 3T magnetic resonance imaging T2 sequence images of the tissue culture plates.

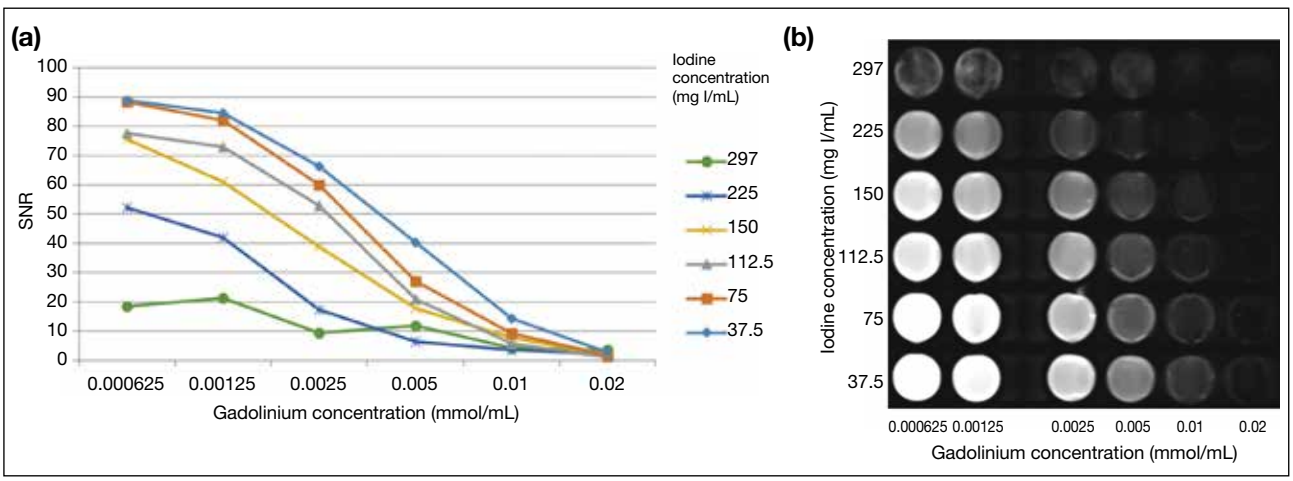

Figure 7. (a) Signal-to-noise ratios against gadolinium concentrations at different concentrations of iodine in 3T magnetic resonance proton density images. (b) 3T magnetic resonance imaging proton density sequence images of the tissue culture plates.

effect was more pronounced at 1.5T. This interesting finding correlates with the findings of Nouh et al.[7] This synergism may be explained by the extra T1 shortening effect of iodine.[11] Significant correlations of iodine concentrations and SNR were found at 3T MR T1 and PD sequences. In the present study, Spearman's rank correlation coefficient test was used, which means the correlation can be linear or non-linear. Nevertheless, the correlation was not found in 1.5T MR T1 and PD sequences.

The results obtained from the present study are within the recommended range of Masi et al,[6] though we investigated the effects of iodine concentrations on MR imaging and fluoroscopic images as well. Masi et al[6] also demonstrated that there was no significant difference between contrast diluted by normal saline and that diluted by albumin. Therefore, normal saline was used in the present study.

The optimal gadolinium concentration found in the present study was higher than that found by Choi et al,[5] whereas the optimal iodine concentration found in the present study was lower. This can be explained by the different aims of the two studies. Choi et al[5] aimed to determine the optimal contrast ratio for simultaneous

computed tomography and MR arthrography; however, the present study included 3T MR imaging.

Nouh et al[7] determined the optimal concentration of two gadolinium contrast agents in MR up to 7T but only one concentration of iodine was used.

There are limitations to the present study. Due to its in vitro setup, it is difficult to achieve a solution with the same chemical composition as joint fluid for dilution. Moreover, fat-saturated sequences were not investigated.

CONCLUSIONS

The optimal ratio of gadolinium and iodine concentrations for 1.5T MR arthrography is 0.0025 mmol/mL (1:200 dilution) gadolinium to 37.5 mg I/mL (12.5% by volume), and that for 3T MR arthrography is 0.00125 mmol/mL (1:400 dilution) gadolinium to 75 mg I/mL (25% by volume) iodine, but the former concentrations suffice for 3T, allowing a simplified setup.

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