



Evaluation of Intra-Aneurysmal Residual Blood Flow with the iMSDE T1-Black Blood Imaging after Flow Diverter Treatment

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Objective: We aimed to evaluate the efficacy of the “improved motion-sensitized driven-equilibrium (iMSDE)”-prepared T1-weighted black blood (T1-BB) MRI for monitoring treatment effect with a flow diverter (FD) for cerebral aneurysms.

Methods: Following the exclusion of concomitant coiling and retreatment cases from 60 consecutive cases of cerebral aneurysms treated with FDs at our institution, 32 with imaging data were included in the analysis. Detectability of residual blood flow within the aneurysms was validated as follows: 1) comparison of MRI sequences (iMSDE-prepared T1-BB images, T1-weighted images [T1WI], and time-of-flight [TOF]-MRA) in cases of incompletely occluded aneurysms and 2) comparison of angiography and MRI sequences in the same period.

Results: 1) The probability of diagnosing intra-aneurysmal blood flow was significantly higher with iMSDE-prepared T1-BB (iMSDE-prepared T1-BB vs. T1WI, $p < 0.001$; iMSDE-prepared T1-BB vs. TOF-MRA, $p < 0.001$). 2) The diagnostic accuracy of residual aneurysmal blood flow was significantly higher with iMSDE-prepared T1-BB than that with T1WI ($p = 0.032$). Furthermore, in cases of incomplete occlusion, the probability of detecting intra-aneurysmal blood flow was significantly higher with iMSDE-prepared T1-BB (iMSDE-prepared T1-BB vs. T1WI, $p < 0.001$; iMSDE-prepared T1-BB vs. TOF-MRA, $p = 0.023$).

Conclusion: Our results demonstrated that iMSDE-prepared T1-BB could help distinguish between blood flow and thrombus within the aneurysms after FD treatment, especially in the early stages of FD treatment.

Keywords ► cerebral aneurysm, flow diverter, thrombosis, MRI

Introduction

A flow diverter (FD) is a useful device for treating cerebral aneurysms because it promotes intra-aneurysmal thrombosis

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and the formation of an endothelium in the parent artery.¹⁻³ This treatment has been expanded and, depending on the characteristics of each case, replaces coil embolization.⁴ Complications may occur during the healing process of FD-treated aneurysms, such as a thromboembolism caused by a thrombus around the device or treated aneurysm or the delayed rupture of aneurysms.⁵⁻⁷ Furthermore, the progression of thrombosis varies in a case-dependent manner; thrombosis may occur immediately after FD treatment in some cases, whereas it may take several months in other cases. Therefore, invasive imaging studies such as angiography and CTA have been used to assess the progression of intra-aneurysmal thrombosis after FD treatment in the clinical setting. However, minimally invasive or noninvasive examinations are preferred because they need to be performed multiple times over an extended period of time.

Improved motion-sensitized driven-equilibrium (iMSDE) is an MR technique that suppresses blood signals in all

directions.⁸⁾ The iMSDE-prepared 3D T1-weighted black blood (T1-BB) imaging has been primarily used to assess cardiovascular and carotid artery lesions as well as intracranial vessel dissection.^{9–12)} We hypothesized that this MR technique without using Gd-based contrast agents was applicable to distinguishing thrombosed aneurysms and might help noninvasively assess intra-aneurysmal thrombosis and residual blood flow after FD treatment. This study was intended to investigate the utility of iMSDE-prepared T1-BB for monitoring FD-treated aneurysms.

Materials and Methods

The Institutional Review Board of Mie University Hospital approved the present study (approval no. H2018-059).

Patients

A prospectively maintained database at Mie University Hospital was searched for patients who underwent FD treatment for unruptured cerebral aneurysms between December 2017 and October 2022. Medical records were retrieved and retrospectively reviewed. Among all aneurysms, cases lacking imaging data, treated with concomitant coil embolization, or retreated were excluded.

Treatment

The oral administration of dual antiplatelet agents (DAPTs; 100 mg of aspirin and 75 mg of clopidogrel) was initiated at least 14 days before treatment. Three days before treatment, platelet aggregation ability was assessed with Verify Now (Accumetrics, San Diego, CA, USA). Patients with more than 200 P2Y12 reaction units (PRUs) were regarded as hypo-responders to clopidogrel, and thus, clopidogrel was changed to 3.75 mg prasugrel before treatment. Patients with less than 50 PRUs were regarded as hyper-responders to clopidogrel, and thus, DAPT was stopped until the day of treatment. All FD treatments were performed under general anesthesia. The Pipeline flex embolization device or Pipeline flex with shield technology (PED; Medtronic, Irvine, CA, USA) or FRED (MicroVention, Aliso Viejo, CA, USA) was selected as the FD device in a case-by-case manner. More than two FDs were used when only one FD did not sufficiently cover the aneurysm. After the deployment of the FD, the microcatheter was exchanged with the occlusion balloon catheter, and angioplasty was performed to improve the apposition of the FD to the vessel wall where necessary. After the treatment, DAPT was continued for 6 months, after which the dose of antiplatelet agents was considered to be reduced based on imaging results.

Imaging

T1-weighted imaging (T1WI), time-of-flight (TOF)-MRA, and iMSDE-prepared T1-BB were performed with MR (Ingenia 3.0T; Philips Healthcare, Amsterdam, the Netherlands) prior to FD treatment, the day after treatment, and 1, 3, 6, 12, and 24 months after treatment in accordance with the protocol of our hospital. Imaging parameters for T1WI were as follows: turbo field echo; repetition time/echo time (TR/TE), 8.2/4.6 ms; field of view (FOV), 260 × 260 mm; matrix, 288 × 288; thickness, 0.9 mm; FA, 10; and acquisition time, 4 minutes 42 seconds. Imaging parameters for TOF-MRA were as follows: fast field echo; TR/TE, 25/3.5 ms; FOV, 200 × 200 mm; matrix, 432 × 238; thickness, 1.0 mm; FA, 18; and acquisition time, 5 minutes 39 seconds. Imaging parameters for iMSDE-prepared T1-BB were as follows: turbo spin echo; TR/TE, 700/27 ms; FOV, 180 × 180 mm; matrix, 224 × 175; thickness, 0.9 mm; refocusing angle, 50; BB pulse MSDE (velocity encoding = 1, 1, 1 cm/s); and acquisition time, 4 minutes 40 seconds. Angiography (Allura Clarity FD 20/20 or Azurion 7 B 20/15; Philips Healthcare) was performed 6 and 24 months after treatment in accordance with our protocol. The occlusion of treated aneurysms was assessed using the O’Kelly–Marotta (OKM) grading system¹³⁾ by DSA, 3D-rotational angiography, and high-resolution cone-beam CT.

Image analysis

Images from T1WI, TOF-MRA, and iMSDE-prepared T1-BB were reviewed first by 2 board-certified neurosurgeons (NT and YS), and then MRI findings were confirmed by using angiographic images. Each reviewer independently judged images, and cases with a mismatched judgement were discussed and a consensus was reached. Reviewed images were evaluated using the following two approaches.

1) Comparison of MRI sequences in cases of incompletely occluded aneurysms

First, we investigated the capacity of MRI to depict the intra-aneurysmal residual blood flow in incompletely occluded aneurysms after FD treatment. As there were no reports of recanalization of FD-treated aneurysms in follow-up within 2 years that have once completely occluded, aneurysms diagnosed as OKM grade B or C on angiography were considered to have been incompletely occluded at an earlier phase. One, 3, 6, 12, and 24 months after the treatment, angiography at the closest time after MRI was used as the reference (i.e., MRI at 1, 3, and 6 months referenced with angiography at 6 months, MRI at 12 and 24 months referenced with angiography at 24 months), and cases with residual aneurysmal blood flow (OKM grade B or C) confirmed by angiography were included in this

evaluation. Residual aneurysmal blood flow was evaluated with each MRI sequence to establish whether they were consistent with the findings assumed from the subsequent angiography.

2) Comparison of angiography and MRI sequences in the same period

Second, at 6 and 24 months after treatment, the ability to accurately evaluate not only residual blood flow but also complete occlusion state was evaluated using the findings of MRI and angiography performed at almost the same time.

Statistical analysis

All statistical analyses were performed using SPSS software, version 28.0 (IBM, Armonk, NY, USA). Differences among the T1WI, TOF-MRA, and iMSDE-prepared T1-BB groups were assessed by the Cochran's Q test with adjustments by the Bonferroni correction. The categorical variables (aneurysmal size, preoperative intra-aneurysmal thrombus, and aneurysmal type) were compared using Pearson's chi-squared tests of Fisher's exact tests with the Bonferroni's post hoc test, as appropriate. P values <0.05 were considered to be significant.

Results

Following the exclusion of cases treated with concomitant coil embolization (14 cases), retreated (5 cases), and lacking imaging data (9 cases) from 60 aneurysms, 32 were included in the present study. The characteristics of patients and treated aneurysms are shown in **Table 1**. Twenty out of 32 aneurysms (62.5%) were extradural internal carotid artery (ICA) aneurysms. Saccular aneurysms were detected in 19 cases (59.4%) and large or giant aneurysms in 21 (65.6%). The most frequently used FDs were the Pipeline flex with shield technology (18 cases, 56.3%).

Illustrative case

Case 1

A 79-year-old woman with an asymptomatic, large, and growing cavernous aneurysm of the right ICA (maximum diameter of 21.6 mm, **Fig. 1A**) was treated with a 4.5 × 25 mm PED (**Fig. 1B**). At 6 months, the patient underwent MRI. We were unable to assess residual aneurysmal blood flow by T1WI (**Fig. 1C**) or TOF-MRA (**Fig. 1D**). This is because the hyperintense region within the aneurysm interfered with distinguish blood flow from thrombus. On the other hand, iMSDE-prepared T1-BB (**Fig. 1E**) demonstrated blood flow in the remaining aneurysm. In this

Table 1 Characteristics of patients and treated aneurysms

Clinical variables	n (%)	n (%)
Total	32 aneurysms	28 patients
Age, median (range)		72.5 (38–85)
Female		23 (82.1)
Location		
ICA		
Intradural	10 (31.3)	
Extradural	20 (62.5)	
MCA	1 (3.1)	
BA	1 (3.1)	
Size		
<10 mm	11 (34.4)	
10–25 mm	17 (53.1)	
≥25 mm	4 (12.5)	
Type		
Saccular	19 (59.4)	
Fusiform	12 (37.5)	
Dissection	1 (3.1)	
Symptoms		
Yes	11 (34.4)	
No	21 (65.6)	
Ruptured		
Yes	1 (3.1)	
No	31 (96.9)	
Partially thrombosed		
Yes	4 (12.5)	
No	28 (87.5)	
Device		
Pipeline	7 (21.9)	
Pipeline shield	18 (56.3)	
FRED	7 (21.9)	
Overlapping		
Single	26 (81.3)	
Double	5 (15.6)	
Triple	1 (3.1)	

BA: basilar artery; ICA: internal carotid artery; MCA: middle cerebral artery

sequence, the high signal intensity in the thrombus area was not uniform, but the presence of low signal intensity areas suggested that the residual blood flow was continuous with the parent artery and its signal intensity was the same as the parent artery. Findings of residual blood flow in the aneurysm were consistent with angiographic findings performed immediately after the MRI (**Fig. 1G** and **1H**).

Case 2

An 83-year-old woman with an asymptomatic, large, and growing cavernous aneurysm of the right ICA (maximum diameter of 10.2 mm, **Fig. 2A**) was treated with a 4.0 × 25 mm PED (**Fig. 2B**). On iMSDE-prepared T1-BB, the high signal intensity of the intra-aneurysmal thrombus indicated rapid thrombosis 1 month after FD treatment (**Fig. 2D**). The signal intensity of the intra-aneurysmal thrombus

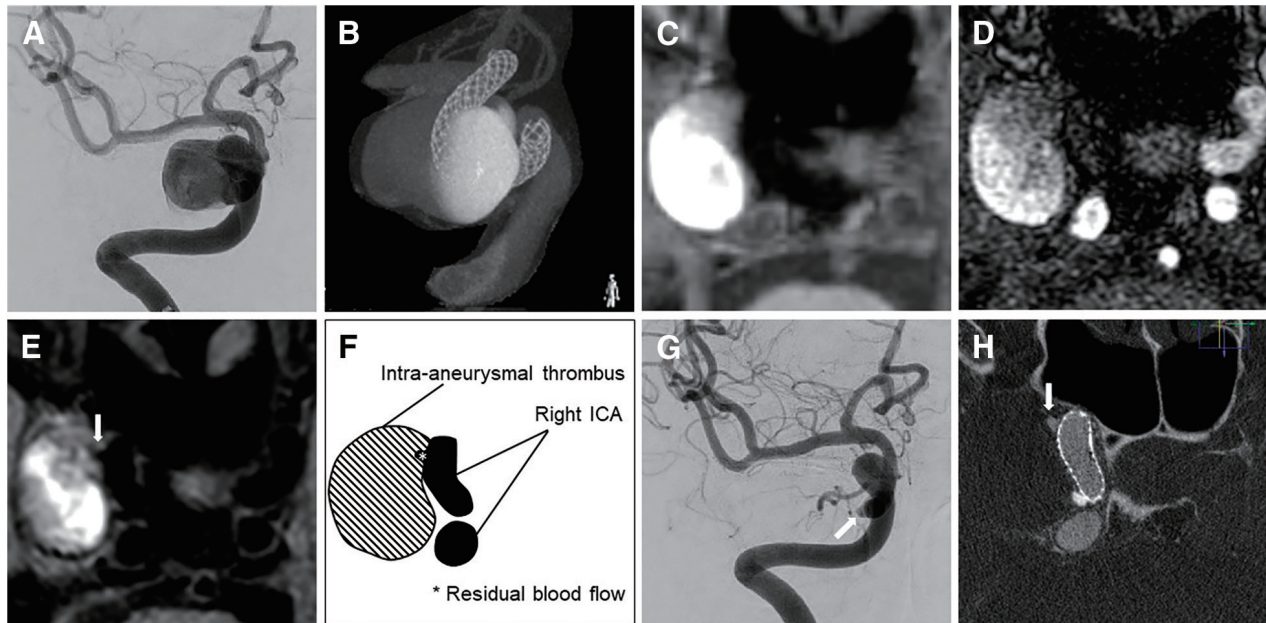


Fig. 1 Angiographic images (A, B, G, and H), MR images (C–E), and a schema of the treated aneurysm (F) 6 months after the FD treatment in illustrative case 1. (A) The frontal view of right internal carotid angiography immediately after the treatment. (B) The 3D image of right internal carotid angiography immediately after the treatment. (C) A T1-weighted image. (D) A TOF image. (E) An iMSDE-prepared T1-BB image. (G) The

frontal view of right internal carotid angiography 6 months after the treatment. (H) An axial image from high-resolution cone-beam CT 6 months after the treatment. White arrows of (E), (G), and (H) and an asterisk of (F) show intra-aneurysmal residual blood flow. FD: flow diverter; ICA: internal carotid artery; iMSDE: improved motion-sensitized driven-equilibrium; T1-BB: T1-weighted black blood; TOF: time-of-flight

gradually decreased. Three months after the treatment, the signal intensity still differed between the intra-aneurysmal thrombus and parent artery (Fig. 2E). At 6 months, the signal intensity of the intra-aneurysmal thrombus contiguous to the parent artery coincided with that of the parent artery, suggesting that intra-aneurysmal blood flow had reopened (Fig. 2F). However, complete occlusion was evidenced, as shown by angiographic findings that performed simultaneously (Fig. 2H and 2I). The iMSDE-prepared T1-BB findings at 6 months were ultimately false positive. On TOF-MRA, the signal intensity within the aneurysm decreased at 1 month and remained at this intensity level until 6 months, but it was difficult to evaluate the signal intensity around the aneurysmal neck and the parent artery due to metal artifacts.

1) Comparison of MRI sequences in cases of incompletely occluded aneurysms

Table 2 shows a summary of MRI obtained at 67 time points in 32 cases before the diagnosis of OKM grade B or C by angiography. Residual aneurysmal blood flow was detected in 14 (20.9%), 35 (52.2%), and 57 images (85.1%) obtained by T1WI, TOF-MRA, and iMSDE-prepared T1-BB, respectively, which was consistent with assumptions from a subsequent angiographic diagnosis. The probability of diagnosing residual aneurysmal blood flow was significantly higher with iMSDE-prepared T1-BB than

with other sequences (iMSDE-prepared T1-BB vs. T1WI, $p < 0.001$; iMSDE-prepared T1-BB vs. TOF-MRA, $p < 0.001$). There were no significant differences in the detection rate with iMSDE-prepared T1-BB when comparing by aneurysmal size, with or without preoperative intra-aneurysmal thrombus, and aneurysmal type.

2) Comparison of angiography and MRI sequences at the same time period

Table 3 shows a summary of MRI obtained at 41 time points in 32 cases and angiography was taken at the same time period. Thirty-one images (75.6%) were obtained at 6 months and 10 (24.4%) at 24 months. MRI and angiographic findings on the presence or absence of residual blood flow agreed in 19 images (46.3%) by T1WI, 26 (63.4%) by TOF-MRA, and 29 (70.7%) by iMSDE-prepared T1-BB. The probability of diagnosing the presence or absence of residual blood flow was significantly higher with iMSDE-prepared T1-BB than that with T1WI ($p = 0.032$). Moreover, when limited to cases with incompletely occluded aneurysms (OKM grade B or C), the agreement rate of iMSDE-prepared T1-BB findings was significantly higher among the three MRI sequences (iMSDE-prepared T1-BB vs. T1WI, $p < 0.001$; iMSDE-prepared T1-BB vs. TOF-MRA, $p = 0.023$). Regarding sensitivity and specificity according to sequences and time periods, sensitivity

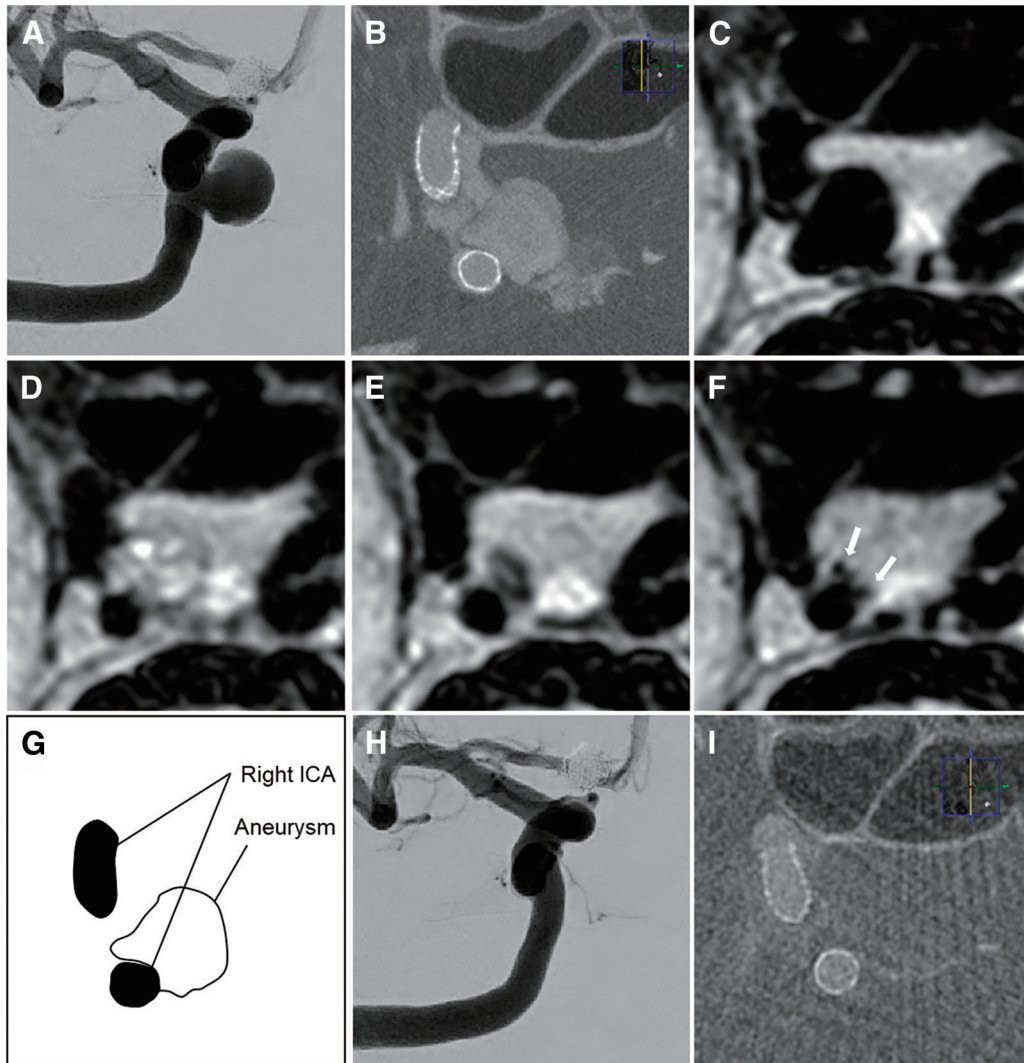


Fig. 2 Angiographic images (**A**, **B**, **H**, and **I**), MR images (**C–F**), and a schema of the aneurysm (**G**) in illustrative case 2. (**A**) The frontal view of right internal carotid angiography immediately after the treatment. (**B**) An axial image from high-resolution cone-beam CT using contrast media immediately after the treatment; an axial slice of an iMSDE-prepared T1-BB image before the treatment (**C**) and 1 (**D**), 3 (**E**), and 6 (**F**) months after the treatment. (**G**) A schema of the aneurysm soon after the treatment. (**H**) The frontal view of right internal carotid angiography 6 months after the treatment. (**I**) An axial image from high-resolution cone-beam CT using contrast media 6 months after the treatment. The area (**F**) indicated by white arrows appears to show reopened intra-aneurysmal blood flow; however, complete occlusion was achieved, as shown in (**H**) and (**I**). ICA: internal carotid artery; iMSDE: improved motion-sensitized driven-equilibrium; T1-BB: T1-weighted black blood

Table 2 Comparison of MRI sequences in cases of incompletely occluded aneurysms

	T1WI		TOF-MRA		iMSDE-prepared T1-BB	
	Yes	No	Yes	No	Yes	No
Residual blood flow	Yes	No	Yes	No	Yes	No
1 month	4	14	12	6	16	2
3 months	5	12	11	6	16	1
6 months	5	13	9	9	16	2
12 months	0	7	2	5	6	1
24 months	0	7	1	6	3	4
Total images (%)	14 (20.9)	53 (79.1)	35 (52.2)	32 (47.8)	57 (85.1)	10 (14.9)

iMSDE: improved motion-sensitized driven-equilibrium; T1-BB: T1-weighted black blood; T1WI: T1-weighted imaging; TOF: time-of-flight

Table 3 Comparison of angiography and MRI sequences in the same time period

		T1WI		TOF-MRA		iMSDE-prepared T1-BB	
		Yes	No	Yes	No	Yes	No
Residual blood flow							
6 months	OKM B/C	5	13	9	9	16	2
	OKM D	2	11	0	13	5	8
24 months	OKM B/C	0	7	1	6	3	4
	OKM D	0	3	0	3	1	2
Total images		7	34	10	31	25	16
Agreement with angiographic findings (%)		19 (46.3)		26 (63.4)		29 (70.7)	

OKM: O'Kelly-Marotta grading system; iMSDE: improved motion-sensitized driven-equilibrium; T1-BB: T1-weighted black blood; T1WI: T1-weighted imaging; TOF: time-of-flight

Table 4 Sensitivity and specificity classified by the sequence and timing of MRI

		T1WI	TOF-MRA	iMSDE-prepared T1-BB
6 months	Sensitivity	0.28	0.50	0.89
	Specificity	0.85	1.00	0.62
24 months	Sensitivity	0.00	0.14	0.43
	Specificity	1.00	1.00	0.67

iMSDE: improved motion-sensitized driven-equilibrium; T1-BB: T1-weighted black blood; T1WI: T1-weighted imaging; TOF: time-of-flight

was the highest at 6 months with iMSDE-prepared T1-BB (sensitivity, 0.89, and specificity, 0.62; **Table 4**).

Discussion

FDs is a device that is used to treat aneurysms through the induction of thrombosis, which reduces intra-aneurysmal blood flow, thereby shrinking the aneurysmal sac, and promotes reendothelialization along the device by providing a scaffold for endothelial cell growth.^{2,3,14,15} On the other hand, during the period when an aneurysm is not completely occluded after FD treatment, increased intra-aneurysmal pressure or the degeneration of the aneurysmal wall may lead to rupture.^{5,7,16–18} Therefore, it is very important to confirm the presence or absence of residual aneurysmal blood flow. This is the first report that the iMSDE method was applied to assess residual blood flow in aneurysms treated with FDs at the time of progressive intra-aneurysmal thrombosis.

Antiplatelet therapy is administered in the perioperative period of FD treatment to prevent thromboembolism or perforator occlusion.⁶ The dose and duration of antiplatelet therapy vary among institutions or operators.¹⁹ Previous studies reported that the administration of clopidogrel for less than 6 months after FD treatment significantly increased ischemic complications,^{20,21} whereas others showed that DAPT with aspirin and clopidogrel for more than 6 months after the treatment did not increase the risk of hemorrhagic complications.²¹ However, the partial thrombosis of

aneurysms has been shown to cause aneurysm inflow jets and changes in intra-aneurysmal shear forces, which may cause the delayed rupture, and antiplatelet therapy may also promote rupture.^{5,7} Therefore, we perform an imaging evaluation as a criterion for decisions regarding dose reductions in antiplatelet therapy.

The timing of intra-aneurysmal thrombosis after FD treatment varies; it may begin as early as immediately after the treatment and requires months to years for complete thrombosis in the aneurysms. Imaging evaluations need to be performed multiple times after FD treatment in order to predict the appearance of neurological symptoms due to early thrombosis or to consider dose reductions in or the termination of antiplatelet therapy. Therefore, minimally invasive or noninvasive examinations are preferred. However, limited information is currently available on the assessment of aneurysmal occlusion after FD treatment. Attali et al. reported that 3D-TOF-MRA was inferior to DSA or contrast-enhanced-MRA in assessing residual aneurysmal blood flow or stenosis of parent arteries after FD treatment.²² Oishi et al. and Irie et al. proposed silent MRA for assessing FD-treated aneurysms and reported that it is useful for assessing blood flow of parent artery, although it is difficult to distinguish blood flow in the aneurysm from aneurysmal thrombosis.^{23,24} High-resolution MRI that Gory et al. proposed could visualize aneurysmal thrombosis after FD treatment, but it is difficult to distinguish a thrombus from brain parenchyma or blood flow in

the aneurysm.²⁵⁾ Duarte Conde et al. proposed subtraction CTA combined with a single-energy metal artifact reduction algorithm as FD-treated aneurysms; however, no usefulness for FDs other than Surpass FD (Stryker Neurovascular, Fremont, CA, USA) was demonstrated.²⁶⁾

The iMSDE method has been used to assess the vessel walls of the intracranial,^{12,27)} coronary,⁹⁾ carotid, and renal arteries,²⁸⁾ as well as the nature of carotid artery plaques.^{10,11)} It suppresses blood flow in any direction, turbulence, or slow flow, and thus, more accurately evaluates the presence or absence of blood flow. We speculated whether this method may be applied to treated aneurysms, in which slow blood flow makes it difficult to distinguish it from a thrombus. Based on the results of this study, iMSDE-prepared T1-BB was feasible and helped distinguish between blood flow and thrombus within the aneurysm, especially in the early stages of FD treatment.

In MRI, the signal of a thrombus changes over time depending on the intracellular or extracellular heme iron status of red blood cells. In the acute phase, heme iron is converted to deoxyhemoglobin intracellularly and shows moderately low intensity on T1WI. Between the acute and subacute phases, heme iron is converted to methemoglobin intracellularly and extracellularly and shows high intensity on T1WI and TOF-MRA. Therefore, it is difficult to distinguish intra-aneurysmal thrombosis with blood flow on TOF-MRA from the acute to subacute phase. However, on iMSDE-prepared T1-BB, the signal of intra-aneurysmal blood flow is completely suppressed and could be discriminated from that of intra-aneurysmal thrombosis. In addition, 3D iMSDE-prepared T1-BB was acquired, allowing us to evaluate the treated ICA aneurysm in thin slices and evaluate the reconstructed images in axial, coronal, and sagittal planes. This is another advantage for assessing intra-aneurysmal thrombosis and residual blood flow.

A drawback of the iMSDE method is that it is difficult to distinguish intra-aneurysmal thrombi from residual blood flow in the chronic phase. This is because in the chronic phase, heme iron is extracellularly converted to hemosiderin, which is less intense on T1WI and TOF-MRA.^{29,30)} Among cases in which iMSDE-prepared T1-BB and angiographic findings were inconsistent, one of the causes of this discrepancy may be the early formation of an intra-aneurysmal thrombus, as illustrated in case 2. Furthermore, an intra-aneurysmal thrombus may have developed in the early phase without the repeated process of thrombosis and thrombolysis. In cases of aneurysms with thrombosis in the early phase, a signal change in an intra-aneurysmal thrombus

from high to low intensity occurs in the early phase. This may increase the difficulty associated with discriminating an intra-aneurysmal thrombus from residual aneurysmal blood flow. This results in high sensitivity but low specificity of the iMSDE method. Conversely, the reason for the higher specificity in T1WI and TOF-MRA was that they could not depict the residual aneurysmal blood flow, and they were forced to assess as complete occlusion.

There are several limitations to evaluations using iMSDE-prepared T1-BB that need to be addressed. This was a retrospective analysis of a small number of cases. Therefore, more cases are needed to confirm the usefulness of iMSDE-prepared T1-BB. Furthermore, aneurysms treated with FDs and concomitant coil embolization were excluded because coils showing low signal intensity on iMSDE-prepared T1-BB were difficult to distinguish from the intra-aneurysmal blood flow. The period of the angiographic evaluation was also too long, ranging from 6 to 24 months after the treatment. Since some cases achieved complete occlusion during this period, an additional evaluation with CT angiography or angiography needs to be considered.

Conclusion

This is the first study to use the iMSDE-prepared T1-BB without Gd-based contrast agents to evaluate FD-treated cerebral aneurysms. This method is useful for visualizing the residual aneurysmal blood flow of FD-treated aneurysms more effectively than conventional MR sequences. In addition, it is less invasive than angiography, CTA, or contrast-enhanced MRI. Further comparative studies using invasive methods are required to limit the phase in which it is able to distinguish an intra-aneurysmal thrombus from residual aneurysmal blood flow by iMSDE-prepared T1-BB.

Disclosure Statement

The authors declare that there are no conflicts of interest.

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