A Novel Technique and New Grading Scale for the Embolization of Cerebral Vascular Malformations

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OBJECTIVE: Effective transarterial embolization of a dural arteriovenous fistula or pial arteriovenous malformation (AVM) requires penetration of a durable occlusive agent into the fistula or AVM nidus. Cyanoacrylate glue often cannot traverse the tortuous vessels that typically supply such malformations, leading to proximal occlusion and recruitment of collateral flow. Other embolic agents, such as polyvinyl alcohol particles, achieve better penetration, but their effects are short lived, often leading to recanalization. The authors sought to overcome these obstacles by developing a technique to enhance glue penetration into the fistula or AVM nidus itself.

METHODS: After placing a guide catheter in the proximal feeding artery, a microcatheter is advanced coaxially to its limit. As glue is injected through the microcatheter, a column of 5% dextrose in water (D5W) is pushed manually through the guide catheter lumen to propel the glue forward. This technique has been bench tested in a standard flow model of vascular malformations, using a pump capable of delivering various rates of D5W. It has also been validated in treating 17 patients with cerebral dural arteriovenous fistulae or AVMs, with real-time adjustment of D5W flow according to the extent of glue penetration.

RESULTS: In the bench model, the extent of glue penetration, as graded by a new scale of liquid agent embolization proposed by the authors, correlated directly with the rate of D5W flow ($P = 0.5$, analysis of variance). In vivo, this technique has enhanced the penetration of glue into the fistula or AVM nidus, resulting in longstanding embolization of these malformations.

CONCLUSION: Coaxial injection of D5W through the guide catheter can propel cyanoacrylate glue through tortuous feeding arteries and can enhance its penetration into dural fistulae and AVMs, leading to more effective endovascular treatment of these malformations.

KEY WORDS: Arteriovenous malformation, Dural arteriovenous fistula, Embolization, Grading scale, *n*-butylcyanoacrylate, Technique

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Transarterial embolization (TAE) has become a mainstay in the treatment of cerebral dural arteriovenous fistulae (dAVF) and pial arteriovenous malformations (AVMs). In some cases, TAE alone may affect cure, palliate symptoms related to increased flow (e.g., tinnitus or congestive heart failure), or convert a high-risk dAVF with cortical venous drainage into a low-risk one (3, 14, 19, 28). In others, TAE can serve an adjunctive role by reducing flow through main arterial feeders, either before or after transvenous occlusion of the affected sinus, microsurgery, radiosurgery, and other therapies (2, 3, 5, 14, 19, 24, 28, 31).

Effective TAE of a dAVF requires penetration of a durable occlusive agent into the fistulous connection (2, 20, 28). Cyanoacrylate glue and mechanical devices (platinum coils, detachable balloons) often cannot traverse the tortuous vessels that typically supply such malformations, leading to proximal occlusion and recruitment of collateral flow (5, 30). Other agents, such as polyvinyl alcohol (PVA) particles, achieve better penetration, but their effects are short lived, often leading to recanalization (2, 27). The use of ethanol can be associated with cranial neuropathy, stroke, and other unacceptable morbidities (5, 29). The same limitations apply to pial AVMs supplied by meningeal branches of the external carotid or vertebral arteries.

We sought to overcome these obstacles by developing a technique to enhance penetration of cyanoacrylate glue into the fistula or AVM nidus itself. *Figure 1* schematically illustrates this method. After placing a guide catheter in the proximal feeding artery of an AVM or dAVF, a coaxial microcatheter is advanced to its limit. As cyanoacrylate glue is injected through the microcatheter under continuous fluoroscopic monitoring, a column of 5% dextrose in water (D5W) is pushed through the guide catheter lumen with a syringe attached to a rotating hemostatic valve. This coaxial flow of D5W around the microcatheter propels glue forward, achieving deeper penetration into the nidus or fistula. The force of manual injection through the syringe can be altered according to the distribution achieved by the glue, allowing real-time adjustment of D5W flow and consequent glue permeation.

MATERIALS AND METHODS

Preclinical Testing

In benchtop experiments, a standard flow model was used to test the D5W push technique. This model consists of two impermeable membranes separated by channels that simulate blood vessels of varying caliber. The models replicate the feeding arteries, nidus, and draining veins of a vascular malformation and were provided by Cordis Neurovascular (Miami Lakes, FL), which uses them to train physicians in the use of Tru-Fill, their proprietary *n*-butylcyanoacrylate (NBCA) glue.

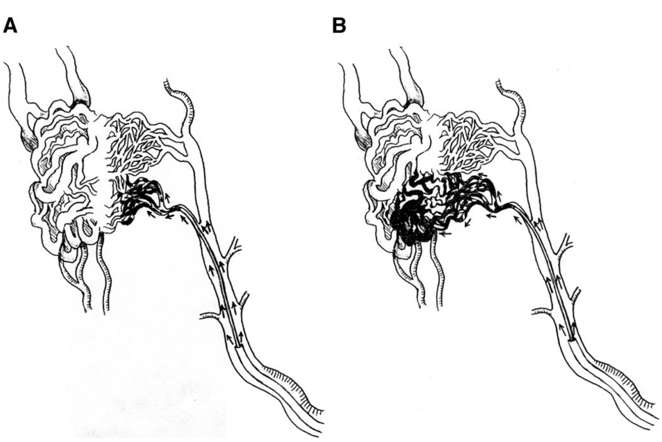

FIGURE 1. *Schematic illustration showing the D5W push technique. After placing a guide catheter in the proximal feeding artery of an AVM or fistula, a coaxial microcatheter is advanced to its limit.* A, *as cyanoacrylate glue (*black*) is injected through the microcatheter, a column of D5W is pushed through the guide catheter lumen with a syringe (*arrows*).* B, *this coaxial flow of D5W around the microcatheter (*small arrows*) propels glue forward, achieving deeper penetration into the nidus or fistula. The force of manual injection through the syringe can be altered according to the distribution achieved by the glue, allowing real-time adjustment of D5W flow and consequent glue permeation.*

The model was perfused continuously with sheep plasma (Hema Resource & Supply, Aurora, OR) using a recirculating pump (Flowtek, Las Vegas, NV). The pump delivers pulsatile flow at frequencies similar to human heart rhythms. A 5-French guide catheter (Envoy; Cordis Neurovascular, Miami Lakes, FL) was advanced to a consistent landmark at the proximal (arterial) end of the AVM model and connected to a digital power injector (Angiomat; Mallinckrodt, Hazelwood, MO) through a rotating hemostatic valve. The injector pushed D5W through the guide catheter at four different rates (0.0, 0.2, 0.4, and 0.6 ml/s) with a force of 1200 lb/inch^2. These parameters were selected after pilot studies suggested that rates of 1 ml/s and more resulted in penetration beyond the venous end of the model.

A microcatheter (Prowler-10; Cordis Neurovascular) was primed with D5W, placed coaxially within the guide catheter, and advanced to a consistent landmark in a simulated feeding artery proximal to the AVM nidus. Tru-Fill was diluted 1:3 volumetrically with ethiodized oil to confer radiopacity and to reproduce ratios typically used in clinical application. The glue and ethiodized oil mixture was then injected manually through the microcatheter, propelled by the flow of D5W through the guide catheter. The injection was terminated when glue refluxed back to a simulated feeding artery aneurysm proximal to the microcatheter tip. All injections were performed by one person (APA), who was blinded to the randomly selected rate of D5W flow.

For each of the four rates, four models were tested. The microcatheter, flow model, and sheep plasma were replaced after each experiment. However, the same guide catheter was used throughout the study. The degree of penetration into the AVM model was assessed radiographically with digital subtraction serialographs using the A-plane of a Philips Integris imaging system (Philips Medical Systems, Bothell, WA). The object-image distance was kept constant throughout. The serialographic images were printed onto radiographic film and then interpreted by two experienced interventional neuroradiologists (GPT, DWL) who were blinded to the rate of D5W flow corresponding to each image. The degree of glue penetration into the flow model was graded on a scale of 1 to 5, using a new classification that we propose for liquid agent embolization of vascular malformations (*Table 1*, *Fig. 2*). The mean score and standard deviation for each rate of flow then was calculated. The four rates were compared using a one-way analysis of variance (21).

TABLE 1. New grading scale for glue embolization of vascular malformations

1. Glue penetration into feeding artery only
2. Glue penetration into proximal nidus or fistula
3. Glue penetration into distal nidus or fistula
4. Glue penetration into immediate draining recipient
5. Glue penetration into distal vein or beyond

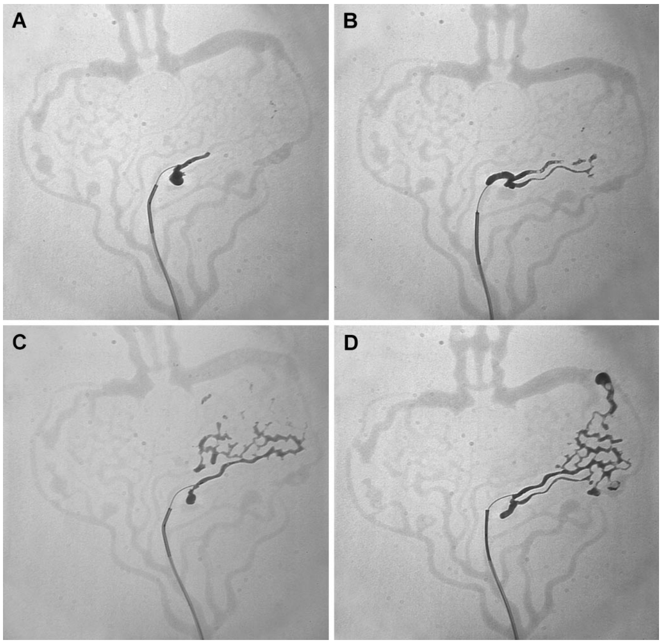

FIGURE 2. *Angiograms illustrating the new grading scale for liquid agent embolization of cerebral vascular malformations (see Table 1). In benchtop experiments, a standard flow model was used to measure the penetration of cyanoacrylate glue. This model simulates the feeding arteries, nidus, and draining veins of an AVM.* A, *glue penetration into feeding artery only.* B, *glue penetration into proximal nidus.* C, *glue penetration into distal nidus.* D, *glue penetration into immediate draining recipient.*

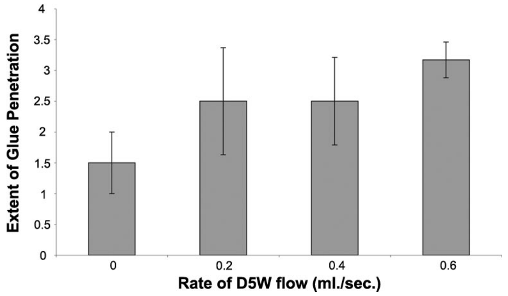

FIGURE 3. *Bar graph illustrating that the extent of glue penetration correlated directly with the rate of D5W flow. The mean score and standard deviation for the four rates of flow are shown (*P = 0.5*, analysis of variance). See* Figure 2 *and* Table 1 *for explanation of the grading scale.*

Clinical Application

The D5W push technique has been validated in treating 17 patients with cerebral dAVFs or pial AVMs supplied by transosseous meningeal branches of the external carotid or vertebral arteries. To date, we have not used it to embolize feeding branches arising from arteries of the subarachnoid space or those supplying spinal dAVFs.

RESULTS

Preclinical Model

The extent of glue penetration, quantified with the new scale proposed in *Table 1* and illustrated in *Figure 2*, correlated directly with the rate of D5W flow (*Fig. 3*). The mean scores (and standard deviations) of glue penetration for rates of 0.0, 0.2, 0.4, and 0.6 ml/s were 1.50 (0.5), 2.50 (0.87), 2.50 (0.71), and 3.17 (0.29), respectively. Using a one-way analysis of variance, this trend of increased glue penetration with increased rates of D5W flow was statistically significant (F test statistic = 3.48, with 3 and 12 degrees of freedom; P = 0.5).

Clinical Usefulness

In the 17 patients in whom this technique has been used, there have been no complications. Because of the potential for real-time adjustment of D5W flow according to the extent of glue penetration, there have been no cases of venous outflow occlusion. There have been no known cases of intracerebral hemorrhage or other bleed. Because of the staged nature of TAE, many of these patients underwent follow-up angiography. No recanalization of the arteries embolized by this technique has been encountered in these ensuing studies. An illustrative case is presented in *Figure 4*.

DISCUSSION

The natural history of cranial dAVFs is highly variable. Although some remain static, incidental findings on imaging studies, others can pursue an aggressive and potentially fatal course (1, 4, 15, 18). Treatment may be indicated to palliate symptoms related to increased flow, to restore perfusion to cerebral territories experiencing vascular steal, or to divert flow away from leptomeningeal veins, aneurysmal varices, and other vessels at risk of hemorrhage.

TAE of arterial feeders to the malformation remains a standard of treatment, either independently (3, 14, 19, 28) or as an adjunct to transvenous occlusion of the affected sinus, microsurgery, radiosurgery, and other therapies (2, 3, 5, 14, 16, 19, 24, 26, 28, 31). The objective of TAE is delivery of a durable occlusive agent directly into the fistulous connection itself (2, 20, 28). A variety of embolic materials have been used, including bare platinum coils, fibered coils, detachable balloons, Gelfoam (Upjohn, Kalamazoo, MI), silk suture, PVA particles, collagen, and cyanoacrylate liquid adhesives. Currently, the most commonly used agents are PVA and NBCA.

NBCA and mechanical devices often cannot traverse the tortuous vessels that typically supply such malformations, leading to proximal occlusion and recruitment of collateral flow, usually from vascular pedicles that are too small to catheterize or too dangerous to embolize (5, 10, 30). Conversely, deposition of embolic agents distal to the nidus or fistula may result in venous infarction or hemodynamic alterations that promote hemorrhage (9). Suspensions of PVA particles achieve better penetration, but their effects are short lived, often leading to recanalization and the need for retreatment (2, 7, 12, 16, 22, 27). These same limitations apply to pial

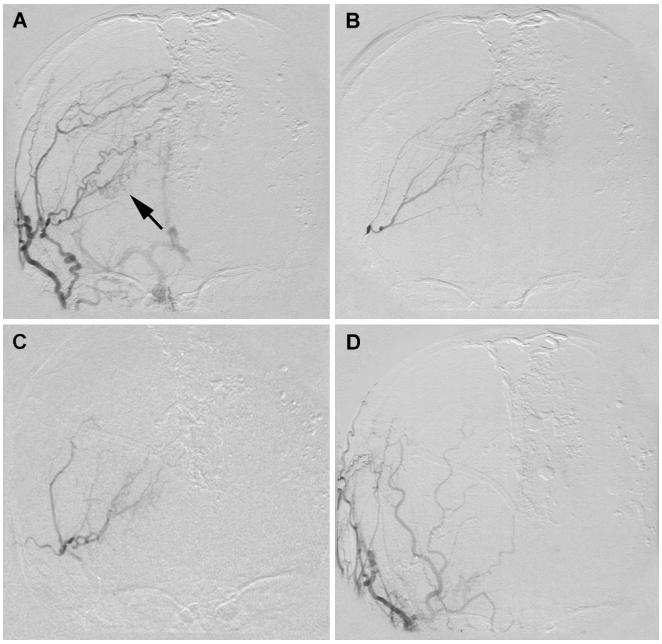

FIGURE 4. *Images obtained from a 17-year-old boy with a right frontoparietal AVM supplied by multiple branches of the internal and external carotid arteries illustrating the D5W push technique.* A, *external carotid artery angiogram performed through a guide catheter, frontal projection. Note the supply to the AVM from the anterior division of the middle meningeal artery* (arrow). B, *angiogram performed through a microcatheter after selective catheterization of this branch. Although the microcatheter was advanced to its limit, a significant distance still remained between its tip and the AVM nidus.* C, *glue cast after NBCA embolization using the D5W push method. Note how the cyanoacrylate glue was propelled into branches of the vessel beyond the microcatheter and into the AVM nidus.* D, *repeat external carotid artery angiogram performed through a guide catheter, frontal projection. Note that the supply to the AVM from the anterior division of the middle meningeal artery has now been eliminated.*

AVMs supplied by meningeal branches of the external carotid or vertebral arteries. We sought to overcome these shortcomings by developing a technique to enhance the penetration of cyanoacrylate glue into the fistula or nidus itself.

Despite the importance of TAE in the management of dAVFs, few reports have emphasized technical aspects of the procedure. In most cases, a concentrated mixture of NBCA and iodized oil is injected using a flow-related method. Some authors have reported better permeation of cyanoacrylate glue by wedging the microcatheter into the feeding artery and arresting blood flow before injection of a more dilute glue mixture (11, 20). However, in its original description, the wedged technique was only possible after approximately 70% of the shunt flow had been eliminated using the conventional flow-related method. Subsequent reports have also emphasized the importance of preparatory embolization of accessory pedicles with the flow-related approach to decrease competing inflow and fragmentation of the glue column. Furthermore, the wedge technique requires navigation to a sufficiently distal segment so that the diameter of the feeding artery matches that of the microcatheter tip. Such positioning is not always possible in the large caliber, tortuous conduits that typically supply dAVFs. Although the use of adenosine to induce systemic hypotension for flow arrest has been reported anecdotally, the safety and efficacy of this adjunct has not been established (23).

For these reasons, the D5W push method has merit in enhancing the penetration of cyanoacrylate glue into the fistula or nidus itself. This technique is indicated for embolizing feeding arteries the tortuosity of which limits the ability to navigate the microcatheter close to the fistulous connection. In general, it works best when the guide catheter can be positioned in the proximal aspect of the same vessel and there are no large branches originating from the intervening segment. This can often be achieved with divisions of the external carotid artery, but less so for those of the internal carotid or vertebral arteries. Thus, feeding vessels within the subarachnoid space may be embolized with the D5W push method, but the greater distance between the guide catheter and microcatheter tips, as well as the numerous branches arising from the intervening segment, dilute the force of the D5W column in propelling the embolic agent distally.

Other strategies for injecting NBCA far beyond the microcatheter tip include delaying its polymerization time by altering the monomer-to-ethiodol ratio or by adding glacial acetic acid (8, 17). However, miscalculating the rate of transit through the fistula or the polymerization kinetics of the glue can lead to unpredictable events, such as proximal occlusion or iatrogenic venous outflow restriction. Furthermore, the use of glue that is too diluted may lead to recanalization. The advantage of the D5W push technique over these methods is the ability to use a concentrated NBCA mixture coupled with dynamic, real-time adjustments that allow precise dispersion of the glue cast at the site of the fistula.

Recently, a nonadhesive liquid embolic agent composed of ethylene-vinyl copolymer dissolved in dimethylsulfoxide has become commercially available (Onyx; MicroTherapeutics Inc., Irvine, CA). Onyx been studied extensively as an embolic agent for cerebral AVMs (6, 13), and its use has been reported in the treatment of dAVFs as well (25). Its nonadhesive property minimizes the risk of gluing the microcatheter to the wall of the feeding artery. This allows more prolonged injection, which should obviate the barriers imposed by tortuosity and long distances between microcatheter tip and nidus. For this reason, the D5W push technique is not likely to augment the use of Onyx. Furthermore, the potential chemical interactions between D5W and the dimethylsulfoxide vehicle have not been characterized.

The benchtop experiments validate the D5W push technique in vitro, but its clinical usefulness is more difficult to quantify. One reason is that dynamic, real-time adjustments of the force of manual injection preclude the ability to correlate the depth of glue penetration with any single rate of D5W flow in vivo. However, it has been our subjective experience that the technique enhances the dispersal of NBCA compared with conventional methods of delivery. For instance, the glue cast depicted in *Figure 4C* is more permeant than what is typically achieved without this adjunctive technique.

Finally, the new grading scale for liquid agent embolization of cerebral vascular malformations proposed in this study may become an important tool for further research and therapy. By specifying the anatomic portion of the vascular malformation permeated by the embolic material, the attendant risk and efficacy of TAE can be refined. Furthermore, this scale can be used for prognostic purposes in helping to define the role and outcome of adjunctive treatments after TAE, such as radiosurgery or microsurgical resection. However, as with the D5W push itself, the clinical usefulness of this grading scale requires further study.

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