Healthy Blue

Medical Policy

Subject:	Mechanical Embolectomy for Treatment of Acute Stroke		
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Description/Scope

This document addresses the use of intra-arterial mechanical embolectomy devices, also known as endovascular thrombectomy, for the treatment of acute thrombotic or embolic stroke. Mechanical embolectomy is designed to reopen occluded blood vessels in the brain by extracting occlusive thrombi or emboli from the cerebral vasculature.

Position Statement

Medically Necessary:

Intra-arterial mechanical embolectomy or thrombectomy is considered **medically necessary** in the treatment of acute ischemic stroke when any of the following criteria sets (I, II, or III) have been met:

Criteria Set I:

A. Angiographic studies have confirmed proximal arterial occlusion of the anterior circulation of the brain, in any of the following anterior intracranial arteries:
   1. Intracranial carotid; **or**
   2. Middle cerebral artery (M1 or M2); **or**
   3. Anterior cerebral artery (A1 or A2); **and**
B. Intra-arterial mechanical embolectomy is performed within 6 hours of onset of symptoms; **and**
C. NIH Stroke Scale (NIHSS) score of 2 or greater; **and**
D. CT or MRI scan has ruled out intracranial hemorrhage or arterial dissection; **and**
E. Procedure is done with a stent retriever device;

or

Criteria Set II:

A. The individual was last known to be well 6 to 24 hours earlier; **and**
B. There is occlusion of the intracranial internal carotid artery or first segment (M1) of the middle cerebral artery; **and**
C. There is a mismatch between the severity of the clinical deficit and the infarct volume, as defined below:
   1. The individual is 80 years of age or older: NIHSS score of 10 or higher and an infarct volume of less than 21 ml; **or**
   2. Less than 80 years of age: NIHSS score of 10 or higher and an infarct volume of less than 31 ml; **or**
   3. Less than 80 years of age: NIHSS score of 20 or higher and an infarct volume from 31 to 50 ml; **and**
D. CT or MRI scan has ruled out intracranial hemorrhage or arterial dissection; **and**
E. Procedure is done with a stent retriever device;

or

Criteria Set III:

A. The individual was last known to be well 6 to 16 hours earlier; **and**
B. The individual has baseline NIHSS score greater than or equal to 6; **and**
C. The individual had a modified Rankin Scale score less than or equal to 2 prior to qualifying stroke (functionally independent for all Activities of Daily Living [ADLs]); **and**
D. There is occlusion of the intracranial internal carotid artery or proximal middle cerebral artery (M1); **and**
E. There is a mismatch between ischemic tissue and infarct volume, as defined below:
    1. Initial infarct volume of less than 70 ml; **and**
    2. A ratio of the volume of ischemic tissue to infarct volume of 1.8; **and**
F. CT or MRI scan has ruled out intracranial hemorrhage or arterial dissection; **and**
G. Procedure is done with a stent retriever device.

Investigational and Not Medically Necessary:

Intra-arterial mechanical embolectomy or thrombectomy is considered **investigational and not medically necessary** in the treatment of acute stroke in all other circumstances when the criteria above have not been met, including, but not limited to, embolectomy or thrombectomy of precerebral arteries.

Rationale

Mechanical removal of emboli or thrombi after an acute stroke, particularly for those who are ineligible for thrombolytic therapy, has been the focus of intense research. Several devices have been approved or cleared by the U.S. Food and Drug Administration (FDA) for the treatment of individuals with acute ischemic stroke (AIS). There are two additional systems that received 510(k) clearance from the FDA; the AXS Vecta™ Aspiration System (Stryker Neurovascular, Fremont, CA) was granted clearance in 2019 and the Riptide™ Aspiration System (Micro Therapeutics Inc., Irvine, CA) was granted clearance in 2020. The 510(k) clearance indicates the systems are substantially equivalent to predicate devices, however there is no peer-reviewed literature published for either device.

EmboTrap® and EmboTrap II® Revascularization Device

Use of the EmboTrap Revascularization device (Neuravi Ltd., Galway, Ireland) was described in the results of the prospective case series ARISE I study (Analysis of Revascularization in Ischemic Stroke With EmboTrap), which involved 40 subjects with large vessel occlusion AIS (Mattle, 2019). Good revascularization rates, defined as modified thrombolysis in cerebrovascular infarction score (mTICI 2b/3) after 3 or fewer passes with EmboTrap were 75%, which is the same as 74% reported in a composite analysis of 8 reported randomized controlled trials (p=0.95). After additional EmboTrap passes or the use of another device, mTICI 2b/3 scores rose to 85%, which was also similar to the composite analysis data (p=0.38). The high revascularization rates in ARISE I converted into 64% good clinical outcomes assessed by modified Rankin Scale (mRS ≤2), vs. 50% in the composite analysis results (p=0.32).

Zaidat (2018a) published the results of EmboTrap use in the follow-up ARISE II study. This single-arm, prospective, multicenter study, evaluated the use of the EmboTrap device to a composite measure based on results of the SWIFT and TREVO 2 trials. A total of 227 subjects from 19 sites with large-vessel occlusions and moderate-to-severe neurological deficits within 8 hours of symptom onset were included in the analysis. The

primary efficacy end point (mTICI ≥ 2b within 3 passes) was achieved in 80.2% of subjects (p<0.0001). After all interventions, mTICI 2c/3 was achieved in 76% of subjects, and mTICI ≥ 2b was 92.5%. The rate of first pass (mTICI ≥ 2b following a single pass) was 51.5%. The primary safety end point, a composite rate of symptomatic intracerebral hemorrhage (sICH) or serious adverse device effects, was 5.3%. Functional independence and all-cause mortality at 90 days were 67% and 9%, respectively.

Brouwer (2018) reported the results of a registry-based study involving 201 subjects with AIS of the internal carotid artery (ICA, 15.5%), middle carotid artery (MCA, 61.2%), the posterior circulation (11.9%), anterior cerebral artery (ACA, 0.5%), and a carotid T-occlusion (10.9%) receiving treatment within the 4.5-hour time window after arrival at the hospital. Intravenous tissue plasminogen activator (IV tPA) was administered to 95 (47.3%) subjects prior to EmboTrap treatment. mTICI 2b–3 was achieved in 170 (84.6%) subjects treated with the EmboTrap, with or without tPA. In anterior circulation occlusions, 85.3% achieved mTICI 2b–3, while 79.2% with posterior circulation occlusions achieved mTICI 2b–3. In the subjects treated with EmboTrap alone (n=166), 143 (86.1%) achieved mTICI 2b–3. In 7 subjects (3.5%) there was a further distal clot in a small vessel requiring additional procedures with a smaller thrombectomy device. Peri-procedural complications occurred in 11 subjects (5.4%; 5 non-flow limiting dissections, 2 vasospasm, 4 emboli to a new uninvolved territory). There were no device-related complications reported. mRS at 3 months were available in 180 subjects, and good functional outcomes were achieved in 95 subjects (47.3%). When corrected for the subjects with pre-existing poor mRS scores (mRS ≥ 3), good functional outcome was achieved in 52.8%. Twenty-six subjects (12.9%) had died at 3-month follow-up.

Valente (2019) published the results of a single-arm, prospective, case series study that involved 29 subjects with large vessel occlusion AIS treated with the EmboTrap II device (Neuravi Ltd., Galway, Ireland). MCA was involved in 90% of subjects (M1 in 80%, M2 in 10%) and terminal ICA was involved in 10%. Successful reperfusion was obtained in 25 subjects (86%), with 4 requiring additional device use (Solitaire, Sophia Plus, or Trevo). Of the subjects treated only with EmboTrap II, successful reperfusion was reported in 76% of cases. Severe focal vasospasm of M1 was observed in one case and was managed with intra-arterial injection of 2 mg of nimodipine. No other device-related complications were reported No distal emboli were reported.

Merci® Retrieval System

The Merci Retrieval System (Concentric Medical, Inc., Mountain View, CA) was evaluated in two prospective non-randomized trials, known as the MERCI trial (Mechanical Embolus Removal in Cerebral Ischemia; [Parts 1 & 2]) and the Multi-MERCI trial [Parts 1 & 2].

Smith (2005) published the results of the MERCI trial. MERCI was a 25-center prospective, nonrandomized trial for individuals with symptoms of acute stroke for less than 8 hours who were not candidates for thrombolytic therapy, either because of contraindications (~25%) or because symptoms were present for more than 3 hours. Study subjects were required to have a National Institute of Health Stroke Scale (NIHSS) score of at least eight (8), exclusion of cerebral hemorrhage by CT scan, and a treatable vessel (intracranial vertebral artery, basilar artery, intracranial carotid artery [including terminal bifurcation] or middle cerebral artery [MCA], first or secondary divisions [M1 or M2]). Most individuals had MCA distribution strokes. Of the 151 subjects enrolled in the trial, 141 had the device deployed. The primary outcome of recanalization, defined as achieving "Thrombolysis in Myocardial Infarction" (TIMI) II or III flow in treated vessels, was achieved in 46% (69/151) of those in an intent-to-treat analysis and in 48% (68/141) of those in whom the device was employed. This was compared to a

"benchmark" of a spontaneous recanalization rate of 18% observed in the control arm of the PROACT-II (Prolyse in Acute Cerebral Thromboembolism-II study), a randomized controlled trial of pro-urokinase for acute ischemic stroke.

Smith (2006) reported the results of the Multi MERCI trial which was designed in part to evaluate the safety and effectiveness of the Merci Retrieval System in conjunction with IV tPA as well as the safety of the next generation design of the device, the L-5 Retriever. A total of 131 participants were initially treated with the L-5 Retriever. Primary outcome was recanalization of the target vessel. Results showed successful recanalization in 75 of 131 (57%) treatable vessels and 91 of 131 (70%) after adjunctive tPA therapy. Secondary outcomes of the Multi MERCI study included mRS and NIHSS scores. At 90 days, 37% of the participants achieved an mRS score of less than or equal to 2 (considered a good outcome). This compares favorably to data from the PROACT-II study which reported an mRS ≤ 2 in 25% of the control arm and 40% of the treatment group. Clinically significant procedural complications occurred in 10 individuals (7.1%) and symptomatic intracranial hemorrhages were observed in 11 (7.8%), a rate of bleeding similar to that seen with thrombolytic therapy alone in other trials. Treatment with the Retriever alone resulted in successful recanalization in 60 of 111 (54%) treatable vessels and in 77 of 111 (69%) after adjunctive therapy. Overall mortality at 90 days was 44% compared to 27% in the control arm of PROACT-II. The investigators observed that good neurological outcomes were more frequent at 90 days in those with successful recanalization compared to those with unsuccessful recanalization (46% vs. 10%, $p<0.0001$) and mortality was less as well (32% vs. 54%, respectively, $p=0.01$). This suggests that restoration of blood flow improves outcomes. The investigators also compared their findings to those from the initial MERCI trial. In the discussion section of the Smith article, the authors point out that in the Multi MERCI trial there was a higher recanalization rate in the retriever alone group (54% vs. 48%), higher final recanalization rate (69% vs. 60%), better 90-day clinical outcome (34% vs. 28% mRS ≤ 2), fewer clinically significant procedural complications (4.5% vs. 7.1%), and lower 90-day mortality (31% vs. 44%). The authors proposed that higher rates of recanalization, when compared to the MERCI trial, were associated with the newer generation thrombectomy device compared with first-generation devices, but these differences did not achieve statistical significance. The authors conclude their report by stating, "…definitive conclusions of clinical efficacy in treating ischemic stroke will require a control group comparison." Indeed, to determine if this treatment improves net outcomes (considering both benefits and risk) in stroke, there must be a comparison with an appropriate control group. It is not clear what the recanalization rate would have been without embolectomy in those who had successful clot removal. Concurrent control groups are also important to evaluate possible unexpected events when intravascular devices are used that may damage arterial endothelium.

Flint and colleagues (2007) published pooled results of the MERCI and Multi MERCI Part 1 trials for the subgroup of participants with occlusions of the intracranial carotid artery (47 enrolled in MERCI and 33 in Multi MERCI). Recanalization was achieved in 53% with the Merci Retriever alone and 63% when used with adjunctive intra-arterial (IA) thrombolytics. At 90 days, 25% of participants had a good neurologic outcome (mRS 0-2), and overall mortality was 46%. The authors noted that the trials had not included a non-treatment arm; therefore, the data could not directly demonstrate the superiority of mechanical thrombectomy for acute intracranial carotid artery occlusions. They also concluded a comparison of mechanical thrombectomy to intravenous thrombolysis within a 3-hour time window was warranted.

FDA clearance through the 510(k) process requires a predicate device and does not require data from randomized trials. In the MERCI clinical trials, results were compared to historical controls based on the PROACT II study of thrombolysis and concerns have been raised about the lack of a control group. Additionally, the MERCI trials

included individuals with different types of occlusions; PROACT II had MCA M1 and M2 occlusions while the MERCI trial also included internal carotid and vertebral basilar systems. In regards to the higher mortality and lack of superior clinical outcomes in the MERCI trial compared to PROACT-II, the MERCI investigators pointed out that their study subjects were older and the variety of affected vessels were associated with more severe strokes carrying worse prognoses. However, the 45% recanalization rate of middle cerebral arteries alone in the MERCI trial compares unfavorably with the 66% rate seen with intra-arterial pro-urokinase in PROACT-II and a recanalization rate of 56% observed in those treated with combined intravenous and intra-arterial (IA) tPA in the Interventional Management of Stroke (IMS) study (IMS Study Investigators, 2004).

Shi and colleagues performed a retrospective pooled data analysis of 178 participants with MCA occlusion that were treated in the MERCI and Multi MERCI trials (2010). They noted that benefit from endovascular revascularization of those with acute ischemic stroke with MCA secondary division (M2) occlusions as compared with MCA trunk (M1) occlusions is unknown. Two groups, one with M1 lesions (n=150, 84.3%) and the other group with isolated M2 lesions (n=28, 15.7%) were evaluated for baseline characteristics, revascularization rates, hemorrhage rates, complications, outcomes, and mortality. Among the 150 subjects with MCA M1 occlusion, 73 were enrolled in MERCI and 77 were enrolled in Multi MERCI. Among the 28 participants with MCA M2 occlusion, 7 were enrolled in MERCI and 21 were enrolled in Multi MERCI. Revascularization rates (TIMI II/III flow) immediately after Merci treatment alone were 46.0% and 71.4% in the MCA M1 group and M2 group, respectively. There were no statistically significant findings for hemorrhage, complications or mortality. Although the data from this study supports the correlation between successful revascularization and the achievement of good clinical outcomes at 90 days post thrombectomy, the authors acknowledged that it was not clear if the trend toward better clinical outcomes in those with isolated M2 occlusions is associated with a higher revascularization rate or with a smaller ischemic area at risk. The greater benefit in the M2 group for revascularization could be due to the fact that a greater number of participants in this group were from the Multi MERCI trial, and better operator and device performance could be a contributing variant.

In a pooled analysis of the MERCI and Multi MERCI studies, Fields and others (2011) evaluated the effect of recanalization on functional outcomes. The TIMI score was used to define the degree of recanalization, and a favorable outcome was defined as an mRS score of 0-2 at 90 days. A total of 305 subjects were included in the analysis. The authors report that the unadjusted odds ratio (OR) for a favorable outcome increased significantly as the TIMI score increased from 0 to 1 (OR, 5.9; 95% confidence interval [CI], 1.7-20.0; p=0.007) and from 2 to 3 (OR. 2.3; 95% CI, 1.2-4.5; p=0.01). The likelihood of death decreased significantly as the TIMI score increased from 2 to 3 (OR, 2.2; 95% CI, 1.1-4.3; p=0.05). In a multivariate analysis, each increase in TIMI grade increased the odds of a good outcome 2.6-fold (95% CI, 1.9-3.4, p<0.0001). The authors concluded by stating:

> These results provide support for the hypothesis that patient outcomes in the context of stroke interventions may be improved by additional attempts to increase the TIMI grade during stroke interventions. Because patients with different TIMI grades may differ from each other at baseline, this hypothesis would require validation in a randomized trial.

Penumbra System®

In September 2007, the FDA granted 510(k) clearance to the Penumbra System (Penumbra, Inc., Alameda, CA) which is a mechanical device designed to reduce clot burden in acute stroke due to large-vessel occlusive (LVO) disease, similar to the Merci Retrieval System. The FDA clearance was based in part on the Penumbra Pivotal

Stroke Trial study, a prospective, multicenter, single-arm study, involving 125 participants with neurological deficits as defined by an NIHSS score of ≥ 8, who presented within 8 hours of symptom onset, and had an angiographic occlusion (Penumbra Pivotal Stroke Trial Investigators, 2009). The results of the study showed neurological recovery and functional outcomes improvement, with 31 of 125 (25%) of the participants having either an NIHSS score of 0 to 1 or ≥ 0-point improvement at discharge. Additionally, 25% of subjects had an mRS score of ≤ 2 at 90 days. The 90-day mRS score was comparable to the subjects in the MERCI Part 2 trial of 27.7% (Smith, 2005), but lower than the treatment group in the PROACT II study of 40% (Furlan, 1999). Given a revascularization rate of 81.6%, the lower mRS score was unexpected and remains unclear. The authors stated that the trial was designed primarily to evaluate the safety and effectiveness of the Penumbra thrombectomy device to reduce clot burden, not functional outcome. They acknowledged that the question of whether mechanical revascularization leads to improved neurological recovery and a better functional outcome when compared to medical management alone will require future prospective, concurrently controlled trials in well-selected subjects presenting with acute ischemic stroke.

Tarr and others conducted a follow-up retrospective case series study of 157 subjects who underwent treatment with the Penumbra system (the POST Trial, 2010). Subject data was followed out to 90 days post-procedure. The primary endpoints used were revascularization of the target vessel (TIMI score 2 or 3), good functional outcome as defined by an mRS score of ≤ 2, and incidence of serious adverse events related to the use of the Penumbra system. The data from the POST trial were compared to those from the Pivotal trial. The report stated that the incidence of intracranial hemorrhage at 24 hours was not significantly different from the Pivotal study data (6.4% vs. 11%), but the rate of all-cause death was, at 20% and 33% respectively ($p<0.05$). Additionally, there was a significantly higher proportion of subjects who were functionally independent after treatment (POST trial, 41% vs. Pivotal, 25%). In the POST study, the authors stated that subjects that had successful revascularization had better outcomes, with significantly lower mortality and a higher rate of good functional outcomes ($p\leq0.01$). The timing of Penumbra treatment in relation to the use of adjunctive treatment was also variable. Thirty-five percent of subjects received IA tPA treatment during treatment with the Penumbra system, 18.5% receiving tPA prior to Penumbra treatment (as a salvage treatment), and 23% received it both before and during Penumbra treatment. The impact of IA tPA treatment was reported as not being significant on revascularization or mortality rates. The adverse event rate was 5.7%, with 2 subjects experiencing dissection, and a single subject each experiencing perforation, intracranial hemorrhage, peripheral hemorrhage, access site hematoma, and cardiac arrest. Three device failures were reported as well, related to fracture or breakage of the device. None of these failures resulted in death. The results of the POST trial are in line with those from the Pivotal trial with regard to the rate of successful recanalization, indicating that the results of the Pivotal study can be replicated. This uncontrolled trial included several approaches to the use of the Penumbra system, with subjects receiving care with the system alone, and in conjunction with IV tPA, IA tPA, and with both IV and IA tPA together. Furthermore, TIMI scores were not adjudicated by a core lab but were assessed at each individual study center. However, the authors argued that this condition reflects real-world use of the Penumbra device.

Tarr and others (2018) published a follow-up POST trial, which described the initial post-market experience with the Penumbra system. This retrospective case series study involved the first 157 consecutive subjects treated with the Penumbra system at 7 stroke centers. The author reported that 87% of the treated vessels were revascularized to TIMI 2 (54%) or TIMI 3 (33%), vs. 82% reported in the Pivotal trial. All-cause death was significantly improved in the POST study vs. the Pivotal study (20% vs. 33%, $p<0.05$). Likewise, the POST study results indicated a higher rate of post treatment functional independence (41% vs. 25%, $p<0.05$). There were 9 serious adverse events

reported (5.7%), including intracranial hemorrhage, dissection, perforation and hematoma. All-cause mortality was 20% (32/157).

Solitaire™ FR Revascularization Device

The Solitaire FR device (Covidien, Mansfield, MA) received FDA 510(k) clearance in March 2012. The FDA determined that this device was substantially equivalent to the Merci Retriever device, based on data from a randomized controlled trial (RCT) submitted to the FDA comparing the Merci and Solitaire devices (the SWIFT trial) (Saver, 2012). The SWIFT trial was a multicenter, randomized, non-inferiority study involving 113 subjects with acute stroke in the proximal carotid arteries. A total of 58 individuals were assigned to receive treatment with the Solitaire device and 55 to receive treatment with the Merci device. The primary efficacy endpoint was successful recanalization without symptomatic intracranial hemorrhage. Secondary efficacy outcomes included time to achieve recanalization, good neurological outcomes at 90 days (as defined as mRS ≤ 2 or NIHSS score improvement ≥ 10), and neurological condition at 90 days. The primary safety endpoint was incidence of device and procedure-related serious adverse events. The reported results demonstrated that the Solitaire group had more frequent successful recanalization (61% vs. 24%, p=0.0001), better time to successful recanalization (36 min vs. 52 min, p=0.038), and more frequent 90-day good neurological outcomes (58% vs. 33%, p=0.017). Additionally, the Solitaire group had a lower incidence of intracranial hemorrhage (both symptomatic and asymptomatic) compared to the Merci group (17% vs. 38%, p=0.02), as well as fewer all-cause deaths at 90 days (17% vs. 38%, p=0.02). No differences between groups were noted with regard to device or procedure-related adverse events. The study was halted early, after the data safety monitoring board and trial steering committee agreed that pre-specified criteria for stopping the trial had been met. The results from this trial were presented at the 2012 International Stroke Conference. The conference presentation acknowledged that "… further study is necessary to prove whether treatment with Solitaire is better than supportive medical care and two such studies addressing that issue are under way in the US."

Pereira and colleagues (2013) report on a prospective case series study involving 202 subjects between 10 and 85 years of age with occlusion of the anterior intracranial artery presenting within 8 hours after onset and who were refractory to IV thrombolysis. All participants were treated with the Solitaire device and a total of 59% of the subjects received intravenously administered tPA before the treatment with mechanical embolectomy. In the intent-to-treat analysis, the rate of the primary outcome of successful revascularization as measured by TICI ≥ 2b after ≤ 3 passes of the study device was reported as 79.2% (160/202). In 42 subjects (20.8%), TICI ≥ 2b was not achieved within the limited number of 3 passes and were considered device treatment failures. In 18 subjects (9%) rescue therapy was performed, which consisted of intra-arterial thrombolysis in 2 subjects, mechanical embolectomy in 13 subjects, and in 3 subjects, combined intra-arterial thrombolysis and mechanical thrombectomy (MT). After rescue therapy, it was determined that 88.1% of subjects (171/194) achieved final successful revascularization. At the 90-day follow-up visit, favorable neurological outcome (mRS, 0-2) was seen in 57.9% of subjects. The frequency of total device- and procedure-related serious adverse events was 7.4%. Intracerebral hemorrhage (ICH) was found in 18.8% of subjects at 24 hours and sICH occurred in 1.5% of the subjects. The mortality rate was 6.9% with a higher proportion found in the male population (5%). An analysis was done between the collateral circulation and outcome, and the authors observed that a good collateral circulation, as defined as grades 3-4 American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology scale, correlated significantly with good (mRS, 0-2) outcomes (p=0.034). Subjects receiving rescue therapy showed a statistically significant lower rate of favorable outcome (33.3%; mRS, 0-2) compared with those who did not (60.3%; p=0.043). The rate of device- and procedure-related serious adverse

events (SAEs) was not significantly elevated in the subgroup of subjects receiving rescue therapy (11.1% vs. 7.2%).

Campbell and others (2014, 2015) reported on the results of the Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial (EXTEND-IA) trial, which was a prospective open-label, blinded endpoint RCT involving 70 subjects with radiologically confirmed intracranial occlusion. Subjects were assigned on a 1:1 basis to treatment with IV tPA alone (n=35) or IV tPA plus mechanical embolectomy with the Solitaire FR device (n=35). All subjects were treated within 6 hours of stroke onset and followed for 90 days post-intervention. While all those involved with the initial treatment were aware of the group assignment, those involved with subsequent clinical and imaging assessments were blind to group assignment. The authors reported that the experimental group showed significantly better outcomes compared to controls with regard to the primary endpoints of probability of reperfusion without symptomatic intracranial hemorrhage at 24 hours (89% vs. 34%; p<0.001). Similarly, the co-primary endpoint of early neurologic improvement as measured by a greater than or equal to 8-point reduction on the NIHSS was also significantly in favor of the experimental group (28% vs. 13%; p<0.001). The secondary endpoint of 90-day mRS was also favorable to the experimental group, with median scores of 1 for the experimental group vs. 3 for the controls (p=0.006). No differences between groups were noted for the incidence of deaths (p=0.18), symptomatic intracerebral hemorrhage (p=0.49), or parenchymal hematoma (p=0.99). Finally, significant and favorable outcomes were reported for tertiary endpoints of reperfusion greater than 90% at 24 hours without symptomatic intracerebral hemorrhage (p<0.001) and median home time within the first 90 days (p=0.006).

Two other similarly designed studies were published in 2015. Jovin and colleagues published the results of the Randomized Trial of Revascularization with Solitaire FR Device versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation large Vessel Occlusion Presenting within Eight Hours of Symptom Onset (REVASCAT) study, which involved 206 subjects with radiologically confirmed intracranial occlusion. Subjects were assigned on a 1:1 basis to treatment with IV tPA alone (n=103) or IV tPA plus mechanical embolectomy with the Solitaire FR device (n=103). Unlike the EXTEND-IA study, subjects were treated within 8 hours of symptom onset. Recruitment was stopped early due to loss of equipoise at the first interim analysis. In addition, the publication of the Goyal, Campbell, and Berkhemer studies had raised ethical concerns of study continuation. Thrombectomy was performed in 98 of the 103 (95.1%) subjects in the experimental group. Additionally, one subject underwent angioplasty after failed thrombectomy and another received interarterial tPA. With regard to the primary outcome, analysis showed significant improvement in the distribution of the mRS score (common OR, 1.7) favoring thrombectomy. The absolute between-group difference in the proportion of subjects who were functionally independent (mRS score, 0-2) was 15.5 percentage points, favoring thrombectomy (43.7% vs. 28.2%; adjusted OR, 2.1). Secondary outcomes also favored the thrombectomy group, with successful revascularization was achieved in 66% of subjects in the thrombectomy group according to core laboratory assessments and in 80% of the subjects according to the assessments of local interventionalists. No significant differences were reported for the rate of symptomatic intracranial hemorrhage (1.9% in both groups; p=1.00) and rates of death (18.4% in experimental group vs. 15.5% in the control group; p=0.60).

Dávalos and colleagues (2017) published the 1-year results of the REVASCAT study. Data was available for 205 of the original 206 subjects involved in the study (99.5%). The authors reported that at 12-months post-treatment the adjusted OR for improvement in mRS score was 1.8 in favor of the experimental group. The proportion of subjects with mRS score 0 to 2 was significantly better in the experimental group vs. controls (44% vs. 30%,

adjusted OR 1.86). They also noted that improvements in mRS scores continued for the first 3 months and were sustained through 12 months in both groups. No differences between groups were noted with regard to overall mortality.

The other study, named Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME), was reported by Saver and colleagues (2015). As with the above trials, subjects (n=196) were assigned on a 1:1 basis to treatment with IV tPA alone (n=98) or IV tPA plus mechanical embolectomy with the Solitaire FR device (n=98). All subjects were treated within 6 hours of symptom onset. In the experimental group, 87 (88.8%) subjects underwent treatment with the embolectomy device. As with the previously reported studies, use of thrombectomy plus intravenous tPA significantly reduced disability at 90 days vs. tPA alone, as measured by mRS score ($p<0.001$). Additionally, the rate of functional independence (mRS score, 0 to 2) was higher in the experimental group than in the control group (60% vs. 35%, $p<0.001$). Successful reperfusion (≥ 90%) at 27 hours, assessed by means of perfusion CT or MRI, was more frequent in the intervention group than in the control group (83% vs. 40%, $p<0.001$). No significant differences between groups were reported with regard to 90-day mortality (9% vs. 12%, $p=0.50$) or symptomatic intracranial hemorrhage (0% vs. 3%, $p=0.12$).

Albers and others (2015) published a follow-up report of the SWIFT PRIME trial that evaluated the relationship between the imaging findings and clinical outcomes in this trial population. The authors reported that there was a "potent relationship" between 27-hour infarct volumes and clinical outcomes (Spearman correlation coefficient [ρ]=0/57, $p<0.001$). They also stated that subjects who had successful reperfusion had significantly better clinical outcomes, with no statistical differences between treatment groups found. In the group of subjects for whom perfusion mismatch data were available, the 27-hour infarct volume was significantly better in the intervention group vs. controls (24 mL vs. 36 mL, $p=0.025$). The size of the initial mismatch volume was also found to be important, with the rate of functional independence reported to be not statistically significant between treatment groups in subjects with small initial mismatch volumes ($p=1.0$). Conversely, for subjects with larger mismatch volumes, the intervention group subjects were reported to have significantly better functional independence scores (62.7% vs. 34.4%, $p=0.002$).

In 2018, Al-Ajlan and colleagues published the results of a follow-up study of data from the REVASCAT trial. Using diffusion-weighted magnetic resonance imaging (n=15) or non-contrast CT data (n=189), blinded assessors determined the pre- and post-infarct volumes. The authors reported significant decrease in median post-treatment infarct size in the embolectomy group vs. the control group (16.3 ml vs. 3.6 ml). In embolectomy group subjects with successful recanalization median post-treatment infarct size was 14.6 ml vs. 92.9 ml in non-recanalized subjects ($p=0.05$). In the control group, the median post-treatment infarct size in subjects with successful recanalization was 1831 ml vs. 52.8 ml in non-recanalized subjects ($p=0.02$). Baseline NIHSS score ($p<0.01$), site of occlusion ($p<0.03$), NCCT Alberta Stroke Program Early Computed Tomography Score (ASPECTS) ($p<0.01$), and recanalization status ($p<0.02$) were all independently associated with post-treatment infarct volume. Baseline NIHSS score ($p<0.01$), time from onset to randomization ($p<0.02$), treatment type ($p<0.04$), and recanalization status ($p<0.01$) were all independently associated with 24-hr. NIHSS score. A significant correlation between infarct volume and 24-hr NIHSS score was reported ($p<0.01$). Subjects in the lowest quartile for post-treatment infarct volume were 4 times more likely to achieve mRS 0-2 vs those in the highest quartile (Rate Ratio, 3.92). Subjects in the highest quartile were 4 times more likely to die vs. those in the lowest quartile (Rate Ratio, 3.88). The authors concluded, "Endovascular treatment saves brain and improves 90-day clinical outcomes primarily through a beneficial effect on the 24-hour stroke severity."

Zaidat (2018b) reported real world performance data of the Solitaire FR device from the North American Solitaire Stent Retriever Acute Stroke (NASA) registry and compared it the results of the SWIFT and TREVO 2 trials. A total of 354 subjects underwent treatment with the Solitaire FR device in 24 centers. The recanalization outcomes reported included a TIMI ≥2 rate of 83.3% (315/354) and TICI ≥2a rate of 87.5% (310/354) vs. TIMI ≥2 rate of 83% in SWIFT and TICI ≥2a rate of 85% in TREVO 2. A total of 42% (132/315) of NASA subjects had a 90-day mRS ≤2 vs. 37% of SWIFT subjects and 40% of TREVO 2 subjects. The 90-day mortality was 30.2% (95/315) vs. 17.2% in the SWIFT trial and 29% in the TREVO 2 trial.

Lee (2019) reported the results of the ROSE ASSIST trial, a retrospective case series study of 303 subjects with AIS due to intracranial atherosclerotic stenosis (ICAS, n=75) or embolism (n=228) treated with the Solitaire device. The primary endpoint, the immediate successful reperfusion rate, was not significantly different between the ICAS and embolism groups after propensity score matching (73.1% embolic vs. 65.8% ICAS-related, p=0.261). The final successful reperfusion grade was also similar in the two groups (79.3 vs. 72.0%, p=0.219). Additionally, the grades and frequencies of ICH and subarachnoid hemorrhage did not differ between groups (p=0.134 and p=0.269, respectively). The authors concluded, "The immediate reperfusion performance in terms of thrombus removal of Solitaire thrombectomy for ICAS-related occlusions was similar to that for embolic occlusions."

A number of small case series studies reporting on the Solitaire device are available (Cohen, 2012; Hann, 2013; Machi, 2012; Miteff, 2011; Mpotsaris, 2012; Roth, 2010). However, the evidence from these small studies is weak and cannot be used to properly evaluate the safety and efficacy of this device. Koh and others conducted a systematic review of these available studies addressing the Solitaire device (2012). Their initial search identified 634 articles, but this number was condensed to 13 when limited to human clinical studies. The number of subjects in these studies ranged from 7 to 56, with a mean of 20. Two of these studies were retrospective comparative studies, two were prospective case series, and the remainder were retrospective case series studies. A total of 262 subjects were included in these publications. Quantitative pooled data analysis was not possible due to significant heterogeneity of study design, inclusion criteria, and subject populations. The authors reported that the mean age of subjects varied from 58.9 to 76.4 years of age. Mean initial NIHSS ranged from 14 to 21.4. Occluded segment included 149 MCAs (56.9%), 59 T-carotids (22.5%), and 54 vertebrobasilar arteries (20.6%). Forty-one cases of 192 MCA or T-carotid occlusions (21.60%) from 11 studies had tandem stenosis of the proximal carotid artery. Eleven studies identified the indications for recanalization therapy. However, the criteria were different for each study.

Trevo® Retriever

The Trevo Retriever device (Concentric Medical, Mountain View, CA) received FDA 510(k) clearance in August 2012 with the indication to treat individuals with acute ischemic stroke due to large intracranial vessel occlusion who are ineligible for or fail intravenous tissue plasminogen activator. The FDA determined that this device was substantially equivalent to the Merci Retriever device, based on data from the TREVO2 study, an RCT of 178 subjects from 27 centers in the U.S. and Europe that compared the Trevo device with the Merci device (Nogueira, 2012). This prospective, open label, non-inferiority study involved 88 subjects randomized to receive treatment with the Trevo device and 90 to be treated with the Merci device. The primary efficacy endpoint was revascularization success defined as TICI ≥ 2, and the primary safety endpoint was a composite of procedure-related adverse events. The authors reported that overall, the Trevo group had significantly fewer vessel

perforations when compared to the Merci group (1 vs. 10, p=0.0182), had higher rates of successful reperfusion (92% vs. 77%, p<0.0068), and had higher rates of 90-day "good" outcomes as measured by mRS 0-2 (40% vs. 22, p=0.0130). No significant differences were reported with regard to any other measures, including symptomatic intracranial hemorrhage, rates of neurological deterioration, and 30- and 90-day mortality.

In a case series study addressing the use of the Trevo Retriever in subjects with acute stroke (San Román, 2012), 60 subjects with stroke were treated in a prospective, single-center study. Of the subjects, 54 had anterior circulation occlusion and 6 had occlusion of the vertebrobasilar circulation. Successful revascularization was obtained in 44 (73.3%) of cases when only the Trevo device was used and in 52 (86.7%) when other devices or additional IA tPA was also required. Good 90-day outcomes were achieved in 27 (45%) subjects, and the mortality rate was 28.3%. Seven subjects (11.7%) presented a symptomatic intracranial hemorrhage. No other major complications were detected. The authors concluded that the Trevo device was reasonably safe and effective in subjects with severe stroke, and that their results support further investigation through multicentric registries and randomized clinical trials.

In 2017, Nogueira and colleagues published the results of the DAWN trial, an unblinded, multicenter RCT involving 206 subjects with occlusion of the intracranial carotid artery or proximal (first segment, M1) middle cerebral artery who had last been known to be well between 6 and 24 hours prior to treatment, who were randomized to treatment with either the Trevo Retriever device plus standard care (n=107) or standard care alone (n=99). Subjects were further stratified into three groups, with group A being 80 years of age or older, having a score of 10 or higher in the NIHSS and an infarct volume less than 21 ml. Group B was younger than 80, had a NIHSS score of 10 or higher, and an infarct volume less than 31 ml. Group C was younger than 80, had an NIHSS score of 20 or higher, and an infarct volume of 31 to less than 51 ml. At 31 months, enrollment in the trial was stopped because of the results of a prespecified interim analysis. The mean score on the utility-weighted mRS at 90 days was 5.5 in the thrombectomy group vs. 3.4 in the control group (adjusted difference [Bayesian analysis], 2.0 points; 95% credible interval, 1.1 to 3.0; posterior probability of superiority, >0.999), and the rate of functional independence at 90 days was 49% in the thrombectomy group vs. 13% in the control group (adjusted difference, 33 percentage points; 95% credible interval, 24 to 44; posterior probability of superiority, >0.999). The rate of sICH did not differ significantly between the two groups (6% in the thrombectomy group vs. 3% in the control group, p=0.50), nor did 90-day mortality (19% and 18%, respectively; p=1.00).

Another RCT reported on the use of mechanical embolectomy beyond 6 hours of onset of symptoms (Albers, 2018). This study, which was stopped early due to the primary efficacy endpoint being met during an interim analysis, involved 182 subjects with occlusion of the cervical or intracranial carotid artery or the proximal middle cerebral artery with an initial infarct volume of less than 70 ml and a ratio of volume of ischemic tissue to initial infarct volume of 1.8 or greater. Subjects were assigned on a 1:1 basis to receive treatment with mechanical embolectomy plus medical therapy (n=92) or medical therapy alone (n=90). Treatment was initiated 6 to 16 hours after the subject was last known to be well, including if they had awoken from sleep with symptoms. Assessments were conducted by blinded assessors with mRS and NIHSS score at 24 hours, 30 days, and 90 days. At 90 days mRS scores were significantly better in the embolectomy group (OR, 2.77, p<0.001). After adjustment for stratification factors, OR was 3.36 (p<0.001). Mortality at 90 days was 14% in the embolectomy group and 26% in the control group (p=0.05). No differences between groups was noted with regard to the rate of intracranial hemorrhage (p=0.75), parenchymal hematoma (p=0.21), or serious adverse events (p=0.18). The authors concluded:

> Endovascular thrombectomy for ischemic stroke 6 to 16 hours after a patient was last known to be well plus standard medical therapy resulted in better functional outcomes than standard medical therapy alone among patients with proximal middle-cerebral-artery or internal-carotid-artery occlusion and a region of tissue that was ischemic but not yet infarcted.

Zaidat and others (2018c) reported results from the TREVO Stent-Retriever Acute Stroke (TRACK) multicenter Registry, which reported real-world results of the use of the Trevo device in 23 centers. A total of 634 subjects were included in the report, and 80.3% of subjects had achieved TICI ≥ 2b, and 90-day mRS ≤ 2 was achieved in 47.9%. The mRS ≤ 2 results changed to 51.4% when restricting the analysis to the anterior circulation and treatment within 6 hours of reported symptoms. The mRS ≤2 results were 54.3% for subjects who achieved complete revascularization. The authors reported a 90-day mortality rate was 19.8%.

In late 2018 Binning and colleagues published the results of a study involving data from the prospective Trevo Retriever Registry. The intent-to-treat population included 2008 subjects with large vessel occlusion with median NIHSS score of 16. The authors reported occlusion sites were ICA (17.8%), MCA (73.5%), posterior circulation (7.1%), and distal vascular locations (1.6%). The results included that mTICI 2b or 3 was achieved in 92.8% of subjects, with 55.3% achieving RS ≤ 2 at 3 months. They also reported that subjects meeting revised 2015 American Heart Association (AHA) criteria for thrombectomy had a 59.7% mRS of 0 to 2 at 3 months, whereas 51.4% treated outside of AHA criteria had mRS of 0 to 2. The symptomatic intracranial hemorrhage rate was 1.7%.

Non-Device-Specific or Mixed-Device Studies

In 2014, Berkhemer and others published the results of the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN). This RCT involved 500 subjects with imaging-confirmed intracranial major vessel occlusion who were eligible for treatment within 6 hours of stroke onset. Subjects were assigned to receive treatment with either usual care or usual care plus intra-arterial treatment, which may have included intra-arterial thrombolysis, mechanical embolectomy, or both. The selection of embolectomy device was left to the discretion of the treating investigator, and any FDA approved or CE marked device was eligible for use. Primary outcome of interest was 90-day mRS score, with secondary outcomes including scores on the NIHSS, Barthel index, EuroQol self-report questionnaire, and the ASPECTS. While the subjects and investigators were not blind to group assignment, radiological assessments were conducted by blinded assessors. In total, 233 subjects were assigned to the experimental group and 267 to the control group. No intra-arterial therapy was undertaken in 37 of the experimental group subjects, mechanical treatment was done in 195 subjects (of which 24 received additional intra-arterial thrombolysis), and 1 subject received intra-arterial thrombolysis only. Of the 195 subjects receiving mechanical therapy, 190 involved the use of retrievable stents (for example, the Penumbra System, Solitaire FR, and Trevo thrombectomy) and the other 5 involved other types of devices (for example, the MERCI retriever). The authors reported that the age-adjusted OR for having a favorable 90-day mRS was 1.67, in favor of the experimental group, regardless of the mRS category except death. The absolute between-group differences in the proportion of subjects who were functionally independent as measured by the mRS scores was 13.5% in favor of the experimental group, with an adjusted OR of 2.16. The NIHSS after 5-7 days was, on average, 2.9 points lower in the experimental group. Recanalization data was available for 394 of 500 subjects, and it was reported that absence of residual occlusion was more common in the intervention group

(75.4% vs. 32.9%). No differences between groups were reported in relation to serious adverse events in the 90-day follow-up period. However, 13 of 233 (5.6%) intervention group subjects had clinical signs of new ischemic stroke in non-downstream vascular tree vs. only 1 control subject. Mortality was no different between groups at any time point measured. The results of this study are promising and demonstrate significant benefit to the use of intra-arterial mechanical interventions.

In 2017 van den Berg and others published the 2-year outcome data from the MR CLEAN study. A total of 391 (78.2%) of the original 500 subjects had data available for the analysis of functional outcomes. The adjusted common OR mRS was 1.68, in favor of the experimental group vs. controls (p=0.007). The authors reported that Subjects in the experimental group were more likely to have a good outcome vs. controls (mRS of 0 to 2, 37.1% vs, 23.9%, respectively, p=0.003). However, among subjects with an excellent outcome (mRS of 0 or 1) no differences between groups were reported (7.2% vs. 6.1%, p=0.64). Additionally, no differences between groups were reported with regard to 2-year cumulative death rate (p=0.46) or the rate of major vascular events (p=0.50). In the sensitivity analysis it was noted that the 103 subjects missing from this 2-year data report had high rates of atrial fibrillation at baseline 35.9 vs. 26.4%, p=0.02), were more likely to be randomized to the control group (62.1% vs. 48.9%, p=0.05), had longer medial time form onset of symptoms to randomization (218 minutes vs. 195 minutes, p=0.003), and were more likely to have poor functional outcomes (mRS or 4 to 5, 57.3% vs. 30.0%, p=0.005).

The Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE) trial was a prospective open-label, blinded endpoint RCT involving 316 subjects with radiologically confirmed intracranial occlusion randomized to undergo treatment with either standard treatment with IV tPA or standard of care plus mechanical embolectomy (Goyal, 2015). Due to the positive outcomes reported in the MR CLEAN trial, the data safety and monitoring board recommended early suspension and interim analysis of the study with only 243 completing the 90-day endpoint. Following analysis, the board concluded that recruitment should be ended and the existing subjects followed to endpoint completion. The final study data included 165 subjects randomized to the experimental group and 150 to the control group. In the experimental group, 14 subjects did not receive the intervention, and 4 were lost to follow-up, leaving 156 subjects completing the trial. The primary outcome of 90-day mRS was assessed by clinicians blinded to group assignment. The common OR of 2.6 was reported, favoring the experimental group (p<0.001). The median mRS at 90 days was 2 in the experimental group and 4 in the control group (p<0.0010). Mortality at 90 days was 10.4% for the experimental group vs. 19.0% in controls (p=0.04). No differences between groups were reported for the incidence of intracerebral hemorrhage (p=0.75). For secondary outcomes, the rate of subjects with a 95 to 100 on the Barthel index at 90 days was 57.7% in the experimental group and 33.6% in the control group (adjusted OR, 1.7). The rate of 90-day NIHSS of 0 to 2 was 5.6% in the experimental group vs. 23.1% in the control group (adjusted OR, 6.5). The authors reported that retrievable stents were used in 130 of the 151 (86.1%) subjects in whom mechanical embolectomy was completed. The Solitaire FR was identified as the device used in 100 (77.0%) of these cases. The identity of the remaining 21 devices was not reported. Finally, in the experimental group 120 of 151 subjects (72.7%) received IV tPA treatment.

Together these studies show the increasing promise of mechanical embolectomy for the treatment of stroke within 6 hours of onset.

In 2017 Dargazanli (2017a) published the findings of a retrospective, non-randomized controlled trial investigating the use of mechanical embolectomy in subjects with minor large vessel occlusion in the anterior circulation. This study involved 301 subjects treated with endovascular therapy with either mechanical embolectomy with a stent retriever or direct aspiration device (n=170), or medical therapy followed by mechanical embolectomy if symptoms worsened (n=131). The mechanical embolectomy group was reported to be younger, have less frequent hypercholesterolemia and left-sided and middle cerebral artery M2 occlusion, and had greater NIHSS values vs. the control group. An excellent outcome, defined as an mRS score of 0 to 1 at 3 months, was achieved in 63.5% (n=191) of subjects overall, with no difference between the 2 groups (OR, 1.15). All-cause mortality within 90 days after symptom onset occurred in 5.0% of participants (n=15) with no difference between the 2 groups. The authors did report a significant difference in the rate of ICH, with it occurring more frequently in the endovascular group (16.5% vs. 6.1%, p=0.008). The authors concluded that individuals with minor-to-mild stroke with large vessel occlusion in the anterior circulation achieved excellent and favorable functional outcomes at 3 months in similar proportions between urgent mechanical embolectomy vs. medical therapy with delayed mechanical embolectomy. They urged further investigation into the use of mechanical embolectomy in this population. It should be noted that the data provided did not stratify results in such a manner to allow differentiation of outcomes in the subjects treated with mechanical embolectomy vs. direct aspiration devices.

This same group (Dargazanli, 2017b) also published the results of a series study involving 138 subjects with large vessel occlusion of the anterior circulation with NIHSS < 8 who received treatment with stent retriever (Trevo or Solitaire devices) or direct aspiration device (Penumbra 5MAX ACE device). The choice of device was left to the discretion of the treating provider. The authors reported successful reperfusion in 81.2% of subjects (n=47 with TICI 2b, n=65 with TICI 3). Excellent outcome (defined as an mRS score of 0 to 1 at 3 months) was achieved in 69 subjects (65.0%), favorable outcome (defined as an mRS score of 0 to 2 at 3 months) in 108 (78.3%), and death occurred in 7 (5.1%). ICH was reported to have occurred in 27 subjects (19.9%) and procedural complications occurred in 11 subjects. Complications included non-occlusive carotid dissections (n=5), arterial perforation (n=1), and vasospasm (n=5). An excellent outcome rate increased with reperfusion grades, with 34.6% of participants with failed/poor reperfusion having excellent outcome in comparison to 61.7% in participants with TICI 2b reperfusion and 78.5% in participants with TICI 3 reperfusion (p<0.001). As with the previous study, these results did not allow differentiation of outcomes in the subjects treated with mechanical embolectomy vs. direct aspiration devices.

Comparative Studies

A small number of nonrandomized comparative studies of different types of endovascular interventions have been published. Broussalis and colleagues (2012) described a study comparing the Merci device with retrievable stents (Trevo and Solitaire devices) in 122 subjects treated with endovascular interventions. A total of 49% of subjects (60/122) underwent treatment with the Merci device, and 51% (62/122) were treated with either the Trevo or Solitaire devices. No data is provided regarding how many subjects received each device in the Trevo-Solitaire group, but the authors noted that there were no statistically significant differences between them. Successful recanalization, as indicated by TICI scores 3 and 2b, was achieved in 82% of subjects treated in the Trevo-Solitaire group vs. 62% of Merci Retriever-treated group (p=0.016). In the 90-day follow-up, 65% of the Trevo-Solitaire group and 35% of the Merci group achieved a good (mRS ≤ 0-2) clinical outcome (p=0.002). Subjects in the Trevo-Solitaire group had significantly less severe intracerebral hemorrhages (10% vs. 28%, p<0.01). A much smaller study by Fesl and colleagues (2012) compared 14 subjects treated with the Solitaire device with 16

subjects treated with older devices (Penumbra separation and aspiration device [n=15], Gooseneck Snare [n=6], Penumbra Thrombus removal ring [n=1], and permanent Wingspan stent [n=2]). TICI scores (> 2b) were achieved in 93% of Solitaire subjects vs. 56% of subjects in the comparison group ($p<0.05$). Favorable outcome, as measured by mRS ≤ 2, was reported as 45% in the Solitaire group and 33% in the comparator group. These studies offer some information on the comparative efficacy of different devices, but do not offer relevant evidence on the comparison of endovascular interventions versus standard stroke care.

In 2017, Hentschel published the results of a study comparing the outcomes between stent and non-stent retriever devices in 166 subjects. The stent retrievers included in this study were the Merci (n=30) and Penumbra devices (n=69), and the non-stent retrievers were the Trevo (n=5) and Solitaire devices (n=62). The non-stent devices were used between 2008 through 2014, and the stent devices were used from 2011 through 2014. The baseline data indicates that the stent cohort had a greater proportion of African Americans ($p=0.04$) and smokers ($p=0.01$). Good clinical outcomes (mRS=0 to 2) were reported to be significantly greater in the stent retriever group vs. the no stent device group (61.67% vs. 22.54%, $p<0.001$). Similar results were noted with regard to 90-day NIHSS score (4.71 vs 2.49, $p=0.008$) and hospital length of stay (8.3 vs. 12.36, $p=0.02$). Recanalization was achieved in 97.01% of the stent device-treated subjects vs. 79.8% of the non-stent subjects ($p<0.001$). The mean number of passes require to achieve success was lower in the stent group (2.23 vs. 2.68, $p<0.001$). The percent of brain salvaged was significantly larger in the stent group (62.3% vs. 28.3%, $p=0.002$). The stent device group has a significantly lower rate of post-treatment hemorrhage (13.43% vs. 40.40%, $p=0.002$), and symptomatic intracranial hemorrhage occurred in 1 stent group subject vs. 7 non-stent group subjects ($p=0.15$). No significant differences between groups was noted with regard to incidence of deep vein thrombosis, decompressive hemicraniectomy or hydrocephalus. These results indicate that the use of stent-type retrievers provide significantly better outcomes in comparison to non-stent devices. However, there are several significant limitations to this study that should be noted. The authors do not describe the device selection process and selection bias may play a role in these results. Additionally, they state in the article that multiple devices were used in several subjects, but they provide no additional information on which devices were used or how many subjects required use of a subsequent device. It is not clear if the subsequent devices were of a similar type and how many subjects were affected.

In 2018, Yi and colleagues published a retrospective study involving 200 subjects who were treated with either the Solitaire (n=102) or Trevo (n=99) devices. They reported that there was no statistically significant difference in NIHSS or mRS outcomes between the 2 groups. However, the Trevo group had shorter procedure time, fewer stent passages, and more one-pass cases than Solitaire group ($p=0.009$, $p=0.014$, $p=0.030$). Additionally, the Trevo group achieved higher successful recanalization (TICI 2b or 3) rate (89.7% vs. 82.3%, $p=0.018$). In multivariate logistic regression analysis, the use of Trevo stent was a predictive for successful recanalization. (OR, 1.40, $p=0.028$). The concluded that the Trevo device results in higher recanalization rates, fewer stent passages, and shorter procedure time than the Solitaire stent.

Pu (2019) conducted a nonrandomized controlled trial involving 89 subjects with AIS assigned to treatment with tPA alone (n=27), tPA+Trevo (n=30), or tPA+Solitaire FR (n=32). The authors reported that at day 1 post-treatment, NIHSS score of the tPA group was significantly lower than that of other two groups ($p<0.05$). However, NIHSS scores for the tPA group was significantly higher than that of other two groups at day 3 and week 3 ($p<0.05$). No significant differences in NIHSS score were reported between the Trevo and Solitaire groups. For both embolectomy groups, the revascularization rate at 90 days was significantly higher, and the mortality rate at 90 days was significantly lower compared to tPA alone ($p<0.05$ for both). No significant differences were found

between the Trevo and Solitaire groups with regard to those outcome measures. However, the incidence of sICH was significantly lower in the Solitaire group than in the Trevo group ($p<0.05$) or the tPA group ($p< 0.01$). Compared to the tPA group, significantly more subjects in both the embolectomy groups had a mRS ≤ 2 points ($p<0.05$). No significant difference was found between the Trevo and Solitaire groups with regard to this measure.

Haussen and colleagues (2019) published the results of a retrospective comparative analysis of the Penumbra 3MAX™ aspiration (Penumbra, Alameda, California) and the 3 mm Trevo for the treatment of distal arterial occlusions. The primary outcome was the rate of distal occlusion first-pass reperfusion as defined by mTICI 2b-3. A total of 137 subjects underwent mechanical thrombectomy, 92 were treated with 3 mm Trevo and 52 were treated with 3MAX. The baseline demographics and occlusion site was comparable between the 2 treatment groups. First-pass mTICI 2b-3 (62% 3 mm Trevo versus 44% 3MAX; p=0.03) and final mTICI 2b-3 (84% 3 mm Trevo versus 69% 3MAX; p=0.05) was higher for individuals treated with 3 mm Trevo; the rate of adjuvant therapy was lower in the 3 mm Trevo group compared with 3MAX (15% versus 31%; p=0.03). The overall safety was comparable between the two groups. The authors concluded that the use of 3 mm Trevo may lead to better outcomes as demonstrated by higher rates of first-pass reperfusion when compared with the 3MAX for the treatment of distal occlusions.

Meta-analyses, Systematic Reviews, and Other Information

Rai and colleagues (2012) described a study comparing subjects who underwent treatment with either IV tPA alone (n=100) or treatment with one of three endovascular procedures (IA tPA, mechanical embolectomy with either the Merci or Penumbra devices or a combination of both, n=120). Overall, the authors reported that there were 45 (20.2%) subjects with an internal carotid artery terminus (ICA-T) occlusion, 107 (48%) with an M1 occlusion, and 71 (31.8%) with an M2 occlusion. Good outcomes were reported in 81 (36.3%) subjects. Mortality was noted in 81 (36.3%) subjects and 27 (12.1%) subjects had significant hemorrhage. Some over-arching observations were that subjects with a favorable outcome had a lower mean age and baseline NIHSS score. Significantly more subjects with a poor outcome had an ICA-T or M1 occlusion, while significantly more subjects with a favorable outcome had an M2 occlusion. In their comparison analysis, good outcomes were seen in 55 subjects (44.7%) in the endovascular group vs. 26 subjects (26%) who received IV tPA (p=0.003). Death rate was not significantly different between groups, nor was the rate of significant hemorrhage. A higher percentage of subjects in the endovascular group had an M1 occlusion while a significantly higher percentage of subjects in the IV group had an M2 occlusion. The authors claimed that these findings demonstrated that for all occlusion sites, subjects undergoing endovascular treatment had significantly higher odds of a favorable outcome than those with IV thrombolysis and the difference was most prominent for ICA-T and M1 occlusions. For M1 occlusions, subjects receiving IV thrombolysis had significantly higher odds of mortality than the endovascular group. A multivariable logistic regression analysis indicated that endovascular therapy, younger age and M2 occlusions were the most significant independent predictors of a good outcome, while a higher NIHSS score and LVO (ICA-T or M1) were the most significant independent predictors of mortality.

A systematic review was published in 2012 that evaluated clinical outcomes from endovascular therapy compared to thrombolysis (Mokin, 2012). The authors limited their analysis to publications that used either thrombolysis or endovascular therapy to treat subjects with acute ICA occlusion. Twenty-eight studies with a total of 385 subjects treated with thrombolysis and 584 subjects treated with endovascular therapy were included in the analysis. No differences in mortality rates were noted between groups (27.3% vs. 32.0%, p=0.12). The endovascular group was

found to have a higher rate of favorable clinical outcomes (as defined by mRS < 2 or Barthel index of 90-100) compared to the thrombolysis group (33.6% vs. 24.9%, p=0.004). The endovascular group had a higher rate of symptomatic intracranial hemorrhage as compared to thrombolysis (11.1% vs. 4.9%, p=0.0011).

Another systematic review of observational studies involving mechanical embolectomy devices (including the Merci, Penumbra, Solitaire or Trevo devices) was published by Almekhlafi and colleagues (2012). The authors identified 16 eligible studies and classified them according to the type of device used. There were 4 studies (n=357) that used the Merci device, 8 studies (n=455) that used the Penumbra system, and 4 studies (n=113) that used a retrievable stent (either the Solitaire or Trevo device). Mean procedural time was 120 minutes for the Merci device, compared to 65 and 55 minutes for the Penumbra and retrievable stents. The successful recanalization rate was 59.1% (211/357) for the Merci group, 86.6% (394/455) for the Penumbra system, and 92.9% (105/113) for the retrievable stent group. Functional independence as indicate by mRS ≤ 2 was achieved in 31.5% of the Merci group, 36.6% in the Penumbra group studies, and 46.9% in the retrievable stent group.

The American Heart Association and American Stroke Association (AHA/ASA) *Focused Update of the 2013 Guidelines for the Early Management of Patients with Acute Ischemic Stroke* (Powers, 2015) recommends that:

2. Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria (Class I; Level of Evidence A). (New recommendation):
    a. Prestroke mRS score 0 to 1,
    b. Acute ischemic stroke receiving intravenous r-tPA within 4.5 hours of onset according to guidelines from professional medical societies,
    c. Causative occlusion of the ICA or proximal MCA (M1),
    d. Age ≥18 years,
    e. NIHSS score of ≥6,
    f. ASPECTS of ≥6, and
    g. Treatment can be initiated (groin puncture) within 6 hours of symptom onset
3. As with intravenous r-tPA, reduced time from symptom onset to reperfusion with endovascular therapies is highly associated with better clinical outcomes. To ensure benefit, reperfusion to TICI grade 2b/3 should be achieved as early as possible and within 6 hours of stroke onset (Class I; Level of Evidence B-R). (Revised from the 2013 guideline)
4. When treatment is initiated beyond 6 hours from symptom onset, the effectiveness of endovascular therapy is uncertain for patients with acute ischemic stroke who have causative occlusion of the ICA or proximal MCA (M1) (Class IIb; Level of Evidence C). Additional randomized trial data are needed. (New recommendation)
5. In carefully selected patients with anterior circulation occlusion who have contraindications to intravenous r-tPA, endovascular therapy with stent retrievers completed within 6 hours of stroke onset is reasonable (Class IIa; Level of Evidence C). Inadequate data are available at this time to determine the clinical efficacy of endovascular therapy with stent retrievers for those patients whose contraindications are time based or not time based (eg, prior stroke, serious head trauma, hemorrhagic coagulopathy, or receiving anticoagulant medications). (New recommendation)
6. Although the benefits are uncertain, the use of endovascular therapy with stent retrievers may be reasonable for carefully selected patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the M2 or M3

portion of the MCAs, anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries (Class IIb; Level of Evidence C). (New recommendation)

7. Endovascular therapy with stent retrievers may be reasonable for some patients <18 years of age with acute ischemic stroke who have demonstrated large-vessel occlusion in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset, but the benefits are not established in this age group (Class IIb; Level of Evidence C). (New recommendation)
8. Although its benefits are uncertain, the use of endovascular therapy with stent retrievers may be reasonable for patients with acute ischemic stroke in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score >1, ASPECTS <6, or NIHSS score <6 and causative occlusion of the ICA or proximal MCA (M1) (Class IIb; Level of Evidence B-R). Additional randomized trial data are needed. (New recommendation)
9. Observing patients after intravenous r-tPA to assess for clinical response before pursuing endovascular therapy is not required to achieve beneficial outcomes and is not recommended. (Class III; Level of Evidence B-R). (New recommendation)
10. Use of stent retrievers is indicated in preference to the MERCI device. (Class I; Level of Evidence A). The use of mechanical thrombectomy devices other than stent retrievers may be reasonable in some circumstances (Class IIb, Level B-NR). (New recommendation)

It must be noted that these new recommendations primarily address the use of "stent retrievers," which would include the Solitaire and Trevo devices, but not the Merci or Penumbra devices. These latter devices are referred to as mechanical clot disruption/extraction devices in the 2013 Guideline (Jauch, 2013), and are mentioned in statement # 10 above as alternatives in some cases. Unfortunately, the guidelines do not provide guidance as to what those circumstances may be.

Broderick and colleagues published the results of the National Institutes of Neurological Disorders and Stroke (NINDS) funded, international IMS III Trial in early 2013. This large, phase III randomized study of IV tPA versus IV tPA followed by intra-arterial therapies was subsequently stopped early due to futility after the first 656 subjects were randomized (434 to endovascular treatment and 222 to IV tPA). The interim analysis by the data management board for this study found no significant differences between the two groups with regard to the blinded primary endpoint (mRS at 90 days), or between any pre-specified secondary outcomes among subgroups. These findings are echoed in the report of another large, randomized trial by the Synthesis Expansion investigators (Ciccone, 2013). This study enrolled 362 subjects randomly assigned to receive IV tPA (n=181) or endovascular therapy (n=181) without initial IV tPA treatment. No significant difference between groups was noted with regard to the blinded endpoint of mRS at 90 days, or any other endpoint including deaths or complications at 7 days. Subgroup analysis also found no significant differences. It should be noted that both these trials involved a variety of endovascular devices, including the Merci Retriever, the Trevo Retriever, and the Solitaire and Penumbra devices. Finally, the results of the NINDS MR RESCUE (Magnetic Resonance and Recanalization of Stroke Clots Using Embolectomy) study were published in the same edition of the New England Journal of Medicine (Kidwell, 2013). The purpose of this randomized controlled, blinded outcome study involving 118 subjects was to compare the effectiveness of treating acute ischemic stroke with mechanical embolectomy using the Merci Retrieval System or the Penumbra System within 8 hours of symptom onset to standard medical treatment and the possible benefits of identifying people who might benefit from mechanical embolectomy with multimodal computerized tomography (CT) or magnetic resonance (MR) imaging. The authors reported that there was no significant

difference between treatment groups (embolectomy vs. medical treatment) or between imaging methods with regard to the primary outcome (90-day mRS), or any secondary outcomes.

In an editorial accompanying the IMS III publication, the author noted that, while there was some data to suggest that there was a trend to significance for newer stent-like devices, further trials were warranted to evaluate the use of these newer technologies (Chemowitz, 2013). He also commented that recruitment for these studies was made difficult by the assumption of superiority of endovascular therapies. He then concluded that, "It is hoped that equipoise will return on the basis of these three trials." Equipoise is an important consideration in medical research. When equipoise is not present, it is not ethical to randomize between two treatments. Chemowitz's comments and the AHA/ASA *Guidelines for the Early Management of Patients with Acute Ischemic Stroke* (Jauch, 2013) both support the need for and appropriateness of additional randomized trials to evaluate the role of mechanical embolectomy in the treatment of stroke.

Multiple meta-analyses addressing the use of mechanical embolectomy were published involving the same pooled dataset from the MR CLEAN, ESCAPE, REVASCAT, and EXTEND-IA trials described above. Overall, 1287 subjects were included in these studies. Saver et al. (2016) reported on time to treatment and functional outcomes. They found that the degree of benefit, as measured by overall mRS score, declined with longer times from symptom onset to arterial puncture (common OR [cOR], 2.79 at 3 hours, 1.98 at 6 hours, and 1.57 at 8 hours). Similarly, the odds of functional independence also declined with longer time to treatment (OR, 2.38 at 3 hours, 2.23 at 6 hours. and 2.03 at 8 hours). Finally, disability outcomes at 90 days followed the same trend, declining with longer time to treatment in the endovascular group (cOR, 2.79 at 3 hours, 1.98 at 6 hours, and 1.57 at 8 hours). Notably, it was found that among 390 participants who achieved substantial reperfusion with endovascular thrombectomy, each 1-hour delay to reperfusion was associated with a less favorable degree of disability (cOR, 0.84) and less functional independence (OR, 0.81), but no change in mortality (OR, 1.12). Touma and colleagues (2016) also investigated the benefits and risks of using stent retrievers in addition to tPA for the treatment of strokes with similar results. They concluded that subjects treated with stent-retriever therapy in addition to tPA had significantly improved rates of functional independence at 90 days compared with those randomized to tPA alone (Relative Risk [RR], 1.72). However, the impact of mechanical embolectomy on all-cause mortality at 90 days was inconclusive (RR=0.82). There were similarly no detectable differences in the risks of intracranial hemorrhage (RR, 1.15) or parenchymal hematoma (RR, 1.18). Goyal (2016) also reported that mechanical thrombectomy led to significantly reduced disability at 90 days compared with control treatment (cOR, 2.49; $p<0.0001$). They found that the number needed to treat with endovascular thrombectomy to reduce disability by at least one level on mRS for 1 subject was 2.6. Interestingly, a subgroup analysis of the primary endpoint demonstrated no heterogeneity of treatment effect across prespecified subgroups for reduced disability ($p_{interaction}=0.43$). Effect sizes favoring endovascular thrombectomy over control treatment were present in several strata, including in subjects aged 80 years or older (cOR, 3.68), those randomized more than 300 minutes after symptom onset (cOR, 1.76), and those not eligible for tPA (cOR, 2.43). They also reported that mortality at 90 days and risk of parenchymal hematoma and symptomatic intracranial hemorrhage did not differ between populations.

Campbell (2016), using the same dataset but limited to subjects treated specifically with the Solitaire device, conducted a meta-analysis to evaluate the efficacy and safety of mechanical thrombectomy using the Solitaire device in anterior circulation ischemic stroke. Their primary analysis involved 787 subjects (n=401 treated with Solitaire and n=386 controls). The cOR for mRS improvement was 2.7 with no heterogeneity in effect by age, sex, baseline stroke severity, extent of computed tomography changes, site of occlusion, or pretreatment with tPA.

Successful revascularization occurred in 77% of those treated with the Solitaire device. The rate of symptomatic intracerebral hemorrhage and overall mortality did not differ between treatment groups.

Gretch (2016) reported the results of a meta-analysis assessing the recanalization rates and long-term functional outcomes of the Solitaire and Trevo devices. This study involved pooled data from 20 trials meeting inclusion criteria, 17 using the Solitaire and 3 using the Trevo, with n=762 and n=210 subjects, respectively. The authors reported that use of the Solitaire device resulted in a lower mortality rate compared to Trevo device (16.2% vs. 22.2%) and achieved a higher rate of functional independence (52.1% vs. 47.6%). Statistical tests, however, failed to demonstrate significant differences between groups in functional outcomes, 3-month mortality rates, or weighted mean recanalization rates. They concluded that no significant differences in functional outcomes, mortality, and symptomatic intra-cranial hemorrhage could be demonstrated between the Trevo and Solitaire devices.

Rodrigues (2016) reported the results of a meta-analysis involving 10 RCTs (n=2925) in pooled analysis addressing the efficacy and safety of endovascular treatment. As with the previously discussed reports above, they reported that endovascular treatment, including thrombectomy, was associated with a higher proportion of participants experiencing good (mRS scores ≤ 2) and excellent (scores ≤ 1) outcomes 90 days after stroke, without differences in mortality or rates for symptomatic intracranial hemorrhage, compared with standard medical care alone. A subgroup analysis of the seven most recent studies yielded an RR=1.56 for good functional outcomes and RR=0.86 for mortality, without heterogeneity among the results of the studies. The authors concluded that the risk of bias was moderate across studies.

A study by published by Haussen (2019) retrospectively evaluated the outcomes of 420 stent retriever procedures, stratifying them by the use of long retrievers (n=221, Trevo 4×30 mm/Solitaire 4×40 mm) vs. short retrievers (n=199, Trevo 4×20 mm/Solitaire 4×20 mm). They reported that subjects in the short retriever group had more frequent hypertension, dyslipidemia, and atrial fibrillation. First-pass mTICI 2b/3 reperfusion was more common in the long retriever group vs. the short group (62% vs 50%; p=0.01). The incidence of parenchymal hematomas type 2, subarachnoid hemorrhage, 90-day modified Rankin Scale score 0-2, and mortality were comparable between groups. In multivariable analysis, the results indicated that long retriever (OR, 2.2; p=0.001), radiopaque device (OR 2.1; p=0.003), and adjuvant local aspiration (OR 2.4; p=0.003) were independently associated with first-pass reperfusion. They concluded that use of longer stent retrievers is an independent predictor of first-pass mTICI 2b/3 reperfusion.

Mokin and others (2018) evaluated pooled real-world data from 830 subjects with anterior circulation acute ischemic stroke in the NASA and TRACK registries to compare outcomes of subjects presenting within the first hours 6 vs. beyond 6 hours of stroke symptom onset. A total of 32.7% (271/830) underwent thrombectomy beyond the first 6 hours of symptom onset. Subjects were stratified to those treated within 6 hours, between 6 and 16 hours, and between 16 and 24 hours. The authors reported that the rates of "good" clinical outcome, defined as mRS of 0-2 at 90 days, were similar between groups (48.1% for ≤ 6 hours, 46.2% for >6 ≤ 16 hours, and 38% for > 16 hours, p=0.08). Mortality was likewise similar (20.6%, 21.6%, and 3.3%, respectively, p=0.06), as was symptomatic intracranial hemorrhage (8.0%, 10.9%, and 5%, respectively, p=0.5). The rates of successful recanalization, defined as TICI 2b/3, were 79.4% in subjects with stroke within 0-6 hours, 72.6% within 6-16 hours, and 85.0% within 16-24 hours (p=0.04). They concluded that the real-world experience in subjects with

anterior circulation AIS treated with the Solitaire and Trevo devices beyond the first 6 hours of symptom onset proved to be equally safe and effective as for individuals with symptom onset within the first 6 hours.

In 2018 the American Heart Association Council on Cardiovascular Radiology and Intervention and Stroke Council published their indications for the performance of intracranial endovascular neurointerventional procedures (Eskey, 2018). In this document they provided the following recommendations:

2. Endovascular therapy with stent retrievers is recommended over intra-arterial fibrinolysis as first line therapy.
4. Use of stent retrievers is preferred over other mechanical thrombectomy devices. The use of mechanical thrombectomy devices other than stent retrievers may be reasonable in some circumstances but is not yet supported by large RCTs.
5. In carefully selected patients with anterior circulation occlusion who have contraindications to intravenous r-tPA, endovascular therapy with stent retrievers completed within 6 hours of stroke onset is reasonable. Inadequate data are available at this time to determine the clinical efficacy of endovascular therapy in such patients (eg, those with prior stroke, serious head trauma, hemorrhagic coagulopathy, or receiving anticoagulant medications).
8. When treatment is initiated beyond 6 hours from symptom onset, the effectiveness of endovascular therapy is uncertain for patients with AIS who have causative occlusion of the ICA or proximal MCA (M1). New trial results addressing this topic will be available in the near future.
9. Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1, (2) AIS receiving intravenous r-tPA within 4.5 hours of onset according to guidelines from professional medical societies, (3) causative occlusion of the ICA or proximal MCA (M1), (4) age ≥18 years, (5) NIHSS score of ≥6, (6) ASPECTS of ≥6, and (7) ability to initiate treatment (groin puncture) within 6 hours of symptom onset.

Use of the Solitaire device in subjects with ASPECTS 0-5 was investigated in the BEYOND-SWIFT registry study (Kaesmacher, 2019). This retrospective, international, multicenter observational study involved 1532 subjects, 237 with ASPECTS 0–5 and 1295 with ASPECTS >5. The overall rates of favorable outcome (mRS 0-3 at day 90) and mortality at day 90 were 40.1% and 40.9%. The authors reported that successful reperfusion was independently associated with favorable outcome (adjusted odds ration [aOR], 5.534), functional independence (aOR, 5.583), reduced mortality (aOR, 0.180), and lower rates of sICH (aOR, 0.235). The mortality-reducing effect remained in subjects with ASPECTS 0-4 (aOR, 0.167).

Mechanical Embolectomy in the Posterior Circulation

Treatment for AIS within the anterior circulation is well established; newer studies are exploring utilizing mechanical embolectomy for posterior circulation occlusions (Meyer, 2020; Stambo, 2020; Watson, 2020; Zhao, 2020). The systematic review conducted by Meyer (2020) found that successful recanalization occurred in 86% (37/43) of individuals. The Thrombolysis in Cerebral Infarction Scale (TICI) measured 3 (2b is successful with ≥ 50% reperfusion) in those with a first past-effect (48.8%, 21/43). sICH occurred in 7% (3/43), 1 perforation and 2 iatrogenic vessel dissections; the in-hospital mortality rate was 9.3% (4/43). Strambo and colleagues (2020) published results of a retrospective cohort study of individuals with posterior cerebral artery occlusions treated with endovascular treatment (utilizing stent retrievers) or best medical therapy. Of the individuals treated with stent retrievers, 68% (13/19) had complete recanalization at 24 hours. Although initial outcomes were promising, the

frequency of sICH and 3-month mortality were similar between those treated with stent retrievers and individuals treated with best medical therapy. Watson and colleagues (2020) published the results of a systematic review for mechanical thrombectomy treatment of acute posterior circulation occlusions. A total of 1612 individuals with acute posterior circulation AIS were treated and successful reperfusion was achieved in 86%. However, there was also an average rate of 16% (132/840, with numerous studies not reporting adverse events) of periprocedural and postoperative complications and a 30% mortality rate. Zhao and colleagues (2020) conducted a meta-analysis and systematic review for the safety and efficacy of mechanical thrombectomy for posterior versus anterior large vessel occlusions. The authors reported that reperfusion rates were similar for anterior and posterior recanalization, but the mortality rate was higher for individuals with posterior occlusions (OR=1.98; 95% CI, 1.37-2.87; p=0.0003).

Meinel (2019) reported the results of a study involving 1739 subjects included in the retrospective observational BEYOND-SWIFT registry who had large vessel occlusion treated with the Solitaire device. Mechanical embolectomy was conducted in subjects with either basilar artery occlusion (n=165) or anterior circulation large vessel occlusion (ACLVO) (n=1574). Complete 90-day follow-up data were available in 152 (91.1%) of the basilar group. It was not clear what percentage of the ACLVO group has complete 90-day data. Compared to the ACLVO group at baseline, the basilar group was significantly different with regard to age (younger), gender (more males), transferred from other hospitals (more frequent), symptom severity and glucose (both higher), anticoagulation pretreatment, hypertension, and dyslipidemia (all lower) ($p<0.05$ for all). Time from symptom onset to groin puncture was longer in basilar group vs. the ACLVO group ($p<0.001$). Recanalization of mTICI 2b/3 was achieved in 90.3% of Basilar group subjects vs. 82.7% of ACLVO subjects (p=0.11). Intracranial stents were used in significantly more basilar group subjects (17.0% vs 2.3%, $p<0.001$). Longer times from symptom onset to groin-puncture were also reported (300min vs 225min, $p<0.001$). The authors reported no significantly differences in the rates of sICH, systemic bleeding, craniectomy, and complication rates. However, subjects in the basilar group had significantly more frequent nonhemorrhagic worsening postoperatively. Overall, the basilar group has worse outcomes, with mRS scores 0-3 reported 46.1% in the basilar group vs. 56.7% in the ACVLO group (p=0.013), and higher mortality rates of 36.2 vs. 24.4%, respectively (p=0.002). However, the authors stated that after adjustment for baseline differences, no significant differences in outcomes were found., with the exception of futile recanalization, which was more frequent in the basilar group (aOR, 2.146). On unadjusted analysis, better outcomes were observed in basilar group subjects vs. those without successful recanalization. However, significantly higher rates of independence at 3 months were found only in the cohort of patients presenting with ACLVO. The authors concluded that in selected individuals, similar outcomes can be achieved with mechanical embolectomy of the basilar artery as those in the anterior circulation, but that additional research was needed to establish proper selection criteria and interventional strategies to avoid futile recanalization.

Liu and colleagues (2020) reported the findings of a randomized, open-label, blinded outcome assessment study involving 131 subjects with vertebrobasilar occlusion presenting at <8 hrs. The trial was terminated early due to high crossover rate and poor recruitment. The intention-to-treat analysis included 130 subjects who were treated with either thrombectomy (n=66) or medical therapy (n=65). The type of thrombectomy devices were not specified but included both stent retrievers and aspiration catheters. The authors reported evidence of a difference in the proportion of participants with mRS 0-3 at 90 days according to treatment (42% in the thrombectomy group vs. 32% in the control group; OR, 1.74). A secondary, prespecified analyses of the primary outcome was done to assess the effect of crossovers. It demonstrated higher rates of mRS 0-3 at 90 days in subjects who received thrombectomy vs. those who received medical therapy alone in both per-protocol analysis (44% vs. 25%, aOR, 2.90) and in the intent-to-treated analysis (47% vs. 24%, aOR, 3.02. at 90-days). Mortality was similar between

groups despite a higher prevalence of sICH in the thrombectomy group (33% vs. 38%, p=0.54). The authors concluded, "There was no evidence of a difference in favorable outcomes of patients receiving endovascular therapy compared with those receiving standard medical therapy alone. Results might have been confounded by loss of equipoise over the course of the trial, resulting in poor adherence to the assigned study treatment and a reduced sample size due to the early termination of the study."

Meyer and colleagues (2021) reported the results of the TOPMOST Study, a multicenter case-control trial involving subjects with primary distal occlusion of the P2 or P3 segments of the posterior cerebral artery treated with either mechanical embolectomy or medical therapy. The type of embolectomy devices used was not specified, but it was stated that both stent retrievers and aspiration catheters were used. Of the 313 subjects with posterior circulation distal medium vessel occlusion (DMVO) receiving, 243 met inclusion criteria, and 184 subjects were compared by treatment group after 1:1 propensity score matching (n=92 subjects in each group, thrombectomy vs. medical therapy). At baseline, diabetes as a cardiovascular risk factor was significantly higher in the control group vs. the thrombectomy group (30 vs. 14, respectively, p=0.006). Additionally, the medical therapy group received intravenous thrombolysis significantly more frequently than and thrombectomy group, both before and after propensity matching, (39% vs. 56%, p=0.01 and 40% vs. 57.7%, p=0.01, respectively). A total of 141 subjects received mechanical thrombectomy, with first pass being done with a stent retriever with or without aspiration in 72% of subjects and 26% of subjects undergoing direct distal aspiration. Successful first pass reperfusion (mTICI 3) occurred in 45.5% of cases. Additional passes increase the overall success rate to 76.2%. Distal embolization to another vessel was reported in 5 subjects (3.5%), with successful recanalization of those locations in 3 subjects. Post-propensity score matching, mean baseline NIHSS scores had decreased from admission in both groups, with there being no significant differences between groups (-2 in the thrombectomy group vs. -1.5 in the medical group, p=0.06). However, there was a significant benefit in favor of subjects in the thrombectomy group with >10 NIHSS score on admission vs. the medical group (mean difference 5.6, p=0.04). No significant differences between groups were also noted in the subgroup of subjects with an mTICI of 2a or lower (p=0.13). In the thrombectomy group two independent factors were identified for predicting successful early neurological improvement, higher NIHSS scores (p<0.001) and successful first pass effect (p=0.04). In the medical group, only the presence of P3 occlusions were predictive of successful early neurological improvement (p=0.021). At 90 days, excellent neurological outcomes (mRS≤1) were reported in 66.2% of thrombectomy group subjects vs. 54.4% of medical group subjects. No p-values were provided for this comparison. sICH was reported in 4.3% of subjects in both groups. Similarly, overall mortality was 4.9% in both groups at 90 days. The authors concluded that the study suggested that "…mechanical thrombectomy for posterior circulation DMVO is a safe, and technically feasible treatment option for occlusions of the P2 or P3 segment of the PCA compared with standard medical treatment with or without IVT." However, additional rigorous studies should be conducted to confirm these findings.

Langezaal (2021) reported the results of an RCT involving 300 subjects with basilar artery occlusion assigned to treatment with either mechanical embolectomy (n=154) or medical therapy (n=146). The investigators used a variety of devices, including the MERCI, Penumbra, Solitaire, and Trevo devices. All subjects were followed for a minimum of 90 days. At baseline the embolectomy group had a significantly high rate of atrial fibrillation (28.6% vs. 15.1%, no p-value provided). Crossover occurred in 3 subjects (1.9%) in the embolectomy group and 7 (4.8%) in the medical therapy group. No significant differences were reported between groups in the number of subjects with favorable outcomes as defined as an mRS 0-3 at 90 days (44.2% vs. 37.7%, p=0.19). Favorable reperfusion (mTICI of 2b or 3) was reported in 72% of the endovascular subjects, but no data was provided for the medical therapy group. However, arterial patency based on CTA was reported in 84.5% in the embolectomy group vs.

56.3% in the medical group (no p-value provided). No differences in 90-day mortality was reported (38.3% vs. 43.2%, respectively, p=0.29). Similarly risk of sICH at 3 days was not significantly different (4.5% vs. 0.7%, p=0.06). The authors concluded,

> Among patients with stroke from basilar-artery occlusion, endovascular therapy and medical therapy did not differ significantly with respect to a favorable functional outcome, but, as reflected by the wide confidence interval for the primary outcome, the results of this trial may not exclude a substantial benefit of endovascular therapy. Larger trials are needed to determine the efficacy and safety of endovascular therapy for basilar-artery occlusion.

Further study is warranted to further identify the impact of mechanical embolectomy on posterior circulation occlusions. The available evidence is currently unclear regarding potential benefits, including reperfusion and functional outcomes.

Non-FDA approved devices

Embolus Retriever with Interlinked Cages (ERIC)

Gruber and colleagues (2018) reported the results of a new device, the Embolus Retriever with Interlinked Cages (ERIC, MicroVention, Tustin, California), in a retrospective case series study involving 183 consecutive subjects treated with either ERIC (49%) or another stent retriever device (51%) as the first device. Successful recanalization was seen in 82% of ERIC subjects and 57% in the control group, respectively (p<0.001). Adding a non-ERIC device to futile ERIC recanalization or vice versa increased final recanalization rates (ERIC: 87%, Controls: 79%). The use of ERIC as a first device resulted in favorable clinical outcome in 50% vs. 35% when another stent retriever device was used (p=0.038). However, the authors noted that this result was due to age, stroke severity, presence of carotid-T-occlusion, and general anesthesia, and not by the device deployed. FDA approval of this device is pending.

ReVive SE Thrombectomy Device

Use of the ReVive SE Thrombectomy Device (Integra LifeSciences, Princeton, NJ) has been described in several studies. Sakai and others (2018) reported on the results of the River JAPAN study, which was a case series study involving 49 subjects with AIS, mainly of the MCA (83.7%), and median NIHSS score of 17. Subjects were followed for 90 days. Post-intervention TICI of ≥ 2a was reported in 73.5% of subjects. Successful recanalization without ICH was reported in 62.5% of subjects, and good neurological outcomes were reported in 66.7% of subjects. Device-related AEs included ICH in 9 subjects (18.4%), intraoperative cerebral artery occlusion in 6 subjects (12.2%), and subarachnoid hemorrhage in another 6 subjects (12.2%). The most frequent procedure-related adverse event was ICH in 9 subjects (18.4%), followed by intraoperative cerebral artery occlusion in 7 subjects (14.3%) and subarachnoid hemorrhage in 6 subjects (12.2%). The rate of serious adverse events at 90 days was 37%, although the authors do not provide specific information regarding what events occurred. Death was reported for 2 subjects, one with worsening ischemic stroke and another with occlusive mesenteric ischemia. Device malfunction was reported in 13 cases (26.5%), of which 5 (10.2%) were considered device related.

Zhang (2019) described the results of the RAPID trial, a prospective case series study involving 100 subjects with AIS of the MCA (n=54), ACA (n=3), ICA (n=22), basilar artery (n=14), and vertebral artery (n=4) treated with the ReVive SE stent retriever. Median NIHSS core was 16. Time from onset to intervention was not reported. The

Revive SE device was used as the only device in 73 (73%) subjects. The other 27 cases involved the use of the Solitaire stent (n=15), while angioplasty with balloon and/or stent was used in 17 cases (including those treated receiving a Solitaire devise). Favorable revascularization was achieved in 92 subjects (n=47 with mTICI 2b and n=45 with mTICI 3), and 6 subjects were recanalized partially to mTICI 2. The overall reperfusion rate without rescue devices was 83.3% in MCA M2 segment, followed by 82.4% in basilar artery, 75.0% in vertebral artery, 68.8% in MCA M1 segment and 66.7% in extracranial segment of ICA. Median time from symptom onset to admission was 187 minutes. The authors reported that additional thromboembolic occlusion of a previously unaffected artery was observed in 5 of 100 cases, and distal embolization events in 5 cases. Intraparenchymal hemorrhage was detected in 7 subjects, post-procedure subarachnoid hemorrhage occurred in 1 subject, and sICH within 24 hours was seen in 2 cases. At 24 hours post-procedure the median NIHSS score was 9 ($p< 0.001$ vs. baseline). A total of 48 subjects achieved favorable outcome (mRS ≤ 2) at 90 days after the intervention, and mortality at 90-day follow-up was 19%.

RECO Flow Restoration Device

In 2021 Cao and colleagues published the results of a trial comparing the RECO Flow Restoration Device (Minitech Medical [Jiang Su] Co., Ltd., China) to the Solitaire FR device in the REDIRECT Study. This multicenter, prospective, open randomized controlled trial involved 138 subjects with LVO treated with either the RECO Flow Restoration Device (n=67) or the Solitaire FR stent retriever (n=69). The authors reported that the primary efficacy endpoint (mTICI grade ≥ 2 within three passes) was not significantly different between groups (91% vs. 87%, respectively, p=0.5861). Reperfusion rate with an mTICI grade 2b/3 was 87% vs. 75% (p=0.1272). Likewise, the rates of sICH (1.5% vs. 7.2%, p=0.1027), serious adverse events within 24 hours after the procedure (6.0% vs. 1.4%, p=0.2050), rate of functional independence (63% vs. 46%, p=0.0609) or 90-day all-cause mortality (13% vs. 23%, p=0.1848) were not significantly different between groups. They concluded, "The RECO stent retriever is effective and safe as a mechanical thrombectomy device for AIS due to LVO." However, additional studies to support these findings are warranted.

These results are promising. Additional data are needed to demonstrate equivalency to the currently available, FDA approved devices.

Conclusion

The available evidence addressing the use of mechanical embolectomy devices is extensive; with earlier studies there was significant heterogeneity with regard to subject populations, devices compared, control or comparison groups and other methodologic limitations. However, more recent data from large, well-designed, and conducted studies (Berkhemer, 2014; Campbell, 2014, 2015; Goyal, 2015; Joval, 2015; Saver, 2015) have demonstrated significant benefits to mechanical embolectomy/thrombectomy in select individuals. Furthermore, recently published postmarketing registry data have demonstrated continued significant benefit to the use of stent retriever devices outside the trial setting. Additional investigation is needed to demonstrate if similar results may be gained with devices that are not yet FDA approved.

Background/Overview

A stroke is a condition where blood flow to the brain is interrupted to the extent that proper brain function is disrupted. Over 750,000 strokes occur annually in the United States. Some strokes are caused by blockage of the

blood vessels to the brain, which frequently results in neurologic emergencies. The use of tissue plasminogen activator (tPA), a drug that dissolves blood clots, is frequently given intravenously within 3 hours of symptoms for treatment of strokes due to blocked blood vessels. Another treatment, called mechanical embolectomy, has been proposed to reopen occluded vessels in the brain, either alone or in conjunction with tPA treatment, by physically extracting occlusive thrombi from the cerebral vasculature.

Several mechanical embolectomy devices have received FDA clearance through the 510(k) process; including the EmboTrap II device, the Merci Retrieval System, the Penumbra System, the Solitaire FR Revascularization Device, and the Trevo Retriever. These devices are designed to be placed into an artery of a stroke victim and, with the guidance of x-ray imaging technology, advanced to the site of the clot in the brain. Once near the site of the blood clot, these types of devices use one of several methods to capture the clot and remove it. It is proposed that by removing the clot, normal blood flow to the brain is restored, which in turn may reduce any damage caused by the lack of blood flow.

There are currently two different design types of mechanical embolectomy devices available in the U.S. The first are referred to as "stent retrievers", which use a stent-like metal structure to ensnare the target clot and remove it. The EmboTrap II device, Penumbra System, Solitaire FR Revascularization Device, and Trevo Retriever are all of this type. The other type involves the use of a metal coil at the end of the device, similar to a corkscrew, which is placed into the clot to remove it. The Merci Retrieval System is of this type.

Definitions

Alberta Stroke Program Early Computed Tomography Score (ASPECTS): A 10-point quantitative topographic CT scan score developed to assess early ischemic changes on pretreatment CT studies in individuals with acute ischemic stroke of the anterior circulation. ASPECTS is determined from evaluation of two standardized regions of the MCA territory, including the basal ganglia level and the supraganglionic level. The abnormality should be visible on at least two consecutive cuts to ensure that it is truly abnormal rather than a volume averaging effect. To compute the ASPECTS, 1 point is subtracted from 10 for any evidence of early ischemic change for each of the defined regions. A normal CT scan receives ASPECTS of 10 points. A score of 0 indicates diffuse involvement throughout the MCA territory.

Embolectomy: Surgical removal of an obstructing clot or foreign material which has been transported from a distant vessel by the bloodstream.

Emboli: Material (usually a blood clot but may be fat or a bone fragment, etc.) that travels through the circulation and eventually obstructs blood flow through a smaller caliber vessel.

National Institute of Health Stroke Scale (NIHSS): A systematic assessment tool that provides a quantitative measure of stroke-related neurologic deficit. The scale is widely used as a clinical assessment tool to evaluate acuity of stroke patients, determine appropriate treatment, and predict patient outcome. It is a 15-item neurologic examination evaluating the effect of acute cerebral infarction on the levels of consciousness, language, neglect, visual-field loss, extraocular movement, motor strength, ataxia, dysarthria, and sensory loss. The Score is intended to be used by a trained observer who rates an individual's ability to answer questions and perform activities. Ratings for each item are scored with 3 to 5 grades with 0 as normal, and there is an allowance for untestable items. The single assessment requires less than 10 minutes to complete.

Neurovasculature: The blood vessel network of the neck and brain.

Plasmin: A proteolytic enzyme that is formed from plasminogen in blood plasma and dissolves the fibrin in blood clots; also called fibrinolysin.

Precerebral arteries: An arterial blood vessel leading to the cerebrum (but not in the cerebrum), including the vertebral artery, basilar artery, carotid artery, and ascending aorta.

Stroke: A condition where blood flow to the brain is interrupted to the extent that proper brain function is disrupted.

Thrombolytics: Drugs that dissolve blood clots.

Tissue plasminogen activator (tPA): An enzyme that dissolves blood clots. It can be produced naturally by cells in the walls of blood vessels, or prepared through the use of genetic engineering. Tissue plasminogen activator is used in the coronary arteries during heart attacks and in the cranial arteries in certain types of strokes.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met:

CPT

	For the following procedure codes when describing embolectomy/thrombectomy of middle cerebral, anterior cerebral or intracranial carotid arteries:
61645	Percutaneous arterial transluminal mechanical thrombectomy and/or infusion for thrombolysis, intracranial, any method, including diagnostic angiography, fluoroscopic guidance, catheter placement, and intraprocedural pharmacological thrombolytic injection(s)

ICD-10 Procedure

03CG3Z7	Extirpation of matter from intracranial artery using stent retriever, percutaneous approach
03CG3ZZ	Extirpation of matter from intracranial artery, percutaneous approach
03CG4ZZ	Extirpation of matter from intracranial artery, percutaneous endoscopic approach

ICD-10 Diagnosis

G45.0-G45.9	Transient cerebral ischemic attacks and related syndromes
I63.30	Cerebral infarction due to thrombosis of unspecified cerebral artery
I63.311-I63.319	Cerebral infarction due to thrombosis of middle cerebral artery
I63.321-I63.329	Cerebral infarction due to thrombosis of anterior cerebral artery

I63.39	Cerebral infarction due to thrombosis of other cerebral artery
I63.40	Cerebral infarction due to embolism of unspecified cerebral artery
I63.411-I63.419	Cerebral infarction due to embolism of middle cerebral artery
I63.421-I63.429	Cerebral infarction due to embolism of anterior cerebral artery
I63.49	Cerebral infarction due to embolism of other cerebral artery
I63.81-I63.9	Cerebral infarction other or unspecified
R29.702-R29.709	NIHSS score 2-9
R29.710-R29.719	NIHSS score 10-19
R29.720-R29.742	NIHSS score 20-42
Z92.82	Status post administration of tPA (rtPA) in a different facility within the last 24 hours prior to admission to current facility

When services are Investigational and Not Medically Necessary:
For the following procedure and diagnosis codes, or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT

	For the following procedure codes when describing embolectomy/thrombectomy of other cerebral or precerebral arteries:
61645	Percutaneous arterial transluminal mechanical thrombectomy and/or infusion for thrombolysis, intracranial, any method, including diagnostic angiography, fluoroscopic guidance, catheter placement, and intraprocedural pharmacological thrombolytic injection(s)

ICD-10 Procedure

03CH3Z7-03CJ4ZZ	Extirpation of matter from common carotid artery [right or left, by approach, with or without stent retriever; includes codes 03CH3Z7, 03CH3ZZ, 03CH4ZZ, 03CJ3Z7, 03CJ3ZZ, 03CJ4ZZ]
03CK3Z7-03CL4ZZ	Extirpation of matter from internal carotid artery [right or left, by approach, with or without stent retriever; includes codes 03CK3Z7, 03CK3ZZ, 03CK4ZZ, 03CL3Z7, 03CL3ZZ, 03CL4ZZ]
03CM3Z7-03CN4ZZ	Extirpation of matter from external carotid artery [right or left, by approach, with or without stent retriever; includes codes 03CM3Z7, 03CM3ZZ, 03CM4ZZ, 03CN3Z7, 03CN3ZZ, 03CN4ZZ]
03CP3Z7-03CQ4ZZ	Extirpation of matter from vertebral artery [right or left, by approach, with or without stent retriever; includes codes 03CP3Z7, 03CP3ZZ, 03CP4ZZ, 03CQ3Z7, 03CQ3ZZ, 03CQ4ZZ]
03CS3ZZ-03CT4ZZ	Extirpation of matter from temporal artery [right or left, by approach; includes codes 03CS3ZZ, 03CS4ZZ, 03CT3ZZ, 03CT4ZZ]

ICD-10 Diagnosis

G45.0-G45.9	Transient cerebral ischemic attacks and related syndromes
I63.00-I63.09	Cerebral infarction due to thrombosis of precerebral arteries
I63.10-I63.19	Cerebral infarction due to embolism of precerebral arteries

I63.20-I63.29	Cerebral infarction due to unspecified occlusion or stenosis of precerebral arteries
I63.331-I63.349	Cerebral infarction due to thrombosis of posterior cerebral or cerebellar artery
I63.431-I63.449	Cerebral infarction due to embolism of posterior cerebral or cerebellar artery
I63.50-I63.59	Cerebral infarction due to unspecified occlusion or stenosis cerebral arteries
I63.81-I63.9	Cerebral infarction other or unspecified
Z92.82	Status post administration of tPA (rtPA) in a different facility within the last 24 hours prior to admission to current facility

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The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	11/11/2021	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Rationale and References sections.
Reviewed	11/05/2020	MPTAC review. Updated Rationale and References sections.
Reviewed	11/07/2019	MPTAC review. Updated Rationale and References sections.
	10/01/2019	Updated Coding section with 10/01/2019 ICD-10-PCS changes; removed codes for bifurcation (ending in Z6) deleted 09/30/2019.
Revised	11/08/2018	MPTAC review. Made minor clarification to MN statement. Updated Rationale and References sections.
	09/20/2018	Updated Coding section with 10/01/2018 ICD-10-CM diagnosis and ICD-10-PCS code changes.
Revised	03/22/2018	MPTAC review. Added new MN criteria for individuals last known to be well 6 to 16 hours earlier. Updated Rationale and References sections.
Revised	01/25/2018	MPTAC review. The document header wording updated from "Current Effective Date" to "Publish Date." Updated formatting in Position Statement section. Added new MN criteria for individuals who were last known to be well 6 to 24 hours earlier. Updated Rationale, Coding, and References sections.
Reviewed	05/04/2017	MPTAC review. Updated formatting in "Position Statement" section. Updated Rationale and References sections.
	10/01/2016	Updated Coding section with 10/01/2016 ICD-10-PCS procedure code changes.
Revised	05/05/2016	MPTAC review. Removed MN criteria related to age. Added NM criteria regarding type of device. Updated Rationale and References sections.
	01/01/2016	Updated Coding section with 01/01/2016 CPT changes, removed 37184, 37185 (no longer applicable); also removed ICD-9 codes.
Revised	08/06/2015	MPTAC review. Clarified medically necessary criteria regarding neuroimaging.
Revised	05/07/2015	MPTAC review. Revised position statement to consider mechanical embolectomy/ thrombectomy medically necessary with criteria. Updated Rationale, Coding and References sections.
Reviewed	11/13/2014	MPTAC review. Updated Rationale and References sections.
Reviewed	11/14/2013	MPTAC review. Updated Rationale and References sections.
Reviewed	11/08/2012	MPTAC review. Updated Rationale, Background, Definitions and References sections.
Reviewed	05/10/2012	MPTAC review. Rationale updated to include Solitaire device. Background, Definitions and References updated.
Reviewed	02/16/2012	MPTAC review. Rationale and References updated.
Reviewed	02/17/2011	MPTAC review. Rationale and References updated.
Reviewed	02/25/2010	MPTAC review. Rationale and References updated.
Reviewed	02/26/2009	MPTAC review. Rationale, Background and References updated.
Reviewed	02/21/2008	MPTAC review. Updated references. The phrase "investigational/not medically necessary" was clarified to read "investigational and not medically necessary" at the November 29, 2007 MPTAC meeting.
New	03/08/2007	MPTAC review. Initial document development.