EMBOLIZATION OF CEREBRAL ARTERIOVENOUS MALFORMATIONS WITH N-BUTYL-2-CYANOACRYLATE

Hon-Man Liu, Yong-Chien Huang, and Yau-Hong Wang

**Purpose:** To determine the safety and effectiveness of arteriovenous malformation (AVM) embolization using liquid adhesives in a series of 103 patients with cerebral AVMs who underwent embolization with n-butyl-2-cyanoacrylate (NBCA).

**Methods:** All embolization procedures were performed using NBCA and a lipiodol mixture delivered by a flow-directed and/or guide-wire directed microcatheter.

**Results:** Using the Spetzler-Martin grading system, there were two cases of grade I AVM, 23 of grade II AVM, 31 of grade III AVM, 37 of grade IV AVM, and 10 of grade V AVM. Eleven patients underwent embolization only; these patients either had evidence of morphologic cure on follow-up angiogram, or showed evidence of a stable condition at 2-years follow-up. Seven patients were not treated owing to technical problems or a positive functional test. All other patients underwent preoperative embolization; 75%–99% obliteration was noted in 39 of these patients, 50%–74% obliteration in 33, and less than 50% obliteration in 13. Embolization-related complications occurred in nine patients, and two patients died as a result of the procedure. Severe neurologic complications occurred in two patients and five patients developed mild or transient neurologic deficit.

**Conclusions:** Endovascular treatment of brain AVMs with an NBCA mixture has a lower complication rate than shown in previous studies using other materials. The percentage of obliteration of the nidus is increased because NBCA penetrates AVMs better than polyvinyl alcohol particles. NBCA can be used at a lower concentration than other acrylates, and therefore causes almost no catheter gluing. The embolic mass formed by NBCA is more biocompatible than that formed by other acrylates.

Arteriovenous malformations (AVMs) are the most common intracranial vascular malformation. Spetzler and Martin proposed a grading scale that assigns points based on the size of the AVM, the eloquence of the surrounding brain, and the pattern of venous drainage [1]. In their paper presenting the grading system, 100 lesions were graded on the basis of radiographic studies. Their results indicate a good correlation between AVM grade and the incidence of neurologic complications. Grade I and II lesions were resected with a very low incidence of surgically induced neurologic deficit, while surgery for grade IV and V AVMs was accompanied by a significant number of neurologic complications.

Over the past 2 decades, the advent of microsurgical techniques has allowed neurosurgeons to undertake the resection of more formidable AVMs. With the development of interventional neuroradiologic techniques, and improvements in fluoroscopic equipment, catheters, embolic agents, angiographic techniques, and understanding of neurovascular anatomy, endovascular embolization of AVMs is now an accepted adjunct to surgical therapy. The purpose of this study was to determine the safety and effectiveness of AVM embolization using liquid adhesives.

**Materials and Methods**

Between 1987 and 1998, 103 patients were referred to our department for assessment and possible endovas-
cular treatment of AVMs. Patients treated with radiosurgery were excluded from this study because of the necessity for long-term follow-up.

The patients’ ages ranged from 12 to 56 years. Forty-five patients presented with hemorrhage only, 29 patients with seizure, 15 patients with neurologic deficits but no history of hemorrhage, and 14 patients with headache. Subsequent computed tomography (CT) or magnetic resonance (MR) imaging revealed AVMs.

Endovascular technique
Prior to or at the time of admission, patient characteristics were reviewed to determine the appropriate therapeutic plan. Referrals were made mainly by neurosurgeons, but neurologists referred a few patients who refused surgical intervention.

Embolization was performed by superselective catheterization of the feeding vessels via the femoral route. Additional intraoperative embolization was performed in three patients because of the complicated anatomy and severe tortuosity of the feeding arteries. In larger AVMs, embolization was usually performed in a series of staged procedures occurring approximately 1 to 4 weeks apart.

Either a guidewire-directed microcatheter (Tracker, Target Therapeutics, Fremont, CA, USA) or a flow-directed microcatheter (Magic, Balt, Montmorency, France) was used to deliver the tissue adhesive. The cyanoacrylate concentration was varied from 25% to 50% by mixing the tissue adhesive n-butyl-2-cyanoacrylate (NBCA; Histacryl, Braun Melsungen, Germany) with an oil-based iodine contrast medium (Lipiodol, Guerbert, Aulney-Sous-Bois, France). Tantalum powder (Nycomed Ingenor, Paris, France) was used as the contrast agent in the mixture at a concentration of 0.5 g/mL. In most cases, the NBCA mixture was injected using a single-column technique. In cases of associated arteriovenous fistula (AVF), 50% to 90% of the NBCA mixture was injected using a “sandwich” technique [2], or microcoils or 6.0 silk thread (2 mm in length).

Embolic strategy
Our strategy was primarily to close the AVM as much as possible. Most embolization procedures (89.3%) were performed before surgical intervention. We tried to decrease the size of AVM nidus in order to occlude the deep arterial feeding arteries and vessels at the margins adjacent to the eloquent area. When an intranidal aneurysm or AVF was present, we tried to close it early in the treatment process. We did not treat the feeder aneurysm. Symptomatic aneurysms were clipped first.

Superselective functional testing was carried out 40 times with 50 mg amobarbital (Amytal, Eli Lilly, Indianapolis, IN, USA) for lesions possibly involved in the eloquent area. Embolization was not performed in the three positive cases.

Results
Radiologic findings
Of the 103 patients with AVMs, the left cerebral hemisphere was involved in 52 patients (50.5%), the right hemisphere in 35 patients (34.0%), and the posterior fossa in 16 patients (15.5%) (Table 1). The largest dimension ranged from 12 to 105 mm (41.5 ± 16.4, mean ± standard deviation, SD) and the volume ranged from 0.6 to 196 mL (24.8 ± 24.4, mean ± SD).

The major arterial groups involved in the supply of the AVMs included the middle cerebral, anterior cerebral, posterior cerebral, and penetrating artery group (lenticulostriate, thalamoperforating, anterior and posterior choroidal, and thalamogeniculate arteries), the basilar artery group (anteroinferior cerebellar and superior cerebellar arteries), and the posteroiinferior cerebellar artery. The blood supply arose from a single major arterial group in 26 patients (25.2%), from two major arterial groups in 34 patients (33.0%), from three major arterial groups in 40 patients (38.8%), and from four major arterial groups in three patients (2.9%). AVFs were found in 12 (11.6%) patients. There were a total of 37 intra-nidal aneurysms (arterial and venous) and 12 flow-related feeder aneurysms. Incidental unrelated aneurysms were found in three patients.

Using the Spetzler-Martin grading, of the 103 AVMs, two were grade I, 23 were grade II, 31 were grade III, 37 were grade IV, and 10 were grade V.

Angiographic obliteration
Table 2 shows the amount of angiographic obliteration in patients with different grades of AVM. Of the
103 patients, 11 (10.7%) had angiographic cure at 2-years clinical follow-up; follow-up angiography was obtained in two of these patients (Fig. 1). One major vascular group supplied the AVMs in all 11 patients. In 39 patients (37.9%), immediate post-embolization angiography revealed 75% to 99% obliteration (Fig. 2). One or two major arterial groups fed 76.9% of these AVMs. In 33 patients (32.0%), immediate post-embolization angiography revealed 50% to 74% obliteration. In 13 patients (12.6%), less than 50% obliteration was shown on immediate post-embolization angiography. No embolization was carried out in seven patients (6.8%). A positive amytal test was obtained in three of these patients and anatomical difficulty in navigating the catheter close to the nidus, preventing a wide margin of safety for the embolization, was encountered in four.

Among the 85 patients with incomplete embolization, two patients died from procedure-related complications; 71 underwent definite microsurgical excision of the AVM 1 to 4 weeks after the embolization, and 12 patients underwent partial surgical excision or palliative treatment.

**Complications**

Among the 96 patients who underwent embolization therapy, nine suffered post-embolization complications. Procedure-related death occurred in two patients. A 36-year-old woman with a right occipital grade III AVM and basilar tip aneurysm became comatose after the first session of embolization. CT showed severe subarachnoid hemorrhage (SAH) and severe brain edema (Fig. 3). She died 3 days after the embolization. A 34-year-old woman with a left temporal grade V AVM was found comatose in the bathroom at home 1 week after the first session of embolization. CT revealed intracerebral hematoma and she died 12 hours later.

**Table 2.** Number of patients in each Spetzler-Martin grade according to the percentage of obliteration of the nidus after embolization in 103 patients with arteriovenous malformation

<table>
<thead>
<tr>
<th>Percentage of obliteration</th>
<th>Spetzler-Martin grade</th>
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<tbody>
<tr>
<td></td>
<td>I</td>
</tr>
<tr>
<td>100</td>
<td>2</td>
</tr>
<tr>
<td>75–99</td>
<td>0</td>
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<tr>
<td>50–74</td>
<td>0</td>
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<tr>
<td>&lt;50</td>
<td>0</td>
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<td>0*</td>
<td>0</td>
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<tr>
<td>Total</td>
<td>2</td>
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*Cases with technical failure or positive amytal test.

**Fig. 1.** Computed tomography scan in a 44-year-old man with severe headache shows subarachnoid hemorrhage. A) Internal carotid artery angiography reveals an aneurysm (arrow) at the genu of the left middle cerebral artery and arteriovenous malformation (AVM) at the posterior temporal lobe. B) The nidus is totally obliterated in the immediate post-embolization angiogram. The aneurysm was clipped surgically. C) Follow-up angiography after 1.5 years shows no evidence of residual or recurrent AVM.
Two patients developed severe neurologic that was attributed to the embolization. One patient had visual deficit (hemianopia) after embolization of a parieto-occipital grade III AVM. CT revealed an infarct in this patient (Fig. 4). The other patient had ataxia due to cerebellar hemorrhage, which occurred as a complication of embolization of a cerebellar grade V AVM. Complete surgical excision of the AVM was performed after embolization in these two patients, and they survived with mild neurologic deficit.

Five patients developed mild or transient neurologic deficit (motor weakness in 3 patients and sensory deficit in 2 patients) after embolization. None of them suffered further decline after surgical excision of the AVM.

**Discussion**

**Embolic material**

According to a review by Frizzle and Fisher [3], only Jafar et al reported treatment of cerebral AVM using NBCA exclusively as the embolic agent [4]. Ours is the first report of a large series of cerebral AVM embolization with NBCA. Many different materials have been used to occlude cerebral AVMs, including metallic coils, balloon catheters, liquid adhesives such as acrylates, and particulate matter. Metallic coils and balloon catheters have not been used in the last decade, except when a large AVF is found inside the AVM.

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*Fig. 2.* Computed tomography scan in a 26-year-old man with severe headache and loss of consciousness shows a large left parietal arteriovenous malformation (AVM) with intracerebral hemorrhage. A) Left internal carotid artery study reveals that the AVM is supplied by the left primitive posterior cerebral artery (PCA), left middle cerebral artery (MCA), and bilateral anterior cerebral artery. B) After the first session of embolization, the blood supply from the left PCA and left MCA is substantially decreased. C) After the third session of embolization, the size of the AVM is further reduced. D) After operation, left common carotid artery (CCA) angiography shows total removal of the large AVM.
Polyvinyl alcohol (PVA), a particulate agent, has several biocompatibility and technical characteristics which makes it suitable for use as an embolic agent. Because it can be compressed and subsequently re-expands on contact with blood, PVA is commonly used as an embolic plug to occlude large vessels. With further technical improvements such as microembolization by superselective catheterization, PVA has been successfully used for embolization of vascular lesions [5, 6]. In experimental and clinical pathologic studies, the degree of tissue reaction to PVA has been inconsistent [7–11]. Recanalized lumina were seen in 18% of PVA-embolized vessels in surgical specimens of human cerebral AVM [12]. The use of PVA in this setting is limited by the difficulty of its preparation and delivery and by frequent catheter obstruction [12, 13].

Isobutyl-cyanoacrylate (IBCA) and NBCA are the two acrylic embolic agents used in the treatment of AVMs. They can penetrate to the nidus of the AVM more effectively than PVA because they are liquids before polymerization. Since the goal of treatment of AVM is the angiographic obliteration of the nidus of the AVM, acrylate has been the embolic agent of choice in many centers. Schumacher and Horton [13] and Wallace et al [14] reported that comprehensive complication rates were lower after acrylic embolization than after PVA embolization.

Embolization of AVM with IBCA has been criticized for complicating the resection of these lesions [4]. Malformations treated with IBCA have been described as brittle and solid masses that are difficult to manipulate without damaging the surrounding softer parenchyma. IBCA-embolized vessels are difficult to cut with microscissors, and continued bleeding from transected embolized vessels that cannot easily be controlled with bipolar coagulation has been described [4].

The use of NBCA for preoperative embolization precludes these problems. NBCA produces a more uniform, higher integrity acrylic column with less fragmentation than IBCA. It forms a mass which is less...
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Fig. 4. This 42-year-old man was admitted because of intractable seizure and occasional blurred vision. A) Right common carotid artery angiography shows an arteriovenous malformation (AVM) in the parieto-occipital lobe. The left posterior cerebral artery (PCA) supplies the posteroinferior part of the AVM. B) Post-embolization left vertebral artery study shows a decreased blood supply from the left PCA. The patient complained of visual field defect after the procedure. C) Computed tomography scan reveals an infarct in the right occipital lobe next to the acrylate mixture (arrow), which was due to inadvertent embolization of the normal branch.

brittle, less rigid, and more elastic than that produced by IBCA. These characteristics have led to NBCA’s increasing acceptance by neurosurgeons.

Microcatheter gluing is a major complication encountered when using IBCA for the embolization of cerebral AVMs. However, catheter gluing did not occur in this series, probably because NBCA has a lower bond strength than IBCA, which decreases the risk of accidental catheter gluing. Using a single column injection method, the procedure is performed slowly under fluoroscopic monitoring. This permits live observation of the progression of glue and the proximal reflux of glue extending along the microcatheter. Once the AVM is filled, or the progression of glue is complete, the syringe is aspirated gently and the microcatheter is quickly removed. We used low concentrations (25%–30%) of NBCA in 83.3% of the cases. This increases polymerization time and reduces the risk of permanently gluing the tip of the microcatheter.

Angiographic obliteration

Angiographic cure of the AVM was achieved in 11 (10.7%) of the 103 lesions in this series (Table 3). All these lesions were classified as grade I or II, and none had more than one major vascular group involved in supplying the lesion. More than 50% obliteration of the AVM was shown on the immediate post-embolization angiography in 80.7% of patients (Table 2).

According to a review by Frizzel and Fisher [3], embolization in 1246 patients with brain AVMs resulted in cure in 5% of patients. The rate of total obliteration in the 572 AVMs embolized using IBCA was 5%. Vinuela reported a series of 283 cases of embolization of cerebral AVMs using acrylic [15]. In 20 (7%) of these cases, it was possible to completely occlude the AVMs with embolization alone, and the AVM was small and had no more than four feeders. More than 50% obliteration was obtained in 210 cases (74.2%). However, these investigators used a calibrated leak balloon catheter in the first 128 cases. This is a more difficult and dangerous technique than using a microcatheter. The calibrated leak balloon technique can cause more complications, such as cerebral hemorrhage due to balloon over-inflation and rupture of the

Table 3. Number of patients with various numbers of supplying vascular groups according to the percentage of obliteration of the nidus after embolization in 103 patients with arteriovenous malformation

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<thead>
<tr>
<th>Percentage of obliteration</th>
<th>Number of supplying vascular groups</th>
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<tr>
<td></td>
<td>1</td>
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<tr>
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<td>&lt; 50</td>
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<td>0*</td>
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<tr>
<td>Total</td>
<td>26</td>
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*Cases with technical failure or positive amytal test.*
arterial feeder, and retention of the catheter due to adhesion of the catheter to the vessel wall. In the remaining 155 cases, they used a microcatheter similar to that used in our series, and the mortality rate related to embolization decreased from 3.9% to 1.3%. However, they did not mention any difference in obliteration rate between these two periods.

Comparison of the obliteration rates in the present study and reports by Wikholm et al [16] and Vinuela [15] indicate that regardless of grading, the likelihood of angiographic cure in cerebral AVMs is about 10% (Table 4). However, embolization can reduce the size by more than 50% in about 70% of AVMs. Occlusion of the deep feeding arteries, the vessels at the margins adjacent to an eloquent area, the intranidal aneurysm, and the high-flow arteriovenous fistulas can be accomplished in about 80% of these AVMs.

**Procedure-related complications**

Procedure-related complications occurred in nine (9.3%) of the 96 patients with embolization. Parenchymal hemorrhage occurred in two patients in our series: one patient died and one had severe cerebellar hemorrhage that required emergency evacuation.

Although the mechanism of hemorrhage following embolization of an AVM has not been studied directly, several theories have been proposed. The pressure in arteries feeding an AVM rises as a result of embolization [17]. If the malformation is not completely embolized by the procedure, residual feeders may be confronted with elevated arterial pressures. Incomplete embolization of an AVM can result in stasis of blood flow in areas of venous dilatation that could lead to venous thrombosis and, again, raise the pressure confronting residual arterial feeders. This is especially likely when the acrylics polymerize in situ in the veins, resulting in venous obstruction. In large AVMs, embolization of more than 30% of the AVM’s volume significantly alters the hemodynamics of flow through the AVM and potentiates the risk of normal pressure breakthrough [2]. The reported incidences of normal pressure breakthrough and venous outflow occlusion with resultant post-embolization intracranial hemorrhage are less than 5% and 1%, respectively [2]. Elevated arterial pressure, progressive venous thrombosis, and normal pressure breakthrough in partially embolized AVMs are possible causes of the bleeding in our two patients.

An AVM-associated aneurysm occurs in about 15% to 20% of cases. In cases of flow-related feeder aneurysm in close proximity to the AVM nidus or intranidal aneurysm, the vessels harboring the aneurysm were the first vessels selected for embolization. The aneurysm was usually embolized with the nidus using a glue cast in our patients. A flow-related feeder aneurysm that is not in close proximity to the AVM nidus or in the proximal trunk poses a difficult dilemma. Embolization in the proximal trunk of the feeder carries a high risk of embolization of normal parenchyma branches, which occurred in one patient who died in our series. In this patient, a wide-based basilar tip aneurysm was associated with the parieto-occipital AVM (Fig. 3). In such cases, an attempt was made to occlude the AVM in the hope that the flow-related aneurysm would regress. The aneurysm ruptured after the first session of embolization in the fatal case with flow-related aneurysm. This might have been due to the increase in pressure at the aneurysm after partial embolization of the AVM. Our case that was complicated with hemianopia after embolization may have been due to inadvertent embolization of the normal branches in the occipital lobe. In cases with mild or transient complications, peri-focal edema after embolization or embolization of tiny normal branches, which are not seen on routine angiography, may have been the cause.

In conclusion, embolization of brain AVMs with an NBCA mixture has a low and acceptable complication rate that is lower than those from previous reports of embolization using other materials. This technique can increase the percentage of obliteration of the AVM nidus compared to PVA because NBCA provides better penetration. NBCA can be used in lower concentration than other acrylics, which makes the procedure more controllable and results in less catheter gluing. This

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**Table 4.** Comparison of results from previously reported series of embolization of cerebral arteriovenous malformations (AVMs) and results from the present study

<table>
<thead>
<tr>
<th>Study</th>
<th>Angiographic obliteration of AVM after embolization</th>
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<tr>
<td>Vinuela [15]</td>
<td>283</td>
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<tr>
<td>Wikholm et al [16]</td>
<td>150</td>
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<tr>
<td>Present study</td>
<td>103</td>
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Results are the percentage of patients with the indicated degree of AVM obliteration. *Cases with technical failure or positive amytal test.
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technique also has the advantage of forming an embolic mass that is more elastic than the mass formed using IBCA.

References