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INSIDE

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completed his internship and residency at Northwestern University Medical Center, becoming chief resident his final year. He then pursued a research fellowship, followed by a clinical fellowship, at the University of Arizona Health Sciences Center. He won a number of awards throughout his years in training.

Dr. Rubin held advancing teaching positions at Case Western Reserve University School of Medicine from 1985 through 1993, moving to a tenured surgery professorship at Northeastern Ohio Universities College of Medicine in 1993. In 2007, he joined Wayne State University's School of Medicine as a professor of surgery.

Dr. Rubin has received 29 grants to pursue his research interests since 1984. He has co-authored 63 articles in peer-reviewed journals and 13 chapters in medical textbooks.

He has been involved with numerous community service projects and programs, and holds positions with the Society of Clinical Vascular Surgery, the VA Surgery Study Section, and the SVS Quality and Performance Measures Committee, among others.

About Yevgeniy Rits, MD:

Yevgeniy Rits, MD, is a vascular surgeon with the Detroit Receiving/Harper Hospital Vascular Center and director of the Vascular Access Center at Harper and Detroit Receiving Hospitals. He completed his undergraduate and medical school degrees at Wayne State University and his residency at William Beaumont Hospital in Royal Oak. He pursued a fellowship in vascular and endovascular surgery at the Mayo Clinic in Rochester, Minnesota, before joining the staff of the DMC in 2008. Dr. Rits is board-certified in both general and vascular surgery. He worked on six clinical postgraduate research studies between 2001-2007 and has made 17 presentations to his peers at conferences and symposia.

Defusing Brain Aneurysm

Introduction:

Interventional neuroradiology (INR) aka neurointerventional surgery (NIS) aka endovascular surgical neuroradiology (ESN) is a newer subspecialty in the field of medicine, specializing in minimally invasive, image-based technologies and procedures for diagnosis and treatment of vascular disorders of the head, neck, and spine.

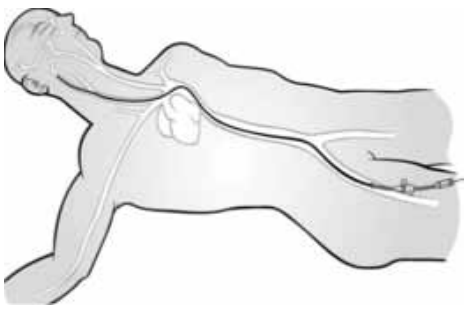
This very young field has made remarkable strides since the early-to-mid 1990s, providing significant improvements in patient outcomes utilizing less invasive interventions and facilitating shorter hospital stays and faster recovery periods. Currently, there are 600-700 such physicians in the U.S. with training backgrounds in neurosurgery, neurology (interventional neurology), and radiology.

Principles:

Under X-ray guidance, using a biplane fluoroscopy machine, selective blood vessels of the neck, brain, and spine are imaged by direct placement of catheters and injecting iodine-based contrast. These images are digitally subtracted from the background, providing high-quality, magnified images of these vessels, often with resolution as small as 0.1 mm.

Access to these cerebral and cervical vessels is commonly from the femoral artery. In select cases, access can also be obtained from the arm or the wrist.

Illustration of femoral access to the neck and brain blood vessels.



s: Interventional Neurologists Offer Solutions

Interventional neurologists Samuel Tsappidi, MD, and Sandra Narayanan, MD, in their lab, with the Siemens biplane angiography table.

In well-trained hands, despite the mild invasiveness of these procedures, they are quite safe, with just a 2-5 mm size cut to the skin at the groin, to treat tiny vessel abnormalities in the brain as small as 1-2 mm.

Benefits and Risks:

As mentioned earlier, one of the major benefits of endovascular approaches to diagnosis and therapy is the limited invasiveness of these procedures to treat significant disorders of the blood vessels in the brain, neck and spine. This facilitates very short stays in the hospital, often a few hours to a day, for most elective therapy of brain aneurysms by coil embolization, or other vascular malformations, including stent placement for narrowed blood vessels in the brain or the neck.

Common risks for these procedures involve stroke, vessel injury at the groin, neck or sometimes, the brain or spine, although relatively infrequent. In patients with kidney failure, use of contrast may be limited and can augment renal failure. Allergies to medications can limit options, especially in emergent situations, although very infrequent in current practice by premedicating such patients.

Diagnostic indications:

Common indications of angiographic evaluations of the vessels of the brain, neck and spine involve conditions, such as brain aneurysms, vascular malformations (arteriovenous malformations - AVMs or dural arteriovenous fistulae - dAVFs), acute strokes, recurrent strokes, compromised blood flow through the vessels

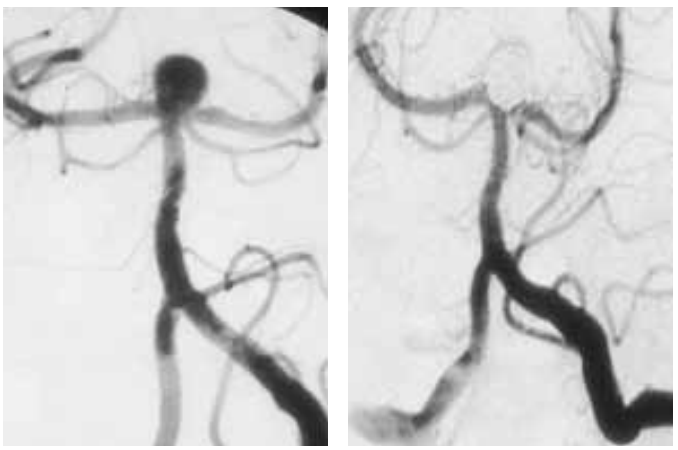
either by injury (dissections), narrowing (stenosis from atherosclerosis), inflammation of the blood vessels (vasculitis), abnormal clots within the arteries or veins (thrombosis), in addition to vasospasm from presence of blood at the brain surface. In addition, certain tumors of the brain or head that are highly vascular are evaluated for presurgical evaluation to minimize blood loss during surgery. Other emergent conditions, such as refractory nosebleeds, acute head and neck tumors with excessive bleeding, and blood loss or compromise from trauma to the head or neck, can also be evaluated for possible therapy.

Treatment options:

Some common conditions treated by specialists in this field are detailed below, along with the latest updates:

a) Brain Aneurysms: Brain aneurysms are abnormal blistering or outpouching of blood vessels in the brain. Often familial and incidental, they have been diagnosed in as high as 5-6% of the normal population. Common presentations include headaches, vision changes, possible strokes, or even mass effect in the brain. Rupture of intracranial aneurysms is relatively rare (0.1-1% each year) and is related to location, size, shape, and certain modifiable risk factors, including uncontrolled hypertension, smoking, recreational drug use (cocaine, amphetamines), or binge drinking. However, ruptured aneurysms have significant impact in outcomes, with about a quarter to a third of these patients not surviving the aneurysmal rupture. About half to a third of the survivors do suffer varying degrees of brain damage and/or other organ dysfunction.

Current treatment options for brain aneurysms involve open-surgical microdissection with placement of titanium clips to pinch/close the aneurysm neck and prevent additional bleeding. Endovascular options include placement of platinum coils or liquid glue within the aneurysm to essentially seal it from the circulation and limit rebleeding. Benefits of endovascular approaches include minimally invasive access from the groin with no requirement of manipulating the brain or opening the cranium. Trials are under way with preliminary data demonstrating better recovery outcomes from endovascular therapy in comparison to open-surgical treatments.

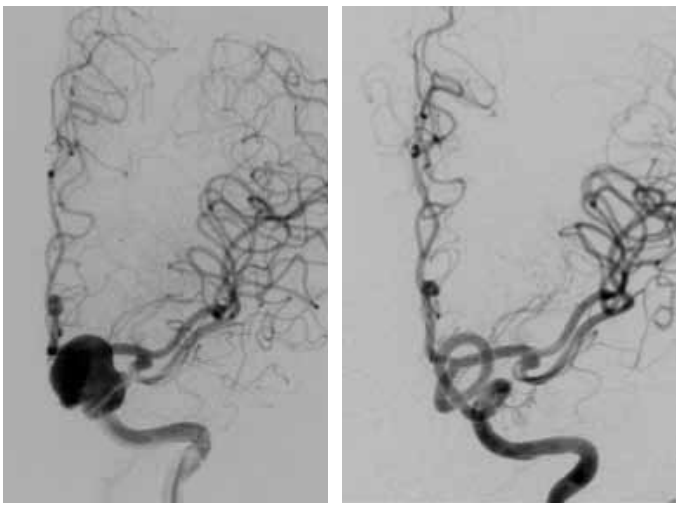


Coil embolization of basilar aneurysm.

Stent assisted coil flow model of a wide based aneurysm using Enterprise stent. Printed with permission from Codman.

Even wide-necked or complex-shaped aneurysms are treatable by balloon remodeling at the neck of the aneurysm or by placing stents to assist coil embolization. Based on various institutions and their experiences, the frequency of endovascular therapy is vastly superseding open-surgical approaches to treat brain aneurysms.

The Pipeline Stent: Reprinted with permission from Covidien.



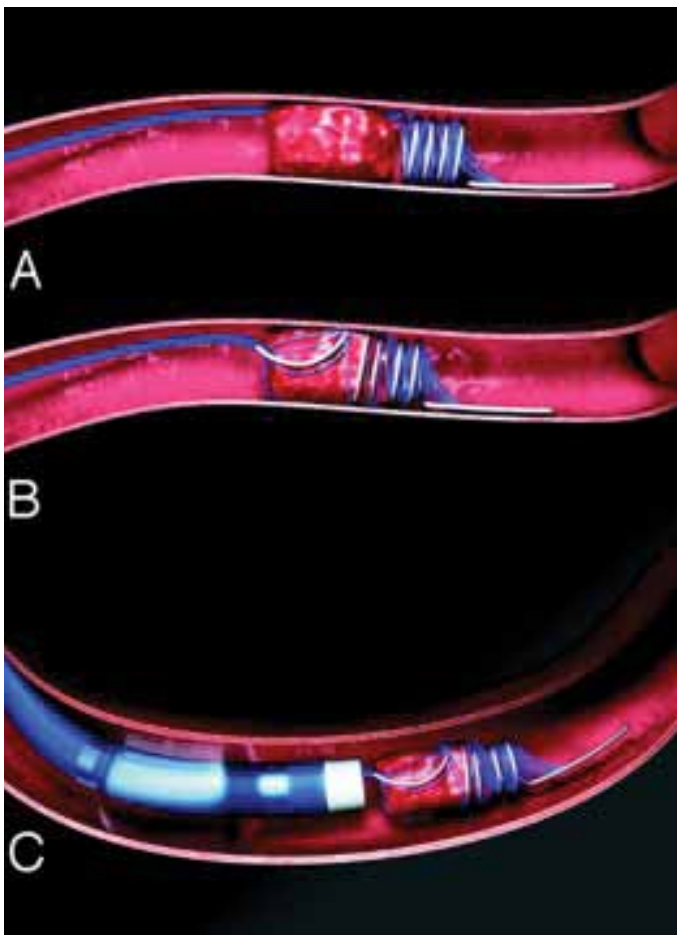
Pre and Post treatment (6 month follow up) angiogram of a giant cavernous aneurysm extending in the brain from the skull base, subsequent to flow remodeling by the Pipeline stent, demonstrating obliteration of the aneurysm and reconstruction of the parent vessel through a newly created intra-aneurysmal channel – Reprinted with permission from Covidien.

Newer approaches for large (>10 mm) or giant aneurysms (>25 mm) and tubular enlargements (fusiform aneurysms) involve remodeling flow through the blood vessels and isolating blood flow to the aneurysm using thick stents with small pore sizes, such as the "Pipeline" embolization device (PED), currently FDA-approved and marketed by Covidien (Dublin, Ireland). These patients typically had minimal treatment options with high risk of rupture or death prior to such therapies.

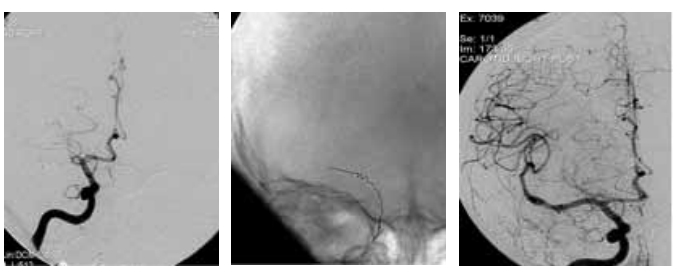
For incidentally diagnosed aneurysms, treatment involves a very short stay in the hospital, lasting less than a day, with no latent recovery period necessary.

b) Acute Ischemic Stroke: There are approximately 800,000 strokes every year (103 per 1000) in the U.S., with 90% comprising sudden compromise of blood flow to the brain. It is the leading cause of disability and the third leading cause of death in the U.S., causing significant financial burden to the U.S. (~80, billion U.S. $ per NIH data, 2008). Current FDA guidelines to reverse or minimize this devastating process involves IV therapy of tissue plasminogen activator (tPA) within a limited-time window. However this has not been shown to be significantly effective for large blood vessel occlusions or significant clot burden. Options in current practice to treat such large vessel occlusions or patients who are contraindicated to medical therapy include devices approved by the FDA under "Humanitarian Device Exemption."

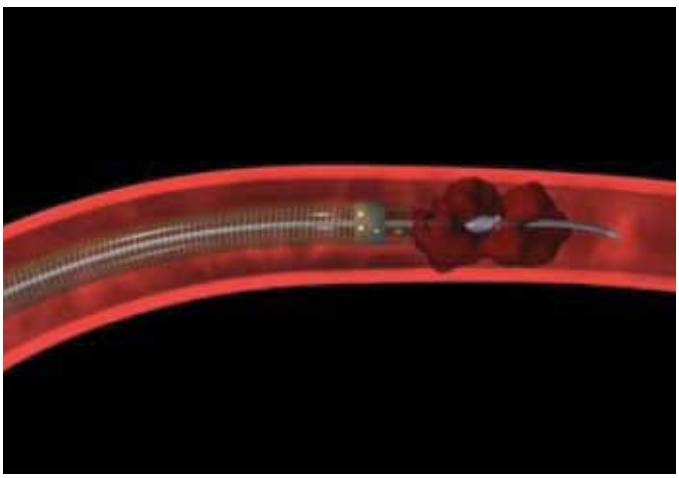
The guiding principle in treatment of vessel blockage by a blood clot in the brain involves re-creating a flow channel, either by mechanical extraction of the clot (MERCI), or gentle aspiration of the clot by negative pressure suction (Penumbra). Both of these devices are FDA-approved and are currently in practice.



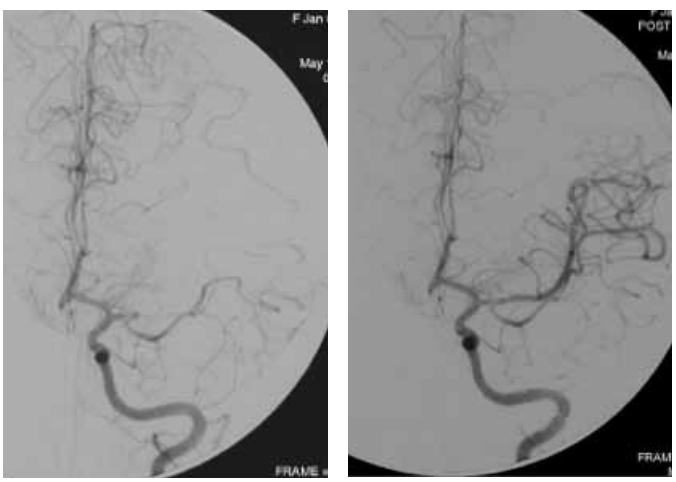
MERCI device principle of mechanical capture and extraction of the clot – Stryker brochure



Cerebral angiogram of the right MCA (middle cerebral artery) occlusion treated with the MERCI device (middle image) with restoration of flow.



Penumbra aspiration device – Reprinted with permission.



Pre and Post aspiration images using the Penumbra System demonstrating a left middle cerebral artery occlusion, subsequently recanalized using the Penumbra Reperfusion catheter – Reprinted with permission.

Several other attempts at clot retrieval include balloon angioplasty, ultrasound-guided clot breakdown, and jet aspiration (ANGIOJET) but are less effective in current practice.

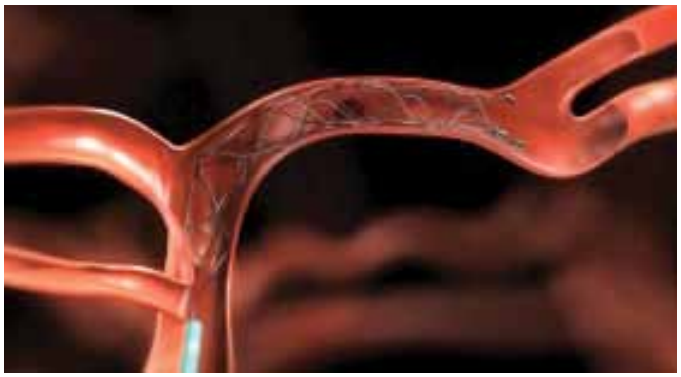
Newer techniques have been introduced, especially in Europe and currently in trials in the U.S. involving

	PROACT II	MERCI	MULTI-MERCI	PENUMBRA	POST
NIHSS	17	20	19	18	16
Recanalization	66%	48-60%	55-68%	82%	84%
Clinical Improvements	40%	28%	36%	25%	40%
Mortality	25%	44%	34%	33%	25%
Symptomatic ICH	20%	8%	10%	11%	7%

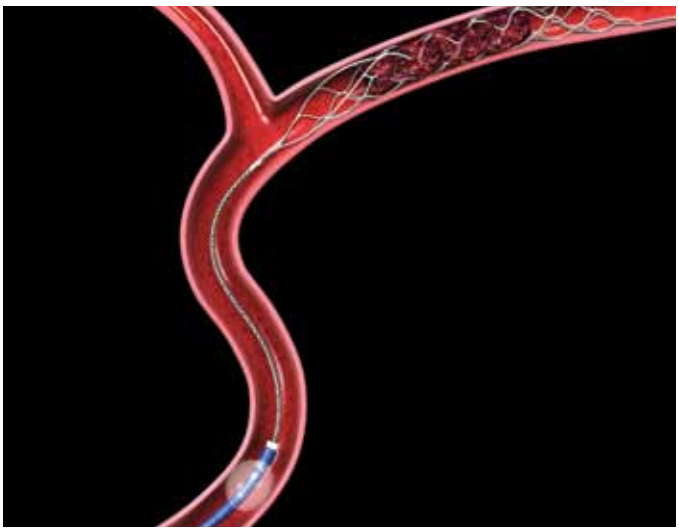
Comparison of the IA thrombolytic (PROACT II), MERCI, and Penumbra device trials.

rapid restoration of flow using retrievable self-expanding stents (SES). The added benefit of these involve shorter time to reopen the blood vessel, with less radiation exposure, thus improving time to restoration of the blood flow to the ischemic brain and thus likely better outcomes.

SOLITAIRE retrievable stent: Among the newest devices about to be introduced to the U.S. (awaiting FDA approval) following successful trials in Europe and U.S. (SWIFT), this "stentriever" has been demonstrated to significantly improve recanalization of the occluded vessel, with reduced bleeding risk, decreased mortality, as well as better clinical outcomes, when compared with the MERCI device.



The SOLITAIRE stent – Reprinted with permission from EV3.



TREVO stent retrieval device – Reprinted with permission from Concentric (Boston Scientific).

Another such device awaiting approval by FDA following completion of a trial in the U.S. is the TREVO stent, marketed by Boston Scientific and available in select centers in the U.S. It follows similar principles to the SOLITAIRE stent in rapid restoration of flow by mechanical entrapment of the clot to the stent-vessel wall with restoration of flow to the distal blood vessel branches, and thus the ischemic brain. Thus, the onus of current acute stroke interventions involve rapid flow restoration to the oxygen-depleted brain within the

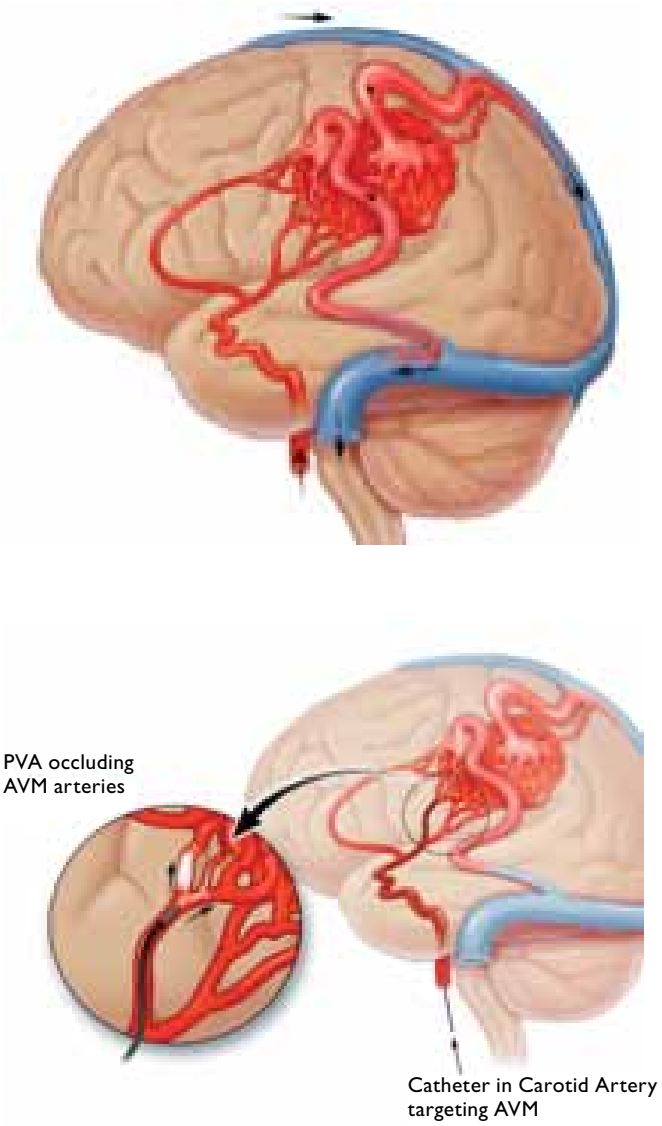


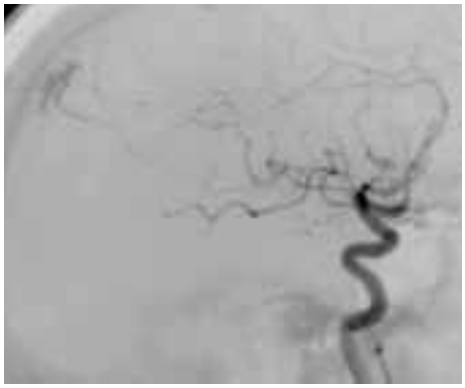
Illustration demonstrating embolization of a brain AVM using embolic materials.

least needed time to improve clinical outcomes, and not infrequently combined with infusion of a thrombolytic.

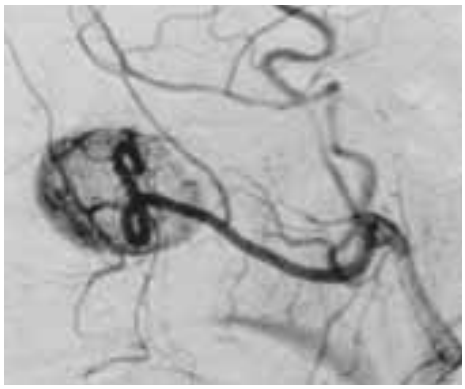
c) Vascular Malformations: Vascular malformations of the brain and spine, include AVMs (arterial-venous malformations – abnormal tangle of blood vessels, often a developmental anomaly) and dural AVMs (involve the dura mater), and typically manifest with seizures, headaches, brain hemorrhage or progressive leg weakness with loss of bladder and bowel control (spine). Typically diagnosed and staged using angiograms and high resolution imaging, such as MRI, they are treated quite frequently by endovascular approaches utilizing liquid agents, such as Onyx (EV3) or nBCA (n-Butyl Cyanoacrylate-Codman). Approaches to treating these involve reduction of the size of the malformation or complete obliteration, based on the size, location, and number of abnormal vessels, among others.

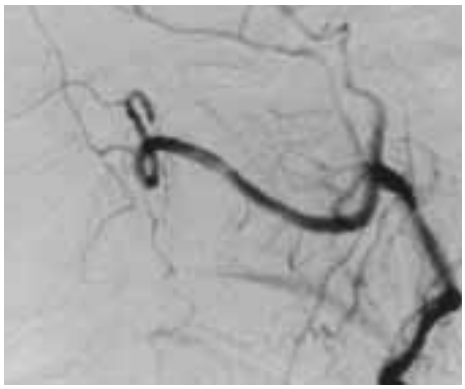
d) Tumors of the Head and Neck: Highly vascular lesions of the head and neck including intracranial tumors such as meningiomas or extracranial tumors (outside the skull), such as "angiomas" involving the neck, nose or below the ears, are often treated by embolization to reduce blood flow to the lesion prior to surgical resection.

Illustration of Onyx (Covidien) within the tangle of abnormal vessels.



Onyx embolization of a dural AV fistula on the top left (External carotid artery injection), with the post embolization images on the bottom left (internal carotid artery), demonstrating the Onyx cast with resolution of the early shunting.





Solitary fibrous tumor of the nasopharyngeal cavity, treated presurgically with embolic particles.

Other commonly performed procedures include carotid artery angioplasty and stenting for cervical carotid stenosis, stenting for extracranial dissections with flow compromise by internal flap, embolizations for refractory epistaxis (nose bleeds) and management of traumatic bleeds.

About Sandra Narayanan, MD:

Dr. Sandra Narayanan is a graduate of the six-year Honors Program in Medicine at the University of Miami School of Medicine. She has completed a neurology residency at University of Miami/Jackson Memorial Hospital, a vascular neurology fellowship at Massachusetts General Hospital, and a three-year fellowship in diagnostic and interventional neuroradiology at Emory University Hospital in Atlanta. She has been on faculty at Wayne State University in the departments of Neurosurgery and Neurology since July 2009.

About Samuel Tsappidi, MD:

Dr. Samuel Tsappidi is double board-certified in vascular neurology and neurocritical care, with additional experience by comprehensive fellowships in diagnostic and interventional neuroradiology. He trained exclusively at Emory University, Atlanta, and currently is on faculty at Wayne State University as an assistant professor in the departments of Neurosurgery and Neurology. For more information, contact him at ***(313) 966-5007****.*

For more information or a consult, call (313) 966-7070.

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