Mechanical recanalization in acute stroke treatment

Pasquale Mordasini, Gerhard Schroth, Jan Gralla*

Institute of Diagnostic and Interventional Neuroradiology, Inselspital, University of Bern, Switzerland

Summary
Endovascular stroke treatment is a rapidly evolving field in neurointerventions. The article reviews the evolution of the different mechanical thrombolysis and stenting techniques and their working principles for endovascular vessel recanalization and reviews the data on the outcome after acute stroke treatment.

Introduction
Ischemic stroke is one of the leading causes of disability and mortality in industrialized countries. Patient outcome mainly depends on the time span between onset of symptoms and revascularization, recanalization rate and the occurrence of symptomatic intracranial hemorrhage (sICH) [1]. Therefore, fast and effective reperfusion in combination with a low rate of sICH is the key to successful stroke treatment. Systemic thrombolysis with intravenously administered tissue plasminogen activator (IV rtPA) and local intra-arterial thrombolysis (IAT) have been shown to be effective to improve patient outcome. However, the time window for treatment and the recanalization rate of both methods are limited [2–4]. Furthermore, the application of thrombolytic drugs increases the risk of sICH [5]. Moreover, recanalization rate is dependent on the site of occlusion: proximal occlusions of large brain supplying vessels such as the internal carotid artery have a limited recanalization rate after either IV rtPA or IAT [3,4]. Therefore, the aim of mechanical recanalization approaches is to improve recanalization rates, reduce the time to recanalization and further expand the window of opportunity. Furthermore, the waiving of thrombolytic drugs is considered to reduce the rate of symptomatic intracranial hemorrhage.

Mechanical treatment approaches
Different techniques and approaches have been advocated for mechanical thrombolysis in acute stroke treatment, which can be divided into: immediate flow restoration using self-expandable stents and thrombectomy.

Stent recanalization
Placement of a permanent intracranial stent achieves immediate flow restoration and recanalization by compressing the thrombus against the vessel wall. Stenting allows fast and effective recanalization without the need of repetitive procedures.
passing of the occlusion site and retrieval attempts. However, this concept has some disadvantages in general and especially in the setting of acute stroke treatment. Thrombus compression may lead to permanent side branch or perforator occlusion. Moreover, permanent stent placement needs double platelet anti-aggregation medication in order to prevent in-stent thrombosis and re-occlusion. This preventive medication may increase the risk of sICH in the setting of acute stroke [6]. Furthermore, an in-stent restenosis rate of bare metal stents has been reported in up to 32% in the treatment of intracranial arteriosclerotic stenosis after a follow-up period of 9 months [7]. The use of different stent systems has been reported in case reports and small case series. In general, self-expandable stents are preferentially used over balloon-mounted stents.

Recanalization rates are reported to be between 79% and 92% with moderate clinical outcome in 33–50% [8,9]. The Stent-Assisted Recanalization in Acute Ischemic Stroke (SARIS) trial is the first FDA approved prospective trial investigating stenting in acute stroke treatment. 20 patients (mean NIHSS 14) were included within 6 h after symptom onset. Recanalization rate was 100% with adjuvant therapies such as angioplasty, IV tPA and IAT applied in 63% of patients. Moderate clinical outcome was achieved in 60% of patients [10,11].

Despite the high recanalization rate reported in these studies, the use of intracranial stenting in acute stroke treatment is debatable due to the risks associated with permanent stent deployment and the recent success of thrombectomy. However, stenting has a clear value in selective cases of rescue therapy.

**Mechanical thrombectomy**

All mechanical thrombectomy devices are delivered by endovascular access proximal to the occlusion site. The various systems can be divided into 3 major groups according to where they apply mechanical force on the thrombus:

(a) Proximal devices apply force to the proximal base of the thrombus. This group includes various aspiration catheters and systems.

(b) Distal devices approach the thrombus proximally but then are advanced by microguidewire and microcatheter across the thrombus to be unsheathed behind it, where force is applied to the distal base of the thrombus. This group includes brush-like, basket-like or coil-like devices.

(c) The most recently developed devices include stent-like devices, which are placed across the thrombus at the occlusion site, deployed within the thrombus and then are retrieved. This group includes various types of self-expandable, retrievable, stent-like devices, so-called stent retrievers.

**Proximal thrombectomy using thrombus aspiration**

Vascular access is usually gained with a 7–8-F sheath. After placement of the guiding catheter, a large dedicated aspiration catheter (4–5-F) flexible enough to pass the tortuosity of the cranial vessels (e.g. carotid siphon) is navigated to the proximal surface of the thrombus. Aspiration force is applied to the thrombus using a 60-ml syringe. The aspiration catheter is then retrieved under constant negative pressure to avoid loss of thrombus material. This approach omits repetitive passing of the occlusion site and after each retrieval of clot fragments, the procedure can be repeated. The advantages of this approach are that it is mechanically simple, fast to apply and inexpensive. Therefore, it is widely used, especially in proximal occlusions where the target vessel has a large diameter and an anatomy favorable for device navigation such as the distal cervical internal carotid artery and the carotid artery terminus. Although first reports on mechanical thrombectomy included the use of aspiration catheters [12,13], only few systematic data have been published on this approach so far. A recent single-center study reported on 22 patients (mean NIHSS 18) treated with aspiration thrombectomy alone with a recanalization rate of 81.9% and a good clinical outcome in 45.5% [14].

**Penumbra System.** The Penumbra System (Penumbra, Almeda, USA) is a modification of the proximal aspiration technique. It has been FDA approved for clot removal in acute stroke treatment in 2007. It consists of a reperfusion catheter attached to continuous aspiration via a dedicated pumping system. A microwire with an olive-shaped tip, called separator, is used to fragmentize the thrombus from proximal to distal and to avoid obstruction of the aspiration catheter by cleaning the catheter tip of clot fragments. Both reperfusion catheter and separator are available in various sizes and diameters (0.26–0.51 in.) to adjust the device to different anatomical settings and to allow thrombectomy even in distal branches such as M2 segments.

The Penumbra System has been investigated in several single-center and multicenter trials. The Penumbra Pivotal Stroke Trial [15] prospectively evaluated 125 stroke patients (mean NIHSS 18) within 8 h after onset of symptoms. Successful recanalization of the target vessel was achieved in 81.6%. Despite the relatively high recanalization rate, favorable clinical outcome was achieved in only 25% of all patients and in 29% of patients with successful recanalization. Overall mortality was 32.8% and sICH occurred in 11.2% with serious adverse events in 3.2%. The high recanalization rate in conjunction with the poor clinical outcome in this trial sparked the discussion on the impact of recanalization using mechanical thrombectomy. However, some single-center studies reported more favorable clinical results with the Penumbra System and then the Pivotal Trial with successful recanalization in 93%, good clinical outcome in 48% and reduced mortality of 11% [16].

**Distal thrombectomy**

Compared to IAT and the use of proximal devices, the use of distal thrombectomy devices is technically more complex. An 8F sheath and balloon catheter of similar size are used. After placement of the balloon catheter in the internal carotid artery, a microcatheter (0.18–0.27 in.) is navigated across the occlusion site to pass the thrombus. The device is then introduced into the microcatheter and unsheathed behind the thrombus. This approach applies the retrieval force to the distal base of the thrombus. The device and thrombus are then retracted into the guide catheter under balloon occlusion and additional aspiration.
Figure 1 74-year-old male patient 4.5 h after acute onset of right hemiplegia and aphasia, at admission NIHSS 18, bridging therapy. (A) Digital subtraction angiogram of the left internal carotid artery, illustrating proximal occlusion (arrow) of the middle cerebral artery (MCA). (B) Application of a stent-retriever: a microcatheter and microwire are advanced beyond the occlusion side (arrow) and placed into the distal branches of the MCA (*). (C) Angiogram immediately after placement of a stent-retriever (Solitaire FR) covering the occlusion (arrow). The device compresses the thrombus and creates a channel; a temporary bypass to the distal branches of the MCA (*). (D) After retrieval of the device 5 min later complete recanalization of the MCA main trunk (arrow) and the distal branches. (E) The stent-retriever device (arrow) after the successful thrombectomy with the entangled clot from the MCA (*). The patient recovered to NIHSS 5 after 24 h, mRS 1 after 90 days.

Clinical observations have shown that thrombectomy using distal devices has the risk of potentially dislodging thrombotic material during retrieval from the occlusion site into a previously unaffected vascular territory. Such embolic events may worsen the patient’s neurological condition. Therefore, distal thrombectomy devices are regularly used in combination with proximal balloon occlusion in the internal carotid artery in conjunction with aspiration from the guiding catheter in order to reduce the risk of thromboembolic events during retrieval. Furthermore, vasospasm and vessel wall damage have been reported more frequently in association with distal thrombectomy devices. Various distal thrombectomy devices with brush-like, basket-like or coil-like designs have been advocated in the past (e.g. Catch, Balt, Montmorency, France; Phenox pCR and CRC, Bochum, Germany), with most of them only available in Europe. The largest clinical experience has been reported on the Merci Retrieval System (Concentric Medical, Mountain View, USA), which is the first device of this group to receive FDA approval in 2004.

Merci Retrieval System. The Merci Retrieval System is somehow the pioneer of intracranial device development for acute stroke treatment. FDA approval was based on the multicenter Mechanical Embolus Removal in Cerebral Ischemia (MERCI) trial [17]. 151 patients (mean NIHSS 20) were evaluated within 8 h after onset of symptoms, who were ineligible for standard IAT. Successful recanalization was achieved in 46% of patients with favorable clinical outcome in 27.7%. Mean procedure time was 2.1 h. Clinically significant procedural complications occurred in 7.1% and rate of sICH was 7.8%. The Multi-MERCI trial [18] was a prospective, multicenter, single-arm registry that included 164 patients (mean NIHSS 19) within 8 h after onset of symptoms. In contrast to the MERCI trial, patients with persistent large vessel occlusion after IV tPA were also included in the study, adjunctive IAT using rtPA and the use of other mechanical recanalization techniques and new generation of Merci devices were allowed. Recanalization success was 57.3% using the Merci device alone and 69.5% in conjunction with other treatment modalities. Favorable clinical outcome was achieved in 36% of patients with clinical significant complications in 5.5% and sICH in 9.8%. Mean time to recanalization was 1.6 h.

The introduction of the Merci device was a landmark of mechanical recanalization in acute stroke treatment. Both MERCI trials demonstrated a significantly
better clinical outcome in patients with successful recanalization.

**Stent retriever.** The most recent developments for mechanical acute stroke treatment are self-expandable, retrievable, stent-like thrombectomy devices. They combine the advantages of intracranial stent placement with immediate flow restoration without the need of permanent device implantation and the advantages of a thrombectomy system with the ability of definitive clot removal. This concept offers a promising new treatment option for acute ischemic stroke with high recanalization rates, marked reduction in procedure time and a marked elevation in the rate of favorable clinical outcome. Stent retrievers are applied in a comparable manner to that of intracranial stents. The occlusion site is passed with a microcatheter (0.21–0.27 in.) and the device is deployed over the entire thrombus. Due to its radial force, the device compresses the thrombus against the contralateral vessel wall leading to immediate partial flow restoration to the distal vessel territory. After an embedding time of 3–10 min the device is retrieved. As for distal thrombectomy devices the use of proximal balloon occlusion and aspiration during retrieval is recommended in order to avoid thromboembolic events.

Several stent retrievers with different designs are currently under development or evaluated in first clinical trials (Trevo, Concentric Medical, Mountain View, USA; PULS and 3D Separator, Penumbra, Alameda, USA; Revive, Micrus, USA; Aperio, Acandis, Pforzheim, Germany; Bonnet and pReSet, Phenox, Bochum, Germany).

The first dedicated combined flow restoration and thrombectomy device for acute stroke treatment was the Solitaire FR (ev3, Irvine, USA). The device is a modification of the Solitaire AB Neurovascular Remodeling Device, originally developed for stent-assisted coil treatment of wide-necked intracranial aneurysms. Within a short period of time several in vivo and clinical studies have reported about the application of the Solitaire FR for acute stroke treatment (Fig. 1).

The first clinical experience was published by Castano et al. [19] in 2010 reporting their initial treatment of 20 patients within 8 h after onset of symptoms. Successful recanalization was achieved in 90% of patients with a favorable clinical outcome in 45%. Mean procedure time was short with 50 min. sICH occurred in 10%. Several other small case series using various stent retrievers have shown similar promising successful recanalization rates (88–91%) and fast procedural times (42–55 min) with comparable rates of favorable clinical outcome (42–54%) [20–22]. Rohde et al. [23] reported their preliminary experience with the Revive system (Micrus Endovascular, San Jose, USA) in the treatment of large vessel occlusion in 10 patients (mean NIHSS 19). The design of the Revive system consists of a closed basket at the distal end of the stent in order to enhance clot removal. Successful recanalization (TICI 2b or 3) was achieved in all patients with favorable outcome in 60% of patients after 30 days. The Solitaire FR with the Intention for Thrombectomy (SWIFT) trial is a randomized trial comparing the efficacy and safety of the Solitaire FR with that of the Merci device. The SWIFT trial was halted by the data monitoring board early in 2011 after inclusion of 126 patients of anticipated 250 patients. The results have not yet been published, but favorable results for the Solitaire FR can be assumed. The Solitaire FR is currently evaluated in the Solitaire FR Thrombectomy for Acute Revascularization (STAR) trial, a prospective, multicenter, single-arm study with an enrolment goal of 200 patients. The study includes patients within 8 h after symptom onset ineligible for or with failed IV rtPA as a bridging therapy or thrombectomy as initial treatment. First results are expected in mid-2012.

**Conclusion**

Immediate flow restoration is the principle goal of ischemic stroke therapy and is associated with better clinical outcome and reduced mortality. The introduction of mechanical approaches has expanded the time window for stroke treatment and broadened the spectrum of stroke patients for treatment. The latest results of MT using stent-retrievers demonstrate high recanalization rates in conjunction with short recanalization times and a low-risk device-related severe adverse event. Furthermore, recent data show that the increased recanalization rate of MT improves clinical outcome.

The future role of MT in acute stroke treatment is not clear yet. Considering the poor recanalization rate and clinical outcome of patients with proximal vessel occlusions and large thrombus burden (e.g. internal carotid artery occlusion), MT is likely to become a first-line treatment.

**References**


