European Radiology (2019) 29:2009–2016
https://doi.org/10.1007/s00330-018-5733-3

MAGNETIC RESONANCE

Spiral flow-generating tube for saline chaser improves aortic enhancement in Gd-EOB-DTPA-enhanced hepatic MRI

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Received: 23 March 2018 / Revised: 11 August 2018 / Accepted: 28 August 2018 / Published online: 25 September 2018
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Abstract

Objectives To evaluate the effect of a spiral tube on contrast enhancement in the hepatic arterial phase (HAP) of gadoxetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance imaging (MRI).

Methods In this retrospective study, we observed 104 patients who underwent dynamic MRI of the liver between October 2017 and December 2017. Three Gd-EOB-DTPA injection protocols were compared: (A) conventional method (undiluted Gd-EOB-DTPA, injection rate 1 ml/s, n = 36); (B) spiral dilution method (1:1 diluted Gd-EOB-DTPA with saline [off-label], injection rate 2 ml/s via spiral tube, n = 38); (C) spiral-flushed method (undiluted Gd-EOB-DTPA, injection rate 1 ml/s via spiral tube, n = 30). We regarded protocol-A as a control. The signal-to-noise ratio (SNR) of the abdominal aorta was calculated using arterial phase images. Image contrast and artefacts were evaluated by two board-certified radiologists, using a four-point scale. Statistical analyses included Dunnett's test, the Kruskal-Wallis test and the Steel test.

Results The SNR of the aorta was significantly higher with protocol-C (25.4 ± 8.8) than protocol-A (20.8 ± 5.4, $p = 0.01$). There was no significant difference in SNR between protocols A and B ($p = 0.47$). The contrast score of protocol-C was significantly higher than that of protocol-A ($p = 0.0019$). There was no significant difference in contrast score between protocols A and B ($p = 0.50$). There was no significant difference in artefacts among the three protocols ($p = 0.96$).

Conclusions Use of a spiral tube with a slow injection protocol contributed to improved aortic contrast enhancement in the HAP of GD-EOB-DTPA-enhanced hepatic MRI.

Key Points

- *Gadoxetic acid shows weaker arterial enhancement at recommended doses, compared with nonspecific gadolinium agents; selection of an appropriate injection protocol is important.*
- *A spiral flow-generating tube improves the transport efficiency of the contrast media, and increases the signal-to-noise ratio of the aorta in hepatic arterial phase.*
- *A spiral flow-generating tube does not contribute to artefact reduction in hepatic arterial phase.*

Keywords Magnetic resonance imaging · Contrast media · Liver

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Abbreviations

CT	Computed tomography
HAP	Hepatic arterial phase
MRI	Magnetic resonance imaging
SNR	Signal-to-noise ratio

Introduction

Gadoxetic acid (Gd-EOB-DTPA) is a hepatobiliary contrast agent used in magnetic resonance imaging (MRI) of the liver [1, 2]. The recommended dose of Gd-EOB-DTPA is 0.025 mmol/kg, which is one-fourth of the recommended dose of nonspecific Gd agents (0.1 mmol/kg) [3]. The T1 relaxivity of Gd-EOB-DTPA, measured in human blood at 1.5-T, is twice that of standard gadolinium chelates [4]. Therefore, the T1 shortening effect of Gd-EOB-DTPA is approximately half that of nonspecific Gd agents in the recommended dose. Thus, selection of an appropriate injection protocol is important in acquiring optimal aortic contrast images in the arterial phase.

Previous reports have shown that a slower injection protocol (1 ml/s vs. 2 ml/s) contributes to increased aortic enhancement and/or reduction in artefacts in the arterial phase of Gd-EOB-DTPA-enhanced MRI [5, 6]. Other reports have shown that a dilution method (Gd-EOB-DTPA diluted 1:1 with saline [off-label] and injected at a rate of 2 ml/s) was more beneficial in minimising artefacts within the arterial phase of Gd-EOB-DTPA-enhanced MRI, relative to the slow injection method (undiluted Gd-EOB-DTPA injected at a rate of 1 ml/s) [7]. In addition, a saline chaser is routinely used in modern contrast-enhanced MRI injection protocols, especially for dynamic studies. The saline pushes the contrast medium bolus to the central blood volume and causes a late peak enhancement at the end of the injection, resulting in increased intravascular contrast enhancement because of the higher efficiency of the injected contrast medium [8–12].

Recently, the spiral flow-generating tube was introduced for clinical use. It generates a spiral flow at the chamber-shaped connecting site; the spiral flow of saline pushes the contrast material bolus into the venous system. Some studies have shown that use of the spiral flow-generating tube increases the effect of a saline chaser and significantly improves arterial enhancement in hepatic dynamic computed tomography (CT) and in CT angiography of the lower extremities [13, 14]. Additionally, a spiral flow-generating tube might be useful for the dilution of contrast material and saline solution by co-injection. However, to our knowledge, the effects of using a spiral flow-generating tube during dynamic MRI have not been analysed. We hypothesised that a saline chaser via a spiral flow-generating tube might push the contrast medium bolus to the central blood volume more efficiently, thereby increasing vessel enhancement, during dynamic MRI. In addition, the use of the spiral flow-generating tube might contribute to artefact reduction in the hepatic-arterial phase (HAP) without complicated mixing procedures, because it can more easily dilute the contrast medium with saline than conventional methods.

The primary purpose of this study was to evaluate the effect of the spiral flow-generating tube on aortic contrast enhancement; the secondary purpose was the evaluation of image artefacts during HAP MRI.

Materials and methods

The Institutional Review Board approved the protocol of this retrospective study and waived the requirement for informed consent.

Connecting tubes

The conventional tube includes a T-shaped joint (medical device; capacity, 2.2 ml; length, 60.0 cm). The spiral flow-generating tube (medical device; capacity, 3.3 ml; length, 57.0 cm; Nemoto-Kyorindo) features a curved circumferential inner surface forming a columnar space (Fig. 1). The inflow opening is tangential to the circumference of the inner surface. This tube makes it possible to dilute contrast media aseptically and easily by injecting both saline and contrast media using an injector at the same time.

Patients and Gd-EOB-DTPA injection methods

Between October 2017 and December 2017, we enrolled 104 patients (71 men, 33 women; mean age, 67.5 years; age range, 27–96 years; mean weight, 61.5 kg; weight range, 41–106 kg) who underwent dynamic MRI with a history or suspicion of liver pathology in our institution. In our institution, an injection rate of 1 ml/s was conventionally applied. In November 2017, the spiral tube was introduced in our hospital. First, we used the same injection protocol (1 ml/s) as for the conventional tube. However, optimal use of the spiral tube for dynamic MRI was unknown; thus, in December 2017, we changed the injection protocol to 2 ml/s with 1:1 dilution with saline, based on previous studies [7]. The application of diluted Gd-EOB-DTPA is off-label; however, previous studies have shown its utility for artefact reduction in HAP [7]. Ultimately, patients underwent hepatic dynamic MRI with one of the following protocols: (A) conventional method (undiluted Gd-EOB-DTPA injected at a rate of 1 ml/s, 40 ml saline flush with the same injection rate) with normal tube (n = 36); (B) spiral dilution method (Gd-EOB-DTPA

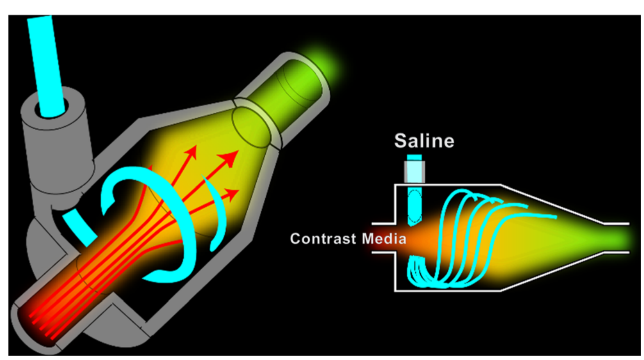


Fig. 1 Within the spiral flow-generating tube, the saline and contrast media flow through a spiral flow-generating chamber, which features a curved circumferential inner surface forming a columnar space

diluted 1:1 with saline [off-label] and injected at a rate of 2 ml/s, 40 ml saline flush with the same injection rate) with spiral flow-generating tube (n = 38); and (C) spiral-flushed method (undiluted Gd-EOB-DTPA injected at a rate of 1 ml/s, 40 ml saline flush with the same injection rate) with spiral flow-generating tube (n = 30). In protocol-B, both contrast media and saline were injected using an injector at the same time to dilute. Table 1 shows patient data for each protocol. Exclusion criterion was severe renal dysfunction (estimated glomerular filtration rate < 30 ml/min/1.73 m^2). No patients were excluded from this study.

MRI protocol

All patients underwent dynamic ultrafast T1-weighted three-dimensional (3D) turbo-gradient-echo sequence (GRE) with fat suppression (mDixon-3D-GRE) on a 3-T scanner (Achieva 3.0T TX, Philips Healthcare) and were injected with 0.025 mmol/kg (0.1 ml/kg) of Gd-EOB-DTPA via one of three injection protocols, followed by injection of 40 ml saline at the same rate, using a power injector. In all examinations, Gd-EOB-DTPA was delivered through a 22-gauge catheter inserted into an antecubital vein.

The patients held their breath in end-expiration. Table 2 describes the sequences and parameters of mDixon-3D-GRE. Images from the protocol were acquired in the transverse plane, with a reception time (TR)/echo time (TE) ratio of 3.20/1.57. Flip angle was 10°, number of acquisitions was 1, field of view (FOV) was 320 × 320 mm, matrix was 304 ×304, and acquisition time was 15.9 s.

The test-bolus comprised 0.125 mmol (0.5 ml) Gd-EOB-DTPA, followed by the injection of 35 ml saline at an equal rate, according to each injection protocol (A to C); images to determine scan timing were acquired in the transverse plane to visualise the abdominal aorta, not the tumour. We defined HAP scan timing according to a previous report [15]. The mean scan delay times were 38.5 s ± 3.9, 29.1 s ± 5.9 and 34.3 s ± 4.4 for protocols A, B and C, respectively.

Quantitative image analysis

All quantitative image analyses were performed by one radiologist with 15 years of experience in abdominal imaging, who was blinded to the study protocol. Operator-defined regions of interest were measured on the abdominal aorta at the level of bifurcation of the coeliac trunk on arterial-phase images and the mean signal intensity was obtained; signal-to-noise ratios (SNRs) of the aorta were calculated by dividing image noise. Image noise was measured in the standard deviation (SD) of abdominal aorta.

Table 2 Magnetic resonance imaging (MRI) parameters for three-dimensional gradient-echo sequence

Sequence	
TR / TE (ms)	3.2 / 1.57
Flip angle (degrees)	10
Field of view (mm)	320
Matrix	304
Voxel size (mm)	0.83 / 0.83 / 2.00
Slice thickness (mm)	2
Acquisition time (s)	15.9
No. of slices	100
No. of acquisitions	1
Bandwidth (Hz / pixel)	719.5
Fat suppression	SPAIR

s second, *SPAIR* spectral attenuated inversion recovery, *TR/TE* repetition time/echo time

Qualitative analysis

Image contrast of the abdominal aorta and the degree of artefacts on arterial-phase images were independently evaluated by two radiologists, each of whom had 8 years of experience with abdominal MRI. The MRI datasets of the 104 patients were randomised, and the readers were blinded to the injection protocols and all patient data.

First, contrast of the abdominal aorta was evaluated using a four-point scale (excellent, good, poor, non-diagnostic) (Fig. 2). Second, the degree of artefacts on arterial-phase images was evaluated using a four-point scale to grade image quality: 4 (excellent) was defined as absence of artefacts, 3 (good) as a slight ringing or motion artefact that did not interfere with diagnosis, 2 (poor) as an artefact interfering with diagnosis, and 1 (non-diagnostic) as an obvious artefact rendering image assessment nearly impossible (Fig. 3).

Table 1 Patient demographic data

	Protocol-A (n = 36)	Protocol-B (n = 38)	Protocol-C (n = 30)	*p*-value**
Age (y)*	69.5 ± 9.1 (56–96)	65.8 ± 13.1 (34–82)	67.3 ± 11.2 (27–82)	0.369
Body weight (kg)*	62.0 ± 11.3 (41–96)	62.5 ± 12.5 (44–106)	59.6 ± 10.9 (42–87)	0.559
Sex (M / F)	27 / 9	27 / 11	17 / 13	0.256

*Data are mean ± standard deviation. Data in parentheses ranges

**Age and body weight: One-way analysis of variance; Sex: Kruskal-Wallis test

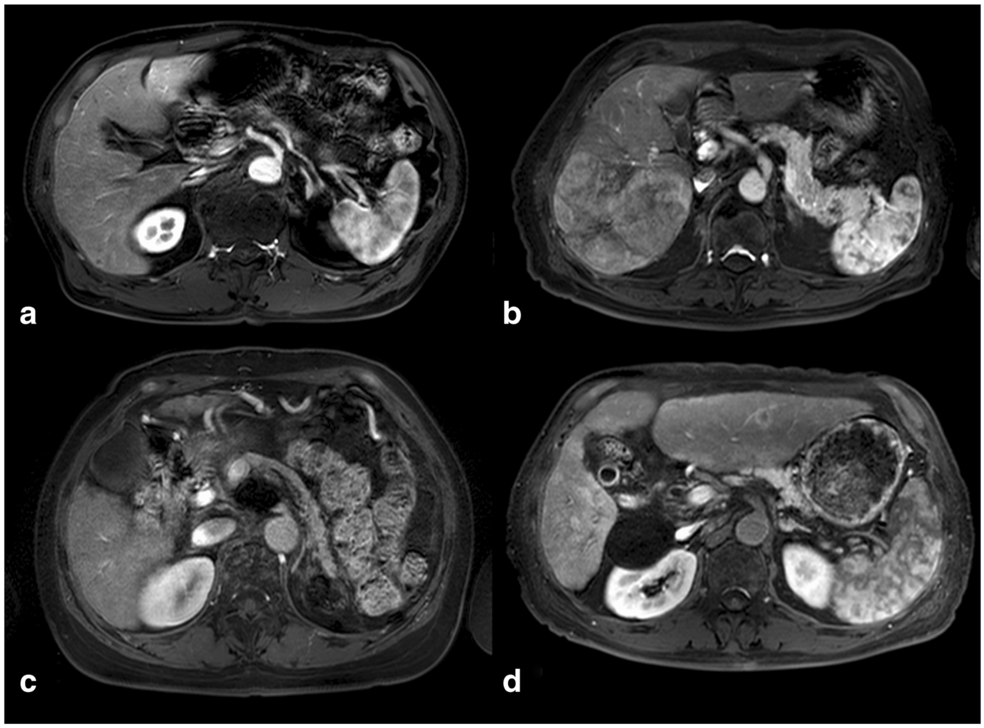


Fig. 2 The contrast of the abdominal aorta was evaluated using a four-point scale (**a**: excellent, **b**: good, **c**: poor, **d**: non-diagnostic)

In cases of interobserver disagreement, the observers discussed and reached consensus. The degree of interobserver agreement for each qualitative assessment was determined by calculating the kappa value.

Statistical analysis

We compared the SNR of the abdominal aorta among the protocols, using one-way ANOVA followed by Dunnett's test.

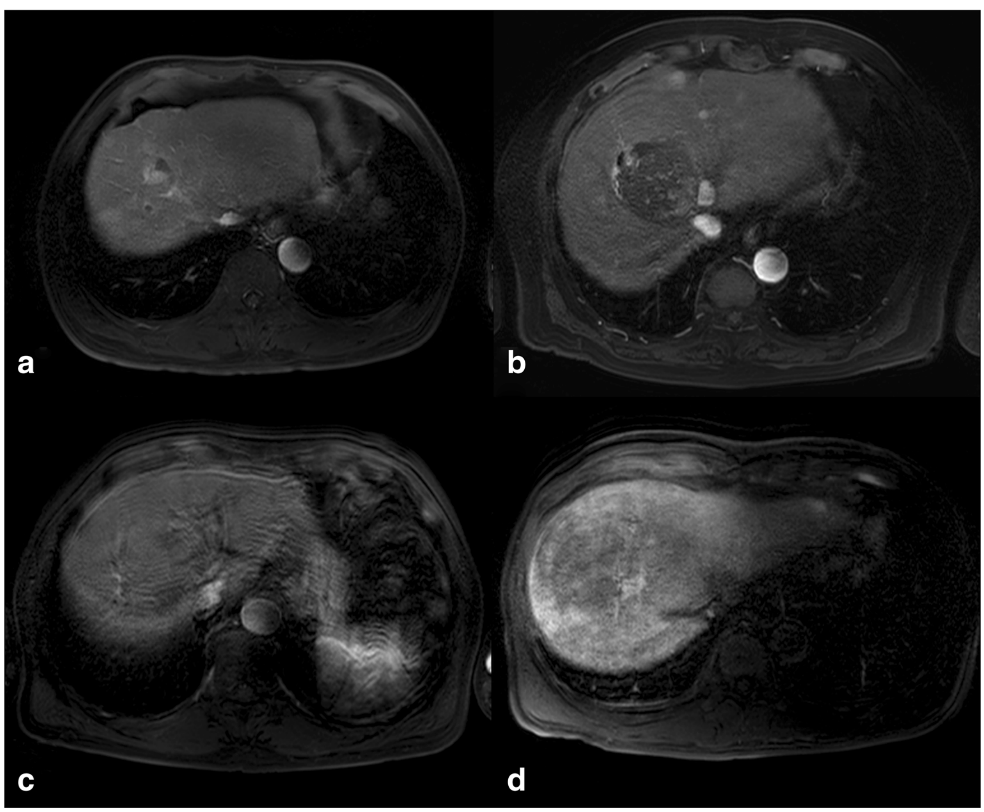


Fig. 3 The degree of artefacts on arterial-phase images was evaluated using a four-point scale (**a**: excellent, **b**: good, **c**: poor, **d**: non-diagnostic)

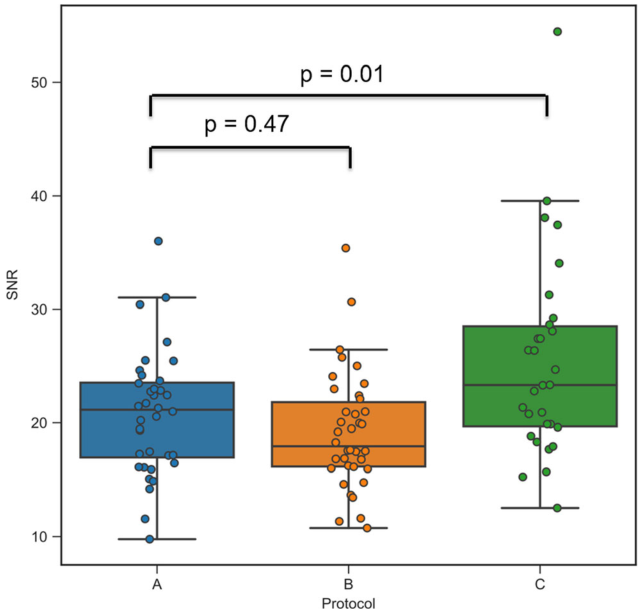


Fig. 4 Box-and-whisker plot shows the results of the quantitative analysis. The signal-to-noise ratio (SNR) of the abdominal aorta during the arterial phase was significantly higher in protocol-C (spiral flush method) than in protocol-A (conventional method) (25.4 ± 8.8 vs. 20.8 ± 5.4, p = 0.01). There was no significant difference in the SNR between protocols A and B (spiral dilution method) (20.8 ± 5.4 vs. 19.2 ± 5.1, p = 0.47)

In qualitative image analysis, the Kruskal-Wallis test was applied to examine intergroup differences for contrast of the abdominal aorta among the protocols, followed by the Steel test. The Kruskal-Wallis test was applied to examine intergroup differences for artefacts among the protocols.

Probability values of < 0.05 were considered statistically significant. Kappa coefficients for interobserver agreement of < 0.20, 0.21–0.40, 0.41–0.60, 0.61–0.80 and 0.81–1.00 were defined as poor, fair, moderate, substantial and nearly perfect, respectively. All statistical analyses were performed with R, version 2.6.1 software (The R Project for Statistical Computing; http://www.r-project.org/).

Results

The three groups were well matched in age (p = 0.37), sex distribution (p = 0.26) and body weight (p = 0.56) (Table 1).

Quantitative analysis

The mean values for SNRs of the abdominal aorta were 20.8 ± 5.4, 19.2 ± 5.1 and 25.4 ± 8.8 for protocols A, B and C, respectively. The overall difference among the three groups was statistically significant (p < 0.001). The SNR of protocol-C was significantly higher than the SNR of protocol-A (p = 0.010). There was no significant difference in SNR between protocols A and B (p = 0.47) (Fig. 4).

Qualitative analysis

The mean scores for abdominal aorta contrast in protocols A, B and C were 3.44 ± 0.65, 3.26 ± 0.76 and 3.90 ± 0.31, respectively. Interobserver agreement was moderate (Kappa = 0.508). The mean score of protocol-C was significantly higher than the mean score of protocol-A (p = 0.0019). There was no significant difference in mean score between protocols A and B (p = 0.50) (Table 3).

The mean scores for the degree of artefacts in protocols A, B and C were 3.25 ± 0.69, 3.18 ± 0.80 and 3.23 ± 0.63, respectively. Interobserver agreement was moderate (Kappa = 0.437). There was no significant difference among the three protocols in the degree of artefacts (p = 0.96) (Table 3).

Figure 5 shows the percentages of scores for abdominal aorta contrast and artefacts of the arterial-phase MR images of the three injection protocols.

Discussion

Our study showed that the SNR of the aorta on the arterial phase images was significantly higher in the spiral-flushed method than in the conventional method; however, there was no significant difference in the SNR of the aorta between the spiral dilution method and the conventional method. Moreover, there was no significant difference in the degree of artefacts among the three methods.

Our clinical study demonstrated that the saline chaser with the spiral flow-generating tube significantly improved aortic contrast enhancement during the arterial phase in Gd-EOB-DTPA-enhanced MRI in both quantitative and qualitative image analyses. A possible explanation for this finding may be that the bolus of contrast

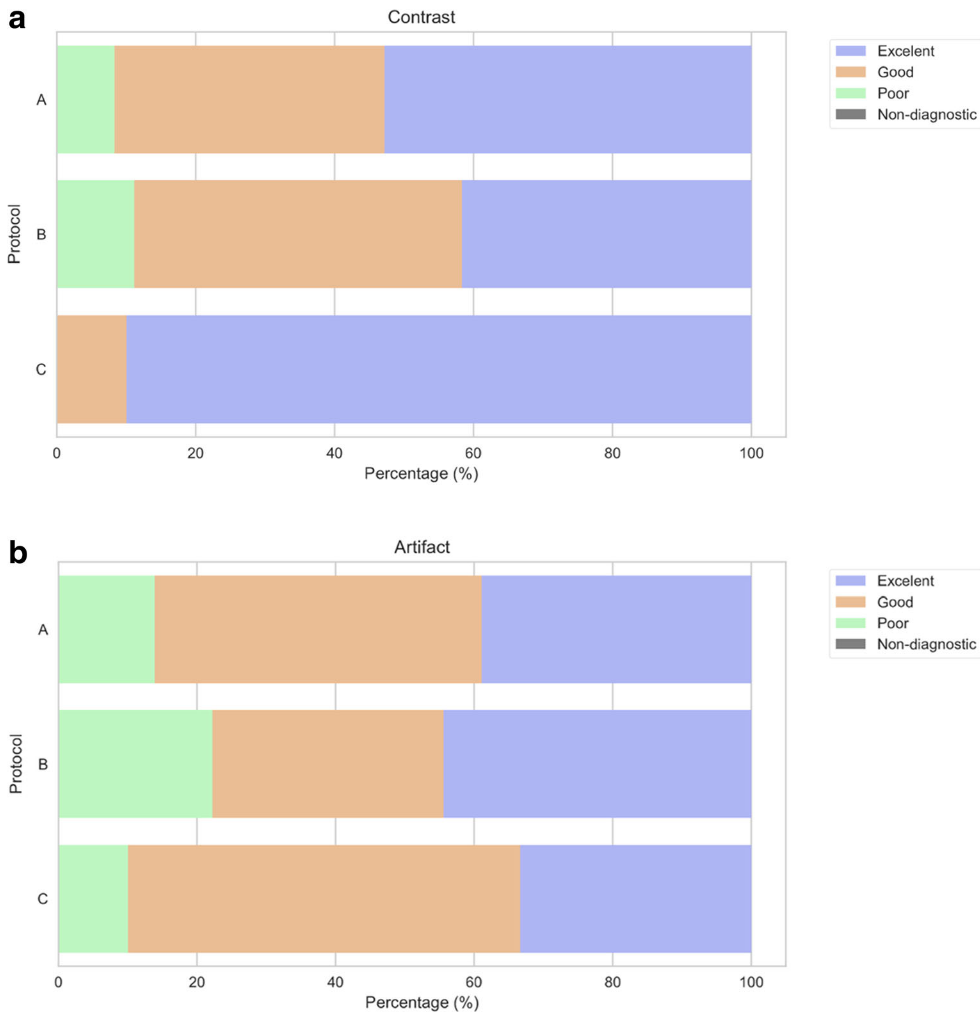
Table 3 Qualitative image analysis (interobserver agreements)

	Protocol-A (n = 36)	Protocol-B (n = 38)	Protocol-C (n = 30)	p-value**
Aortic contrast*	3.44 ± 0.65	3.26 ± 0.76	3.90 ± 0.31	0.00018
Artifact*	3.25 ± 0.69	3.18 ± 0.80	3.23 ± 0.63	0.96

*Data are mean ± standard deviation

**Kruskal-Wallis test

Fig. 5 Bar graph shows the results of qualitative analysis: the percentages of scores for (**a**) abdominal aorta contrast and (**b**) artefacts of the arterial-phase MR images of the three injection protocols. **a** There was a significant difference between protocols A and C (p = 0.0019), but not between protocols A and B (p = 0.50). **b** There was no significant difference among the three protocols (p = 0.96)



material is pushed forward into the venous system more efficiently when saline solution is injected with a spiral flow-generating tube, resulting in greater aortic enhancement. Previous studies have shown that flow in a smooth tube is laminar at a low flow rate and turbulent at a high flow rate [16]; the velocity of saline varies throughout the vein, such that saline cannot effectively push contrast material during laminar flow. Therefore, some studies have shown a decreased effect of a saline chaser at lower injection rates [8]. The spiral flow-generating tube did not generate laminar flow and the velocity of saline might not be changed in the vein as it would in the case of laminar flow. Some dynamic CT studies have shown that spiral flow was effective at an injection rate of approximately 3–4 ml/s [13, 14], and we found a similar effect in spiral flow at low injection rates, such as 1 ml/s, in this examination. According to the study by Kidoh et al, the use of a spiral flow-generating tube increased the effect of the saline chaser and significantly improved the SNR of the aorta during the arterial phase of hepatic dynamic CT [13]. Masuda et al reported the CT number of the abdominal aorta to the arteries of the foot upon CT angiography of the lower extremities [14]. Theoretically, the dilution method using the spiral flow-generating tube might also increase the transportation efficiency of the contrast material; however, this method reduces the concentration of contrast material because of its greater total volume of saline and higher injection rate, relative to the other two methods. In this study, the increase in transportation efficiency might be counteracted by the reduction in contrast material concentration.

In our study, the use of the spiral flow-generating tube did not contribute to artefact reduction. Previous studies demonstrated that dilution of Gd-EOB-DTPA may reduce the frequency of artefacts [7, 17]. Kim et al demonstrated that 1:1 diluted Gd-EOB-DTPA, with saline at a rate of 2 ml/s, was more beneficial in minimising the artefact in HAP of dynamic MRI, compared with slow injection of undiluted Gd-EOB-DTPA at a rate of 1 ml/s [7]. The spiral flow-generating tube can more easily dilute the contrast medium with saline during concurrent injection. Therefore, we predicted that the use of the spiral flow-generating tube might contribute to artefact reduction during HAP without the requirement for complicated mixing procedures, compared with previous reports [7, 17]. Conversely, our study showed that the spiral dilution method did not statistically reduce the degree of artefacts, compared with the conventional method. We cannot readily explain this phenomenon, but offer the following suggestions that may have contributed to it: (1) a relatively small sample size; (2) contrast media may not mix uniformly with saline in our spiral dilution method, compared with previous dilution methods; and (3) there were few artefacts overall, possibly because oxygenation is provided for some patients with breath-hold failure in our institution.

There are some limitations in our study. First, we examined only the SNR of the abdominal aorta and did not evaluate the tumour and hepatic enhancement. Therefore, we cannot directly prove the utility of the spiral flow-generating tube in clinical practice for Gd-EOB-DTPA-enhanced MRI. Second, we did not evaluate differences in the cardiovascular statuses of the three patient groups. This may have contributed to differences in enhancement among the protocols. To minimise this effect, we adopted a test bolus injection protocol in dynamic MRI. Third, the volume of contrast material differed among patients according to body weight, which resulted in a variable injection duration of contrast material that may have influenced signal intensity (e.g. by flux per body size and recirculation effect). However, there was no significant difference in BW among the three groups, and previous reports suggested that the influence of injection duration is relatively small at short injection durations [18]. Fourth, the application of diluted Gd-EOB-DTPA (protocol-B) is an off-label use. However, the co-injection of contrast material and saline has been widely reported as a common practice and appears to be justified. Finally, this was a retrospective study and the sample size was small.

In conclusion, the use of a spiral flow-generating tube with a slow injection protocol contributed to improved aortic contrast enhancement in the arterial phase of GD-EOB-DTPA-enhanced hepatic MRI.

Funding The authors state that this work has not received any funding.

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Takeshi Nakaura.

Conflict of interest Yuba Koji declares a relationship with the following company: Nemoto Kyorindo; however he did not analyse and control the data or evaluate the results.

The other authors declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry One of the authors (Takeshi Nakaura) has significant statistical expertise.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- Retrospective
- Observational
- Performed at one institution

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