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Summary

A prototype endovascular electromechanical clot extraction device was fabricated using a combination of shape memory polymer (SMP) and shape memory nickel-titanium alloy (nitinol). Five embolic vascular occlusions were created in four rabbits by injecting thermally coagulated blood through a 4.0F catheter in the common carotid artery. Angiography immediately after clot injection showed complete or partial occlusion of the common carotid artery. Post-treatment angiography showed complete (2/5), partial (2/5), or no (1/5) restoration of blood flow.

Most strokes are caused by cerebral thrombo-embolic arterial occlusion and are conventionally treated with intravenous thrombolytic drugs. Drawbacks associated with this treatment, including the narrow (3-hour) therapeutic window and strict exclusion criteria imposed to mitigate the risk of hemorrhage, have prompted the development of alternative non-pharmacological therapies. We report on the use of an electromechanical embolectomy device in a rabbit acute arterial occlusion model.

Description of Technique

Device Use and Fabrication

The prototype device consisted of an electromechanical microactuator mounted on the distal tip of either a Prowler-14 microcatheter (1.9F distal shaft, Cordis Corporation, Miami Lakes, FL) or a custom-made 1.5F stainless steel 55-cm long hypotube with a 20-cm long distal flexible coil section (Heraeus Vadnais, St. Paul, MN). A device is shown in Fig 1. The microactuator was comprised of a shape memory polymer (SMP) shell over a shape memory nickel-titanium alloy

(nitinol) wire backbone with attached copper leads to deliver a current. The microactuator maintains a straight rod shape until the applied current, provided by a dc power supply, induces electro-resistive (Joule) heating of the nitinol wire, causing the microactuator to transform into a corkscrew shape capable of retrieving a blood clot. At body temperature, the overlying SMP is in a glassy (high elastic modulus) state and maintains the nitinol corkscrew in a straight form for endovascular delivery. Once in position beyond the clot, Joule heating is initiated. As the surrounding SMP is heated by conduction to its characteristic glass transition temperature ($T_g \approx$ 80 °C), it transitions to its low-modulus rubbery state, allowing the nitinol to resume its corkscrew shape. When the current is turned off, the nitinol and the SMP cool and the elastic modulus of the SMP approaches its original glassy value, providing enhanced stiffness to the nitinol corkscrew and resistance to deformation (i.e., stretching) during blood clot extraction.

Superelastic nitinol wire (SE508 wire, Nitinol Devices & Components, Fremont, CA) with a diameter of 97 μm was wrapped around an aluminum mandrel and heated in a furnace at 500 °C for 10 min to program the corkscrew shape. The nitinol reverts to the programmed corkscrew shape at temperatures at or above its Austenite finish temperature (A_f= 5-18 °C). To route current flow through the nitinol corkscrew for Joule heating, two polyimide-insulated 40 AWG copper wire leads approximately 100 cm long were connected to the nitinol wire at each end of the corkscrew using gold crimp tubes which also served as radiopaque markers. The diameter of the copper wire including insulation was 95 μm. The copper wire lead attached at the distal end of the nitinol corkscrew was wound back around the length of the corkscrew (Fig 1), permitting both copper wire leads to emerge from the same (proximal) end of the corkscrew.

A thermosetting urethane SMP formulation developed in-house (1) was used to encase the copper-wound nitinol. A teflon tube (inner diameter = 305 μm) was placed over the straightened

copper-wound nitinol corkscrew and the SMP resin was injected into the tube. The cast SMP resin was then thermally cured and the teflon tube was removed, revealing a straight SMP rod encapsulating the copper-wound nitinol wire.

Intervention

The animal experiments were conducted at the University of California Davis Medical Center (Sacramento, CA) in accordance with the National Institutes of Health Public Health Service Policy on Humane Care and Use of Laboratory Animals and approved by the Institutional Animal Care and Use Committees of the University of California, Davis, and Lawrence Livermore National Laboratory. Five occlusions were treated in four anesthetized New Zealand White rabbits (weight 3-4 kg). A 4.0 French sheath was placed in the right or left femoral artery and a 4.0 F catheter was directed into the common carotid artery (CCA; lumen diameter 1.5-2.0 mm) under fluoroscopic and roadmap guidance using iohexol contrast (Omnipaque 300, Amersham Health, Princeton, NJ); baseline angiography was performed. Blood collected from a marginal ear vein was thermally coagulated and a clot 0.2-0.3 cm^3 in volume was injected through the catheter into the CCA. Angiography was performed to evaluate the resulting vascular occlusion and additional clot was injected if necessary. Under fluoroscopic guidance, the clot extraction device was delivered through the catheter in its straight form, positioned into the external carotid artery (ECA) distal to the occlusion, and actuated to assume its corkscrew form by applying a dc current of 0.6-0.8 A for 3-5 s until actuation was complete (the copper-wound nitinol was visible by fluoroscopy). The device and catheter were then withdrawn simultaneously. The sheath was inspected and any lodged clot was collected. Angiography was performed after each extraction attempt. The results are summarized in Table 1. Angiographic images of the second rabbit are shown in Fig 2.

Discussion

Non-pharmacological vascular reperfusion methods have exhibited the potential to broaden stroke patient eligibility by extending the therapeutic time window and reducing the contraindications related to the risk of hemorrhage (2). In particular, the U.S. Food and Drug Administration recently approved the use of the Merci Retrieval System (Concentric Medical, Inc., Mountain View, CA), a spring-like endovascular thrombectomy device to retrieve the clot up to 8 hours after the onset of stroke (3, 4). In the clinical study evaluating the safety and efficacy of the Merci system, up to six extraction attempts were made before the effort was considered a failure, with three attempts made on average (4). Similarly, in this study multiple attempts were usually required. This may at least in part be due to the fact that fragmentation of the injected clot occurred due to the small lumen of the 4.0 F catheter, confirmed on benchtop injection of clot through the catheter.

Several potential performance-enhancing modifications to the current device have been identified, including a flexible distal tip, a tighter corkscrew, and a means of securing the clot (e.g., aspiration into the guide catheter) for withdrawal from the body. Flow arrest, as in the Merci system (2, 3), could facilitate clot extraction and reduce the risk of distal embolization. To reduce the risk of thermal injury to the vessel during device actuation, the actuation temperature (i.e., the T_g of the SMP) would be minimized but maintained sufficiently above body temperature to prevent spontaneous actuation in the body. The T_g of the SMP can be tailored from approximately 34 to 86 °C by adjusting the chemical composition (1). Because the glass transition is gradual, actuation can be achieved at temperatures ~10 °C below the nominal T_g. Previous studies of energy-dissipating interventional therapeutic devices that generate

temperatures and total energy dissipated on the same order-of-magnitude as the SMP-nitinol device have resulted in no thermal damage (5). Future studies may include histological examination of tissue harvested at the site of actuation at various post-treatment timepoints to assess the extent of thermal injury, if any. In addition, further studies are necessary in larger animals, as this would allow the use of larger catheters, injection of intact clot, and evaluation of the device in vessels similar in size to the human internal carotid artery.

This preliminary study suggests that an SMP-nitinol device may have application in the treatment of acute stroke or other thrombo-embolic disease.

References

1. Wilson TS, Small W, IV, Benett WJ, et al. **Shape memory polymer therapeutic devices for stroke.** *Proc SPIE* 2005;6007:157-64
2. Nesbit GM, Luh G, Tien R, et al. **New and future endovascular treatment strategies for acute ischemic stroke.** *J Vasc Interv Radiol* 2004;15:S103-10
3. Gobin YP, Starkman S, Duckwiler GR, et al. **MERCI 1: a phase 1 study of mechanical embolus removal in cerebral ischemia.** *Stroke* 2004;35:2848-54
4. Smith WS, Sung G, Starkman S, et al. **Safety and efficacy of mechanical embolectomy in acute ischemic stroke: results of the MERCI trial.** *Stroke* 2005;36:1432-8
5. Maitland DJ, Metzger MF, Schumann D, et al. **Photothermal properties of shape memory polymer micro-actuators for treating stroke.** *Lasers Surg Med* 2002;30:1-11

TABLE 1: Summary of mechanical embolectomy results

Rabbit	Occlusion Site	Angiographic Deficit	No. of Extraction Attempts	Clot Retrieved from Sheath?	Angiographic Findings Post-Treatment
1	R CCA	Filling defect	1	Yes	Complete restoration
2	R CCA	Complete occlusion	3	Yes	Complete restoration
3	R CCA	Complete occlusion	3	Yes	Partial restoration
	L CCA	Complete occlusion	5	No	Complete occlusion
4	R CCA	Complete occlusion	5	Yes	Partial restoration

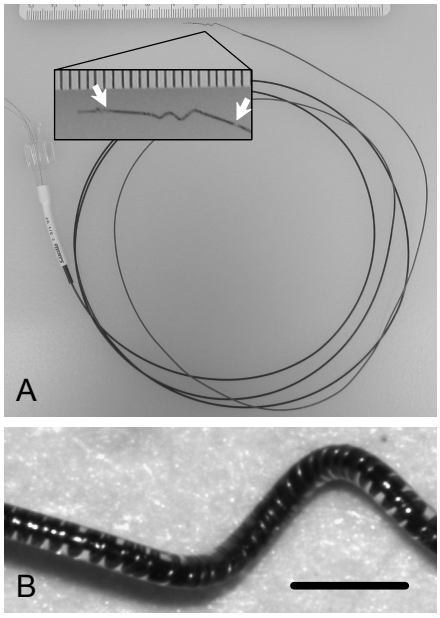

FIG 1. Electromechanical embolectomy device in its corkscrew form.

A, The SMP-nitinol corkscrew microactuator is mounted at the distal end of a microcatheter. The copper leads (and nitinol wire) extend from the proximal end of the microcatheter for connection to the power supply. A close-up of the microactuator showing the radiopaque gold markers (arrows) is shown in the inset. Scale divisions in millimeters.

B, Microscope image of the microactuator showing the copper-wound nitinol wire encapsulated by SMP. The diameter of the microactuator is 0.3 mm (0.012 in). Scale bar = 1 mm.

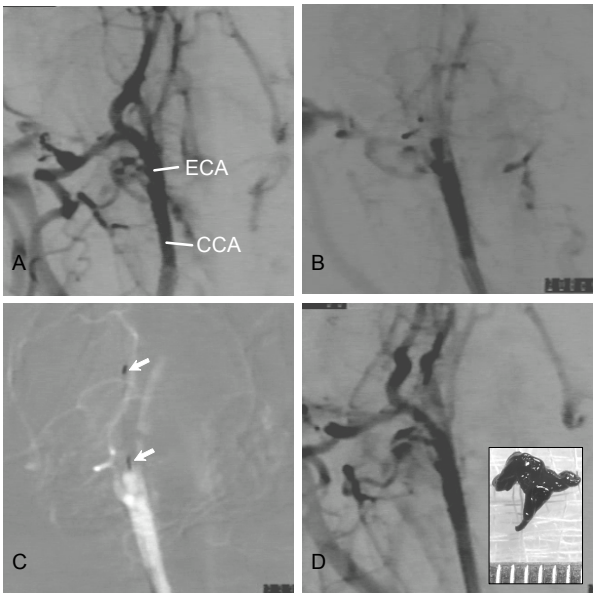

FIG 2. Angiographic images of the second rabbit.

A, Baseline angiogram of the right CCA and branch vessels acquired before clot injection.

B, Angiogram showing occlusion of the CCA.

C, Fluoroscopic image showing placement of the device into the ECA distal to the occlusion (radiopaque markers indicated by arrows). The copper-wound nitinol was visible on the fluoroscopy monitors but not on the video tape recording used to capture the image.

D, Post-treatment angiogram showing complete restoration of blood flow. A photograph of the retrieved clot is shown in the inset (scale divisions in millimeters).