Mechanical Thrombectomy for Acute Ischemic Stroke
Thrombus–Device Interaction, Efficiency, and Complications In Vivo

Jan Gralla, MD; Gerhard Schroth, MD; Luca Remonda, MD; Krassen Nedeltchev, MD; Johannes Slotboom, PhD; Caspar Brekenfeld, MD

Background and Purpose—Mechanical thrombectomy is a promising new modality of interventional stroke treatment. The various devices differ with regard to where they apply force on the thrombus, taking a proximal approach such as aspiration devices or a distal approach such as basket-like devices. The study compares the in vivo effectiveness and thrombus–device interaction of these 2 approaches.

Methods—Angiography and embolization with a radioopaque whole blood thrombus was performed in 10 swine. Mechanical thrombectomy was performed in 20 cranial vessels using a proximal aspiration device (Vasco35) and a distal basket-like device (Catch) with and without proximal balloon occlusion. Fifty-six retrieval attempts were made.

Results—The proximal device allowed fast repeated application with a low risk of thromboembolic events (3%) and vasospasm, but it had a significantly lower success rate (39.4%) in retrieving thrombotic material than the distal device (DD) (82.6%; odds ratio, 7.3; 95% CI, 2.0 to 26.4). The compaction of the thrombus during retrieval with DD increased the risk of vessel wall irritation significantly \( (P<0.01) \) and complicated retrieval into the guiding catheter. The number of embolic events was significantly higher with DD (26%; odds ratio, 11.3; 95% CI, 1.35 to 101.6) unless proximal balloon occlusion was used.

Conclusions—The proximal and the distal approaches to mechanical thrombectomy proved to be effective at achieving recanalization of cranial vessels. The proximal device is faster in application and allowed repeated attempts with a low complication rate. The DD is more successful at removing thrombotic material, but its method of application and attendant thrombus compaction increase the risk of thromboembolic events and vasospasms. (Stroke. 2006;37:3019-3024.)

Key Words: animal models ■ embolic stroke ■ interventional neuroradiology ■ stroke

Intra-arterial thrombolysis has improved the prognosis of patients with acute ischemic cerebrovascular stroke. The time window for effective intra-arterial thrombolysis is brief, and the outcome depends on the length of time between onset of symptoms and recanalization and the recanalization rate. Recent studies examined whether mechanical thrombectomy can accelerate the process of recanalization, increase the recanalization rate, and even expand the window of opportunity. Some authors report a benefit from mechanical thrombectomy compared with thrombolysis. Most studies have relied on primarily clinical data in advocating various devices for this novel and rapidly developing technique of endovascular intervention.

All mechanical thrombectomy devices are delivered by endovascular access proximal to the occlusion site. The various devices can be divided into 2 major groups according to where they apply force on the thrombus: proximal devices (PDs) apply force to the proximal base of the thrombus (this group includes various aspiration catheters); distal devices (DDs) approach the thrombus proximally but then are advanced by guide wire and microcatheter past the thrombus to be unsheathed behind it, where force is applied to the distal base of the thrombus (this group includes snare-like, basket-like, or coil-like devices). Two commercially available DDs are the Catch device (Balt) and the Merci Retrieval System (Concentric Medical, Inc). No in vivo studies have yet systematically compared these 2 major principles of mechanical thrombectomy in the treatment of acute cerebrovascular stroke.

The present study uses an animal model using a radio-opaque whole blood thrombus to compare the in vivo effectiveness of the proximal approach (PD Vasco 35 catheter) to the distal approach (DD Catch device) with regard to thrombus–device interaction, retrieval success, and complication rates.

Methods

Animals

All procedures are approved by the responsible local animal care committee. Ten swine ranging in weight from 43 to 48 kg were used in this study. General anesthesia was maintained by 2% isoflurane.
and 2 L/min N₂O inhalant. Expired carbon dioxide levels were kept between 30 and 35 mm Hg. The animals were euthanized after the experiments.

### Thrombus Preparation

In acute cerebrovascular stroke, whole blood thrombus or “red thrombus” predominates in the occluded vessel.¹⁴ To reproduce the situation in human stroke, thrombi of 25×3 mm were generated. We therefore prepared the blood clot for selective thromboembolization by mixing 10 mL autologous blood with 25 IU bovine thrombin (Dade Behring Inc). To increase x-ray absorption, 1 g barium sulfate was added. After mixing for 10 s, the blood was injected into a silicone tube (3 mm; ClinicoMedical) and incubated for 60 minutes at room temperature. The radio-opacity allows visualization of thrombus movement in real time as well as detection of the dislocation of fragments to peripheral vessels.

The thrombus was then washed in physiological saline solution and incubated for an additional 20 minutes before application. The radioopaque barium sulfate does not cause local or systemic reactions during the study interval.¹³

### Study Protocol

Surgery was performed on each animal through a groin approach for preparation of the common femoral artery and vein under general anesthesia. A 9 French catheter sheath (Arrow International Inc.) was introduced into the common femoral artery and flushed continuously with heparinized physiological saline (10 U/mL). A central venous catheter was placed in the common femoral vein for constant venous access.

Selective intra-arterial digital subtraction angiography was performed on a biplane high-resolution angiography system (Toshiba CAS500). Selective angiography was done on the lingual artery (LA) and internal carotid artery (ICA). Two vessels per animal were occluded. The mean vessel size was 2.7 mm for both proximal and distal clot retrieval (range 2.4 to 3.2 mm). After thrombus application, the guiding catheter was removed for 5 minutes to restore arterial flow and allow embedding of the thrombus (Figure 1).

The 4.2 French in diameter Vasco +35 catheter (Balt) for thrombus aspiration and the Catch device (Balt) were used for mechanical thrombectomy (Figure 2). Aspiration was performed by vacuum suction with a 20-mL syringe. The Catch device was delivered using a microwire (SilverSpeed 14; MTI) and Vasco 21 microcatheter (Balt). To assess the influence of proximal balloon occlusion on the success rate and complications such as thrombus dislocation and vasospasm, the devices were tested with (half of the occlusions) and without proximal balloon occlusion using a 9 French Merci balloon guider (Concentric Medical, Inc) in the common carotid artery.

The number of attempts for a device to retrieve the thrombus was limited to 5 attempts per thromboembolic occlusion. After the fifth attempt without success, the clot retrieval was rated as failed. During the study, a total of 20 vessels (10 LA and 10 ICA) were occluded, and 56 retrieval attempts were performed. A follow-up angiography was performed to evaluate the recanalization rate and detect potential complications.

The following data were recorded: (1) thrombus movement and distal dislocation, fragmentation, and thromboembolization; (2) recanalization rate using the thrombolysis in myocardial infarction scale (TIMI; 0 to 3);¹⁵ (3) number of vasospasms in case of recanalization using a grading scale:¹⁶ 0, no narrowing; 1, slight narrowing (<25% reduction in lumen diameter); 2, moderate nar-

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**Figure 1.** Digital subtraction angiography in anterior–posterior projection (a) of the cranial common carotid artery (CCA) in swine showing the origins of the ICA, the LA, and the maxillary artery (MA). After selected thromboembolization of the ICA (b, without digital subtraction angiography; c, with digital subtraction angiography) with a radiopaque thrombus (>) using a 7 French guiding catheter (*), total occlusion of the vessel is documented in the control angiography (d).

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**Figure 2.** The Vasco +35 microcatheter (4.2 French) is a dedicated aspiration device with a blunt tip (ID 1.02 mm). The approach allows aspiration and force application at the proximal base of the thrombus (a). To deliver the Catch device, the thrombus is passed by microwire and microcatheter. The basket-like Catch device is unsheathed behind to the obstruction, and the site of force is the distal base of the thrombus (b).
rowing (25% to 50% stenosis or 50% to 75% stenosis affecting only a short segment of vessel); and 3, severe narrowing (50% to 75% stenosis affecting a long segment of vessel or any stenosis >75%); (4) vessel dissection or perforation; (5) success rate and time per attempt; and (6) site where thrombotic material was lost during retrieval.

Student t test was used for between-group analysis and Mann–Whitney test for comparison of vasospasm grading. The odds ratio (OR) and 95% CI were applied to compare the probability of successful thrombus retrieval and embolization rate with the 2 devices.

Results

Proximal Device

Efficiency and Complications

Overall, 10 occlusions were treated with the PD. In 7 of 10 occlusions (70%) the PD led to total recanalization of the vessel (TIMI 3), and in 30% (3 of 10), no recanalization could be achieved (TIMI 0). In all 33 attempts performed with the PD (mean 3.3 attempts per occlusion; range 2 to 5), the device was easily navigated to the thrombus. In none of the occlusions, total clot removal was achieved on the first attempt. Thrombotic material was removed successfully in 13 of 33 attempts (39.4%) but could not be removed in the remaining 20 attempts (60.6%). During 4 attempts (12.1%), the thrombus was lost in the carrying vessel. In none of the attempts, the thrombus was dislocated distally in the carrying vessel, and in 1 attempt (3%), a thromboembolic event occurred in different vessels. The mean vasospasm rating after recanalization was 1.6 (range 0 to 2), and no dissection or perforation occurred. Proximal balloon occlusion had no significant influence on the success and embolization rates or vasospasm.

The mean time between introduction of the device into the sheath and the first retrieval attempt was 9 minutes. The mean time per attempt for subsequent attempts was slightly shorter (6.3 minutes). The mean time in case of successful recanalization with proximal aspiration was 20.7 minutes.

Distal Device

Efficiency and Complications

Overall, 10 vessel occlusions were treated with the DD. The distal approach allowed total recanalization (TIMI 3) in 8 of 10 occlusions (80%). In 2 occlusions, the thrombotic material was partially removed, but no recanalization was achieved (TIMI 0). A total of 23 attempts (mean 2.3; range 1 to 3) were made with the DD. In 2 occlusions, the very first attempt led to complete thrombus removal and recanalization. In 19 of 23 attempts (82.6%), the device was able to remove thrombotic material, and in only 4 attempts (17.4%), it failed to retrieve any clot. This retrieval success was significantly higher than the results in the PD trial (OR, 7.3; 95% CI, 2.0 to 26.4). In 2 attempts (2 of 23; 8.7%), the initial passage of the microcatheter led to distal dislocation of the thrombus in the carrying vessel (unrelated to the proximal balloon occlusion). In 6 of 23 attempts (26%), thrombotic material was lost during retrieval in the carrying vessel and led to thromboembolic occlusion of a different vessel (Figure 4). This rate is significantly higher than with PD (OR, 11.3; 95% CI, 1.3 to

Thrombus–Device Interaction

Evaluation of the thrombus–device interaction revealed that the PD typically led to an initial elongation of the thrombus. In the 20 unsuccessful attempts, aspiration produced initial movement of the thrombus, but the applied force was not sufficient for retrieval or fragmentation of the thrombus. In 9 attempts, the proximal base of the thrombus entered the microcatheter tip during aspiration. This phenomenon led to a significantly higher retrieval rate compared with the attempts without thrombus entering the catheter tip (OR, 20.3; 95% CI, 3.1 to 132.3). Once the applied force exceeded the adhesion force of the thrombus in the vessel, the clot returned to its original shape and could be pulled into the guiding catheter (Figure 3). No thrombotic material was lost at the tip of the guiding catheter.

Figure 3. Total thrombus retrieval after successful navigation of the aspiration catheter (tip —) to the proximal surface of the thrombus. During initial aspiration, the proximal base of the thrombus enters the tip of the microcatheter (a) and is elongated during retrieval (a and b). Total retrieval into the guiding catheter (*) was achieved without fragmentation or dislocation of thrombotic material (c through e).
The risk of embolic events using DD was considerably lower with proximal balloon occlusion (1 of 11; 9.1%) than without (5 of 12, 41.6%; OR, 7.1; 95% CI, 0.7 to 75.2). In 1 occlusion, a dissection occurred, but no perforation of a vessel was found. The mean vasospasm rating of 2.6 (range 1 to 3) for the DD was relevantly higher than that for the PD (1.6). In 1 case, severe vasospasm hindered any additional retrieval attempts. The occurrence and grade of vasospasm were independent of the use of proximal balloon occlusion.

The time of the initial attempt per occlusion was mean of 14.1 minutes. In contrast to PD, the mean time per attempt increased with each successive attempt (mean 18.3 minutes). This increase in time was mainly attributable to the procedure for repositioning the device into the microcatheter and navigation of the microwire and microcatheter distally to the thrombus. Therefore, the mean time in case of successful recanalization was significantly \( P < 0.01 \) prolonged to 42.1 minutes compared with PD (20.8 minutes; Table).

### Thrombus–Device Interaction

Device navigation showed that the guide wire and microcatheter could be advanced easily past the thrombus and the device unsheathed distally to the thrombus. In none of the attempts, thrombus penetration was observed, the devices always passing between the thrombus and vessel wall. Restriction of the distal space because of branching of the vessel or distal obstruction made deployment of the device more difficult and time consuming. Typically, retrieval of the DD began with compaction of the thrombus. In successful thrombus retrieval, the thrombus was partially caught in the proximal third of the basket-like device and pushed sideways into the guiding catheter (Figure 5). Because of the compaction, retrieval into the tip of the guiding catheter was complicated. In 6 of 23 attempts (26%), small fragments of the thrombus were sheared off at the tip of the guiding catheter. In another attempt, the device compressed and lost the thrombus in the carrying vessel; the resulting obstruction could not be passed with either the guide wire or the microcatheter.

### Results for Proximal and Distal Mechanical Thrombectomy

<table>
<thead>
<tr>
<th></th>
<th>PD</th>
<th>DD</th>
<th>Level of Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of attempts</td>
<td>33</td>
<td>23</td>
<td>NA</td>
</tr>
<tr>
<td>Mean time (min) per attempt ( \pm \text{SD} )</td>
<td>6.3 ( \pm ) 4.7</td>
<td>18.3 ( \pm ) 9.2</td>
<td>( P &lt; 0.01 )^*</td>
</tr>
<tr>
<td>Mean time (min) per recanalization ( \pm \text{SD} )</td>
<td>20.7 ( \pm ) 3.5</td>
<td>42.1 ( \pm ) 6.1</td>
<td>( P &lt; 0.01 )^*</td>
</tr>
<tr>
<td>Mean vasospasm rating</td>
<td>1.6</td>
<td>2.6</td>
<td>( P &lt; 0.01 )†</td>
</tr>
<tr>
<td>Total recanalization, TIMI 3</td>
<td>70%</td>
<td>80%</td>
<td>1.71 (0.2–13.4)</td>
</tr>
<tr>
<td>Success rate of clot removal per attempt</td>
<td>39.4%</td>
<td>82.6%</td>
<td>7.3 (2–26.4)</td>
</tr>
<tr>
<td>Total incidence of thromboembolism</td>
<td>3%</td>
<td>26%</td>
<td>11.3 (1.3–101.7)</td>
</tr>
<tr>
<td>Clot fragmentation at guiding catheter tip</td>
<td>0%</td>
<td>23%</td>
<td>NA</td>
</tr>
<tr>
<td>DD incidence of thromboembolism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% without proximal balloon occlusion</td>
<td>41.6%</td>
<td>91.1%</td>
<td>(0.7–75.2)</td>
</tr>
<tr>
<td>PD success rate</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>% without clot entering catheter tip</td>
<td>18.2%</td>
<td>20.3</td>
<td></td>
</tr>
<tr>
<td>% with clot entering catheter tip</td>
<td>90.1%</td>
<td>(3.1–132.3)</td>
<td></td>
</tr>
</tbody>
</table>

NA indicates not applicable; *Student \( t \) test; †Mann–Whitney test.
eter. Furthermore, in 2 attempts (2 of 23; 8.7%), thrombotic material was pressed into small side branches and cut off by the device. In none of the 23 retrieval attempts did the device fracture.

Discussion

In this first study to compare the 2 major principles of mechanical thrombectomy, the proximal and the distal approach were found to be effective for thrombus retrieval under testing conditions. The study revealed a slight benefit from DD over PD in the rate of total recanalization. Furthermore, the distal approach was highly successful as measured by the number of attempts with attain retrieval of some thrombotic material and the number of attempts necessary to achieve total recanalization. Shifting the application of force to the distal base of the thrombus with DD proves therefore to be very successful from the mechanical point of view. By advancing the complex device past the thrombus and unfolding it distally, the thrombus can be pushed back to the guiding catheter. To be advanced past the thrombus, the device must be as small in diameter as possible. Surprisingly, even without flow arrest, we encountered only 2 minor distal dislocations of the thrombus in the carrying vessel during the passing procedure. Therefore, this method for deployment of the device was relatively safe. The device always passed between the vessel wall and thrombus, in doing so never penetrating the thrombus. The trajectory of the device was therefore not in line with the thrombus but rather at a steep angle to the vessel wall (Figure 6). Because of this circumstance, the thrombus was mostly not totally caught within the basket-like device. A small part of the thrombus was carried in the device, whereas the remaining part was pushed sideways, becoming liable to flow and dislocation. Moreover, the pushing maneuver caused compaction of the thrombus, increasing its diameter. This might hinder additional passing attempts and makes the thrombus prone to flow and shearing at the tip of the guiding catheter. The risk of thromboembolic events was therefore higher without proximal flow arrest. Although not significant, DD might be beneficially applied in conjunction with balloon occlusion. Furthermore, in contrast to PD, large-sized guiding catheters might reduce the risk of thrombus shearing.

The present study also revealed that DDs have a relevant higher risk and severity of vasospasm, hindering reperfusion in case of recanalization. This may be as well attributable to the irritation caused by the procedure for advancing past the thrombus, the force trajectory of the device, and resulting compaction of the thrombus. If the thrombus has extended into small side branches, a phenomenon sometimes seen after previous unsuccessful retrieval attempts with thrombus compaction, the DD cuts off this thrombotic material in the main carrying vessel.

The distal approach demands a mechanically more complex device than the proximal approach. The repeated passing and the need to reposition the device in the microcatheter after unsuccessful retrieval increase recanalization time. Al-

Figure 5. Thrombectomy in the left ICA using a distal retrieval device (Catch device; top and bottom markers >) without proximal balloon occlusion (*). During retrieval, the thrombus is caught by the device (a). Compaction of the thrombus attributable to the pulling maneuver (b and c) and a small remaining fragment in the carrying vessel. Because of the compaction, the major part of the thrombus is lost and remains in the tip guiding catheter (d), and only a small fragment of the thrombus is retrieved (e).

Figure 6. Because of the observed passing procedure between vessel wall and thrombus, the trajectory of the force applied might increase vessel wall irritation and clot dislocation sideways to the basket-like DD.
though fewer attempts are necessary than with PD, the time to achieve total recanalization is much longer. In addition, the design of the device requires space distal to the occlusion site, limiting access to the thrombus if there is distal branching or bifurcation.

Compared with the DD, the approach of the PD is uncomplicated and its design mechanically simple. Without the need for time-consuming repositioning and passing procedures, the PD allowed repeated fast retrieval attempts. Because it does not require passing procedures, no distal dislocation occurred. Analysis of the thrombus–device interaction shows that the thrombus was initially elongated during PD retrieval. Both of these characteristics appear to have reduced irritation to the vessel wall and thus lowered the risk and severity of vasospasm compared with DD. Furthermore, the in-line position of the thrombus behind the PD decreased the risk of thromboembolic events attributable to flow. Accordingly, we found proximal balloon occlusion to have only a minor influence on the embolization rate. However, per attempt, the success rate for retrieving thrombotic material was relatively low. The limiting factor for successful aspiration was the amount of suction the tip of the microcatheter could apply to the proximal base of the thrombus. In more than half of all attempts, the force created at the tip of the PD by suction with the 20-mL syringe was insufficient, thus preventing removal of the thrombus. In case the proximal end of the thrombus entered the microcatheter during aspiration, the chance of thrombus retrieval increased significantly. These results indicate that microcatheter diameter, tip shape, and the syringe size influence the success rate and point out room for device improvement.

Disclosures

None.

References


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Stroke. 2006;37:3019-3024; originally published online October 19, 2006;
doi: 10.1161/01.STR.0000248457.55493.85

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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