



Chronological Changes in Embolization for Cerebral Arteriovenous Malformations: Impact of Endovascular Treatment Device Advancements

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Objective: Although embolization of cerebral arteriovenous malformations (AVM) is widely performed as an adjunctive therapy before microsurgery or radiosurgery, there is no high-level evidence to ascertain its effectiveness. However, the technology for endovascular devices has improved. Therefore, this study aimed to identify the chronological changes in AVM embolization due to advances in endovascular treatment devices.

Methods: This retrospective study included 24 patients who underwent 31 embolization procedures between January 2018 and August 2023. Embolization plus microsurgery, embolization plus radiosurgery, and embolization alone were performed in 15 (62.5%) patients and 21 embolization procedures, 2 (8.3%) patients and 2 procedures, and 7 (29.2%) patients and 8 procedures, respectively. We assessed chronological changes in endovascular treatment devices and evaluated clinical outcomes (ideal position of microcatheter, vessel perforations, symptomatic complications) from January 2018 to December 2020 and from January 2021 to August 2023 based on the chronological changes in endovascular treatment devices.

Results: Intermediate catheters were employed in 29 (93.5%) procedures. Brands of intermediate catheters and microcatheters significantly changed around 2021. No differences were observed in the embolic materials. The ideal position of the microcatheter was achieved significantly more in 2021–2023 than in 2018–2020 (72.1% vs. 48.4%, $p = 0.04$). Vessel perforation by microcatheters in 2018–2020 and 2021–2023 occurred in 3 (18.8%) and 1 (6.7%) procedures ($p = 0.32$), respectively. Symptomatic complications in 2018–2020 and 2021–2023 occurred in 3 (18.8%) and 0 ($p = 0.08$) procedures, respectively. Complete obliteration was achieved in 18 of 24 patients (75.0%). Favorable clinical outcomes (modified Rankin Scale score 0–2) were observed in 20 of 24 (83.3%) patients at the final follow-up.

Conclusion: The advancement in endovascular devices for AVM has enabled effective and safe embolization, potentially enhancing the outcomes of microsurgical interventions.

Keywords ▶ arteriovenous malformation, endovascular device, chronological change, intermediate catheter, microcatheter

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Introduction

The vessel structure in cerebral arteriovenous malformation (AVM) differs between patients, hindering the establishment of optimal AVM management. Although embolization for AVM is performed in most cases as an adjunct treatment before microsurgery or radiosurgery,¹⁾ limited reports have proven the effectiveness and safety of preoperative and curative embolization.^{2–7)} In addition, the intra- or peri-nidal positioning of the microcatheter is the most important factor for the safe and successful embolization of an AVM.^{8,9)} Over the years, embolization techniques for AVM have advanced, including the use of non-adhesive liquid embolic

materials and transvenous approaches.¹⁰⁾ In addition, the technology for endovascular devices, including intermediate catheters, microcatheters, and microguidewires, has improved.^{11–14)} Thus, advancements in endovascular treatment devices may gradually make safe embolization possible. Therefore, we aimed to investigate the chronological changes in AVM embolization due to advances in endovascular treatment devices and evaluate the clinical outcomes based on two treatment periods.

Materials and Methods

Study design

This retrospective study was approved by the ethics committee of University of Tsukuba Hospital and conducted in accordance with the tenets of the Declaration of Helsinki. Owing to the retrospective nature of the study, the Institutional Review Board waived the requirement for written informed consent, offering participants an opt-out option, in compliance with the Personal Information Protection Law and National Research Ethics Guidelines in Japan. The study procedures adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Patients

Among the 39 patients who underwent interventions for AVM at our hospital between January 2018 and August 2023, 31 procedures in 24 patients who underwent embolization were analyzed (**Fig. 1, Table 1**). Eight patients who did not undergo embolization procedures and 7 patients who participated in clinical trials for AVM were excluded. The mean age of the patients was 39.0 ± 20.3 years. Eight (33.3%) patients were male, and 19 (79.2%) experienced hemorrhagic onset. The mean nidus size was 23.8 ± 16.1 mm. Spetzler-Martin grade 1–2 and 3–4 were observed in 14 (58.3%) and 10 (41.7%) patients, respectively. Fifteen (62.5%) patients underwent microsurgery with preoperative embolization and 21 embolization procedures. Two (8.3%) patients underwent radiosurgery with pre-radiosurgical embolization and 2 embolization procedures. Seven (29.2%) patients underwent embolization alone and 8 embolization procedures; 1 patient underwent transarterial and transvenous embolization.

Treatment

The treatment strategy was determined at a cerebrovascular conference comprising cerebrovascular surgeons and neurointerventionalists. For patients in whom surgical

removal was difficult, treatment strategy was determined at a neuroradiation therapy conference. During this period, our hospital had four main operators, all of whom were experienced board-certified neurointerventionalists. Cerebral angiography was performed using Azurion 7 (Philips, Amsterdam, the Netherlands). All patients underwent general anesthesia for the procedures. After the insertion of a 6Fr guiding sheath into the femoral artery, a heparin bolus of 80 U/kg was administered with a targeted activated clotting time of 150–200 s. A guiding sheath was inserted proximal to the target vessel and an intermediate catheter was inserted proximal to the feeding arteries using a microcatheter. The microcatheter was introduced into the intra- or peri-nidus to the maximum extent possible. Transarterial embolization was performed after superselective angiography confirmed imaging solely of the nidus. Post-embolization, all patients were evaluated for hemorrhagic complications via cone-beam computed tomography. Heparinization was reversed and patients were transferred to the intensive care unit. The following patient information was collected from the medical records: age, sex, onset type, size, Spetzler-Martin grade, method of treatment, number of embolization procedures, devices (intermediate catheters, microcatheters, and embolic materials), ideal position of microcatheter, vessel perforation by endovascular devices, complications during microcatheter removal, symptomatic complications, and modified Rankin Scale (mRS) score at the final follow-up. The intermediate catheters used during this period were 4.2Fr ASAHI FUBUKI (ASAHI INTECC, Aichi, Japan), TACTICS (TECHNOCRAT, Aichi, Japan), Guidepost (Tokai Medical Products, Aichi, Japan), and SOFIASELECT (MicroVention Terumo, Aliso Viejo, CA, USA). The microcatheters used during this period were Marathon (Medtronic, Minneapolis, MN, USA), DeFrictor Nano (Medico's Hirata, Osaka, Japan), Scepter (MicroVention Terumo), Magic (Balt, Montmorency, France), and microcatheters for coil embolization. Cyanoacrylate and Onyx (Medtronic) were used as embolic materials. Onyx was the first choice; however, cyanoacrylate was used in patients with a severe tortuous feeding artery wherein Onyx could complicate microcatheter removal. The ideal position of the microcatheter was defined as being at the intra- or peri-nidus (**Fig. 2**). Complications during microcatheter removal were defined as the inability to remove the microcatheter or hemorrhagic complications immediately after microcatheter removal. Symptomatic complications were defined as requiring additional treatments and worsening of mRS score ≥ 1 .

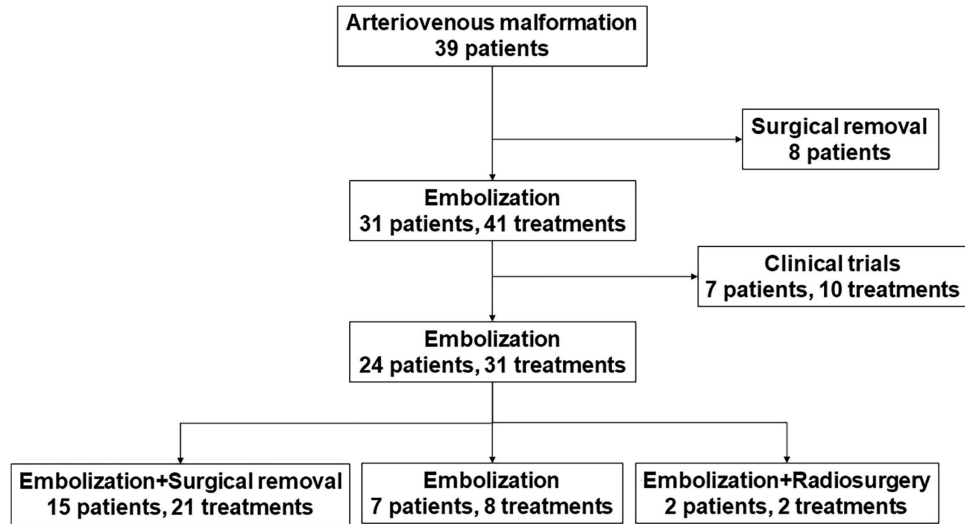


Fig. 1 Patient data.

Table 1 Patient characteristics

	Overall	Embolization + microsurgery	Embolization alone	Embolization + radiosurgery
Patients	24	15	7	2
Embolization procedures	31	21	8	2
Age, years	39.0 ± 20.3	35.4 ± 19.3	44.1 ± 20.0	22, 73
Male	8 (33.3%)	4 (26.7%)	4 (57.1%)	0 (0%)
Hemorrhage	19 (79.2%)	10 (66.7%)	7 (100%)	2 (100%)
Size, mm	23.8 ± 16.1	28.7 ± 16.7	14.9 ± 12.9	11, 26
Spetzler-Martin grade				
1–2	14 (58.3%)	10 (66.7%)	3 (42.9%)	1 (50.0%)
3–4	10 (41.7%)	5 (33.3%)	4 (57.1%)	1 (50.0%)
Complete obliteration	18 (75.0%)	13 (86.7%)	4 (57.1%)	1 (50.0%)
Modified Rankin Scale score 0–2	20 (83.3%)	13 (86.7%)	5 (71.4%)	2 (100%)



Fig. 2 Ideal microcatheter position. The ideal position of the microcatheter for transarterial embolization of arteriovenous malformation is shown. (A) Three-dimensional image of a representative patient. (B) Ideal position of the microcatheter. The microcatheter (A and B, white arrow) is inserted into the peri-nidus, and the nidus and shunt are clearly contrasted by the microcatheter angiography. (C) Non-ideal position of the microcatheter. The microcatheter (A and C, black arrow) is inserted only as far as the feeding artery proximal to the nidus, and the nidus is unclear on microcatheter angiography.

We conducted the following analyses: (1) Assessment of chronological changes in endovascular treatment devices and (2) Evaluation of clinical outcomes between January 2018 and December 2020 (Period I, 12 patients and 16

embolization procedures) and January 2021 and August 2023 (Period II, 12 patients and 15 embolization procedures) based on the chronological changes in endovascular treatment devices.

Statistical analysis

Continuous variables are expressed as mean \pm standard deviation, and discrete data are expressed as counts and percentages. Differences in background factors between groups were evaluated using Fisher's exact test for discrete data. SPSS (version 27.0; IBM, Armonk, NY, USA) was used for all analyses. $p < 0.05$ was considered statistically significant.

Results

Embolization treatments included one procedure in 19 (79.2%) patients, 2 procedures in 4 (16.7%) patients, and 4 procedures in 1 (4.2%) patient. A total of 74 vessels were embolized. The number of embolized vessels per procedure included 1–2 vessels in 19 (61.3%) procedures, 3–4 vessels in 9 (29.0%) procedures, and 5–6 vessels in 3 (9.7%) procedures (**Table 2**).

The utilization of intermediate catheters and microcatheters has undergone significant changes since 2021. Therefore, the study period was divided into two groups: Period I between January 2018 and December 2020 and Period II between January 2021 and August 2023.

Chronological changes in endovascular treatment devices

Intermediate catheters were used in 29 (93.5%) embolization procedures; 4.2Fr ASAHI FUBUKI (15 procedures, 48.3%) was the most common during the entire research period, followed by Guidepost (10 procedures, 32.3%) and TACTICS (three procedures, 9.7%). The 4.2Fr ASAHI FUBUKI and TACTICS are now less frequently used, having been replaced by Guidepost after 2021 (**Fig. 3A**). The 4.2Fr ASAHI FUBUKI, TACTICS, and Guidepost were used in 11, 3, and 0 procedures between 2018 and 2020, and 4, 0, and 10 procedures between 2021 and 2023, respectively. The use of intermediate catheters changed significantly after 2021 (**Fig. 4A**, $p < 0.001$). In total, 77 microcatheters were employed across 74 vessels. The most commonly used microcatheters were the DeFrictor Nano in 43 (58.1%) vessels, followed by Marathon in 23 (31.1%) vessels, Magic in 5 (6.8%) vessels, and Scepter in 2 (2.7%) vessels. The use of Marathon has decreased since 2020, whereas the use of DeFrictor Nano has seen a significant increase and is now considered mainstream (**Fig. 3B**). Marathon and DeFrictor Nano were used in 22 and 6 vessels between 2018 and 2020, and 1 and 37 vessels between 2021 and 2023, respectively. The use of microcatheters changed

Table 2 Number of embolization procedures and embolized vessels

Patients	24
Embolization procedures	31
Procedure	
1	19 (79.2%)
2	4 (16.7%)
4	1 (4.2%)
Total embolized vessels	74
Number of embolized vessels	
1	12 (38.7%)
2	7 (22.6%)
3	4 (12.9%)
4	5 (16.1%)
5	2 (6.5%)
6	1 (3.2%)

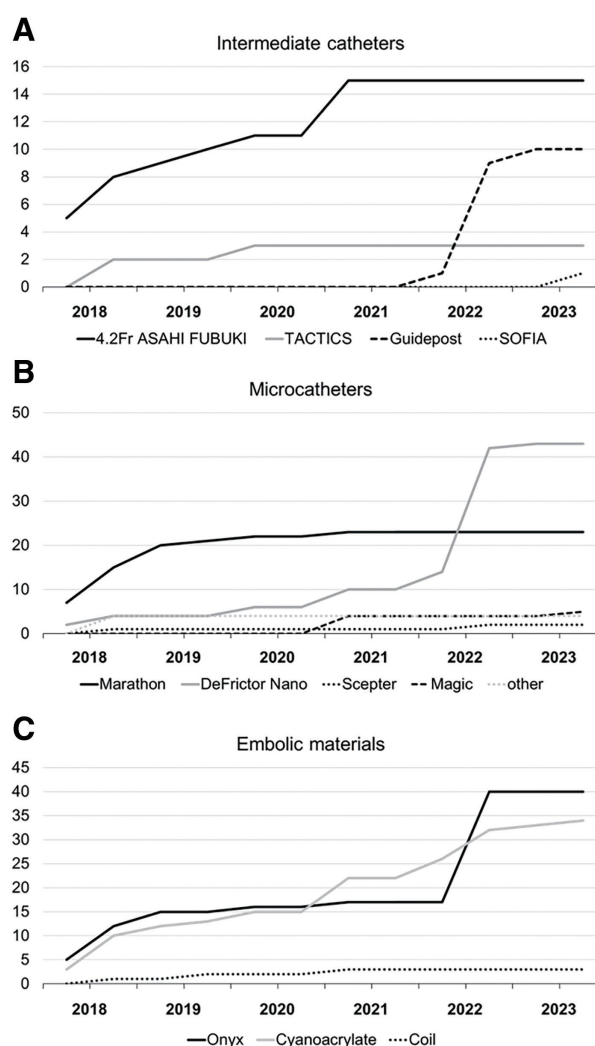


Fig. 3 Chronological changes in endovascular treatment devices. Chronological evolution of endovascular treatment devices utilized throughout the study duration, including (A) intermediate catheters, (B) microcatheters and (C) embolic materials.

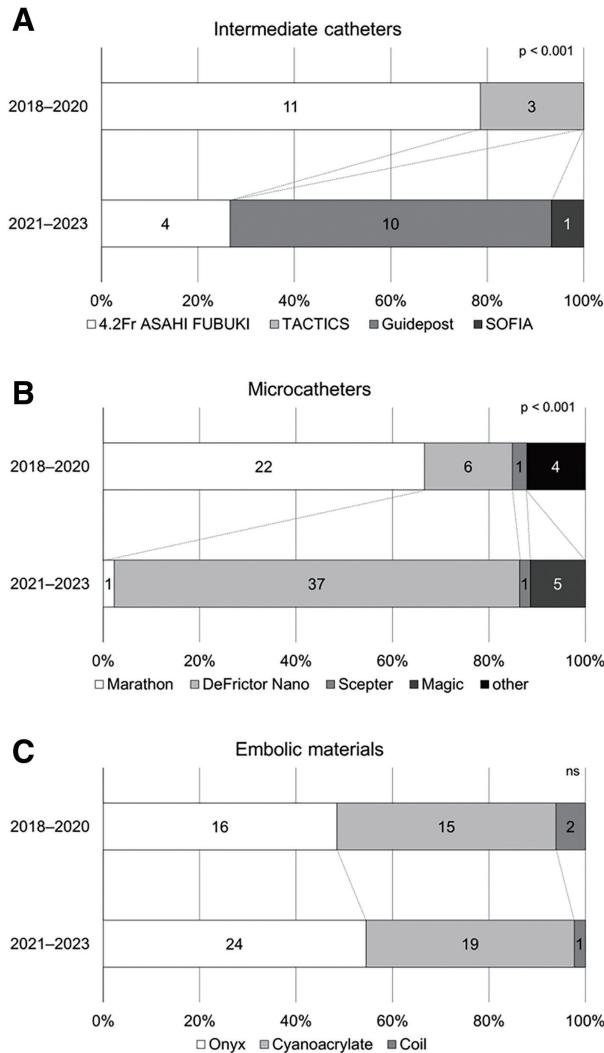


Fig. 4 Comparison of endovascular treatment devices around 2021: **(A)** Intermediate catheters, **(B)** microcatheters and **(C)** embolic materials.

significantly around 2021 (**Fig. 4B**, $p < 0.001$). Among the embolic materials, Onyx was used in 40 (54.1%) vessels and cyanoacrylate was used in 34 (45.9%) vessels. However, no chronological changes were observed in the use of embolic material (**Fig. 3C** and **Fig. 4C**).

Evaluation of clinical outcomes

There were significantly more patients with Spetzler-Martin grade 3–4 in Period II than in Period I (66.7% vs. 16.7%, $p = 0.01$). The ideal position of the microcatheter was achieved significantly more in Period II than in Period I (72.1% vs. 48.4%, $p = 0.04$). Symptomatic complications occurred only in Period I, with 2 (6.5%) of ischemic and 1 (3.2%) of hemorrhagic complications. Vessel perforation by microcatheters in Period I and II occurred in

3 (18.8%) and 1 (6.7%) patients, respectively. None of the 4 patients with vessel perforation experienced symptomatic complications. There were no complications during microcatheter removal (**Table 3**). Complete obliteration was achieved in 18 of 24 patients (75.0%). Of the 15 patients who underwent microsurgery with preoperative embolization, 13 (86.7%) underwent complete removal of AVM. Among patients who underwent embolization alone, 3 (42.9%) of 7 patients underwent palliative embolization and 4 (57.1%) underwent curative embolization, of whom 1 patient experienced recurrence and was cured with additional embolization. The mRS score of 0–2 at the final follow-up was observed in 20 of 24 (83.3%) patients (**Table 1**).

Discussion

In this study, we found that advancements in endovascular devices for cerebral AVM have enabled safer embolization procedures, potentially enhancing the outcomes of microsurgical interventions.

Endovascular embolization for AVM is considered a multimodal therapy.¹⁵⁾ A previous study suggested that preoperative embolization may reduce intraoperative bleeding during microsurgery and contribute to safe AVM treatment.⁶⁾ However, review articles have reported that the need for preoperative embolization is limited, given that embolization increases complications.^{4,16)} Moreover, pre-radiosurgical embolization reportedly reduces obliteration rates despite increasing complications.^{17–19)} Nonetheless, adjunctive embolization for AVMs is commonly performed, despite its unproven utility, likely attributed to the inherent variability in the angioarchitecture of each AVM and the challenge of assessing adjunctive embolization outcomes using numerical data. However, with recent advancements in technology, we believe that embolization for AVM has become safer than that in previous studies. Therefore, we investigated chronological changes in the treatment and results of AVM embolization.

Although the study period was limited to 5 years, endovascular devices have changed significantly. The 4.2Fr ASAHI FUBUKI and TACTICS intermediate catheters were predominantly used in Period I, whereas Guidepost was increasingly used in Period II. TACTICS and Guidepost have the same outer diameters: a distal diameter of 3.2 Fr and a proximal diameter of 3.4 Fr. However, the inner lumen of Guidepost is larger than that of TACTICS; TACTICS has an inner lumen of 0.035 inches, whereas

Table 3 Complications and clinical outcomes

	Total	Period I	Period II	p
Patients	24	12	12	
Embolization procedures	31	16	15	
Age, years	39.0 ± 20.3	35.9 ± 20.2	42.0 ± 20.8	0.47
Male	8 (33.3%)	1 (8.3%)	7 (58.3%)	<0.001
Hemorrhage	19 (79.2%)	8 (66.7%)	11 (91.7%)	0.13
Size, mm	23.8 ± 16.1	22.4 ± 15.4	25.3 ± 17.4	0.68
Spetzler-Martin grade				0.01
1–2	14 (58.3%)	10 (83.3%)	4 (33.3%)	
3–4	10 (41.7%)	2 (16.7%)	8 (66.7%)	
Ideal position of microcatheter	46/74 (62.2%)	15/31 (48.4%)	31/43 (72.1%)	0.04
Complications of embolization procedures				
Vessel perforations	4 (12.9%)	3 (18.8%)	1 (6.7%)	0.32
Complications during microcatheter removal	0	0	0	–
Symptomatic complications	3 (9.8%)	3 (18.8%)	0	0.08
Hemorrhage	1 (3.2%)	1 (6.3%)	0	
Ischemia	2 (6.5%)	2 (12.5%)	0	

Guidepost has a proximal lumen of 0.039 inches and a distal lumen of 0.035 inches. Thus, the Guidepost provides a wider range of microcatheter options. In particular, TACTICS can only contain the DeFrictor Nano, whereas Guidepost can contain both DeFrictor Nano and Marathon, leading to its increase. Regarding microcatheters, although the Marathon microcatheter was primarily used in Period I, DeFrictor Nano microcatheter use increased in Period II. The DeFrictor Nano microcatheter has an external tip diameter of 1.3 Fr and is compatible with dimethyl sulfoxide (DMSO).²⁰⁾ Although the 5 mm tip of this microcatheter cannot be seen on radiography, it has better distal access than the Marathon.²⁰⁾ Notably, no differences were observed in the embolic materials employed in this study. Cyanoacrylate is often selected for patients with tortuous feeding arteries because of concerns regarding microcatheter trapping. Moreover, Magic is incompatible with DMSO. Although it may be possible to replace Onyx in the future, microcatheter limitations must be considered.

When investigating clinical outcomes due to chronological changes in endovascular devices, there was a trend toward more effective and safer embolization in Period II. The microcatheters were better inserted into the intra- or peri-nidus in Period II (72.1%) compared with Period I (48.4%). In addition, there were fewer vessel perforations in Period II than in Period I, although the difference was not significant. Hemorrhagic complication is the most common complication in endovascular embolization for AVM occurring in 9.7%–19.8% of patients.^{2,3,7)} Symptomatic complications (9.8%) in this study were similar to those reported previously.^{2,3,7,21,22)} However, despite the fact that

the patients in Period II had higher grades than those in Period I, symptomatic complications decreased in Period II. The tortuous, narrowed, and complex vascular structure of AVMs can cause problems in achieving superselective embolization.²³⁾ The microcatheter is deflected against the vessel wall and inserted in the distal vessels. Thus, the microcatheter in tortuous vessels may prevent the all-around transmission of energy and occasionally lead to sudden forward motion resulting in vessel injury.²⁴⁾ Conversely, an intermediate catheter inserted sufficiently distally will provide a more stable position for the microcatheter and prevent it from springing forward or sagging even in tortuous and complex vascular structures.²³⁾ Furthermore, the combination of a smaller-diameter intermediate catheter and a microcatheter with distal trackability may allow the microcatheter to be safely inserted into the intra- or peri-nidus, which may have reduced symptomatic complications. Thus, as further advances in endovascular devices are expected in the future, neurointerventionalists should closely monitor the devices.

Nevertheless, this study had certain limitations. First, this was a single-center retrospective study with a limited sample size. As endovascular devices continue to advance, verifying their effectiveness and safety in multiple institutions is crucial. Second, improvements in the skills of neurointerventionalists during the study period may have influenced the clinical outcomes. All neurointerventionalists had been engaged in endovascular treatment for over 10 years and had sufficient experience. Third, the impact of intermediate and microcatheters on microsurgery in patients who underwent preoperative embolization was not

investigated. The impact of endovascular device advancements on microsurgery needs to be assessed at multiple institutions and with a larger number of patients.

Conclusion

Technological advancements in endovascular devices for AVM, such as intermediate catheters and microcatheters, enable the effective and safe introduction of a microcatheter into intra- or peri-nidal feeding arteries, facilitating safe embolization. This advancement may have a beneficial impact on microsurgical procedures.

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Disclosure Statement

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