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

NEUROVASCULAR NEWS

Winter 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
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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.

Please Join Us

Ischemic and Hemorrhagic Update: Current Practices and Future Directions

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Flow diversion for the treatment of intracranial aneurysms: A totally new concept

Christopher S. Ogilvy, MD and Ajith Thomas, MD

As a result of significant advances in endovascular neurosurgery over the past 20 years, there has been a rapid evolution in technology. The typical concept of treating aneurysms endovascularly involves placing platinum coils inside the aneurysm with a micro catheter. This induces thrombosis and aneurysm obliteration, and this technology is still utilized in many patients with saccular aneurysms today. However in certain aneurysms, we are currently using a completely new technology which involves placement of a flow diverting stent in the parent artery. This induces stagnant flow in the aneurysm and ultimate thrombosis (Figure 1). This becomes useful in aneurysms that are more fusiform in shape and large and giant lesions (greater than 2.5 cm). The BIDMC Brain Aneurysm Institute has one of the largest experiences using this device in New England.

Figure 1: Concept of the Pipeline™ Endovascular Device. The device is placed in the parent artery and by virtue of its low porosity, there is stagnation of blood flow in the aneurysm with gradual thrombosis.

The Pipeline™ Embolization Device (PED; EV 3/Covidien Vascular Therapies, Mansfield, MA) is a braided mesh cylinder composed of 48 strands of 25% platinum and 75% cobalt – nickel alloy. The pore size is 0.02 to 0.05 mm. The device is deployed using a microcatheter advanced from the femoral artery in the groin. The device was approved by the FDA in April 2011. Dual antiplatelet therapy with aspirin and Plavix is required before and after deployment of the PED.

Case report: This 66-year-old woman presented with double vision. She was found to have a partial left VIth nerve palsy. Investigation with MRI imaging revealed a large intracavernous aneurysm of the left carotid artery measuring 17x10x15 mm (Figure 2). Angiography confirmed a large intracavernous aneurysm (Figure 3) as well as a 4 mm anterior communicating artery aneurysm. After discussion with the patient and her family it was decided to proceed with placement of a Pipeline™ Endovascular Device in the carotid artery to treat the cavernous sinus aneurysm. The patient tolerated the procedure well and was discharged on post-treatment day two. Follow up angiography at four months demonstrated complete obliteration of the aneurysm with the carotid artery normal in contour and diameter (Figure 4). The patient had worsening of her double vision at six weeks after treatment and gradual complete resolution of symptoms. This clinical worsening likely correlated with thrombosis and edema of the aneurysm followed by contraction. She underwent elective clipping of the anterior communicating artery aneurysm without incident.

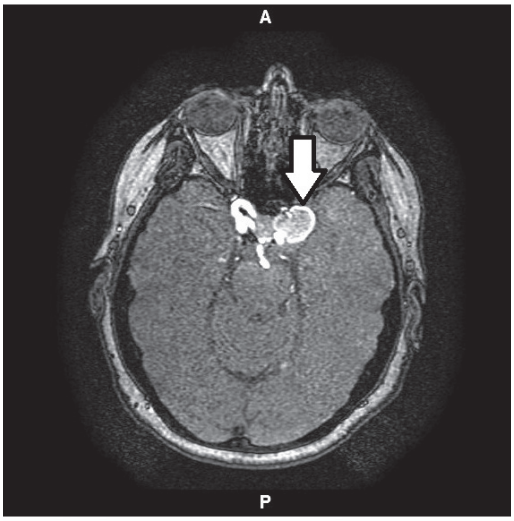

Figure 2: Axial MRI of patient with large, symptomatic cavernous carotid segment aneurysm (arrow).

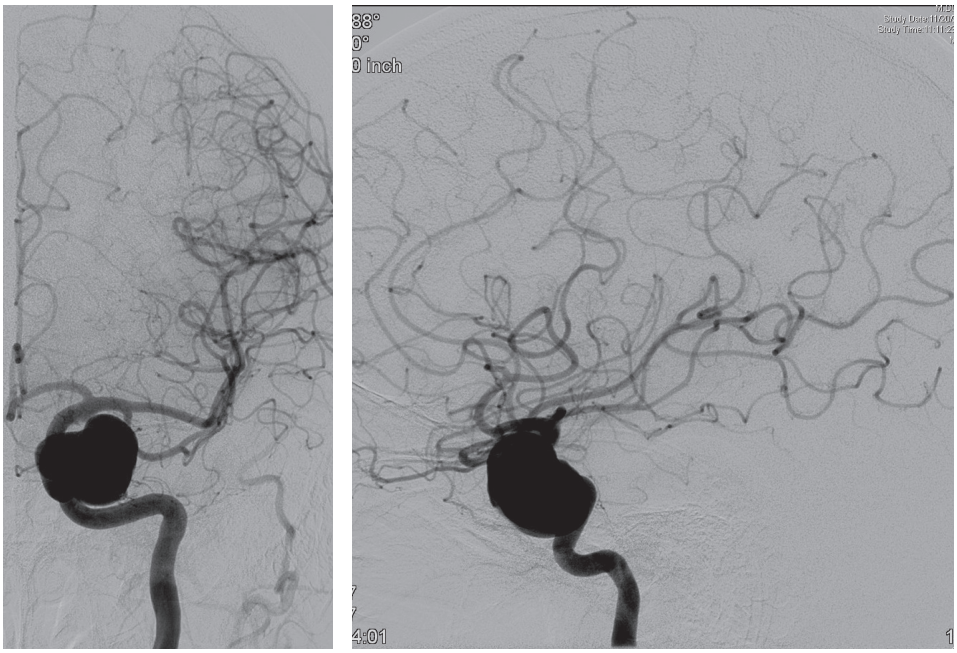

Figure 3: AP (A) and lateral (B) cerebral angiogram demonstrating the large intracavernous carotid artery aneurysm.

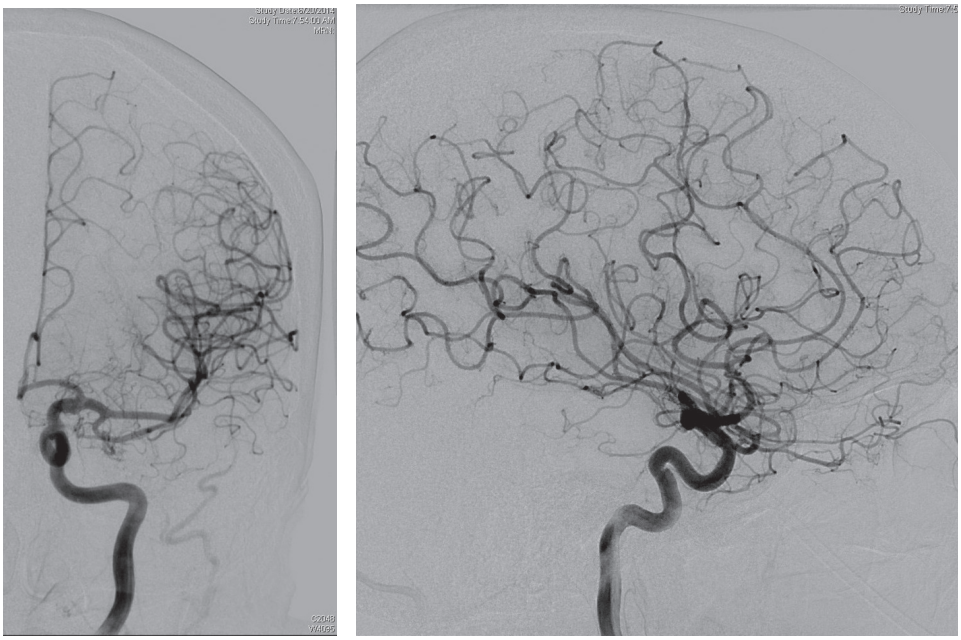

Figure 4: AP (A) and lateral (B) cerebral angiogram four months after treatment with complete obliteration of the aneurysm and visualization of the carotid artery.

In studies performed to date, the 12 month complete occlusion rate of aneurysms using the pipeline endovascular device range from 75-96%, with many remaining lesions demonstrating near complete obliteration. This device is not meant for all intracranial aneurysms and there is concern using it where branch vessels are present or there are small perforating arteries. Careful patient selection is a large factor in achieving excellent results.

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Stent-assisted coiling is a valuable treatment modality for brain aneurysms

Ajith Thomas, MD, Matthew Fusco, MD, and Christopher S. Ogilvy, MD

Saccular aneurysms of the brain have a risk of rupture that varies based on the size, location, and other risk factors. In 1995, the FDA granted approval for a new method of treating such aneurysms with detachable coils made of platinum. Initially named after the inventor as GDC, or Guglielmi Detachable Coils, this minimally invasive approach (endovascular) treatment involves going through a tiny groin incision by manipulating a catheter from the femoral artery in the thigh into the aneurysm in the brain. This method has found increasing popularity. By the end of the first decade of this millennium, about 60% of the aneurysms in the United States were treated by this technique, termed coiling, and this percentage continues to increase.

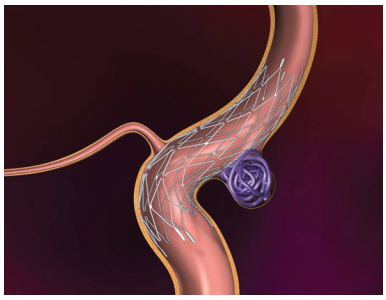

Figure 1

However, wide-necked aneurysms such as the one shown at left (Figure 1) were not amenable to primary "coiling." Coils placed in a wide-necked aneurysm could prolapse and block the parent artery from which the aneurysm developed. Such an occlusion of the parent artery could lead to a stroke. This problem was solved with the development of an expandable stent – the Neuroform stent. Though various stents were available for use in other arteries such as coronary arteries, none possessed the flexibility to be navigated into the tortuous arteries of the brain. The Neuroform stent underwent the first safety trials in 2001 and in 2010, a better version, Neuroform EZ, was launched. The Neuroform stent dramatically changed the endovascular management of aneurysms as wider subsets of aneurysms could be treated with this method (Figure 2). Soon after, the Enterprise stent was developed by another company for similar indications. A wide-necked aneurysm is defined by a neck diameter of greater than 4 mm or a dome-to-neck ratio greater than 2. While balloon-assisted coiling is another way to treat this with coils, stents are easier to deploy.

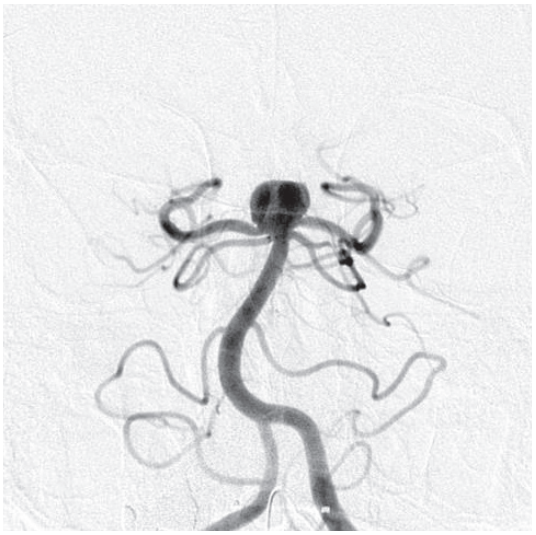

Figure 2

Illustrative case: a 65-year-old female presented with a history of headaches which had been present for three months. Her internist ordered an MRI scan of her brain, which demonstrated an anterior communicating artery aneurysm between the frontal lobes. She was referred to the BIDMC Brain Aneurysm Institute. The aneurysm measured 6 mm and was pointing upwards. We estimated a 2% risk of rupture per year given the size and location. The patient was anxious to proceed with treatment. The aneurysm was complex (Figures 3a and 3b) because of several small perforators and three branches associated with the aneurysm. Surgery would have had a high risk of memory deficits secondary to perforator injury from clipping of the aneurysm.

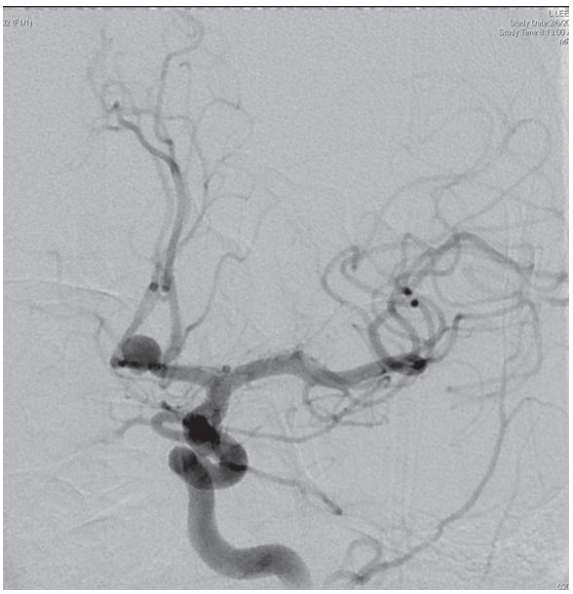

Figure 3a

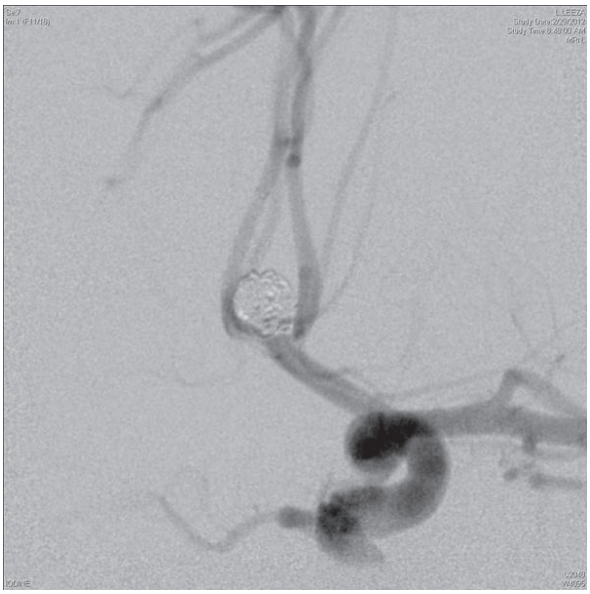

Figure 4a

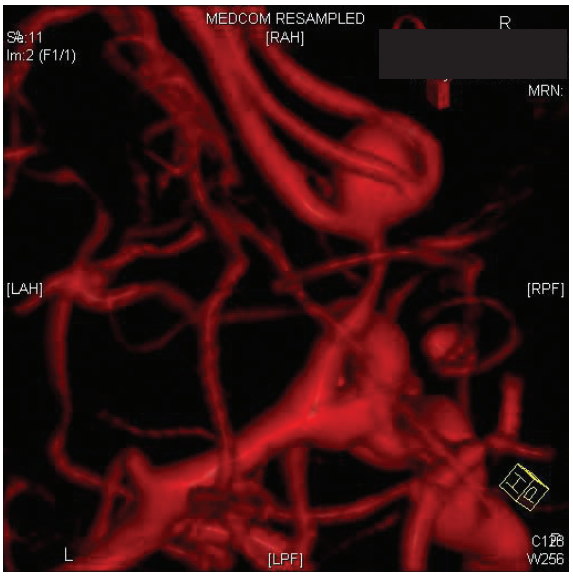

Figure 3b

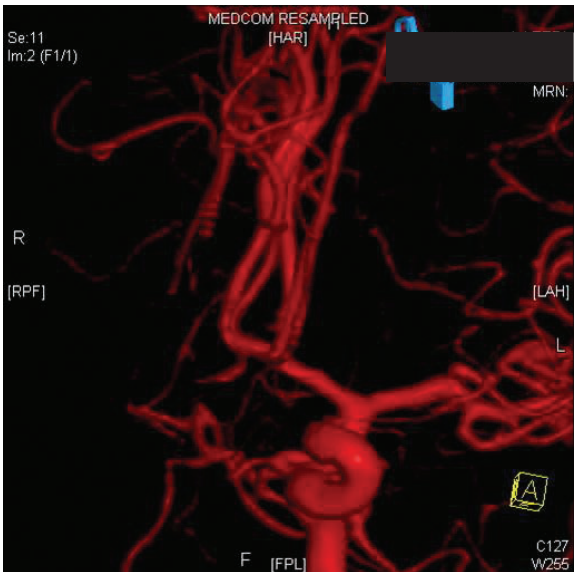

Figure 4b

Primary coiling would have been difficult secondary to the wide neck of the aneurysm and the multiple branches arising from the aneurysm. Therefore, at the multidisciplinary conference, a decision was made to treat the aneurysm with stent-assisted coiling.

The patient was started on Plavix 75 mg and aspirin 325 mg once daily two weeks prior to treatment. Treatment consisted of a Neuroform stent, which was placed from the left A1 segment into the right A2 segment of the anterior cerebral artery. The aneurysm was then coiled with Target coils without any difficulty. Complete obliteration of the aneurysm was obtained (Figure 4). The patient was discharged home the following day, neurologically intact. Plavix was maintained for three months following which the patient will continue to be on aspirin 81 mg.

Though the Pipeline Flow diverter has been very useful for large aneurysms, the Neuroform stent and Enterprise stent are still very valuable for treating smaller aneurysms that have wide necks.

Time is Brain!

Recent high quality stroke trials demonstrate: Endovascular treatment is highly efficacious

An update about recent randomized controlled trials in stroke

Parviz Dolati, MD, Magdy Selim, MD, PhD, and Matthew Fusco, MD

Introduction:

Endovascular treatment of acute ischemic stroke represents several therapeutic interventions, including both drugs and devices introduced through catheters or microcatheters placed in the intracranial arteries using a percutaneous approach. Three past trials, including Interventional Management of Stroke (IMS) III, Magnetic Resonance and REcanalization of Stroke Clots Using Embolectomy (MR RESCUE), and SYNTHESIS EXPANSION, evaluated the therapeutic efficacy of endovascular treatment in patients with acute ischemic stroke in comparison to the standard IV tPA1-5. The results of these trials showed no significant difference between the two treatment arms. These results were expected to affect the practice of endovascular treatment for acute ischemic stroke. However, because of significant limitations and increasing criticisms regarding the technical aspects and patient selection in those trials, many investigators around the world conducted three newer studies, which were randomized trials. These recent studies, which will be discussed here, have shown more promising results. They include:

1) **MR CLEAN**
2) **ESCAPE**
3) **EXTENDED IA**

***MR CLEAN*[6], is a **M**ulticenter **R**andomized **CL**inical trial of **E**ndovascular treatment for **A**cute ischemic stroke in the **N**etherlands. The study compared intra-arterial therapy (IAT) with no IAT. IAT consisted of intra-arterial thrombolysis with Alteplase or Urokinase, mechanical treatment, or both. Mechanical treatment included clot retrieval, direct aspiration, sonolysis, or use of modern devices, including retrievable stent (stent-retriever) at the discretion of the physician. The control arm did not receive IAT. However, both arms included best medical management, which included intravenous tPA.

Patients with an intracranial proximal (large vessel) arterial occlusion of the anterior circulation confirmed by CTA who could be treated within six hours after stroke onset were eligible. The primary outcome was the score on the modified Rankin scale at 90 days. Treatment effect was estimated with ordinal logistic regression (shift analysis). Secondary outcomes were the National Institute of Health stroke scale score at 24 hours, vessel patency at 24 hours, infarct size on day five, and the occurrence of major bleeding during the first five days.

Five hundred patients were randomized (233 in the IAT arm; 267 in the control arm). This sample size provided a power of 80% to detect a shift, leading to a 10% reduction in poor outcome after stroke; careful implementation of the intervention could save approximately 1% of all new stroke cases from death or disability annually.

The data was presented at the World Stroke Congress in October 2014, and the results were recently published in the *New England Journal of Medicine*. In a blinded assessment of mRS 0-2 at 90 days, endovascular treatment demonstrated statistically significant positive outcomes for stroke patients treated with IAT (33% vs. 19%). There were no safety concerns in terms of hemorrhage or mortality.

***ESCAPE* – **E**ndovascular treatment for **S**mall **C**ore and **A**nterior circulation **P**roximal occlusion with **E**mphasis on minimizing CT to recanalization times.** This was a phase 3 prospective trial with 316 randomized patients from invited centers, headquartered at the University of Calgary of Canada. The treatment arms were endovascular thrombectomy or thrombolysis using currently available technology at the site, which included Solitaire stent, Penumbra aspiration, and

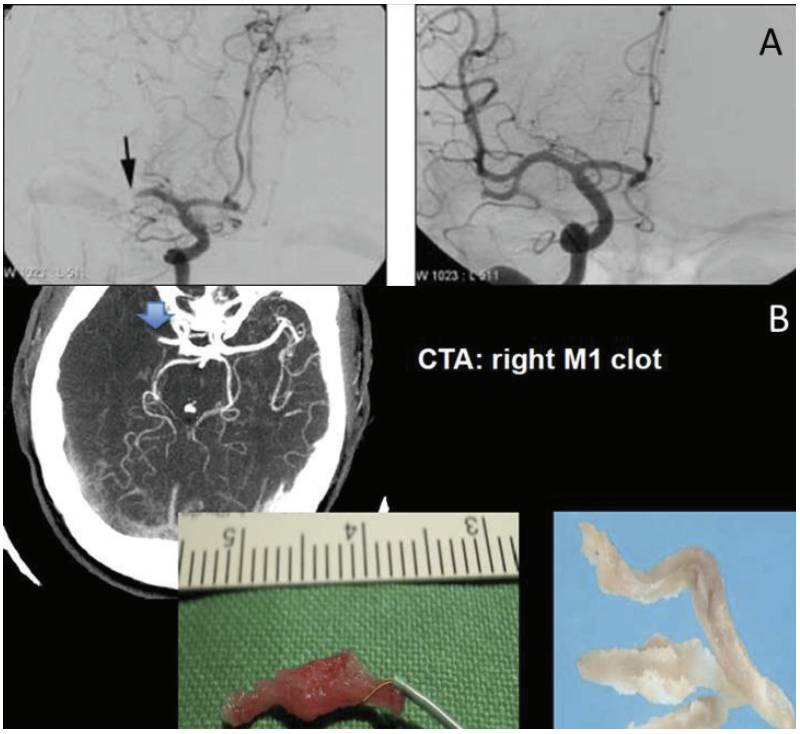

Figure 1: A) cerebral angiography. *Left:* Pre-treatment angiogram shows complete occlusion of proximal right middle cerebral artery (black arrow). *Right:* Post-treatment angiogram shows complete recanalization, which correlated with immediate neurological recovery.
B) CTA also shows the right M1 occlusion and we can also see the retrieved clot.

Trevo stent-retrieval devices. The control arm was medical management only. Patients must have had an intracranial, anterior, large vessel occlusion (LVO) confirmed by CTA. One of the determining criteria in this study was that patients had a small core infarct as measured by ASPECTS score of 6-10. Patients must have been randomized within 12 hours of onset. Avoiding patient selection bias and applying better diagnostic and modern endovascular tools resulted in overwhelming efficacy in the endovascular arm. Therefore, the study has been halted by the Data and Safety Monitoring Board (DSMB) for efficacy. The data will be presented at the International Stroke Conference in February 2015.

***EXTEND-IA*[7] – Ex**tending the **T**ime for **T**hrombolysis in **E**mergency **N**eurological **D**eficits – Intra-Arterial was a phase 2 prospective trial with 70 randomized patients sponsored by the National Stroke Research Institute of Australia. The treatment arm was endovascular treatment plus IV tPA. The control arm was IV tPA only. Patients must have had an intracranial, anterior, LVO confirmed by CTA. Patients also must have had a perfusion mismatch on CT or MRI. Treatment was to be initiated within six hours of onset. This study has an imaging surrogate outcome. It also has been halted by the DSMB for efficacy in favor of IAT based on the overwhelming surrogate outcome.

Conclusion:

The positive results of these trials indicate that utilization of advanced brain and vascular imaging techniques to improve patient selection, and recent improvement in endovascular technologies and devices, could translate into better outcomes for acute ischemic stroke patients with large vessel occlusion. Low enrollment rate per center (selection bias), randomizing patients only based on a hypodensity on plain CT scan (not LVO on CTA), and using older endovascular techniques were the major limitations in previously published studies, especially IMS-III 1-5. When CTA was used in patients with IMS-III and confirmed large vessel occlusion, targeted therapy resulted in mRS score <1 in 35% IAT vs 19% in IV, and improvements in recanalization rate by 20%. MR CLEAN, ESCAPE, and EXTEND-IA provide evidence that IAT is superior to best medical management in stroke patients with large vessel occlusion, and will undoubtedly change the landscape of stroke management and systems of care (Figure 1).

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