

# Delivering the diluted contrast agent with saline via a spiral flow tube improves arterial enhancement for contrast enhancement of magnetic resonance angiography of the neck

## A retrospective study

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### Abstract

A contrast agent can be pushed by a saline solution more effectively through a spiral flow tube than through a conventional T-shaped tube in contrast-enhanced magnetic resonance angiography (CEMRA). To compare the degree of contrast enhancement and signal stability in the carotid artery by using CEMRA between a spiral flow tube and a T-shaped tube.

A total of 100 patients were analyzed in this retrospective study. The first 50 patients underwent CEMRA of the carotid artery with the T-shaped tube, while the last 50 patients used the spiral flow tube. Gadoterate meglumine was diluted with saline to make a total volume of 20 mL. Injection was performed with a bolus rate of 2.5 mL/s for 8 seconds. Five regions of interest (ROIs) were placed on the contrast-enhanced area in each carotid artery and the signal intensity (SI) in the ROI was used for the analysis. The ROIs on the brain stem were also placed and the average SI in this ROI was used as a reference signal. The enhancement of the artery ( $E_{\text{artery}}$ ) was calculated as a normalized signal using the following equation:  $E_{\text{artery}} = \text{SI in the ROI of the carotid bifurcation} / \text{SI in the ROI of the brain stem}$ . Signal homogeneity in the contrast-enhanced area ( $\text{SH}_{\text{enhance}}$ ) was assessed by calculating the coefficient of variation from the SI in the 5 ROIs. The value of  $\text{SH}_{\text{enhance}}$  and  $E_{\text{artery}}$  between the data obtained from the spiral flow tube and the T-shaped tube were compared.  $P$ -values  $< .05$  were considered significant.

We found a significant difference in  $\text{SH}_{\text{enhance}}$  between the data obtained from the spiral flow tube ( $0.20 \pm 0.060$ ) and the T-shaped tube ( $0.24 \pm 0.056$ ) ( $P = .001$ ). The  $E_{\text{artery}}$  values significantly increased by 15% (spiral flow tube, median 14.1 with interquartile range [IQR] 11.8–15.4 vs T-shaped tube, median 12.3 IQR 11.3–14.0,  $P = .02$ ) using the spiral flow tube.

These findings suggest that, by using the Spiral flow tube, the homogeneity of the contrast-enhanced signal intensity in the carotid artery was significantly improved without decreasing the signal intensity in CEMRA.

**Abbreviations:** ASSET = array spatial sensitivity encoding technique, CEMRA = contrast-enhanced magnetic resonance angiography, CTA = computed tomographic angiography, DSA = digital subtraction angiography,  $E_{\text{artery}}$  = enhancement of artery, IQR = interquartile range, MRI = magnetic resonance imaging, PC = phase-contrast, ROIs = regions of interest, SD = standard deviation,  $\text{SH}_{\text{enhance}}$  = signal homogeneity in the contrast-enhanced area, SI = signal intensity,  $\text{SI}_{\text{artery}}$  = the mean signal intensity in the enhancement area inside the carotid artery,  $\text{SI}_{\text{stem}}$  = the mean signal intensity in the brain stem during pre-contrast imaging, TOF = time-of-flight.

**Keywords:** carotid artery, contrast-enhanced magnetic resonance angiography, magnetic resonance angiography

Editor: Neeraj Lalwani.

The authors have no conflicts of interest to disclose.

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How to cite this article: Hamaguchi A, Fujima N, Hamaguchi N, Hayashi T, Kodera S. Delivering the diluted contrast agent with saline via a spiral flow tube improves arterial enhancement for contrast enhancement of magnetic resonance angiography of the neck: A retrospective study. *Medicine* 2019;98:52(e18526).

Received: 30 March 2019 / Received in final form: 22 November 2019 /

Accepted: 29 November 2019

<http://dx.doi.org/10.1097/MD.00000000000018526>

## 1. Introduction

Proper treatment of carotid steno-occlusive diseases requires a comprehensive assessment of the underlying vascular morphology because it is crucial to detect and evaluate the severity of the stenosis in arterial lesions for further therapeutic decision-making.<sup>[1–3]</sup> Digital subtraction angiography (DSA) is the gold standard for diagnosis of vasculature, however, because of neurological complications related to DSA,<sup>[4]</sup> computed tomographic angiography (CTA) or contrast-enhanced magnetic resonance angiography (CEMRA) has been widely used for the assessment of carotid steno-occlusive diseases in clinical practice.<sup>[5,6]</sup> In contrast, time-of-flight (TOF) and phase-contrast (PC) MRA are also widely used because of their noninvasive nature. However, TOF- and PC-MRA have a major limitation, turbulent flow, which is caused by certain flow characteristics. This unstable flow condition causes arterial signal dephasing and signal loss, which is frequently observed in carotid bifurcation and makes it difficult to evaluate carotid arterial stenosis.<sup>[7,8]</sup> In

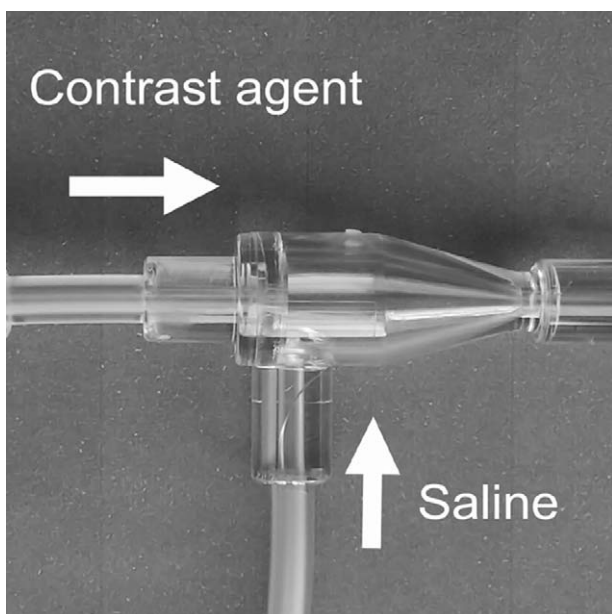
contrast, the depiction of the vasculature in CEMRA is not significantly influenced by such signal loss by unstable arterial flow because of its high arterial signal obtained with the use of contrast agents. Additionally, one advantage that CEMRA has over CTA is that it does not cause radiation exposure. Therefore, CEMRA is more useful for the evaluation of cervical arteries compared with other techniques, as it provides sufficient visualization and less invasiveness. However, an appropriate amount and injection rate of contrast agent with additional saline flush is required in CEMRA image acquisition.<sup>[9]</sup> Specifically, a previous investigation of CTA described the utility of a spiral flow tube to obtain stronger enhancement and more homogeneous density in arterial vessels than that obtained by the use of a conventional T-shaped tube.<sup>[10]</sup> A spiral flow tube has a specifically shaped chamber larger than the tubing at the connecting site, which enables saline solution to push the contrast agent more effectively than it can through a conventional T-shaped tube. Spiral flow tubes are expected to improve the visibility of arterial vessels in CEMRA relative to that of a conventional T-shaped tube (Fig. 1).

The purpose of this study was to compare the degree of contrast enhancement and signal stability in the carotid artery between CEMRA with either a spiral flow tube or a conventional T-shaped tube.

## 2. Materials and methods

### 2.1. Patients

From February 2015 to November 2017, we retrospectively analyzed a total of 103 patients who underwent neck CEMRA with the suspicion of steno-occlusive arterial disease. Three subjects were excluded because of poor image quality. Thus, 100 patients were included in the final analysis. This study group comprised 63 men and 37 women, with a median age of 75 years with interquartile range (IQR) 68–72 (age range, 32–98 years).



**Figure 1.** A specifically shaped chamber generates spiral flow for pushing the contrast agent effectively.

The first 50 patients were scanned with the T-shaped tube (MR-20; Nemoto, Tokyo, Japan) and the last 50 patients with the spiral flow tube (Nemoto Spiral Flow; Nemoto, Tokyo, Japan). This study was approved by the Institutional Review Board of Sapporo Azabu neurosurgical Hospital. The requirement for written informed consent was waived because of the retrospective design of this study.

### 2.2. MRA procedure

A 3.0T magnetic resonance imaging (MRI) scanner (Discovery 750 3.0T ver.24; GE Healthcare, Milwaukee, MI) with 12-channel receiver coils was used to perform neck CEMRA. The scan range was from the aortic arch to the anterior commissure–posterior commissure plane. CEMRA used a spoiled gradient-echo imaging sequence with the following acquisition parameters: field of view =  $240 \times 240 \text{ mm}^2$ , matrix =  $384 \times 256$  pixels, repetition time = 4.3 ms, echo time = 1.5 ms, flip angle =  $25^\circ$ , BW =  $\pm 83.33 \text{ kHz}$ , slice thickness = 1.2 mm, slab thickness = 91.2 mm, coronal slab orientation, number of excitations = 1, and acquisition time = 48 seconds. Parallel imaging was performed using an array spatial sensitivity encoding technique (ASSET) algorithm. ASSET parameters were set to an acceleration factor of 2. An asymmetric k-space sampling scheme (partial Fourier factor of 80%) and zero interpolation were applied in all 3 axes to minimize the echo time and acquisition time. The phase-encoding order was elliptical centric for neck CEMRA. Two-phase MR images were acquired for pre- and post-contrast imaging, while pre-contrast imaging was used for the measurement of the reference signal. A 20- or 22-gage catheter was placed at the right antecubital vein. Gadoterate meglumine (0.1 mmol/kg; Magnescape, Terumo, Tokyo, Japan) was used as the contrast agent in each patient and was diluted with saline to make a total volume of 20 mL.<sup>[11]</sup> The contrast agent was injected as a bolus at a rate of 2.5 mL/s for 8 seconds; it was followed by a 30 mL saline flush by using a power injector (SONIC SHOT GX; Nemoto, Tokyo, Japan). Detailed information for the injection of contrast agent with saline flush through both the T-shaped tube and spiral flow tube is summarized in Table 1. Fluoroscopic triggering was performed to determine the appropriate scan timing. For fluoroscopy, a coronal slice was angulated to capture the aortic arch and common carotid arteries. Dynamic imaging acquisition was performed using a 0.6 second interval per phase. When the contrast agent bolus reached the common carotid arteries, the CEMRA acquisition was started manually under fluoroscopic control.

### 2.3. Data analysis

From the CEMRA dataset, the depicted common and internal carotid arteries were reconstructed into a curved multiplanar

**Table 1**

**Dose and infusion time determination.**

Patient weight, kg	Gd-DOTA, mL	Saline, mL	Total, mL	Infusion time, s
40–60	8	12	20	8
61–80	12	8	20	8
81–100	16	4	20	8
100>	20	0	20	8

The bolus of the contrast agent was flushed with 30 mL saline for all patients.

stretch view by using commercially available image analysis software (Advantage Windows ver4.6; GE Healthcare, Milwaukee, MI).

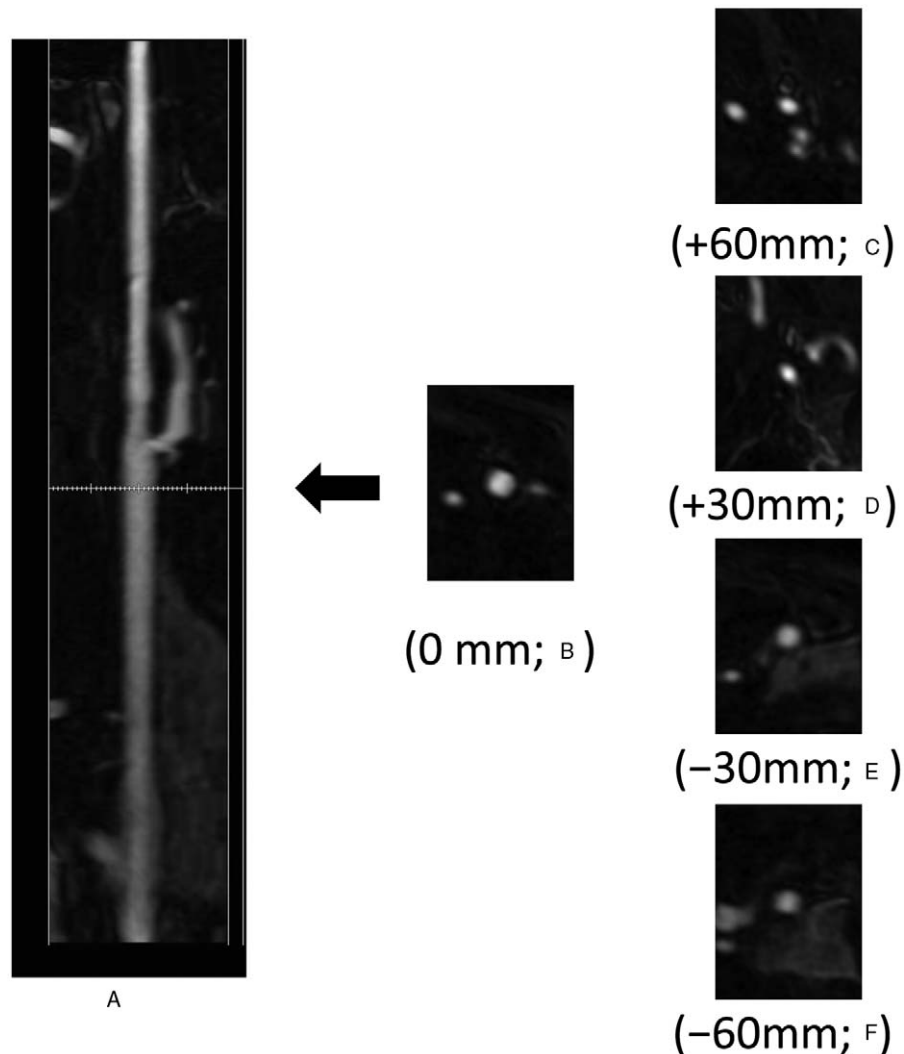
Each carotid artery was assigned to 1 of the following 3 categories that were based on the degree of carotid artery stenosis: 0,  $\leq 50\%$  luminal narrowing; 1, from 50% to 70% luminal narrowing; and 2,  $\geq 70\%$  luminal narrowing. When multiple luminal lesions were detected in the same region, the most severe stenosis was used for analysis.

Enhancement areas were delineated as large as possible inside the carotid artery with oval regions of interest (ROIs) by a radiological technologist with 23 years of experience. For each artery, 5 ROIs were placed on the multiplanar stretch view. At first, an ROI was measured on carotid bifurcation. Additionally, we displaced the location of the ROI by 30 and 60 mm in the superior direction and by 30 and 60 mm in the inferior direction, followed by measurements (Fig. 2). Then, the ROIs on the brain stem were also placed during pre-contrast imaging. The mean signal intensity in these ROIs in the enhancement area ( $SI_{\text{artery}}$ ) and brain stem ( $SI_{\text{stem}}$ ) were used for the analysis. The signal

homogeneity in the contrast-enhanced area ( $SH_{\text{enhance}}$ ) was calculated as a coefficient of variation among the 5  $SI_{\text{artery}}$  values in each carotid artery. Furthermore, the enhancement of the artery ( $E_{\text{artery}}$ ) was also calculated as a normalized signal in the carotid artery, according to the following equation:  $E_{\text{artery}} = SI_{\text{artery}} \text{ on carotid bifurcation} / SI_{\text{stem}}$ .

#### 2.4. Statistical analysis

First, to assess the presence of bias in the patient characteristics between the spiral flow tube and conventional T-shaped tube patient groups, nominal variables were compared using Fisher exact test (for sex, diabetes mellitus, and hypertension). Depending on the distribution and variances, Student *t* test (for body weight) or Wilcoxon rank-sum test (for age, height, and carotid artery stenosis) was performed. Second, the  $SH_{\text{enhance}}$  values between the spiral flow tube and conventional T-shaped tube data were compared by performing Student *t* test (as the normality of data distribution was verified according to Shapiro-Wilk test, and equal variances were observed according to F-test)



**Figure 2.** A base position (0 mm; B) was decided on a carotid bifurcation in the curved multiplanar stretch view (A) (arrow); 4 ROIs were subsequently displaced from the location in the superior direction by 60 (+60 mm; C), and 30 mm (+30 mm; D) and the inferior direction by 30 (−30 mm; E) and 60 mm (−60 mm; F). ROIs = regions of interest.

**Table 2**  
**Patient demographics and indicator.**

Patient demographics	Spiral flow tube	T-shaped tube	P-value
Number of patient	50	50	
Gender			.10*
Male	27	36	
Female	23	14	
Body weight, kg, mean (SD)	60.28 ± 14.30	59.5 ± 12.55	.77 <sup>†</sup>
Height, cm, median (IQR)	156 (151–165)	163 (153–166)	.13 <sup>‡</sup>
Age (y), median (IQR)	75 (69–82)	74 (65–83)	.57 <sup>‡</sup>
Hypertension	31	31	>.99*
Diabetes mellitus	15	16	>.99*
Carotid artery stenosis			.89 <sup>‡</sup>
≤50% luminal narrowing	43	42	
50%–70% luminal narrowing	2	5	
≥70% luminal narrowing	5	3	
SH <sub>enhance</sub> , mean (SD)	0.20 ± 0.060	0.24 ± 0.056	.001 <sup>†</sup>
E <sub>artery</sub> , median (IQR)	14.1 (11.8–15.4)	12.3 (11.3–14.0)	.02 <sup>‡</sup>

E<sub>artery</sub> = enhancement of artery, IQR = interquartile range, SD = standard deviation, SH<sub>enhance</sub> = signal homogeneity in the contrast-enhanced area.

\* Fisher exact test.

<sup>†</sup> Student *t* test.

<sup>‡</sup> Wilcoxon rank-sum test.

and E<sub>artery</sub> values were compared by performing Wilcoxon rank-sum test (as the normality of data distribution was not verified). All statistical tests were 2-sided. *P*-values <.05 were considered indicative of statistical significance. The values were presented as the mean and standard deviation (SD) or the median and IQR. All statistical analyses were performed by using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).<sup>[12]</sup>

### 3. Results

There were no significant differences in the patient characteristics (body weight, height, sex, age, and carotid artery stenosis) between the spiral flow tube and T-shaped tube patient groups (Table 2). We found a significant difference in SH<sub>enhance</sub> between the spiral flow tube group (0.20 ± 0.060) and the conventional T-shaped tube group (0.24 ± 0.056) (*P* = .001). The median of E<sub>artery</sub> values increased by 15% in the spiral flow tube versus the T-shaped tube (14.1 with IQR 11.8–15.4 vs 12.3 with IQR 11.3–14.0, *P* = .02) (Table 2).

### 4. Discussion

In this study, we found a significant difference in SH<sub>enhance</sub> between the spiral flow tube and conventional T-shaped tube groups, with the spiral flow tube showing 15% greater enhancement of the neck. Previous studies have stated that the spiral flow tube improved arterial enhancement in coronary CT angiography<sup>[10]</sup> that was given following saline flush, although the performance of the spiral flow tube in MRI was unclear. These findings indicated that the spiral flow tube contributed to arterial enhancement and homogeneity of CEMRA in carotid arteries.

The 15% enhancement in E<sub>artery</sub> obtained by the use of the spiral flow tube in our study can be explained by the turbulent flow generated by the chamber used at the connecting site in the

tube. This finding is in agreement with those of previous studies that demonstrated an increase in arterial enhancement by use of a spiral flow tube instead of a conventional T-shaped tube, followed by a saline flush.<sup>[10,13]</sup> An important physicochemical property of the contrast agent is viscosity. Because of sufficient mixing in the chamber, the diluted solution using the spiral flow tube would be lower viscosity than that using the conventional T-shaped tube. The use of high concentration contrast agent injected at high rates may not increase iodine delivery to vessel of interest, resulting in a contrast enhancement weaker than expected.<sup>[14]</sup> Similarly, the unstable diluted solution using a T-shaped tube may result in weaker enhancement than that using a spiral flow tube. Furthermore, the contrast agent and saline solution were mixed sufficiently by turbulent flow, and the mixed solution provided a stable bolus injection. This type of mixing may explain how the spiral flow tube enhanced arterial homogeneity.

The spiral flow tube can be used for the assessment of other parts of a patient. The vascular information during the early dynamic phase is well known to be important to MRI of the liver with a hepatobiliary contrast agent. In comparison to the slow injection of undiluted contrast agents, this dilution method has been shown to reduce severe ghosting artifacts.<sup>[15]</sup> A dilution method using a spiral flow tube may provide greater flexibility in the injection time.

For stepping-table (multistation) CEMRA, the imaging was acquired by a 2-phase contrast injection scheme. However, the amounts of contrast agents for each phase have been low relative to those used in the single-phase injection technique. The present findings of improved efficiency and stability show that this two-phase contrast injection scheme improved arterial enhancement.<sup>[16,17]</sup>

This study had several limitations. First, the bolus tracking method was adopted to determine the scan timing. The rise in the arterial signal from when the scan started was decided by a senior technologist, not by auto-detection, and the timing of the scan start varied with each individual operator. The image contrast of CEMRA with an elliptical centric *k*-space order was sensitive to variables. Thus, our present findings were influenced by variables. A second limitation was that this result was based on first-pass enhancement. We did not evaluate the enhancement in the venous phase. By providing a push of the residual contrast agent into the central venous system, the spiral flow tube improved the enhancement.<sup>[18,19]</sup> On the other hand, after the circulation of the blood, the residual contrast agent was washed out from the subclavian vein. In the venous phase, the enhancement provided by the spiral flow tube may be similar to that of a conventional tube.

In conclusion, by using a spiral flow tube, the homogeneity of the contrast-enhanced signal intensity in the carotid artery was significantly improved without decreasing the signal intensity in CEMRA.

### Acknowledgments

The authors thank Enago for editing this manuscript.

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