Mechanical Thrombolysis in Acute Ischemic Stroke With Endovascular Photoacoustic Recanalization

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**Background and Purpose**—We present the results of the endovascular photoacoustic recanalization (EPAR) treatment for acute ischemic stroke from the Safety and Performance Study at 6 centers in Europe and North America. The objectives of mechanical thrombolysis are rapid vessel recanalization and minimal use of chemical thrombolysis.

**Methods**—This study was a prospective, nonrandomized study. The National Institutes of Health Stroke Scale (NIHSS) score and the modified Rankin Scale (mRS) score were recorded before treatment. The presence of recanalization was assessed by angiography. To measure outcome, follow-up examinations were performed at 24 hours, 7 days, and 30 days after stroke onset.

**Results**—Thirty-four patients (median NIHSS 19) were enrolled. Ten patients had internal carotid artery occlusion, 12 patients had middle cerebral artery occlusion, 11 patients had vertebrobasilar occlusion, and 1 patient had posterior cerebral artery occlusion. The overall recanalization rate was 41.1% (14/34). Complete EPAR treatment was possible in 18 patients (median NIHSS 18), with vessel recanalization in 11 patients (61.1%) after EPAR. The average lasing time was 9.65 minutes. Incomplete EPAR treatment (16/34, median NIHSS 19) was defined as intention to treat with EPAR and that the EPAR microcatheter entered the patient. Additional treatment with intraarterial application of rTPA occurred in 13 patients. An adverse event associated with use of the device occurred in 1 patient. Symptomatic hemorrhages occurred in 2 patients (5.9%). The mortality rate was 38.2%.

**Conclusions**—This study demonstrates the safety and technical feasibility of EPAR. This new technique may provide another treatment option in the therapeutic armamentarium for patients with acute ischemic stroke. ([Stroke. 2004;35:1112-1116.]

Key Words: laser • endovascular therapy • stroke, acute • stroke, ischemic • thrombolysis

In this report, we present the results of the Safety and Performance Study of a new solely mechanical clot fragmentation device based on laser technology (endovascular photoacoustic recanalization [EPAR]; Endovasix Inc). The emulsification of the thrombus is a mechanical thrombolysis and not a direct laser-induced ablation. The photonic energy is converted to acoustic energy at the fiberoptic tip through creation of microcavitation bubbles. The tip of the 3-French hydrophilically coated catheter is 1 mm in diameter with 5 windows, each of them with 1 fiberoptic (Figure 1). The vaporization and re-liquefication of the cavitation pocket induces a suction of the thrombus through the lateral windows into the tip. Inside the tip the clot is emulsified, and the tip contents are discharged as subcapillary-size particles (in vitro: 1 to 10 μm). The objectives of this mechanical thrombolysis device are rapid recanalization and minimization of the use of chemical thrombolytics to avoid symptomatic hemorrhages.

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occlusion of the internal carotid artery (ICA), anterior cerebral artery, middle cerebral artery (MCA), posterior cerebral artery (PCA), basilar, and vertebral arteries with a minimum of vessel diameter of 2 mm (according to M1, A1, and P1) and TIMI 0 to 1 flow.

All patients with the following criteria were excluded: (1) known pregnancy; (2) evidence of aneurysm or dissection in target vessels; (3) patients with uncontrolled bleeding diathesis; (4) markedly increasing improvement of neurologic symptoms by time of treatment initiation; (5) evidence of intracranial hemorrhage; (6) patients with uncontrolled hypertension >200 mm Hg systolic and 120 mm Hg diastolic; and (7) evidence of intracranial tumor or large infarct resulting in significant mass effect with midline shift.

The neurological status was assessed at admission using NIHSS and modified Rankin Scale (mRS), and at 24 hours, 7 days, and 30 days using NIHSS, mRS, Glasgow Outcome Scale, and Barthel Index. The vessel patency was confirmed 24 hours and 30 days post-procedure by CT-angiography, MR-angiography, or transcranial Doppler.

MedPass International (Paris, France) was the contract research organization for this study. The contract research organization’s responsibilities include monitoring patient data, ensuring that the investigational plan is followed, and verifying that complete, timely, and accurate data are submitted.

Before treatment, 2000 U normal heparin was administered as an intravenous bolus, followed by continuous infusion at 500 U/h for 4 hours. After diagnostic angiography, the 3-French hydrophilic-coated EPAR microcatheter was coaxially inserted through a 6-French guiding catheter. The EPAR microcatheter was navigated distally across the occlusion under road map technique using a 0.014-inch microwire. A superselective angiogram through the microcatheter was performed to demonstrate that the blood clot was completely crossed. After initially flushing the microcatheter with the blue indigo carmine (standard 0.8% for infusion), the catheter was continuously flushed with indigo carmine using a syringe pump at a rate of 1 mL/min. Indigo carmine, which is an inert blue dye, is used as a coolant and for absorption of the green wavelength light. Treatment of the blood clot occurred by activating the power generator and by pulling the EPAR microcatheter slowly back through the blood clot.

Results
Thirty-four patients were enrolled (Table 1 to 3). The mean age of the patients was 67.6 years (range of 27–87 years). There was 1 apparent protocol violation with inadvertent treatment of a patient aged 87 years.

The median NIHSS score at admission was 19 (range 6–39). The mean delay (±1 SD) from stroke onset to EPAR treatment was 6.37 hours (±3.97) for all patients, 4.60 hours (±0.70) in patients with anterior circulation occlusion, and 8.78 hours (±5.27) in patients with posterior circulation occlusion. Angiography showed occlusion of the ICA in 10 patients, MCA in 12 patients, vertebrobasilar territory in 11 patients, and PCA in 1 patient.

Safety and Hemorrhages
A device-related adverse event occurred in 1 patient with fatal outcome. The cause was ballooning of the distal catheter and vessel rupture during a hand injection with 1-mL syringe, even though a 3-mL syringe was recommended by the company.

Symptomatic intracranial hemorrhage (ICH) within 24 hours of treatment occurred in 2 (5.9%) of the patients, 1 of whom had received adjuvant rTPA. Symptomatic ICH was previously defined as causing an increase in the NIHSS score of ≥4 points. In 1 case, dense blood clot exceeding 30% of the infarct volume was seen, and in another there was symptomatic hemorrhagic transformation of the brain stem. Two patients had a slight asymptomatic subarachnoid hem-
orrhage (SAH) at the postprocedural CT because of dissection of M2 branch with the microwire. This side effect is not directly device-related because microwire manipulation at the occlusion site is frequently used and the dissection was not the consequence of microcatheter manipulation.

**Recanalization**

The overall recanalization rate was 41.1% (14/34). The 34 patients were divided into 2 groups: complete and incomplete treatment. Complete treatment was defined as a case in which treatment with the EPAR system could be applied as intended by the protocol, whether recanalization occurred. Complete treatment was possible in 18 of 34 patients; immediately after EPAR therapy, vessel recanalization occurred in 11 of 18 patients (61.1%, defined as TIMI 2 to 3, Table 2). Figure 2 illustrates 1 case of complete treatment with recanalization with EPAR alone.

Incomplete treatment was defined as intention to treat with EPAR, including those cases in which the EPAR microcatheter entered the patient but the treatment could not be completed as per the protocol. Incomplete treatment occurred in 16 patients, 3 of whom had recanalization. Reasons for incomplete treatment were tortuous vessel anatomy (n=7), premature termination of treatment (n=3), procedure terminated after 10, 30, and 67 seconds of lasing time and iatrogenic decision to change to intraarterial rTPA application, untreated because of local high-grade stenosis (n=2), unable to treat because of problems with laser function or back-up catheter availability (n=2), guidewire perforation before treatment (n=1), and an adverse event subsequent to catheter failure (n=1). In 7 of 16 patients, the laser was not fired.

The average lasing time in the complete-treated patients was 9.65 minutes (1.33 to 19.92); the average lasing time in the incomplete treated group was 1.50 minutes (0 to 6.45). Adjunctive treatment with use of intraarterial rTPA was administered in 13 patients: 6 from the complete treatment group and 7 from the incomplete treatment group. Adjunctive treatment with stent occurred in 4 patients; 1 was deployed in the MCA and 3 in the vertebrobasilar territory.

**Outcome**

Thirty days after treatment, 5 of 34 patients (14.7%) had recovered to mRS score 0 to 2. This represented 22.2% of the complete treatment group (4/18) and 36.4% of those in whom treatment was complete and in whom recanalization was seen (4/11). Mortality was 38.2%. NIHSS improvement ≥ 50% occurred in 20.6% (7/34) of all patients, in 22.2% (4/18) of treatment-complete patients, and in 36.4% (4/11) of treatment-complete patients with recanalization (Table 3).

**Discussion**

Evolution in the treatment of acute ischemic stroke has been remarkably slow since the results of the National Institute of

### TABLE 1. Clinical Data: Division Into Anterior and Posterior Circulation

<table>
<thead>
<tr>
<th></th>
<th>Anterior Circulation</th>
<th>Posterior Circulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>22</td>
<td>12</td>
</tr>
<tr>
<td>Average age</td>
<td>69.3</td>
<td>64.8</td>
</tr>
<tr>
<td>Male</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Female</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Entering NIHSS (median)</td>
<td>21</td>
<td>15</td>
</tr>
<tr>
<td>Complete treatment</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Incomplete treatment</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Mean time to treat (h)</td>
<td>4.60 (3.53–6.20)</td>
<td>8.78 (2.90–17.73)</td>
</tr>
<tr>
<td>Mean lasing time (min)</td>
<td>5.43 (0.00–19.92)</td>
<td>8.65 (0.47–18.90)</td>
</tr>
<tr>
<td>Additional rTPA</td>
<td>7 of 22 patients (4–70 mg)</td>
<td>6 of 12 patients (15–55 mg)</td>
</tr>
<tr>
<td>Pretreatment</td>
<td>1 patient 17 mg rTPA intraarterial</td>
<td>1 patient 5 mg rTPA intraarterial</td>
</tr>
<tr>
<td></td>
<td>1 patient 10 mg rTPA intraarterial</td>
<td>1 patient 20 mg rTPA intravenous</td>
</tr>
</tbody>
</table>

### TABLE 2. Changes of TIMI Flow Before and After EPAR Treatment and Final TIMI

<table>
<thead>
<tr>
<th></th>
<th>TIMI Before EPAR (Mean)</th>
<th>TIMI After EPAR* (Mean/% TIMI 2–3)</th>
<th>Final TIMI (Mean/% TIMI 2–3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n=34)</td>
<td>0.1</td>
<td>0.9/41</td>
<td>1.1/41</td>
</tr>
<tr>
<td>Anterior circulation (n=22)</td>
<td>0.1</td>
<td>0.7/26</td>
<td>0.9/32</td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>0</td>
<td>1.1/50</td>
<td>1.3/50</td>
</tr>
<tr>
<td>Complete treatment (n=8)</td>
<td>0</td>
<td>1.2/58</td>
<td>1.6/67</td>
</tr>
<tr>
<td>Posterior circulation (n=12)</td>
<td>0</td>
<td>1.4/70</td>
<td>1.6/70</td>
</tr>
<tr>
<td>Posterior circulation Complete treatment (n=10)</td>
<td>0</td>
<td>1.3/61</td>
<td>1.4/61</td>
</tr>
<tr>
<td>Complete treatment (n=18)</td>
<td>0</td>
<td>0.2/0</td>
<td>0.8/25</td>
</tr>
</tbody>
</table>

* n=27. Seven patients were not treated with EPAR but the catheter was inserted.
Neurological Disorders and Stroke (NINDS) study were reported. LIT was pursued, followed by several reports about neurological symptoms developed with a NIHSS score of 6 and mRS of 4. The angiogram revealed distal basilar artery occlusion (A, B) and hypoplastic distal right vertebral artery, which was used for the access. EPAR treatment was followed with complete recanalization under local anesthesia (C, D). Two passes of the occlusion were necessary, with an overall lasing time of 5.22 minutes without adjunctive treatment. The TIMI improved from 0 to 2. MR angiography after 24 hours (E) and 30 days (F) showed patent vessels. MR after 3 days (G, transverse T2-weighted image) and after 30 days (H, transverse FLAIR) with pontine and partial PCA infarct. The neurological symptoms improved with NIHSS 0, mRS 1, Glasgow Outcome Scale 1, and Barthel Index 100 after 30 days.

TABLE 3. Clinical Data of all Patients and Division Into Complete and Incomplete Treatment

<table>
<thead>
<tr>
<th>All Centers</th>
<th>All Patients</th>
<th>Complete Treatment</th>
<th>Complete Treatment: Recanalized</th>
<th>Complete Treatment: Not Recanalized</th>
<th>Incomplete Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>34</td>
<td>18</td>
<td>11</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Average age</td>
<td>67.6</td>
<td>66.0</td>
<td>64.5</td>
<td>68.4</td>
<td>69.4</td>
</tr>
<tr>
<td>Male</td>
<td>17</td>
<td>9</td>
<td>6</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Female</td>
<td>17</td>
<td>9</td>
<td>5</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Time to treat (h)</td>
<td>6.37</td>
<td>6.22</td>
<td>7.55</td>
<td>4.32</td>
<td>6.68</td>
</tr>
<tr>
<td>Recanalization rate n (%)</td>
<td>14 (41.1)</td>
<td>11 (61.1)</td>
<td>3 (18.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic ICH</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mortality n (%)</td>
<td>13 (38.2)</td>
<td>7 (38.9)</td>
<td>4 (36.4)</td>
<td>3 (42.9)</td>
<td>6 (37.5)</td>
</tr>
<tr>
<td>Entering NIHSS (median)</td>
<td>19</td>
<td>18</td>
<td>19</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>NIHSS 50% decrease at day 30 n (%)</td>
<td>7 (20.6%)</td>
<td>4 (22.2)</td>
<td>4 (36.4)</td>
<td>0</td>
<td>3 (18.7)</td>
</tr>
<tr>
<td>MRS 0–2 at day 30 n (%)</td>
<td>5 (14.7)</td>
<td>4 (22.2)</td>
<td>4 (36.4)</td>
<td>0</td>
<td>1 (6.2)</td>
</tr>
</tbody>
</table>
anatomy were ICA occlusions (71% [5/7]). Nevertheless, our results of recanalization of the posterior territory were in the upper range of the reported recanalization rates (50% to 75%).4,5,24,25

The incidence of symptomatic hemorrhage was low, in accordance with the prediction that reduction of fibrinolytics should reduce the risk of symptomatic ICH. Our overall rate of symptomatic ICH (5.9% [2/34]) was in the same order as the NINDS cohort (6.4%) for intravenous rTPA application and intraarterial application of different fibrinolytics (range 7% to 14%).1,2,8,16,26 Given that one of the hemorraghes occurred in a patient who received adjuvant rTPA, the rate for patients treated solely with EPAR could be as low as 2.9%.

In conclusion, the Safety and Performance Study demonstrated the safety and technical feasibility of EPAR. This new technique may provide another treatment option in the therapeutic armamentarium for patients with acute ischemic stroke. EPAR offers the possibility of a multimodal treatment strategy that starts with mechanical thrombolysis resulting in rapid recanalization, followed by the opportunities to administer fibrinolytics for residual or peripherally distributed thrombus via the same catheter or to deliver a stent or perform PTA to treat an underlying stenosis.

The results are limited to the small sample size, which makes it difficult to draw strong conclusions from the results. Further research is needed to circumstantiate these early results.

Acknowledgments

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