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Prototype Laser-Activated Shape Memory Polymer Foam Device for Embolic Treatment of Aneurysms

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ABSTRACT

Conventional embolization of cerebral aneurysms using detachable coils is time-consuming and often requires re-treatment. These drawbacks have prompted the development of new methods of aneurysm occlusion. We present the fabrication and laser-deployment of a shape memory polymer expanding foam device. Data acquired in an *in vitro* basilar aneurysm model with and without flow showed successful treatment, with the flow rate affecting foam expansion and the temperature at the aneurysm wall.

Keywords: aneurysm, laser, shape memory polymer foam

1 INTRODUCTION

Cerebral aneurysm rupture occurs in approximately 30,000 people per year in the United States, with most resulting in death or neurological debilitation. Drawbacks of current endovascular treatment using detachable embolic coils [1] to fill the aneurysm include the time-consuming delivery of multiple coils and the need for re-treatment due to compaction of the coils and associated re-exposure of the aneurysm wall [2, 3]. Further, when the aneurysm neck is greater than 4 mm, complete occlusion using coils is achieved in only 15% of the cases [1]. In these instances, the wide neck allows the coils to migrate or unravel from the aneurysm into the parent artery, potentially increasing the risk for aneurysm re-growth and rupture [4].

Recently, shape memory polymer (SMP) foam based on DiAPLEX Company, Ltd. (a subsidiary of Mitsubishi Heavy Industries) polyurethane has been investigated as a material to occlude aneurysms with promising embolic performance [5] and biocompatibility [5, 6]. SMPs can be formed into a specific primary shape, reformed into a stable secondary shape, and then controllably actuated to recover the primary shape. A review of SMP basics and representative polymers was given by Lendlein and Langer [7]. For SMPs that are actuated thermally, raising the temperature of the polymer above the glass transition temperature (T_g) results in a decrease in the elastic modulus from that of the glassy state (~10^9 Pa) to that of an elastomer (~10^6 to 10^7 Pa). For SMP foams, this drop in modulus translates to an expansion force during thermal actuation (<1 kPa at recovered strains over 50%) that is much less than the force required to rupture an aneurysm wall (700-5000 kPa) [8, 9]. Upon cooling, the original modulus is nearly completely recovered and the primary form is stabilized. When the T_g of the SMP is above body temperature (37°C), an external heating mechanism such as photothermal (laser heating) or electrical (resistive heating) is required [10].

Researchers at Lawrence Livermore National Laboratory (LLNL) have developed an endovascular treatment technique to deliver thermally-deployed SMP foams [11]. This paper presents fabrication of LLNL-synthesized SMP foam devices and laser deployment in a polydimethylsiloxane (PDMS) basilar necked aneurysm model. Experimental analysis of the photothermally deployed foams in the model under bounding parent artery flow conditions (high and zero flow) is also presented.

2 MATERIALS AND METHODS

2.1 SMP FOAM

The chemically blown foam was based on LLNL SMP which is comprised of hexamethylene diisocyanate (HDI), N,N,N',N'-tetrakis(2-hydroxypropyl)ethylenediamine (HPED), and triethanolamine (TEA). Dye (Epolight™ 4121, Epolin, Inc.) was added during processing to aid laser light absorption. The predominantly open cell foam had a T_g of 45°C, dye concentration of ~900 ppm (absorption coefficient ~10 cm^{-1}), density of 0.020 g/cc, and calculated volumetric void fraction of 98.4%, allowing for a theoretical volume expansibility from a fully condensed state of 60x. Thought not available at the time of this study, higher and lower T_g foams can be made by adjusting the relative amounts of HDI, HPED, and TEA [12].

2.2 PROTOTYPE DEVICE FABRICATION

A spheroid (11 mm x 10 mm) was cut from the LLNL SMP foam using a scalpel and hollowed out by hand using a ball-tipped drill bit. The foam was positioned over a cylindrical light diffusing fiber (made in-house from LLNL SMP) such that the open end of the spheroid faced proximally and collapsed using a crimping machine (Model W8FH, Interface Associates) at 93°C (see Fig. 1). Upon reaching the collapsed diameter the device was allowed to cool to room temperature and then released from the machine. The device maintained the collapsed form prior to actuation as shown in Fig. 1(b).

To fabricate the diffusing fiber, LLNL SMP (T_g=81°C) was cast in a teflon tube (inner diameter=300 μm) over a 100 μm core cleaved optical fiber. The resulting SMP rod was then media blasted with 100 μm sodium bicarbonate particles to create a diffusing surface. A ST connector was added to the proximal end of the optical fiber for coupling to the laser light source, an 810 nm continuous-wave diode laser pigtailed into a 100 μm core optical fiber (Model UM7800/100/20, Unique Mode). An overlying thin-walled stainless steel hypotube (inner diameter=356 μm, outer diameter=508 μm, Heraeus Vadnais, Inc.) was incorporated to add stiffness to the optical fiber for device delivery. Approximately 80-90% of the light was emitted radially, with the remaining light emerging from the distal end of the diffuser. The SMP formulation was specifically designed to be optically transparent so as not to absorb the laser wavelength (absorption coefficient=0.01 cm^{-1} at 810 nm).

2.3 BENCHTOP DEPLOYMENT OF FOAM

With the diffusing fiber inside the collapsed device, the proximal end of the optical fiber was coupled to the 810 nm diode laser. The PDMS aneurysm model (Fig. 2) was filled with 21°C water and the collapsed device was delivered into the aneurysm. Though water at 37°C (body temperature) would have provided a more accurate representation of physiological conditions and heat flow, the relatively low T_g of the available foam (45°C) required a lower water temperature to prevent spontaneous expansion prior to laser heating (the glass transition begins to occur ~10°C below the nominal T_g). Flow rates varied between 0 and 148 cc/min where 0, 70, and 148 cc/min were typically used because they represent blocked, diastolic, and systolic flow in the basilar artery [13], respectively. Laser powers varied between 1 and 8.6 W. The foam expansions were video recorded and the temperature was measured by a needle probe thermocouple (HYP1, Omega) protruding slightly into the aneurysm at the dome apex. While this single thermocouple may not represent the maximum temperature in the aneurysm, it provides a means of comparing the effects of the various laser powers and flow rates.

3 RESULTS

Figure 3 shows a combined timeline of laser power, flow rate, temperature, and images of the foam expansion. The flow in the aneurysm prevented sufficient heating of the outer region of the foam and, thus, prevented full expansion during ~200 s of 148 cc/min flow and 8 W of laser power. Not until the flow was reduced did the foam fully expand. When the flow was reduced to 0 cc/min, the apex temperature quickly increased by over 20°C. A subsequent experiment in which the flow was maintained at 0 cc/min and the laser power was set to 8.6 W resulted in full expansion of the foam within 60 s with a temperature rise of ~30°C (not shown in figures).

Rapid overheating associated with zero flow and the cooling impact of high flow were further demonstrated in a fully expanded foam undergoing laser heating (not shown in figures). At 148 cc/min, the steady state apex temperature rise was limited to 1, 2, and 3°C for laser powers of 2, 4, and 6 W, respectively. At 0 cc/min, the apex temperature increased by approximately 10, 20, and 30°C within the first minute of laser heating for 2, 4, and 6 W, respectively.

To overcome the cooling effect of flow, the foam was doped with additional dye to increase laser heating; the hollow spheroid was coated with a solution of ~4400 ppm dye in tetrahydrofuran followed by vacuum drying to remove the solvent. Figure 4 shows the results of foam deployment at a flow rate of 70 cc/min as the laser power was gradually increased to 8.6 W over ~190 s. Full expansion was achieved in ~180 s and the apex temperature never exceeded 2°C. A subsequent experiment using the same foam spheroid under the same flow condition (70 cc/min) in which the laser power was increased to 8.6 W more quickly (over ~100 s) showed similar results (not shown in figures).

4 DISCUSSION AND CONCLUSION

The foam device presented here will require several significant modifications before it is clinically viable. First, foam with a higher T_g will need to be used to prevent spontaneous expansion in the body. Second, the foam device would need to be delivered through a microcatheter with a lumen diameter of 300-600 μm, requiring a reduction in the current collapsed diameter (1800 μm). Work on lower density foams with greater volume expansion is in progress. By further removing volume (e.g., holes, dimples, channels, etc.) without sacrificing embolic performance, foam devices capable of filling a 10 mm aneurysm may potentially be compacted to the ~500 μm diameter necessary for microcatheter delivery. Third, due to the impact of flow on foam expansion, the device may require some engineering of the flow via a baffle to reduce the flow near the aneurysm neck or a balloon to block flow [14] in the parent artery during laser heating. At a temperature of ~67°C (~30°C above body temperature), thermal damage of arterial tissue occurs within a few minutes [15], a timescale similar to that of device deployment. To avoid causing thermal damage to the already compromised aneurysm wall under zero or low flow conditions, the optimal combination of foam T_g, laser power, dye concentration, and flow will need to be determined.

This preliminary study demonstrated that SMP foams can be laser deployed in an *in vitro* aneurysm model. The flow rate affected the deployment. Zero flow resulted in fast, full expansion with overheating at the aneurysm wall. Low (diastolic) flow resulted in slow, full expansion with minimal temperature increase at the aneurysm wall. High (systolic) flow resulted in incomplete expansion. Advances in the materials with the basic techniques presented here suggest the potential for a single device that can treat a 10 mm aneurysm.

Acknowledgments

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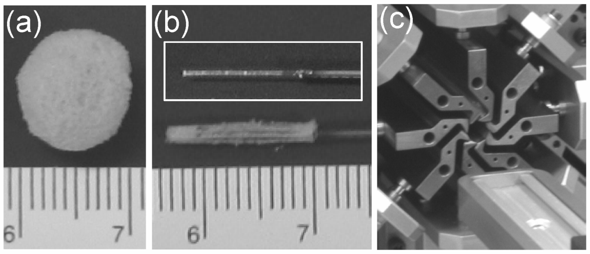
Fig. 1. LLNL SMP hollow foam spheroid prior to collapse, 11.0 x 10.0 mm, (a) and post-collapse, 1.8 x 13.0 mm, on the light diffusing fiber (b). The open end of the spheroid is facing right. The light diffusing fiber is shown in the inset in (b) coupled to a red diode laser. (c) Image of the eight-blade cylindrical crimping machine with heated blades used to collapse the foam.

Fig. 2. (a) Clear PDMS (Sylgard 184, Dow Corning) generic basilar necked aneurysm model made in-house (dome dimensions: 11.3 mm apex to neck, 11.7 mm wide). The model consists of two PDMS halves pressed between polycarbonate plates with stainless steel alignment pins. The positive molds used to cast the PDMS were machined from polycarbonate stock using a computer-controlled rapid prototyping mill (Roland MDX-650). The thermocouple port permits measurement of the temperature at the apex of the aneurysm dome. The device is inserted into

the model via a Touhy Borst valve. A peristaltic pump (model 505Du, Watson-Marlow, Ltd.) provided flow through the system.

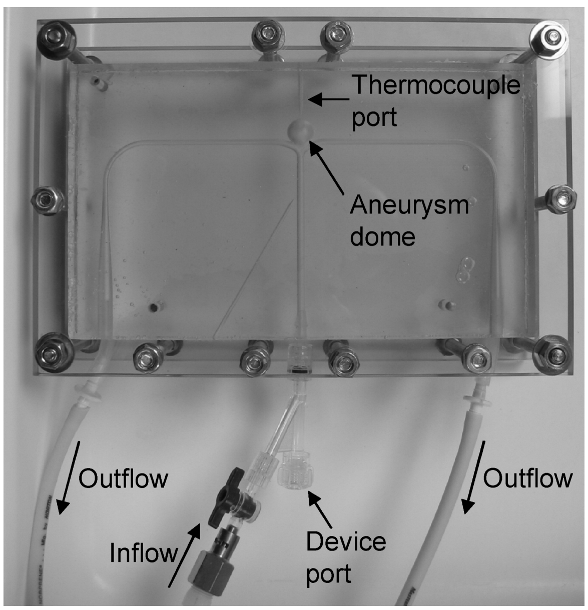
Fig. 3. Temporal history of aneurysm apex temperature, foam expansion, flow rate, and laser power. The bars above the plot display the laser power and flow rate timelines. The plot shows the corresponding apex temperature and the letters (A-H) on the plot correspond to the foam expansion images. Full expansion was prevented by convective cooling due to the high flow rate (148 cc/min) and did not occur until the flow was turned off (0 cc/min).

Fig. 4. Apex temperature and expansion of the foam at a flow rate of 70 cc/min. The darker color of the foam is due to the added dye. The laser power was gradually increased to 8.6 W over ~190 s. The large arrow indicates the time of full expansion (~180 s from laser on).



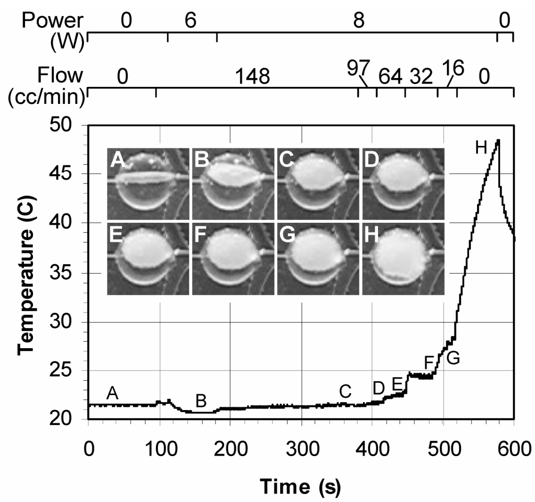
(a)
(b)
(c)
6
7
6
7

Fig. 1



Thermocouple
port
Aneurysm
dome
Outflow
Outflow
Inflow
Device
port

Fig. 2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(W)
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6
8
0
Flow
(cc/min)
0
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97
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A
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H

Fig. 3

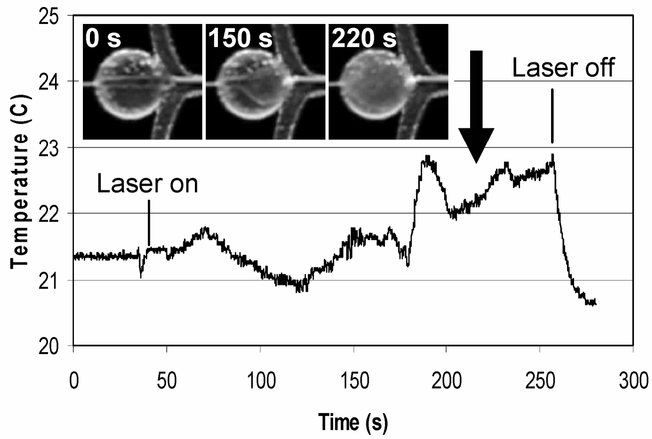
0 s
150 s
220 s
Laser on
Laser off
Temperature (C)
Time (s)

Fig. 4