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.

**Medically Necessary:**

Intra-arterial mechanical embolectomy or thrombectomy is considered **medically necessary** in the treatment of acute ischemic stroke when the following criteria have been met:

- Individual is 18 years of age or older; AND
- Angiographic studies have confirmed proximal arterial occlusion of the anterior circulation of the brain, in any of the following anterior intracranial arteries:
  - Intracranial carotid; OR
  - Middle cerebral artery (M1 or M2); OR
  - Anterior cerebral artery (A1 or A2); AND
- Intra-arterial mechanical embolectomy is performed within 6 hours of onset of symptoms; AND
- NIH Stroke Scale (NIHSS) score of 2 or greater; AND
- CT or MRI scan has ruled out intracranial hemorrhage or arterial dissection.

**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 stroke and are currently under investigation.

**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].

The MERCI trial 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 (Smith, 2005). 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.

The Multi MERCI trial was designed in part to evaluate the safety and effectiveness of the Merci Retrieval System in conjunction with intravenous tissue plasminogen activator (IV tPA) as well as the safety of the next generation design of the device, the L-5
Retriever (Smith, 2006). 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 modified Rankin Scale (mRS) and NIHSS scores. At 90 days, 37% of the participants achieved a 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 a 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.

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 (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.

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 a 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=0.011). 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 neurologic 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 a 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.

As a follow-up study, Tarr and others conducted a 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 a 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<0.01). 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.

**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 thrombolysis in cerebral infarction (TICI) \( \geq 2b \) after \( \leq 3 \) passes of the study device was reported as 79.2% (160/202). In 42 subjects (20.8%), TICI \( \geq 2b \) 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 symptomatic ICH (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 \((11.1\% \text{ vs. } 7.2\%)\).

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 \((89\% \text{ vs. } 34\%, p<0.001)\). Similarly, the co-primary endpoint of early neurologic improvement as measured by greater than or equal to 8 point reduction on the NIHSS was also significantly in favor of the experimental group \((28\% \text{ vs. } 13\%, p<0.001)\). 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 Bérkhemer 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 \((\text{common OR}=1.7)\) favoring thrombectomy. The absolute between-group difference in the proportion of subjects who were functionally independent \((\text{mRS score, 0-2})\) was 15.5 percentage points, more frequent in the intervention group than in the control group \((83\% \text{ vs. } 40\%, p=0.001)\). Successful reperfusion \((\geq 90\%)\) at 27 hours, assessed by means of perfusion CT or MRI, was more frequent in the intervention group than in the control group \((83\% \text{ vs. } 40\%, p=0.001)\). No significant differences between groups were reported with regard to 90 day mortality \((9\% \text{ vs. } 12\%, p=0.50)\) or symptomatic intracranial hemorrhage \((0\% \text{ vs. } 3\%, p=0.12)\).

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 \((\text{mRS score, 0 to 2})\) was higher in the experimental group than in the control group \((60\% \text{ vs. } 35\%, p=0.001)\). Successful reperfusion \((\geq 90\%)\) at 27 hours, assessed by means of perfusion CT or MRI, was more frequent in the intervention group than in the control group \((83\% \text{ vs. } 40\%, p=0.001)\). No significant differences between groups were reported with regard to 90 day mortality \((9\% \text{ vs. } 12\%, p=0.50)\) or symptomatic intracranial hemorrhage \((0\% \text{ vs. } 3\%, p=0.12)\).

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.

There is currently one case series study addressing the use of the Trevo Retriever in subjects with acute stroke (San Román, 2012). This prospective, single-center study included 60 subjects with stroke. 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.

**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 Alberta Stroke Program Early Computed Tomography Score (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 one 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 odds ratio 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 odds ratio 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.

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 safety and monitoring board recommended early suspended 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 odds ratio 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.

**Meta-analyses, Systematic Reviews, and Other Information**

A small number of nonrandomized comparative studies of different types of endovascular interventions have been published. Broussalis and colleagues described a study comparing the Merci device with newer retrievable stents (Trevo and Solitaire devices) in 122 subjects treated with endovascular interventions (2012). Forty-nine percent 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 Thrombolysis in Cerebral Infarction [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 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]). Successful recanalization (as indicated by TICI scores > 2b) was achieved in 93% of Solitairesubject 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.

Rai and others 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) (2012). 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 internal carotid artery (ICA) occlusion. Twenty-eight studies with a total of 385 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) *Guidelines for the Early Management of Patients with Acute Ischemic Stroke* (Jauch, 2013) recommends that:

5. When mechanical thrombectomy is pursued, stent retrievers such as Solitaire FR and Trevo are generally preferred to coil
retrievers such as Merci (Class I; Level of Evidence A). The relative effectiveness of the Penumbra System versus stent retrievers is not yet characterized. (New recommendation)

6. The Merci, Penumbra System, Solitaire FR, and Trevo thrombectomy devices can be useful in achieving recanalization alone or in combination with pharmacological fibrinolysis in carefully selected patients (Class IIa; Level of Evidence B). Their ability to improve patient outcomes has not yet been established. These devices should continue to be studied in randomized controlled trials to determine the efficacy of such treatments in improving patient outcomes. (Revised from the previous guideline)

7. Intra-arterial fibrinolysis or mechanical thromboectomy is reasonable in patients who have contraindications to the use of intravenous fibrinolysis (Class IIa; Level of Evidence C). (Revised from the previous guideline)

8. Rescue intra-arterial fibrinolysis or mechanical thromboectomy may be reasonable approaches to recanalization in patients with large-artery occlusion who have not responded to intravenous fibrinolysis. Additional randomized trial data are needed (Class IIb; Level of Evidence B). (New recommendation)

9. The usefulness of mechanical thromboectomy devices other than the Merci retriever, the Penumbra System, Solitaire FR, and Trevo is not well established (Class IIb; Level of Evidence C). These devices should be used in the setting of clinical trials. (Revised from the previous guideline)

It should be noted that Statements 5, 6, 8, and 9 all include cautionary statements or comments regarding the uncertainty regarding the efficacy of mechanical embolectomy devices. Additionally, they specifically state that "Their ability to improve patient outcomes has not yet been established. These devices should continue to be studied in randomized controlled trials to determine the efficacy of such treatments in improving patient outcomes." These guideline recommendations note the lack of data showing improved clinical outcomes and reinforce the need for additional randomized data.

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.

Conclusion

The available evidence addressing the use of mechanical embolectomy devices is extensive; with earlier studies there was significant heterogeneity with regard to patient 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.

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 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.

**Definitions**

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.

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.

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

03CG3ZZ-03CG4ZZ

Exirpation of matter from intracranial artery [by 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

I63.8-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

**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
03CH3ZZ-03CJ4ZZ Extirpation of matter from common carotid artery [right or left, by approach; includes codes 03CH3ZZ, 03CH4ZZ, 03CJ3ZZ, 03CJ4ZZ]
03CK3ZZ-03CL4ZZ Extirpation of matter from internal carotid artery [right or left, by approach; includes codes 03CK3ZZ, 03CK4ZZ, 03CL3ZZ, 03CL4ZZ]
03CM3ZZ-03CN4ZZ Extirpation of matter from external carotid artery [right or left, by approach; includes codes 03CM3ZZ, 03CM4ZZ, 03CN3ZZ, 03CN4ZZ]
03CP3ZZ-03CQ4ZZ Extirpation of matter from vertebral artery [right or left, by approach; includes codes 03CP3ZZ, 03CP4ZZ, 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
I63.8-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

References

Peer Reviewed Publications:


Government Agency, Medical Society and Other Authoritative Publications:


**Index**

Mechanical embolectomy
Mechanical thrombectomy

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**

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<thead>
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<th>Status</th>
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<tr>
<td>Revised</td>
<td>01/01/2016</td>
<td>Updated Coding section with 01/01/2016 CPT changes, removed 37184, 37185 (no longer applicable); also removed ICD-9 codes.</td>
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<tr>
<td>Revised</td>
<td>08/06/2015</td>
<td>Medical Policy &amp; Technology Assessment Committee (MPTAC) review. Clarified medically necessary criteria regarding neuroimaging.</td>
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<td>Revised</td>
<td>05/07/2015</td>
<td>MPTAC review. Revised position statement to consider mechanical embolectomy/ thrombectomy medically necessary with criteria. Updated Rationale, Coding and Reference sections.</td>
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<td>11/13/2014</td>
<td>MPTAC review. Updated Rationale and Reference sections.</td>
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<td>11/14/2013</td>
<td>MPTAC review. Updated Rationale and Reference sections.</td>
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<td>11/08/2012</td>
<td>MPTAC review. Updated Rationale, Background, Definitions and Reference sections.</td>
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<td>05/10/2012</td>
<td>MPTAC review. Rationale updated to include Solitaire device. Background, Definitions and References updated.</td>
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<td>MPTAC review. Updated references. The phrase &quot;investigational/not medically necessary&quot; was clarified to read &quot;investigational and not medically necessary&quot; at the November 29, 2007 MPTAC meeting.</td>
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**New**

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Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

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