The Brain Aneurysm Institute
at Beth Israel Deaconess Medical Center
Multidisciplinary Care of Patients with Hemorrhagic and Ischemic Stroke

NEUROVASCULAR NEWS Summer 2015

The Brain Aneurysm Institute has special expertise in the evaluation and treatment of the following conditions:

Ischemic
- Acute stroke (thrombolysis)
- Carotid artery stenosis
- Vertebrobasilar artery stenosis
- Intracranial artery stenosis
- Moya-Moya disease
- Spinal cord disease

Hemorrhagic
- Brain hemorrhage
- Subarachnoid hemorrhage
- Unruptured aneurysms
- Arteriovenous malformations (AVMs)
- Cavernous malformations
- Other brain vascular malformations
- Spinal cord malformations

The Institute also provides the following endovascular procedures:
- Balloon test occlusions
- Sclerotherapy of congenital venous malformations
- Tumor devascularization
- Vertebroplasty
- WADA test

As well as embolization for:
- Dural sinus thrombosis
- Epistaxis
- Extra-cranial vascular malformations


Christopher S. Ogilvy, MD
Director
Brain Aneurysm Institute


Ajith Thomas, MD
Co-Director
Brain Aneurysm Institute

The Beth Israel Deaconess Medical Center (BIDMC) Brain Aneurysm Institute, under the direction of Christopher S. Ogilvy, MD, and co-director Ajith Thomas, MD, was established in 2013 for the management and care of patients with routine and complex intracranial and extracranial blood vessel disorders. In order to provide the best care for patients with blood vessel abnormalities in the central nervous system, a group of experts joined forces to form the BIDMC Brain Aneurysm Institute. The concept of the Institute is to make available to patients with cerebrovascular problems all modalities of treatment currently available, which includes minimally invasive procedures such as endovascular therapy, radiosurgery, and open cranial surgery, when indicated.

You Can Help
Declare September as National Brain Aneurysm Awareness Month.

Senator Edward Markey has introduced a resolution in Congress to make September "National Brain Aneurysm Awareness Month".

1 in 50 people will develop a brain aneurysm. If a brain aneurysm is diagnosed early with proper screening, it can be treated before it ruptures. Lives can be saved if people know the risks, the signs, and when to get help. It is critical that you help raise awareness of brain aneurysms, including methods of early detection and treatment. The Brain Aneurysm Foundation asks you to please sign below to support S. Res. 176 and H. Res. 259 to make September National Brain Aneurysm Awareness Month.

www.bafound.org

We are available to accept referrals of patients on an emergent or non-urgent basis.

Direct Transfer Line
617-667-7000; Page "9COIL"

Direct Emergency Department Access
617-754-2494

Physician Referral for Non-Urgent Cases
brainaneurysm@bidmc.harvard.edu or call 617-632-9940

bidmc.org/brainaneurysm

Dramatic change in stroke care: Five major studies confirm safety and efficacy of endovascular treatment of ischemic stroke

Christopher S. Ogilvy, MD, Ajith Thomas, MD, Parviz Dolati, MD, Lucy He, MD, and Christoph J. Griessenauer, MD

There are five major large volume multi-center randomized trials which have been published in the New England Journal of Medicine in 2015 that document the safety and efficacy of intra-arterial treatment of acute ischemic stroke. The studies have associated acronyms of MR CLEAN(1), EXTEND IA(2), REVASCAT(4), SWIFT Prime(5), and ESCAPE(3). While the studies do have differences in entry criteria and endpoints for outcome, all of the studies demonstrate significant benefit of using intra-arterial therapy for clot retrieval in large vessel occlusion at various intervals after symptom onset.

The big difference between these published studies and previous studies on intra-arterial therapy for stroke rests with the devices used to retrieve thrombus from occluded vessels. Older devices for retrieval were much less efficacious in vessel opening and complications associated with hemorrhage were higher. The current studies use "stent – retriever" devices. The concept of this device is shown in Figure 1. A stent is attached to a wire and as the stent is deployed in the thrombus inside the occluded vessel, the tynes of the stent intercalate with the clot in such a fashion that as the stent is withdrawn, it pulls the clot out of the vessel. Other techniques can be used to augment this process system such as a balloon on the catheter into which the stent is withdrawn. By inflating a balloon in the carotid artery, one can reverse flow with aspiration of blood and encourage the clot to be withdrawn from the occluded vessel. The widespread utilization of this type of device has dramatically and rapidly changed stroke therapy.

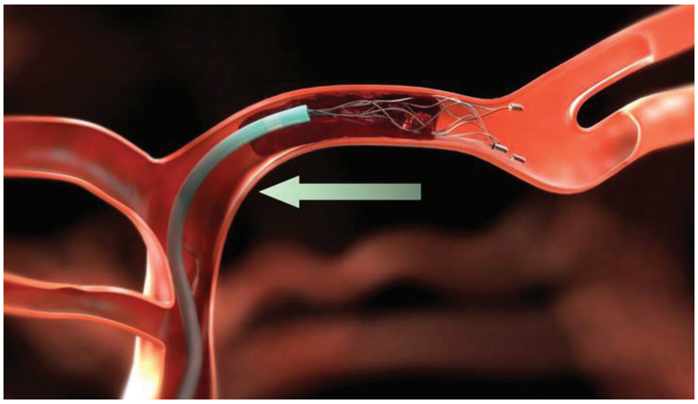


Figure 1: Mechanism of action of a stent retriever.

What this means for the practicing emergency room physician and stroke neurologist is that a stroke is a true emergency.. The studies also document that the interval of time allowed to elapse between vessel occlusion and vessel opening relate directly to patient outcome, extended care facility utilization, and complications. The longer a vessel is occluded the worse is the outcome. This can be calculated in minutes from time of vessel occlusion. The implication of this is obvious. Acute stroke from large vessel occlusion should now be managed in a fashion similar to acute myocardial infarction from vessel occlusion. Patients need to be rapidly assessed and mobilized to centers where they can be appropriately treated for large vessel occlusion.

Rapid patient assessment usually involves a neurologic examination combined with radiologic imaging. Typically a CT scan of the brain is obtained to evaluate for the presence or absence of intracranial hemorrhage. CT angiography is utilized with the infusion of IV contrast material and rapid CT acquisition to evaluate the patency of and largest intracranial vessels. When vessel occlusion is documented, further information can be gleaned from the CTA study to evaluate perfusion in the amount of tissue "at risk". The tissue "at risk" is evaluated by comparing infarcted tissue with tissue that remains viable yet with poor perfusion.

Given this data, the current structure of how a patient with potential large vessel occlusion is managed is coming into question. Patients are being carefully monitored to evaluate time of symptom onset, time of arrival to the hospital, administration of intravenous tPA, and subsequent "time to needle" for intra-arterial therapy.

In order to hasten the evaluation and decision-making process in patients with potential large vessel occlusion, sites in Europe and in the United States have developed ambulance vehicles that contain CT scanners to evaluate patients with stroke. The feasibility of more widespread utilization of such vehicles is currently under investigation.

A typical good result of the patient that was rapidly mobilized to the hospital and found to have a large vessel occlusion with subsequent vessel opening is shown in Figure 2. As can be seen, an obvious cutoff of contrast material in the middle cerebral artery is seen in Figure 2A. There is subsequent excellent flow several minutes later, after using a stent-retriever device (Figure 2C). Patients can enter the emergency room aphasic and hemiplegic and after clot removal can have only minimal if any deficit.

Certainly not all patients with stroke have large vessel occlusion. The next steps for consideration is how to rapidly mobilize stroke patients to centers where expeditious clinical and radiologic evaluations can be performed and treatments delivered. In New England, the emergency medicine services are partnering with hospitals to try to derive the best strategies to maximize rapid care to those patients who require therapy and accurately diagnose those patients who do not. This is an extremely exciting time with great potential benefits for patients with acute ischemic stroke. We are faced with a completely new paradigm in treatment and the exciting possibility of reducing long-term neurologic deficits and cost of care to patients and society.

References

1. Berkhemer OA, Fransen PSS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al.: A randomized trial of intraarterial treatment for acute ischemic stroke. **N Engl J Med 372**:11–20, 2015
2. Campbell BCV, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al.: Endovascular therapy for ischemic stroke with perfusion-imaging selection. **N Engl J Med 372**:1009–1018, 2015
3. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al.: Randomized assessment of rapid endovascular treatment of ischemic stroke. **N Engl J Med 372**:1019–1030, 2015
4. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al.: Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke. **N Engl J Med**:2015
5. Saver JL, Goyal M, Bonafe A, Diener H-C, Levy EI, Pereira VM, et al.: SolitaireTM with the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke (SWIFT PRIME) trial: protocol for a randomized, controlled, multicenter study comparing the Solitaire revascularization device with IV tPA with IV tPA alone in acute ischemic stroke. **Int J Stroke Off J Int Stroke Soc 10**:439–448, 2015

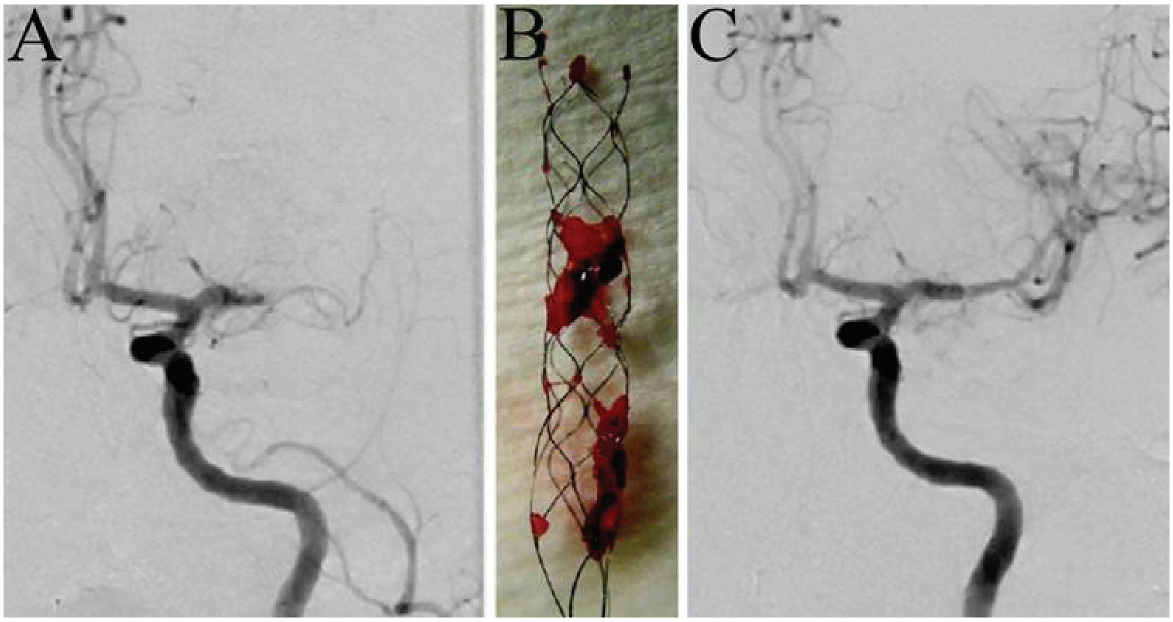


Figure 2: 69 year old patient presented with left middle cerebral artery stroke (NIHSS 16) (Panel A). A stent retriever was deployed and clot was removed (Panel B). Within 36 minutes from femoral artery puncture the middle cerebral artery was completely reopened (Panel C). At 36 hours the patient's NIHSS was 2.

Moyamoya: Diagnosis, Treatment and Prognosis

Lucy He, MD, Christopher S. Ogilvy, MD, and Ajith Thomas, MD

Moyamoya is a rare and progressive disease that affects the arteries which supply blood to the brain. Initially described and characterized in Japanese children, moyamoya translates literally into "puff of smoke" – a characteristic pattern seen on angiograms of affected patients (3). In moyamoya, there is progressive occlusion of the larger intracranial blood vessels over time and the body responds by attempting to recruit additional blood supply (usually from the brain surface, dura or bone) to help perfuse the brain. This leads to the characteristic appearance of "puff of smoke" on angiograms [Figure 1].

Moyamoya can be present in one or both sides of the brain and can affect the blood vessels of the anterior or posterior circulation and effects adults and children alike. Symptoms of the disease include headache, seizures, vision problems, strokes or transient ischemic attacks and often these are worse then the patient is dehydrated due to under perfusion of the brain. Moyamoya can also be associated in patients with sickle cell disease, Downs's syndrome, and other arteriopathies. Patients with moyamoya are at risk for stroke, transient ischemic attacks, and/or intracranial hemorrhage. The natural history of this disease is one of progressive vessel occlusion and as the body becomes unable to provide alternative blood flow, stroke invariably occurs (4).

Treatment for moyamoya is aimed to provide improved blood flow to the brain either through direct bypass or through an indirect procedure known as encephaloduroarteriosynangiosis (EDAS) (2). At BIDMC, the treatment depends on a variety of factors including patient symptoms, age, caliber of blood vessels on angiogram, severity of moyamoya, and history of strokes. For patients who undergo a direct bypass, an artery beneath the scalp is directly connected to one on the surface of the brain to increase blood flow extracranial to intracranial artery bypass or EC-IC bypass). For patients who undergo the indirect procedure, an artery beneath the scalp is laid over the surface of the brain and over time the body

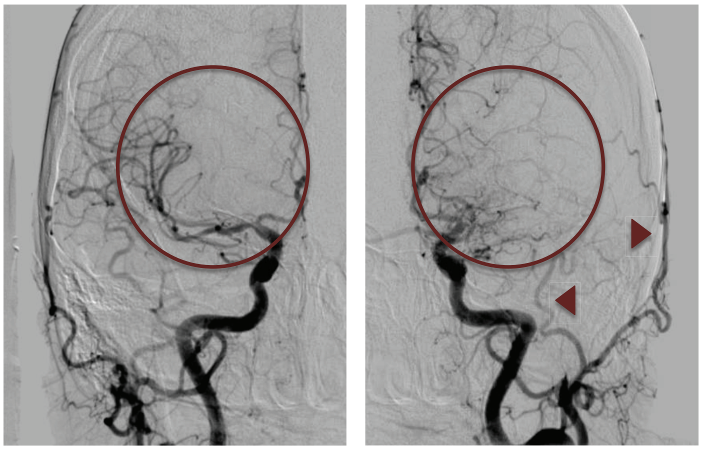


Figure 1: Angiogram from a patient with moyamoya. The left panel shows the normal side (right sided injection) with filling of the middle cerebral artery (circled). The right panel shows the side with moyamoya, note the lack of a middle cerebral artery and the characteristic puff of smoke (circled); also note that the body as attempted to recruit blood supply from vessels from the scalp and bone (arrowheads).

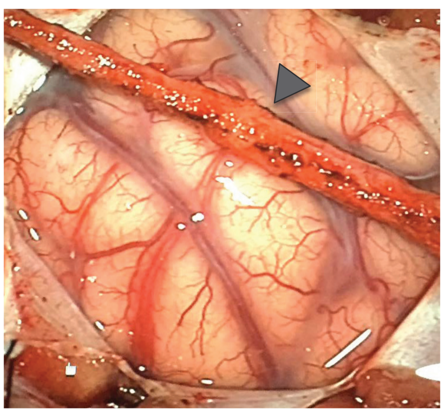
will recruit new blood vessels to form to supply the brain (EDAS). Both cases are performed under general anesthesia, with careful monitoring of the patients blood pressure and volume status during the procedure and afterwards to avoid putting the patient at risk for hypoperfusion stroke. For either procedure, the majority of patients are able to leave the hospital within a few days of surgery and are maintained on aspirin therapy afterwards.

In the direct bypass procedure, the superficial temporal artery (STA) runs beneath the scalp and it is carefully mapped out with an ultrasound over the skin. Then the skin is opened carefully along the course of the artery to avoid any damage to the vessel itself. The skull is exposed and an oval window of bone is temporarily removed. The brain is exposed and a blood vessel from the brain, usually a branch of the middle cerebral artery (MCA), is dissected free and prepared for bypass. Next the small cuts are made in the MCA and STA and these arteries are carefully sewn together under the microscope to allow increased blood supply and flow to the brain – direct bypass. The bone window is replaced with special titanium plates and the muscle and skin closed. Patients are monitored closely after surgery for signs of stroke and/or hemorrhage.

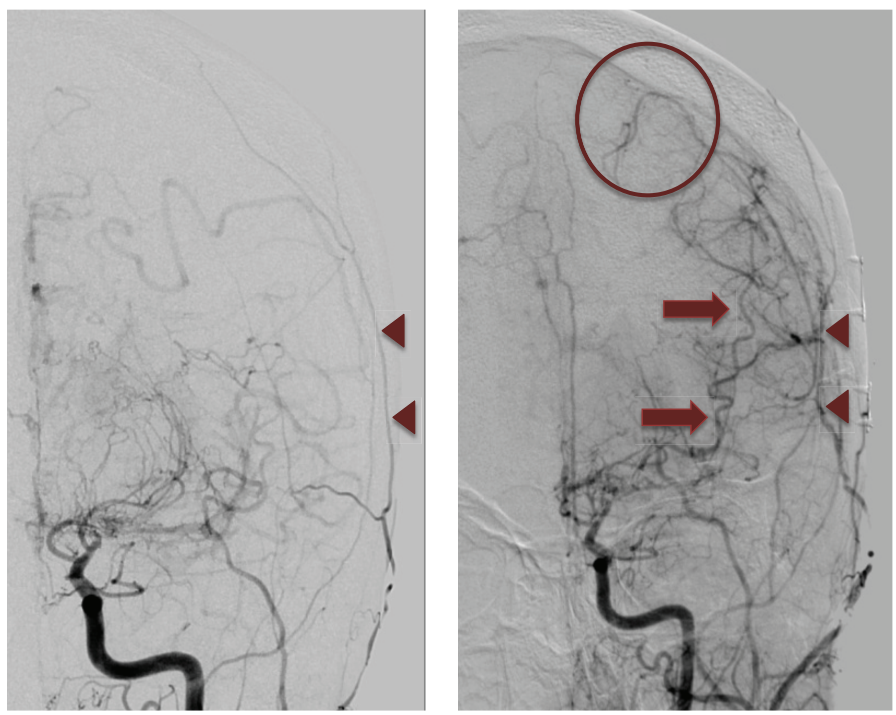
In the EDAS procedure, the STA is again carefully mapped out and dissected. A window of bone is temporarily removed and the brain exposed. At this point, the dissected STA is then carefully laid over the surface of the brain and tacked into place with fine sutures under the microscope. The bone window is replaced and the muscle and skin are closed with sutures [Figure 2]. Over time, special growth factors from the spinal fluid and blood will allow for small collateral vessels to form and provide increased blood flow to the brain. Sometimes small holes are created in the skull near the original surgery to also allow collateral vessels from the scalp to form over the surface of the brain. Patients are monitored closely after surgery to avoid low blood pressure and to observe for any signs of bleeding.

After surgery patients can expect to experience improvement in their neurologic symptoms from moyamoya and decrease their risk for future stroke (1). Around 6 months to one year after surgery, patients will get an angiogram to assess the degree of revascularization. The results can be very stunning with the degree of new ingrowth of blood vessels to feed the brain compared to before surgery [Figure 3].

Moyamoya is a disease that leads to progressive occlusion of the arteries that normally supply the brain and places patients at risk for severe and debilitating strokes. Treatment involves facilitating revascularization of the brain through procedures that provide new large bore blood vessels in direct bypass or indirect EDAS procedures. After surgery, patients can have significant improvement in the recruitment of blood flow to their effected brains and also improvement in symptoms from TIAs and/or seizures and/or cognition.



▲ **Figure 2:** Picture taken from an EDAS procedure from the microscope. The superficial temporal artery (arrowhead) has already been carefully dissected out and the brain exposed. It is shown laid carefully over the brain surface just prior to anchoring the vessel to the surface of the brain.



▲ **Figure 3:** Angiogram from a patient with moyamoya six months after her EDAS and burr hole procedure. The left panel shows the preoperative state with left middle cerebral artery occlusion and the classic moyamoya appearance. The superficial temporal artery that was used for surgery is seen as well (arrowheads). In the right panel, the superficial temporal artery (arrowheads) as been laid over the brain and allowed to form new blood vessels to the previously effect regions of the brain (arrows). Additional blood vessels are seen to form from the areas near the top of the skull where additional burr holes were drilled (circle).

References:

1. Agarwalla PK, Stapleton CJ, Phillips MT, Walcott BP, Venteicher AS, Ogilvy CS: Surgical outcomes following encephaloduroarteriosynangiosis in North American adults with moyamoya. **J Neurosurg 121**:1394–1400, 2014

2. Lin N, Aronson JP, Manjila S, Smith ER, Scott RM: Treatment of Moyamoya disease in the adult population with pial synangiosis. **J Neurosurg 120**:612–617, 2014

3. Scott RM, Smith ER: Moyamoya disease and moyamoya syndrome. **N Engl J Med 360**:1226–1237, 2009

4. Smith ER, Scott RM: Moyamoya: Epidemiology, presentation, and diagnosis. **Neurosurg Clin N Am 21**:543–551, 2010

Multidisciplinary management of brain arteriovenous malformations (AVMs)

Christopher S. Ogilvy, MD, Ajith Thomas, MD, Christoph J. Griessenauer, MD

Brain arteriovenous malformations are clusters of direct connections from arteries to draining veins without a normal intervening capillary bed. The three main components of an AVM are one or more feeding arteries, the nidus is the site of the arteriovenous shunt, and the draining venous structures. AVMs are high flow, low resistance shunts which create a significant increase in pressure on the venous side of the lesion and cranial circulation. AVMs appear on MRI studies as a cluster of flow voids (Figure 1).

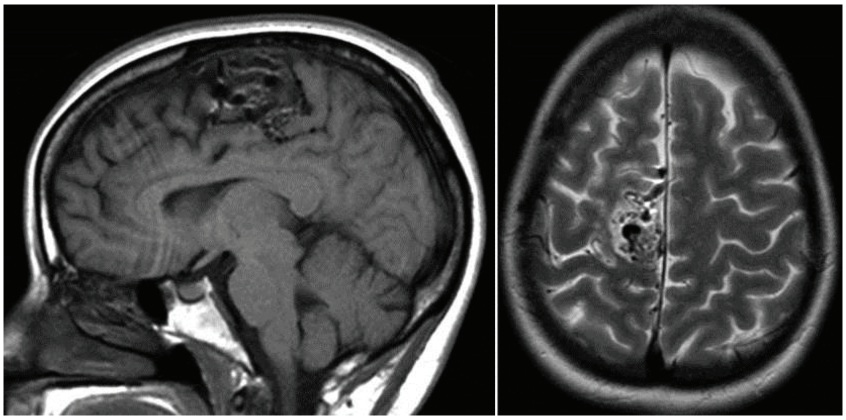


Figure 1: Edema surrounding an AVM on MRI.

Patients who harbor brain arteriovenous malformations typically present with clinical signs and symptoms of intracranial hemorrhage or seizures. There are two age peaks of presentation for patients with brain AVMs. The first of these is during childhood and the second is in patients in adulthood between ages of 20 and 60 years old. Headaches may result from the presence of an AVM. However, many patients with AVMs have headaches that are unrelated to the lesion. With improved imaging modalities, many AVMs that are being detected are asymptomatic and unruptured.

There are a number of studies where the natural history of brain AVMs have been analyzed. The rupture rate is reported to be between 0.9% per year and 4% per year for unruptured AVMs. Once a hemorrhage has occurred, the rupture rate is higher for the first year or two after the hemorrhage at a rate of 6 to 7% per year. Patients age and medical comorbidities certainly factor into the decision-making process when evaluating the patient with a brain AVM. In older patients with lesions that are higher risk for treatment, clinical observation may be the best option.

Treatment of brain AVMs is complex and often multidisciplinary. It is best to have a team of treating physicians familiar with the various techniques and the associated risks and benefits. Direct surgery can be used to excise an AVM with microsurgical techniques. Embolization of part or all of the AVM can be undertaken utilizing endovascular techniques. While embolization may be curative, this occurs in only 5 to 10% of AVM patients. Embolization is usually used as an adjunct to subsequent surgical excision or treatment with stereotactic radiosurgery. Stereotactic radiosurgery is a technique where a variety of radiation sources can be utilized to focus the radiation dose on the AVM with a low surrounding dose to the normal brain tissue.

A recent study was published which evaluated the risks of continued observation in patients with unruptured brain AVMs and compared this to the risks of treatment. The ARUBA trial results were reported after enrollment of 223 patients with unruptured AVMs at 39 clinical sites in nine countries. The study was stopped prematurely after the primary endpoint of stroke or death was reached and found to be significantly lower in the observational arm compared to the interventional arm (1). However, the study is quite controversial in that many of the patients never reached completion of the treatment. Therefore, the management of patients with brain AVMs remains a complex decision-making process attempting to balance the natural history of the disease for a given individual against the predicted treatment related risks.

Given the complexity of decision-making in the management of brain AVMs, it is often of benefit to have a multidisciplinary team for the detailed discussions of risks and benefits of treatment of each modality and of projected combined treatment. In addition, the patient's age and overall medical condition is extremely important in balancing the risks of observation with no treatment compared to the risks of treatment. A team should consist of the surgeon experienced in the removal of brain AVMs, endovascular experts who routinely treat AVMs, and individuals who perform radiosurgery on a regular basis. The ARUBA data presented earlier has not significantly changed our management strategies for patients with brain AVMs. Young patients with low-grade lesions are often treated with surgical excision or embolization followed by surgical excision (Figure 2). Older patients with higher risk lesions for treatment are typically followed clinically without intervention.

One major advantage in the treatment of brain AVMs is to have the same individuals who perform endovascular treatments and open surgical resections. There is a greater appreciation for the detailed angio- architecture acquired during embolization procedures. Armed with this information, the surgeon has a much better sense of the anatomy and physiology of the AVM on the day of surgical excision. By having been the individual who treated the patient with embolization on anywhere from 1 to 3 previous treatments, the surgeon has time to digest the remaining details of the AVM for surgical excision. While it is difficult to prove how this helps statistically, individuals who perform embolization and then the surgery can attest to the increased safety and efficacy of this type of approach.

If indeed the person performing embolization is a different individual from the one performing surgical resection, there has to be excellent and detailed communication between the two individuals regarding the anatomy and physiology of the AVM. Review sessions should be undertaken with all parties involved to understand the different components of the AVM, where embolization has been performed, and what remains for subsequent surgical or radio-surgical obliteration. Working in a center that manages a high volume of AVM patients facilitates an increased understanding of the pathophysiology and management of brain AVMs. At the BIDMC Brain Aneurysm Institute, many patients with brain AVMs are evaluated and managed on a weekly basis. Our team of physicians work together to arrive at rational and safe treatment plans based on all of the factors discussed above.

References

1. Mohr JP, Parides MK, Stapf C, Moquete E, Moy CS, Overbey JR, et al.: Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. **Lancet 383**:614–621, 2014

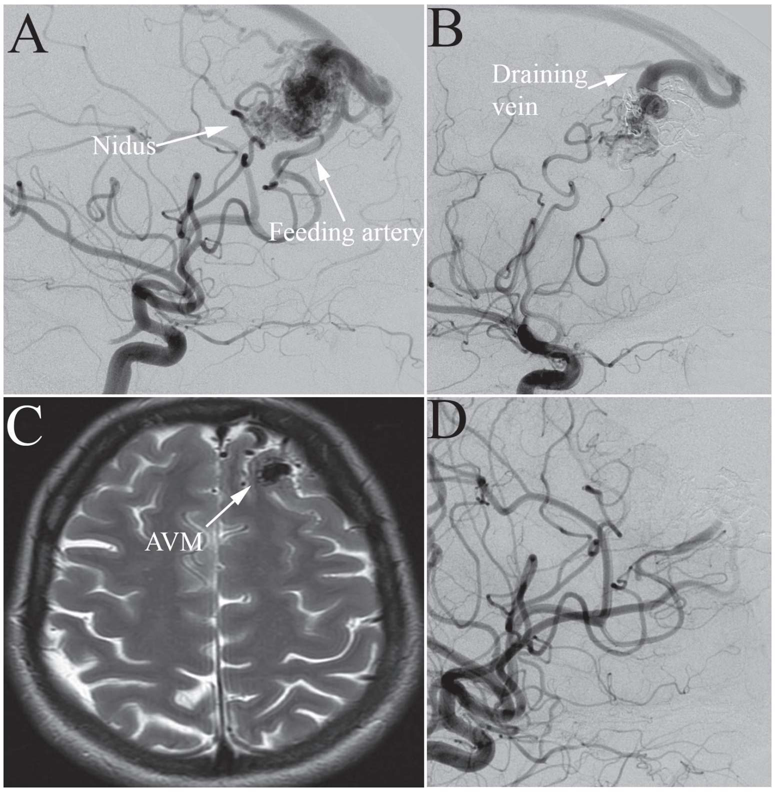


Figure 2: 32 year old female presenting with headaches found to have left medial frontal Spetzler Martin grade 2 AVM. The patient favored treatment and was preoperatively embolized with Onyx® (*Covidien, Mansfield, MA*) and subsequently underwent a craniotomy for AVM resection. Neurologically she did well throughout the course of her treatment. Panels A and B show the Spetzler-Martin grade 2 AVM on a lateral injection of the left internal carotid artery before and after embolization, respectively. Intraoperatively, the detachable Apollo™ Detachable Tip microcatheter tip (*Covidien, Mansfield, MA*) (*white arrow*) used for Onyx injection was visualized in the main feeding artery (Panel C). Postoperative lateral angiogram of the left common carotid artery showed complete resection of the AVM (Panel D).

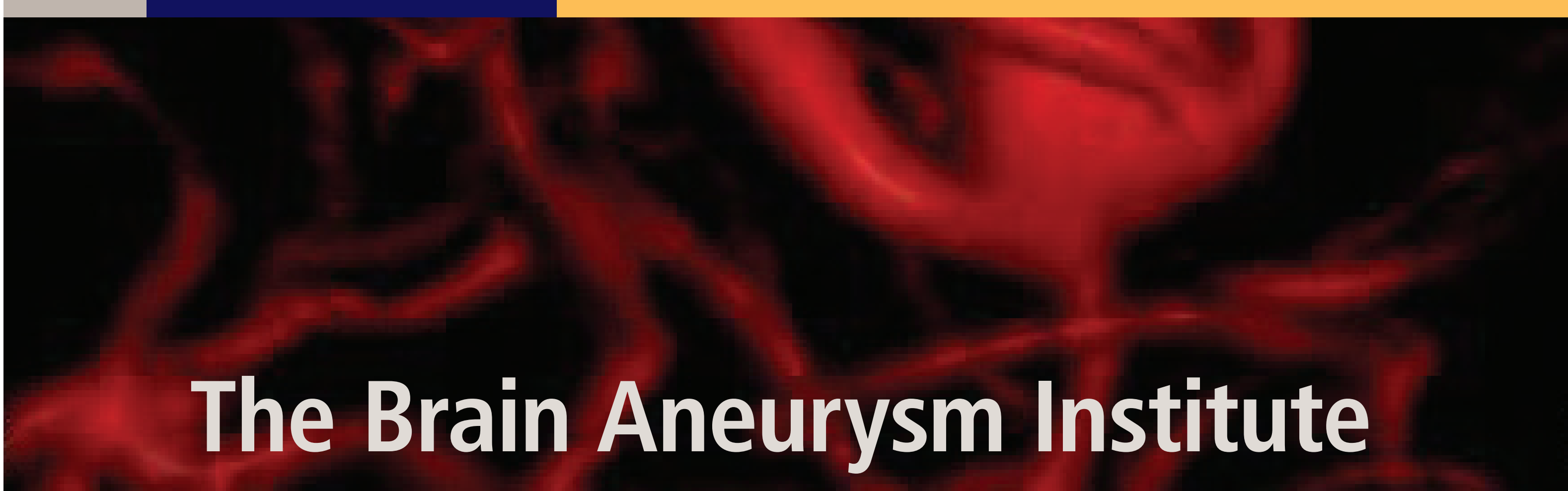
Beth Israel Deaconess Medical Center

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Brain Aneurysm Institute
110 Francis Street, Suite 3B
Boston, MA 02215

Beth Israel Deaconess Medical Center

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL



The Brain Aneurysm Institute

NEUROVASCULAR NEWS

Summer 2015