A Shape Memory Polymer for Intracranial Aneurysm Coils: An Investigation of Mechanical and Radiographic Properties of a Tantalum-Filled Shape Memory Polymer Composite

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A Shape Memory Polymer for Intracranial Aneurysm Coils: An Investigation of
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Memory Polymer

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF FIGURES

SUMMARY

An intracranial aneurysm can be a serious, life-threatening condition which may go undetected until the aneurysm ruptures causing hemorrhaging within the brain. Currently, the most typical treatment method is by embolism of the aneurysm with platinum coils. However, in about 15% of the cases treated by this method, the aneurysm eventually re-opens (Kallmes, Kallmes, Cloft, and Dion, 1998). The solution to the problem of aneurysm recurrence may be in developing more bio-active materials, including certain polymers, to use as coil implants. These devices have shown favorable results in embolizing aneurysms in animal studies compared to bare platinum devices (Kallmes et al., 2003).

A few published reports have established that completely polymeric devices are capable of enhancing treatment outcomes (Murayama et al., 1997, 1999, 2002, 2003). However, these materials have required surgical implantation because they could not be inserted with a catheter. In this research, a shape memory polymer will be investigated as a potential candidate for aneurysm coils. The benefit of a shape memory polymer is that a small diameter fiber can be fed through a micro-catheter, and then change its shape into a three-dimensional configuration when heated to body temperature. Furthermore, being polyurethane, it is biologically safe for implantation and would be cheaper to produce than platinum devices.

In this research, a shape memory polymer was tested to determine the modulus of the material near body temperature, the magnitude of stress generated during shape recovery, the exact temperature at which recovery occurs, and the behavior of prototype coils in a simulated aneurysm model. In addition, composite specimens containing 3% tantalum filler were examined to determine the mechanical effect of adding this radio-opaque metal. Thermo-mechanical testing showed that the material exhibited a shape recovery force a few degrees above T_g. The effects of the metal filler were small and included a depression of T_g and recovery stress. Shape memory coils deployed inside a simulated aneurysm experimental model demonstrated that typical hemodynamic forces would not hinder the shape recovery process.

The x-ray absorption capability the tantalum-filled material was characterized using x-ray diffractometry and clinical fluoroscopy. Diffractometry revealed that increasing tantalum concentration increased the x-ray absorption coefficient of the material; however, not as the rule of mixtures would predict. Fluoroscopic imaging of the composite coils in a clinical setting verified the radio-opacity of the material.

INTRODUCTION

Intracranial aneurysms affect between 2% and 6% of the world population (Horowitz, Samson, and Purdy, 1997; Ahuja et al., 1993). Every year, over 25,000 people suffer from subarachnoid hemorrhage due to aneurysm rupture in the United States alone. About half of these cases result in death, with 10-15% of the patients dying before getting to the hospital. Even the survivors have a 50% chance of permanent neurological damage (Emory Healthcare, 2004).

An aneurysm is a simply described as a weak spot, or defect, on the wall of an artery which becomes more compliant than a healthy vessel. Having less resistance to counteract hemodynamic forces, the weak area bulges outward. Aneurysms are more likely to form at high pressure regions in the circulatory system, such as at bifurcations. The aneurysm shape will vary from patient to patient, but it is commonly depicted as a roughly spherical or oblong protrusion from the artery wall. An important feature of the aneurysm is the neck. The neck is the interface region that links the parent vessel with the protrusion. It is characterized by its diameter, which is usually smaller than the largest dimension of the aneurysm. In general, the diameter of the aneurysm "dome" is an indication of the danger that rupture will occur.

Treatment of intracranial aneurysms has evolved from invasive surgical techniques to include interventional methods over the past several decades. The first form of treatment involved brain surgery to place a clip around the neck of the aneurysm to separate it from the parent vessel. With the development of microcatheter technology, endovascular treatment has emerged. Endovascular methods are minimally invasive and

pose less of a risk to older or medically sensitive patients. Currently, the most common endovascular treatment is embolization of the aneurysm by placing soft platinum coils inside the aneurysm. A catheter is navigated inside the circulatory system from the groin to the head where a platinum wire is deposited into the sac of the aneurysm. The wire is manufactured so that its natural shape is a helical coil. Thus, when the wire is pushed from the catheter, it forms into a coil and fills the aneurysm cavity. Several of these coils are inserted into an aneurysm so that blood flow into the aneurysm is blocked. With stagnant blood around the coils, clotting occurs that leads to thrombus formation. Total occlusion of the aneurysm from the parent artery results if a dense interconnected matrix of thrombus and scar tissue form across the neck of the aneurysm.

In a recent study interventional aneurysm therapy with coils has been shown to be better for patients than surgical clipping (Molyneaux et al., 2002). However, the long term clinical studies of platinum coil embolization have shown that there may be up to a 15% chance that the treated aneurysm will re-canalize (Kallmes et al., 1998). The cause of this outcome has been the subject of many studies in recent years. A vast majority of research concluded that the re-canalization problem is due to a combination of unorganized thrombus, limited fibrous scar tissue, and undeveloped neointima covering the neck of the aneurysm (Byrne et al., 1997; Kallmes et al., 1999). Without a stable matrix of tissue covering the entrance to the aneurysm, eventually the thrombus loosens, and blood flow is re-established into the defect.

Platinum is a relatively inert metal in the body, and therefore does not promote significant cellular response which would cause scar tissue formation. Also, it has been shown that there is limited endothelial cell adhesion on the bare metal surface of platinum

coils (Piotin et al., 2000). Because of the minor biological response and lack of cellular adhesion, platinum coils do not encourage the body's natural mechanisms of scarring and increases the risk of re-canalization.

In light of the risk of aneurysm recurrence with platinum coils, improved interventional devices are needed. One solution is to develop bioactive coils that do encourage a biological response within the defect. There has been several research efforts aimed at attaching a bioactive material such as a synthetic polymer or collagen, to the surface of the coils (Kallmes et al., 2003). It has been shown that these enhancements do indeed lead to more scarring and stable thrombus formation in animal studies.

Another coil modification that is currently being tested in clinical trials is hydrogel-coated coils (Cloft and Kallmes, 2004). A hydrogel is a loose network of polymer chains that rapidly absorb water. This absorption of water causes the hydrogel to swell. Hydrogel is considered to be very biocompatible. When a hydrogel-coated coil is deployed into an aneurysm, the hydrogel coating absorbs water from the blood and expands. The result is that blood flow is restricted more effectively because of the expansion of the hydrogel. One drawback of this type of device is that once deployment occurs, it may be very difficult to retract the coil back into the catheter if needed. Usually after five minutes of exposure to blood the hydrogel has fully expanded.

When making material enhancements to aneurysm coils, there are at least five issues to address. These are: biocompatibility, adherence of the coating, mechanical response of the coils, visibility to x-ray imaging, and cost. The issue of biocompatibility will examine the biological response of the body to the implant and potential for long term degradation or leaching of the coil material. Secondly, a coating must be stabilized

on the coil so that it will not come off during delivery. When collagen is polymerized onto platinum metal coils, the surface bond is very weak, and the coating can easily be removed by sliding through the catheter. Surface modification techniques such as ion bombardment are now being investigated to improve the surface bond (Murayama et al., 1997).

Another issue facing the design of enhanced coils is the effect a coating will have on mechanical behavior (i.e. stiffness, friction, and shape recovery). Typically coils are inserted into the aneurysm by manually pushing the coil from the catheter with an introducer wire. Most coils used in aneurysms have a core diameter of less than 0.40 mm and are very flexible. A coating that increases the stiffness of the coil could cause a puncture of the aneurysm wall. Furthermore, the coating must not interfere with the recovery of the wire to the natural helical shape. Obtaining a bioactive coating on a coil without compromising the mechanical properties is currently a challenge.

When aneurysm coils are implanted, the doctor relies on x-ray imaging to determine if the devices are placed properly. It is imperative that the coils are securely deployed inside the aneurysm and will not migrate out into the parent vessel. The only way to know for sure if the devices are located correctly is by real-time x-ray fluoroscopy. Platinum coils are quite radio-opaque, but polymers are typically not. Therefore, polymeric devices used in embolotherapy must have radio-opaque fillers or coatings added to them.

In the end, whether or not an enhanced coil is accepted into practice will be determined by cost. Currently the cost of one standard platinum coil is between $500 and $1000 (Kallmes et al., 1998). Typically 10 to 15 coils are implanted into an aneurysm.

A new type of coil must demonstrate improved cost-to-benefit ratios before physicians will switch from established devices to new devices and insurance companies will reimburse for them.

The impetus behind this research is to establish the feasibility of using a novel block co-polymer polyurethane material to replace platinum in the design of a new type of aneurysm coil. This material has the special property of shape memory, which means that it can be made to form a programmed shape after it is warmed. The physical behavior of the shape memory polymer, (SMP), may allow for complex three-dimensional coil configurations or customized shape coils that would be impractical with metal devices. A clinical study by Cloft, Joseph, Tong, Goldstein and Dion (2000) concluded that coils which can assume a three-dimensional configuration after deployment are advantageous for occlusion of aneurysms. As with the current coils, a SMP coil could be delivered as a straight fiber via a micro-catheter. Then upon emerging from the catheter into the aneurysm cavity, shape recovery would take place within seconds. The shape which is achieved can be a helical coil or practically any three-dimensional structure which may more efficiently block off the aneurysm.

The SMP material used in this research is comprised of polyurethane. In laboratory studies, polyurethane-coated platinum coils have been shown to promote significantly faster aneurysm occlusion than metal coils in animal studies (Ahuja et al., 1993). Completely polymeric coils have been surgically implanted in rabbit model aneurysms, and were shown to have improved effects over metal coils by promoting a greater cellular response (Murayama et al., 2003). Many types of polyurethanes are safe for use in the human body. Currently, polyurethanes are being tested for use in artificial

vascular grafts and scaffolds for tissue engineering (Lamba, Woodhouse, Cooper, 1998). Published research describing the biological response inside an aneurysm coiled with a SMP device has not been found.

With the application of aneurysm treatment as a driving force, this research investigates the mechanical behavior of SMP and SMP-metal composite material with thermo-mechanical testing. Thermo-mechanical analysis will be conducted to characterize the modulus change with temperature. Also, recovery stress generated in the material during shape change will be measured. Differential scanning calorimetry will be used to identify the molecular transition regions. Also, actual-sized, prototype SMP coils will be fabricated and deployed into a glass aneurysm experimental model to characterize the response of the device to simulated in-vivo flow conditions.

Radio-opacity of the implanted coil is crucial to accurate placement of the device. X-ray visibility can be achieved through the addition of a radio-dense filler such as tantalum. However, the effect of this filler on the shape recovery property cannot be predicted. This research intends to compare the mechanical properties of unfilled and tantalum-filled SMP specimens. Also absorption of low-energy copper $K\alpha_1$ x-rays in the SMP composite will be measured by x-ray diffractometry. The radio-opacity of metal-filled SMP coils will be examined with high-energy medical diagnostic x-rays using clinical fluoroscopic equipment at Emory University Hospital.

BACKGROUND

This research focuses on the application of a shape memory polymer (SMP) with metallic filler for use in a medical device to treat aneurysms. A shape memory polymer is a material that is engineered to recover a programmed shape after being heated above a certain activation temperature. This process is capable of strain recoveries of several hundred percent, and it can be repeated over many cycles. Shape memory alloys (SMAs) are well-known examples of shape-programmable materials that have been studied for many decades. Only recently have polymeric materials been developed that exhibit this unique property. In the last five to ten years, there has been an accelerating effort to learn more about the physical behavior of SMPs.

What allows the shape memory effect in polymers is the presence of two separated molecular phases, a hard segment and a soft segment. The hard segment is responsible for creating physical cross-links that "lock-in" the programmed shape, and has a higher glass transition temperature, $T_{g(hard)}$, than the soft segment, $T_{g(soft)}$. During the processing stage (i.e. extrusion, injection molding, etc.), the material is at or above the melting temperature, T_{melt}. All of the polymer chains have high degrees of mobility. Once the material cools down to $T_{g(hard)}$, the configuration of the hard segments is "stored" by physical cross-links. At temperatures between $T_{g(soft)}$ and $T_{g(hard)}$, the soft segments allow the material to deform to a temporary shape while the physical cross-links of the hard segments store strain energy. Below $T_{g(soft)}$, the material is completely glassy, and will hold a deformed shape without external constraint. When the material is heated back above $T_{g(soft)}$, the soft segments are too mobile to resist the strain energy

stored in the bonds of the hard segments. This results in an unconstrained recovery from the temporary deformed shape to the original "stored" shape. At temperatures higher than $T_{g(hard)}$, the physical cross-links of the hard segments release, thus erasing the "memory" of the polymer. Whatever shape the material has when the material is cooled below $T_{g(hard)}$, will be the programmed shape. And because the polymer is a three-dimensional network, a SMP can fully recover near 100% strain in all three dimensions.

The typical representation of the thermo-mechanical cycle of a SMP is shown in Figure 1 (Liu et al., 2003). In step one, the material, already heated to $T_{g(soft)}$ undergoes a high-strain deformation to a temporary shape. The second step consists of cooling the material while under constraint to hold the deformation. At some point, the stress required to hold the deformation diminishes to zero. In step three, there is a heating process back to $T_{g(soft)}$. If the recovery of the material is constrained, path 3a will be followed resulting in a recovery stress opposing the constraint. If there is a strain-free recovery, path 3b will be followed.
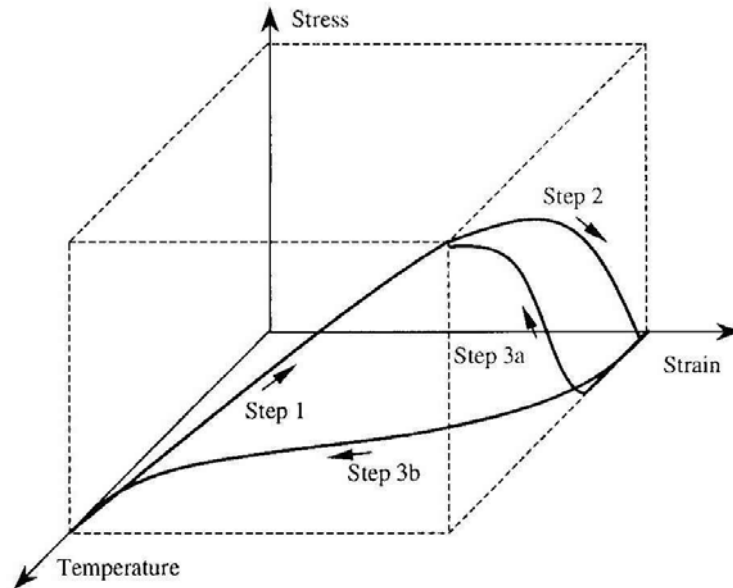
Figure 1. Stress-strain-temperature behavior of a shape memory polymer (Liu et al., 2003)

Figure 2 further illustrates the material behavior during unconstrained shape recovery (Gall et al., 2002).
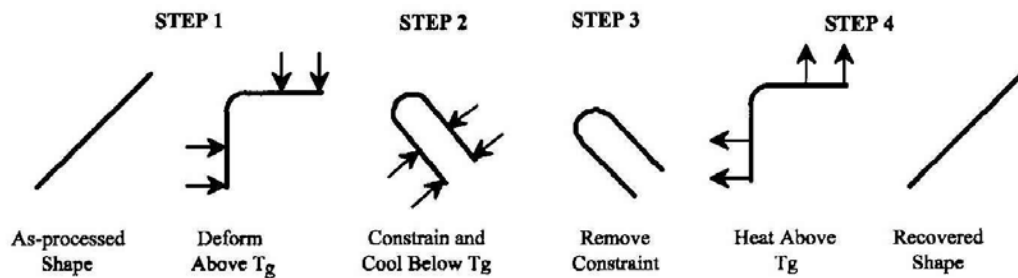
Figure 2. Steps involved in unconstrained shape recovery (Gall et al., 2002)

One of the benefits of SMPs over SMAs is that the shape recovery temperature can be engineered to occur over a wide range. Often the recovery temperature can be customized by adjusting the fraction of the hard and soft phases. Consequently, SMPs can be produced to function in the range of body temperature. Also, SMAs are limited to less than 10% strain recovery. As already mentioned, SMPs can recover strains of several hundred percent.

Other advantages SMPs have over SMAs are that they are lightweight and much less expensive to produce. A key point in favor of SMPs in biomedical applications is that biodegradable SMPs can be manufactured. Researchers at Massachusetts Institute of Technology have engineered a multiblock copolymer SMP that is biodegradable and biocompatible to use in self-tightening sutures (Lendlein and Langer, 2002).

A drawback, however, for SMPs is that the recovery force is relatively weak compared to SMAs. The shape recovery in an SMA is due to a martensitic phase transition, and the recovery stresses are in the range of 200 to 400 MPa. Current SMPs, have recovery stresses that are typically between 1 and 3 MPa (Liu et al., 2003; Lendlein and Langer, 2002). In some structural applications, SMP may not be able generate enough force during recovery to be viable. For example, there has been interest in designing a SMP stent for arteries. The ideal SMP stent would be fed as a straight fiber through a catheter to the damaged artery. As the fiber is pushed into the bloodstream it would warm to the activation temperature and quickly expand into a helical coil to hold the artery walls open. However, the constraint of the artery wall acting against the recovery force of the SMP device is such that it would prevent the device from fully deploying. Efforts are underway to increase the recovery force of SMPs by adding reinforcement to the polymer matrix with carbon or glass fibers or ceramic filler particles (Gall et al., 2002; Liu et al., 2003).

In some biomedical applications, a weak recovery force may be advantageous. Soft tissues in the human body typically undergo mechanical stresses more similar to the range for SMPs than for SMAs. In small, fragile blood vessels, such as in intracranial aneurysms, the high recovery forces exhibited by SMAs cannot be tolerated. It is important to fully understand the mechanical behavior of an SMP material before it can be safely used in the body.

Polymeric materials in the body are usually hard to detect using x-ray diagnostic imaging. To increase radio-opacity in polymers, radio-dense fillers may be added. The two most common fillers that are used are barium sulfate and tantalum. Both of these

fillers have been safely used in various polymeric materials which are implanted into the body. A common example is the use of tantalum or barium sulfate in acrylic bone cement (polymethylmethacrylate) for percutaneous vertebroplasty (Royal Australasian College of Surgeons, 2003). High loading filler fractions are often required to achieve good x-ray visibility. It depends on the location of the implant, but 40% to 60% weight filler fraction is not uncommon. This amount of filler can have a significant effect the mechanical properties of the composite. One of the objectives of this research is to examine the effect of a radio-opaque filler on the modulus and shape recovery of a SMP composite.

EXPERIMENTAL PROCEDURE

<u>Material Processing</u>

The shape memory polymer used in this research was donated by The Polymer

Technology Group, Inc[i]. It is specifically designed to have a glass transition temperature

of 33° C. Often during interventional neurological procedures, a cool saline solution is

injected into the blood stream along with the interventional device. Thus, having a shape

memory recovery temperature a few degrees lower than 37° C is preferred. Tantalum

metal powder (325 mesh) obtained from Alpha Aesar was used as a filler in the polymer

composite.

In order to conduct thermo-mechanical tests on the material, thin strip specimens

were prepared. To create prototype coils for use in the simulated aneurysm model, small

diameter fibers were produced. The SMP polymer is a thermoplastic material with a

melting temperature of about 140° C. To fabricate fibers with a diameter on the order of

0.35 mm, an extrusion processing procedure was considered. However, a typical

extruder was not be used because this would require a large quantity of polymer. Thus, a

custom-made extruder was fabricated for the purpose of extruding fibers with a small

quantity of SMP material. The extruder apparatus consisted of a 9.8 mm diameter hollow

aluminum tube and a threaded 9.4 mm diameter stainless steel rod. At the end of the

aluminum tube, a bronze end cap was attached with a 1.5 mm hole drilled through the

center. To produce thin strip specimens, a separate extruder was constructed that had an

aluminum end cap with a 1.5 mm x 16 mm rectangular slit. Images of the customized

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[i] The Polymer Technology Group, Inc. 2810 7th Street, Berkely, CA, 94710. Telephone: 510-841-8800.

extruders are shown in Figures 3 and 4. A thermocouple was attached to the outside of the aluminum tubes to measure the temperature during the extrusion process.

To make an extruded fiber or strip, the SMP pellets were inserted into the hollow tube followed by the threaded push rod. The extruder assembly was set on a hot plate to be heated to 140° C. When the melting temperature of the polymer was reached, the push-rod was advanced by hand toward the end cap. The pressure of the push rod on the melted polymer, forced the material through the opening in the end cap. Cooling of the extruded material to room temperature was not accelerated.
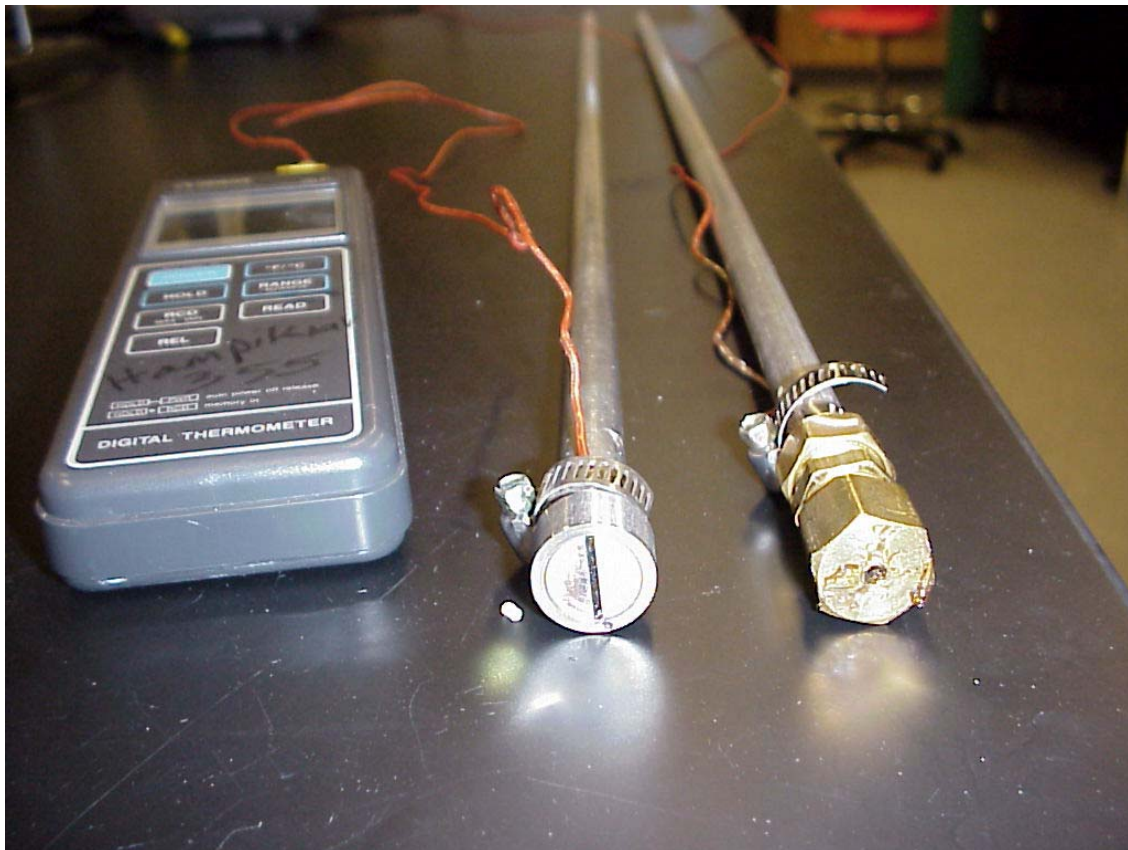

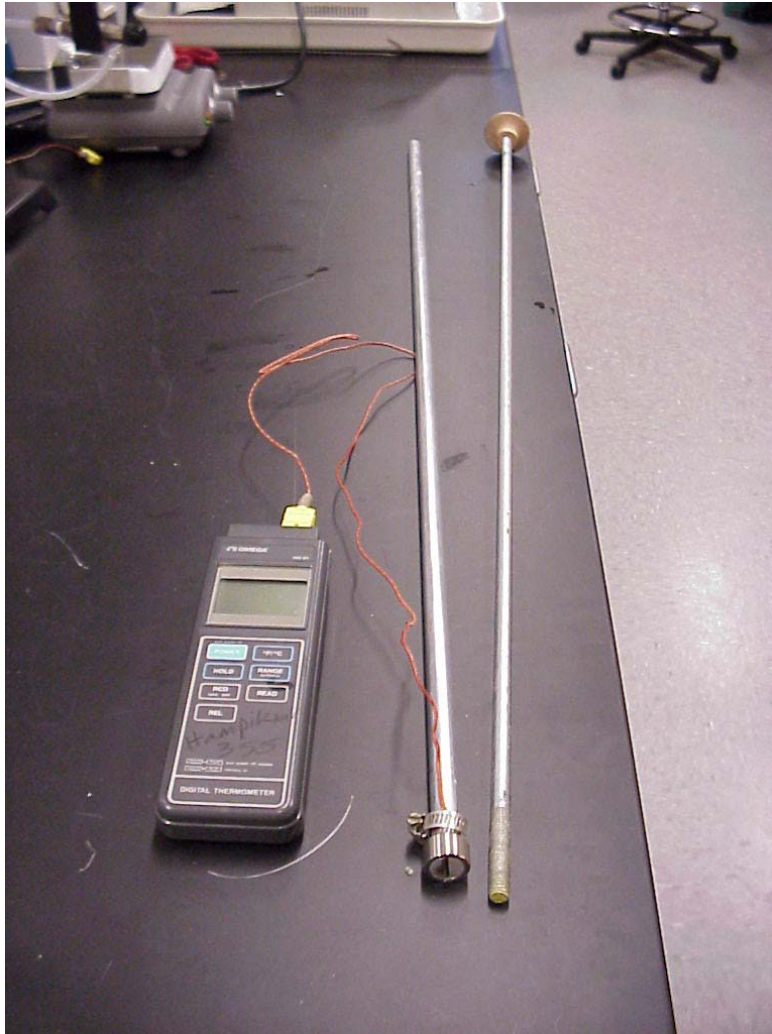Figure 3. Custom-made extruders used to make SMP fibers and strips.

Figure 4. Extrusion apparatus with attached thermocouple.

Fibers were drawn to the desired diameter. Diameters of the produced fibers varied from 0.25 to 0.45 mm. Strip specimens were produced by the slotted-end extruder in the same fashion as the fibers, except the material was not drawn. For thermo-mechanical testing of the SMP strips, uniformity of thickness was critical to get accurate results. It was observed the extruded strips did not have uniform thickness. To solve this problem, the extruded strips were compressed with a mounting press to create thin, uniform strips. The press was heated to 110° C and applied a pressure of 1200 psi for approximately 30 seconds. This created SMP specimens that were approximately 0.30 +/- 0.02 mm thick.

For the tantalum-filled material, a metal volume fraction of 3% was chosen. With a polymer density of 1.08 gm/cm^3, this corresponds to a weight fraction of approximately 50%. To make the composite material, a specialized blending procedure was adopted. Because the push-rod extruder had no way of mixing metal powder with polymer at the melt temperature, consistent particle distribution could not be assured. Therefore, a technique was developed to first mix the metal into a viscous solution of the polymer dissolved in toluene. The procedure involved dissolving the SMP material in toluene to create a viscous solution. Tantalum metal powder was then added to the solution and vigorously mixed. At a high viscosity, the particles remained suspended in the solution. The polymer-solvent-metal solution was poured into glass dishes for evaporation of the solvent. After 48 hours of air drying, the film of composite material was further dried in an 85° C oven overnight to evaporate the remainder of the toluene. Following drying, the film was cut into small pellets to be extruded into fibers and strips. Figure 5 shows two SEM images of a composite SMP specimen containing 3% tantalum. For consistency, all

of the unfilled specimens for this work were also processed using the specialized solution processing procedure.

Shape programming in the unfilled and composite specimens was conducted as follows. The processed material was heated to the rubbery state (> 33° C), allowing the material to be easily deformed. At this point, the specimen was shaped around a mold. To create a programmed shape of a helical coil from a fiber, the fiber was wound around a metal rod and clamped in place. A heat gun was used to heat the shaped SMP material secured to the mold up to a temperature of 100° C. At this temperature, the shape would be programmed into the material in about 60 seconds. The specimen was cooled below 33° C before removing from the mold.
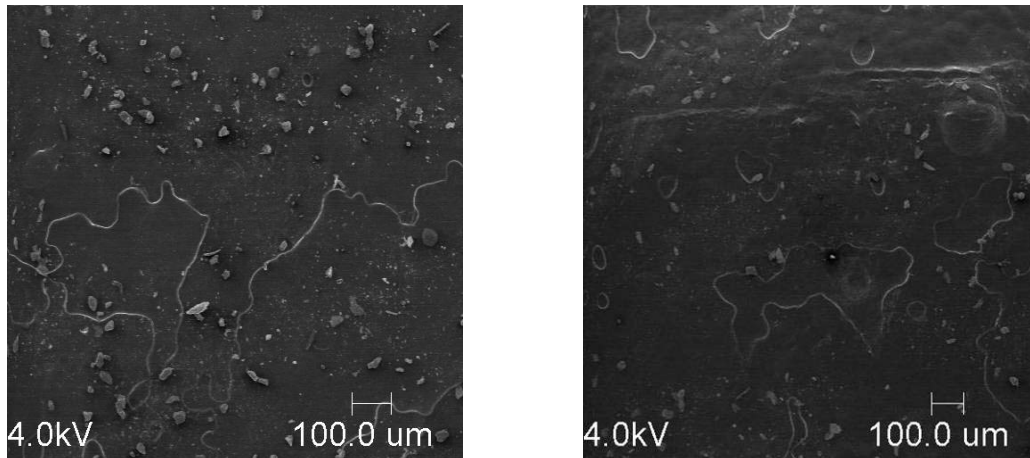
Figures 5a (left) and 5b (right). SEM micrographs showing SMP-tantulum composite material with 3% metal by volume.

Material Testing

       A shape memory polymer material has a unique thermo-mechanical cycle. A characteristic property of SMPs is a dramatic decrease in modulus around the glass transition temperature. The ability of SMPs to store and recover strains of several hundred percent and generate a recovery force during heating to the activation temperature is the most useful quality of the material. To investigate the thermo-mechanical behavior of the unfilled and composite SMP specimens, a dynamic mechanical analyzer (DMA) was utilized. Two DMA tensile tests were conducted: a dynamic, single frequency modulus test to characterize the change in modulus versus temperature, and an iso-strain test with increasing temperature to determine the recovery stress during the shape recovery.

       The test specimens for the modulus test were unfilled polymer and 3% (by volume) tantalum-polymer composite. Each of the rectangular test specimens were 4 to 6 mm wide and 10 to 15 mm long. The thickness of the specimens was between 0.24 +/- 0.02 mm and 0.33 +/- 0.02 mm. The specimens were carefully measured and the dimensions entered into the DMA software. After mounting the specimens in the clamps of the DMA, the material was cyclically loaded at a frequency of 1 Hz from room temperature up to 55° C at a heating rate of 3° C / min. The stress-strain response of the material at a given temperature was recorded and converted into a complex modulus for that temperature. Then, DMA software was used to separate the storage and loss modulus from the complex modulus. Knowing the storage modulus versus temperature enables one to predict the change in the material's stiffness as it is heated.

Test specimens for the recovery stress test also consisted of unfilled SMP and 3% (by volume) tantalum-SMP composite. The dimensions of the specimens for this test were similar to the modulus test. In preparation for the test, the specimens were shape-programmed to have an outward bow at mid-length (see Figure 6). After this programming step, the specimens were flattened as shown in Figure 7. Upon heating above the transition temperature, these programmed specimens would re-form the bow shape, effectively shortening the length of the strip. If a constraint were applied to the specimen to prevent the ends from retracting during the shape recovery, then a recovery stress would be generated acting against the constraint. To record the magnitude of the recovery stress, a DMA iso-strain test was performed using the shape-programmed specimens that had been straightened. The strips in the straight configuration were mounted in the clamps of the DMA and a constant tensile strain of 0.1% was applied. As the temperature was ramped from room temperature to 55° C at a rate of 3° C/min, the recovery stress was recorded as the strips attempted to resume the programmed shape.

In addition to the thermo-mechanical tests, the molecular transition regions in the polymer were investigated by differential scanning calorimetry (DSC). The purpose of the DSC tests was to identify major molecular transitions, such as the glass transition and melting point, in the un-filled and composite material. These tests were conducted to confirm the glass transition temperature, reveal the effect of metal filler on the molecular transition regions, and identify a secondary molecular transition in the region of the programming state temperature.
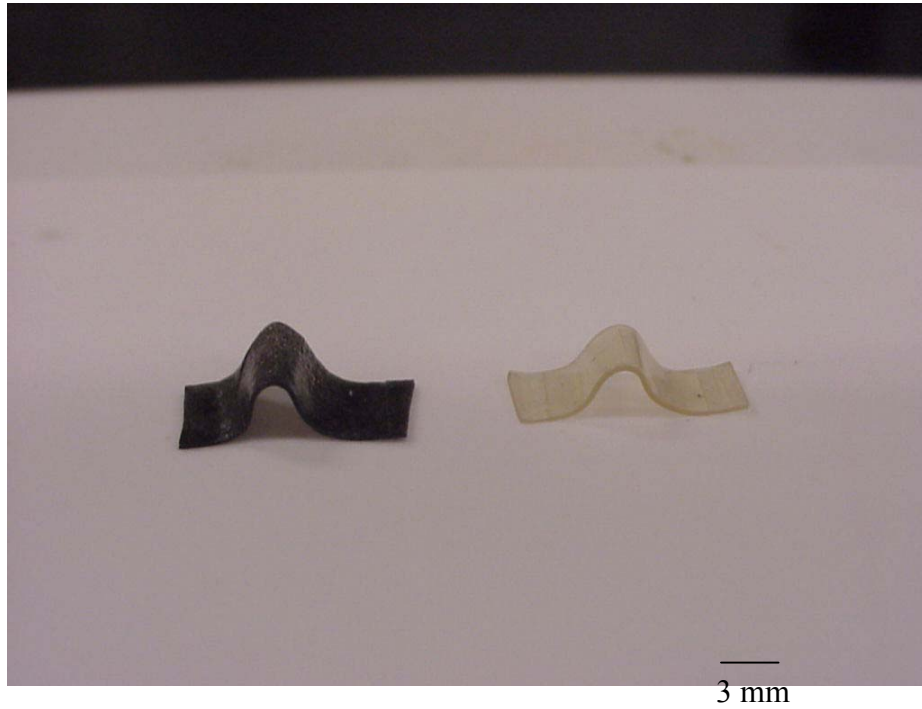
Figure 6. Shape-programmed strip specimens for recovery stress test. Tantalum-filled polymer (left) and unfilled polymer (right) were shape-programmed to have a mid-length bow as shown.
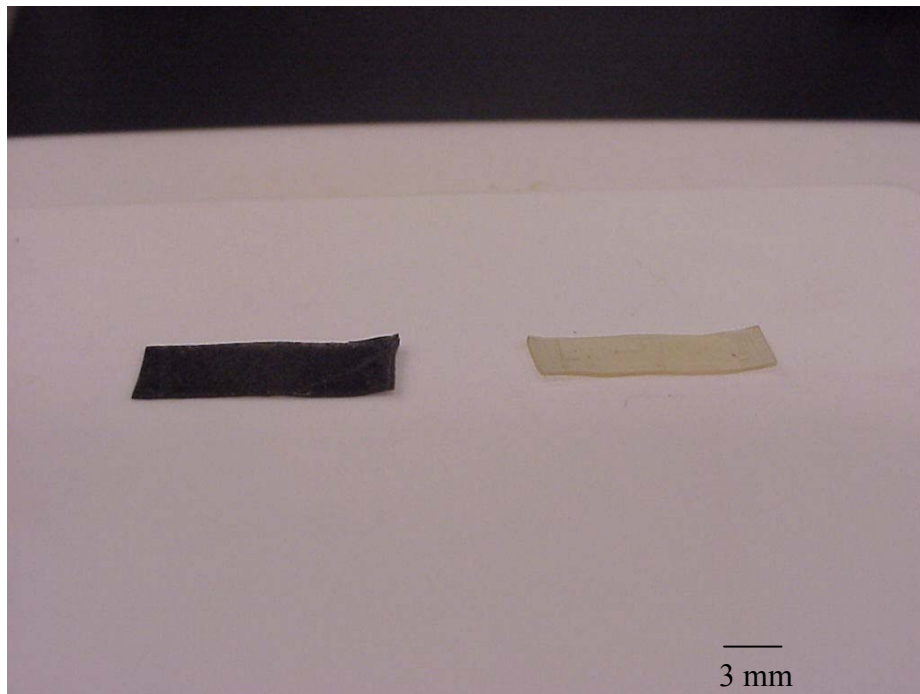

Figure 7. Recovery stress test specimens after temporary deformation.

Simulated Aneurysm Experimental Model

To determine the feasibility of SMP aneurysm coils an experimental model was built to test the shape memory recovery and mechanical behavior of prototype coils under simulated hemodynamic conditions. Five millimeter diameter glass tubing was fabricated into a T-shape to roughly imitate an arterial bifurcation in the brain. A "berry" shaped aneurysm was created in the wall of the glass tubing on the opposite side of the stem of the "T". This position would maximize the fluid forces inside the cavity. The glass aneurysm had a maximum outside diameter of 15 mm with a neck dimension of approximately 4 mm.

Clear plastic tubing was connected to each outlet of the glass model. A pump was connected to the stem of the "T," with a ball valve in-line to control the flow rate. The pump was placed in a sump that was heated by a hot plate to a temperature of approximately 42° C. This temperature was selected because the recovery test showed that the maximum recovery force occurs at this temperature. Also, at this temperature the modulus of the material is lower which allows a true examination of the deformation of the coil under stress. In an actual device, the maximum recovery force of the SMP material should occur at or below 37° C.

Connected to one end of the horizontal conduits of the glass model was the return line to the sump. To the other horizontal outlet, a tube was connected that fed the hemostasis y-valve. From the side-port of the hemostasis valve, a pressure gage was connected. Through the valve, a catheter was inserted which would deploy the SMP coils inside the glass model. A syringe port on the side of the introducing catheter allowed a

dye to be injected into the system to reveal flow patterns. A photograph of the

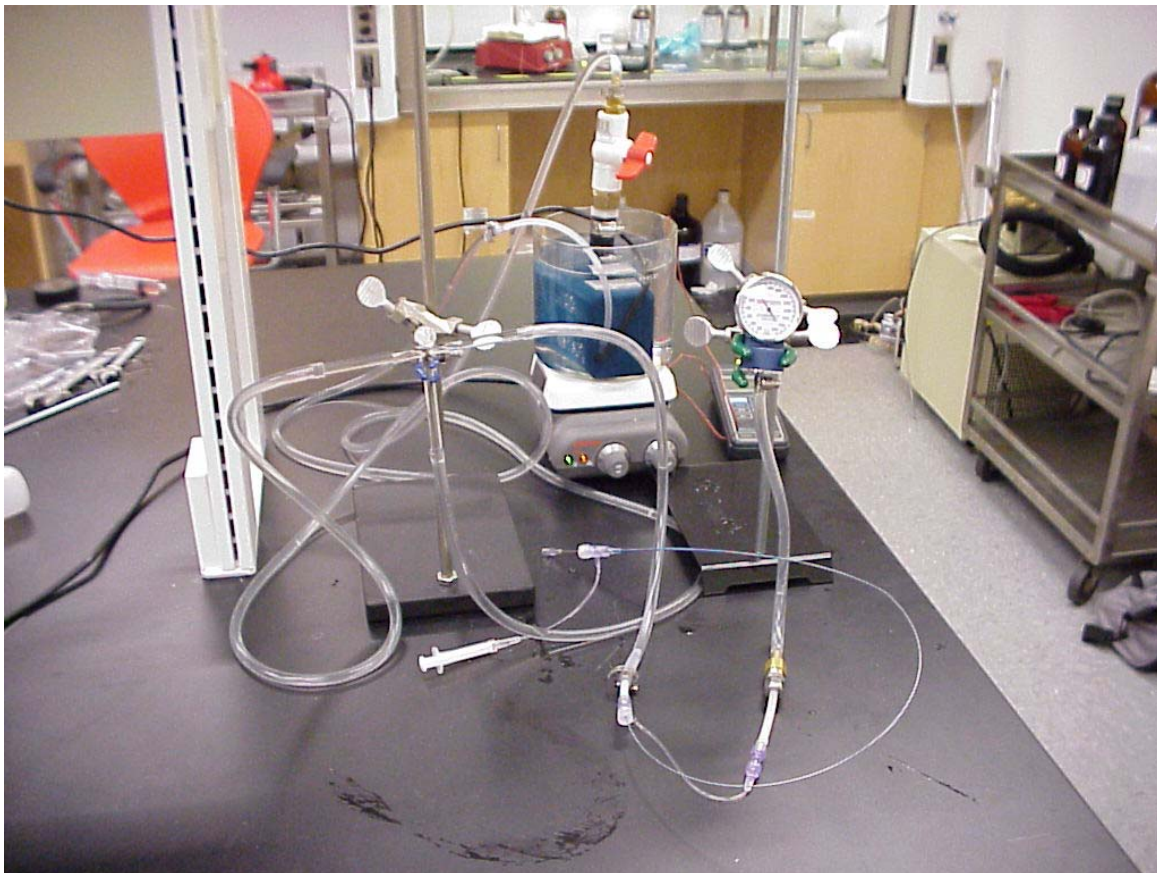experimental model is shown in Figure 8.

Figure 8. Simulated aneurysm experimental model for simulating in-vivo flow
conditions.

Helical coils were shape-programmed from 0.35 mm diameter SMP fibers. These coils had outer diameters of approximately 10 mm and lengths varying from 30 to 40 mm (see Figure 9). After being programmed, the coils were subsequently straightened so that they could be inserted into the catheter (see Figure 10). The SMP fibers could be pushed from the catheter using an introducer wire. Even with a pressurized system, the coils could be deployed into the glass aneurysm in a manner very similar to an actual interventional procedure.

Coils with tantalum filler were not examined in the simulated aneurysm model. The reason this was not done was because there was difficulty in making 0.35 mm fibers from the composite material using the custom-made extruder. While attempting to produce the small diameter fiber, the fibers would break during the drawing process. The comparatively large metal particles weakened the tensile strength of the material leading to fiber failure.
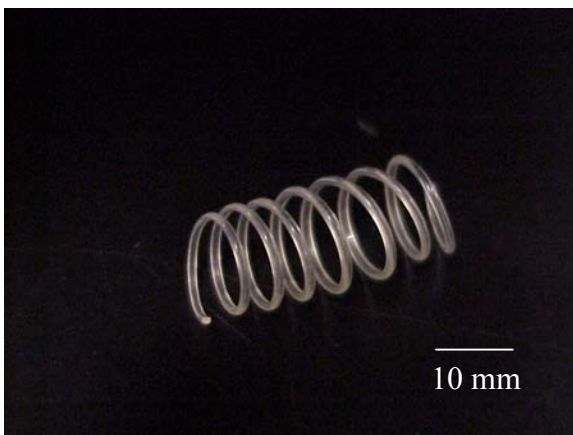
Figure 9. SMP fiber programmed with helical coil configuration.
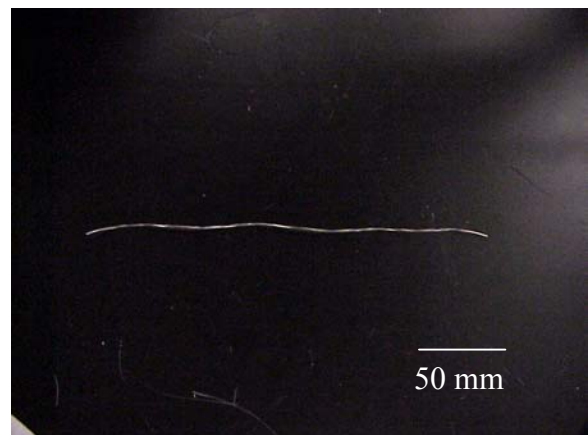
Figure 10. Straightened SMP coil prepared for catheter delivery.

Flow velocity in the cerebral vasculature is approximately 60 cm/s, and the pressure cycles between systolic and diastolic pressure (Ferguson, 1972). For this model, the flow rate was adjusted so that the velocity of heated water through the model would be approximately 60 cm/s. An assumption of a constant pressure of 140 mm Hg was chosen for this model for simplicity. The effects of pressure on the coils should be maximized under this assumption.

Radio-Opacity Testing

  To examine the effect of the tantalum filler on the radio-opacity of the material, unfilled and filled specimens were examined using x-ray diffractometry. The diffractometer was set to scan at angles close to zero in order to measure photon absorption through the thickness of the rectangular strip specimens. The thickness of the specimens was approximately 0.30 +/- 0.03 mm. The diffractometer generated characteristic Cu $K\alpha_1$ x-rays having a wavelength of 1.54 angstroms and energy of 8.04 keV. Three specimens were tested for x-ray opacity. Diffraction patterns were obtained for unfilled, 1%, and 3% tantalum by volume.

  Specimens of SMP-metal composite coils were examined for radio-opacity using clinical fluoroscopic imaging equipment at Emory University Hospital in Atlanta, Georgia. The specimens examined contained 3% tantalum by volume. The coils were immersed in approximately 50 cm of water inside a plastic container. Figure 26 shows an x-ray image of the tantalum-filled SMP coils taken by the fluoroscope at Emory. These three coils had diameters of 0.25, 0.45, and 0.088 mm.

RESULTS

Thermo-mechanical Testing

Specimens were produced from unfilled SMP material and composite-SMP material with 3% tantalum by volume. All of the specimens were processed from a thermoplastic SMP material obtained commercially. A homogenous dispersion of metal particles in the polymer matrix was attained by mixing the metal powder into a viscous solution of the polymer and toluene. Evaporation and drying of the solvent led to cast films of composite material which was cut into small pieces. These pieces were extruded into fibers and strips using a custom-made extruder (see Figures 2 and 3). The unfilled specimens were created with the same procedure, except without the addition of metal. Scanning electron microscope examination of the composite material (see Figure 4) showed good distribution of filler, without significant clumping.

For mechanical testing of polymers and other viscoelastic materials, dynamic testing is required since the mechanical response is time dependent. Therefore, a dynamic mechanical analyzer (DMA) was used in the testing of the SMP material. For DMA thermo-mechanical testing, uniform, thin rectangular strips were created by compressing the as-extruded specimens with a thermoplastic mold press. Metal-filled and unfilled test strips were tested for modulus change with respect to temperature. Shape memory polymers have the property of large modulus change over a short temperature range. The graph of the single frequency modulus test for the unfilled SMP material is shown in Figure 11. In viscoelastic materials, the storage modulus corresponds to the recoverable elastic strain. The loss modulus is that component of

25

stress which is out of phase with strain. Since it lags behind the strain, it represents the

viscous response of the material. The storage modulus gives a measure of stiffness of the

material, while the loss modulus is related to the energy that is dissipated by heat

(Findley, 1976). At the glass transition temperature, the material can absorb more heat

because of the increased mobility of polymer chains. Therefore, a maximum in the loss

modulus would occur at a temperature of T_g. In Figure 11, the maximum of the loss

modulus curve occurs at a temperature of 36.0° C. Between 27° C and 55° C, the storage

modulus of the unfilled SMP material drops from approximately 1400 MPa to 55 MPa.

The modulus test for the composite material with 3% tantalum by volume is

shown in Figure 12. The peak of the loss modulus occurs at a slightly higher

temperature, 39.0° C, than in the unfilled material. Also, the storage modulus at 27° C, is

about 22% higher than in the unfilled material. This is expected since a rigid filler

usually increases the modulus in a composite system.

The storage modulus decreases more steeply in the 27° C to 55°C range in the

composite material than the unfilled material. However, the moduli of the two systems

above T_g are very close to each other. Note the similarity of the storage and loss modulus

curves above T_g in the combined plots in Figure 13. This supports the conclusion that

addition of 3% volume fraction of metal filler into the SMP material has very little effect

on the modulus above T_g. For cardiovascular implants, a material with a low, tissue-

friendly modulus is desirable. The modulus of platinum is 168 GPa. Young's modulus

for the 3 volume percent tantalum-SMP composite at 37° C is approximately 1 GPa.

Thus, coils made of this material would have less than 1% of the stiffness of currently

used coils.

Next, DMA testing was conducted to investigate the magnitude of the recovery stress for the unfilled and composite material. Figure 13 shows the graph of the recovery stress of the two specimens as the temperature is increased. The unfilled specimen
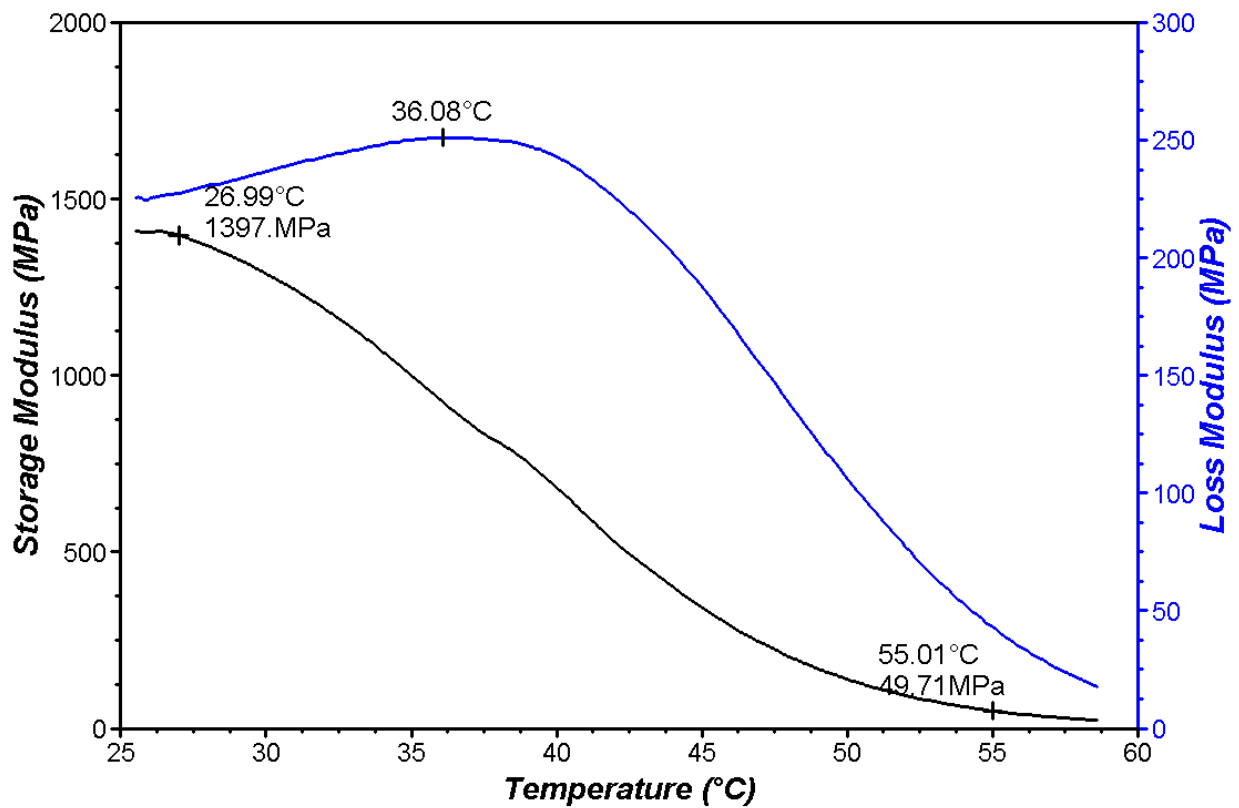

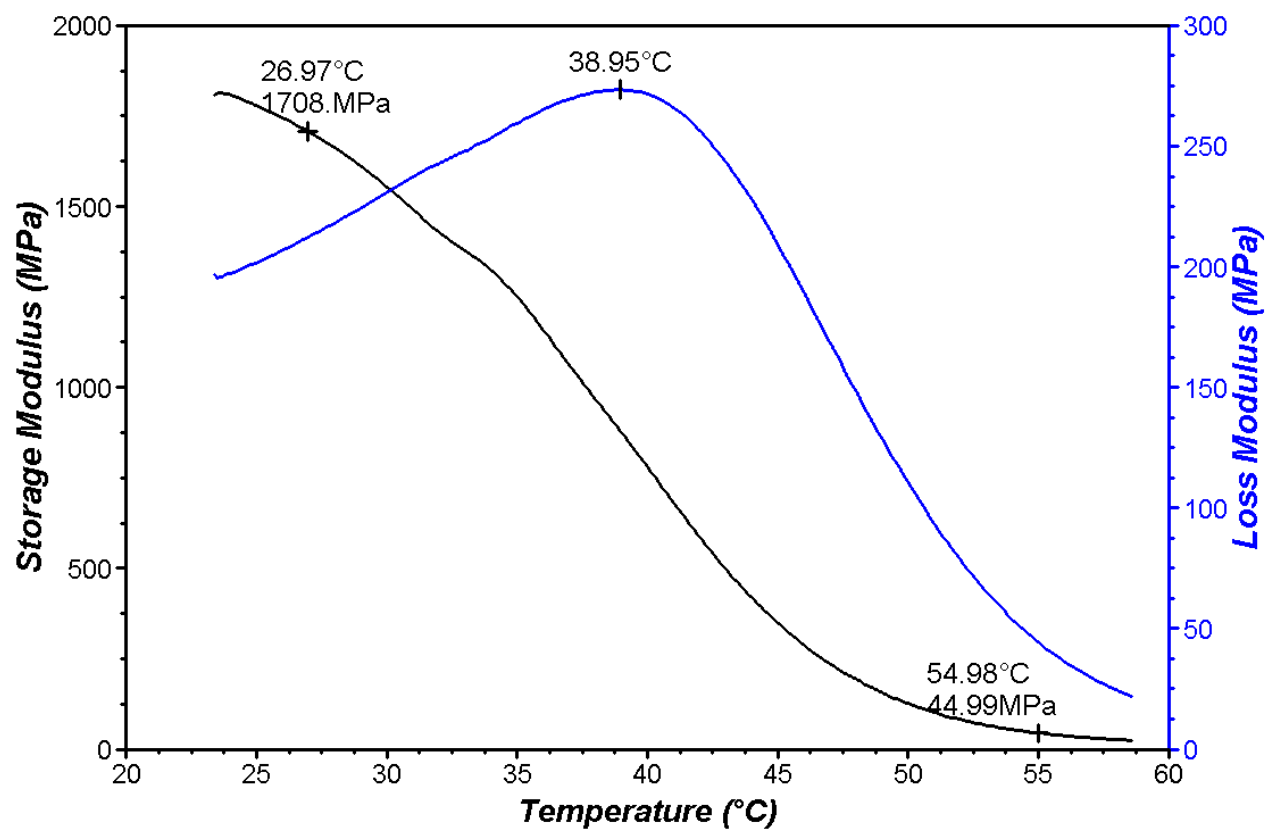Figure 11. Modulus versus temperature behavior of unfilled SMP near T_g.

Figure 12. Modulus versus temperature behavior of 3% tantalum-filled SMP composite near T_g.
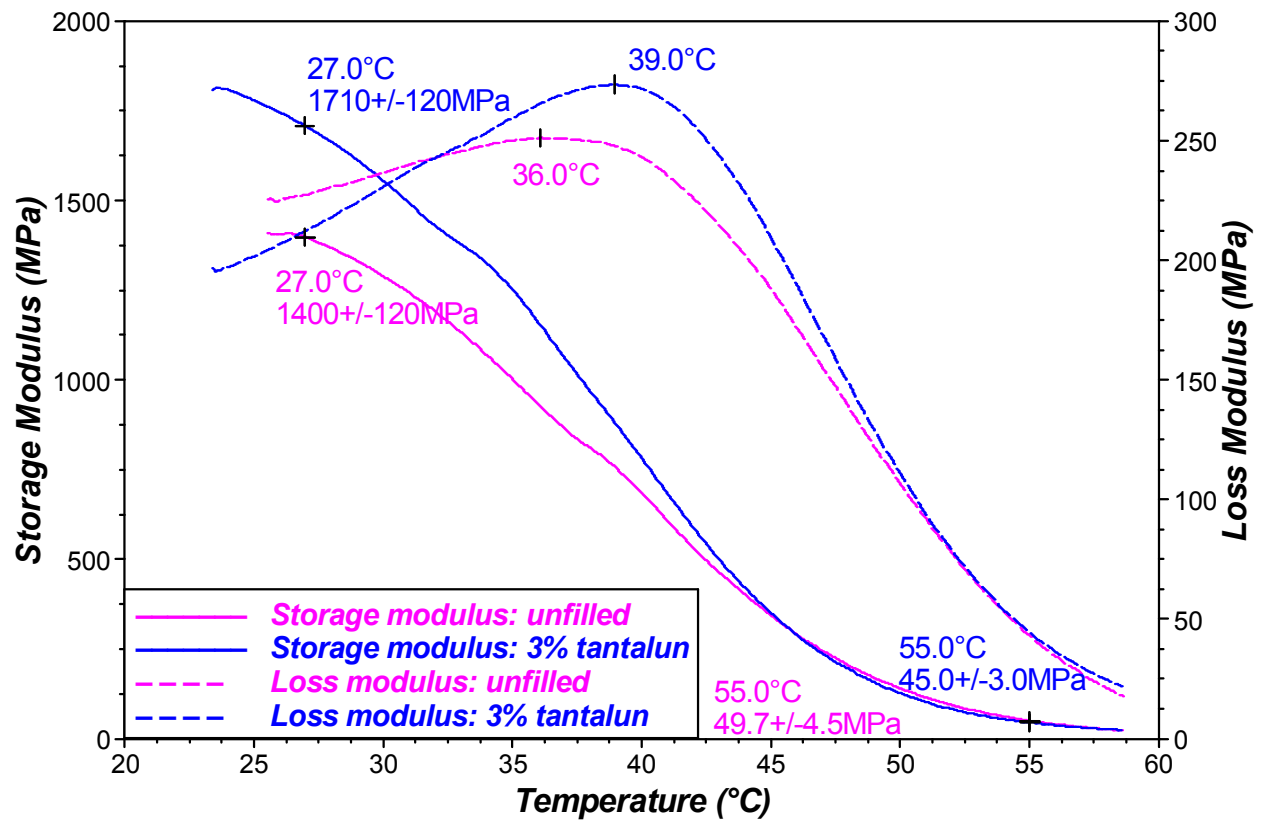
Figure 12b. Combined plots of the storage and loss moduli for unfilled and composite material.

shows an initial decrease in stress as the temperature increases from about 25° C to 30°

C. Then from about 30° C to about 40.4° C, the stress acting against the 0.1 % strain

constraint steadily increases to a value of about 0.18 MPa. As the graphs show, the

recovery stress then decreases after the peak at 40.4° C. Referring back to the modulus

test, at 40° C, the unfilled material has lost about 65% of its modulus at room

temperature. The maximum recovery stress temperature does not correspond to the peak

of the loss modulus curve. From these observations, it seems likely that recovery begins

to occur as the modulus, or stiffness, of the material decreases to a certain threshold. The

strain energy stored in the hard segments can overcome the soft segment's resistance to

deformation at a certain temperature and modulus. Under constraint, the recovery force

continues to increase as the temperature rises above T_g and the recovery stress competes

against the applied strain. Above some temperature, 40.4° C in this case, the recovery

stress is too weak to

overcome the compliance of the material and the applied strain. The shape recovery

could occur at these temperatures, but not at 0.1% strain. In fact, when the strain applied

by the DMA was released at 55 C, all tested specimens fully recovered to the

programmed bow shape. The steep decline in the curves near 55° C does not represent

another transition point. As the DMA established an equilibrium temperature of 55° C,

the heating rate slowed, and more time elapsed between one data point and the next. The

apparent sudden change in slope of the stress and force curves represent is due to stress-

relaxation in the material.

For the composite specimen, some notable differences were seen. The maximum

recovery stress was lower than the unfilled specimen. Also, the temperature of the

30

maximum recovery stress was lower by about five degrees. Furthermore, the recovery stress in the composite appears to occur over a broader range than in the unfilled material. An initial decrease in stress upon initial heating of the specimen was not evident.

It appears that the unfilled material undergoes a large stress reduction at the first stages of heating when compared to the recovery stress. This behavior is most likely due to thermal expansion of the polymer causing the dissipation of strain energy. The fact that this effect is not seen in the composite specimen is not completely understood.

As pointed out above, the recovery stress and maximum stress temperature are obviously affected by the filler. A lower recovery force may be expected in the composite because 3% of the polymer volume has been replaced by a rigid filler. The filler does not contribute to the shape recovery response, but it does increase the modulus. It seems reasonable that the stress an SMP material is capable of generating would be reduced in proportion to the stress required to deform the material back to an original shape. It must be pointed out, though, that other work in this area has shown that SMPs reinforced with ceramic nanoparticles and continuous fibers have demonstrated a greater recovery stress than non-reinforced polymer (Gall et al., 2002). The behavior may be governed by the size and shape of the reinforcement, whether it is particles, short fibers, or continuous fibers.
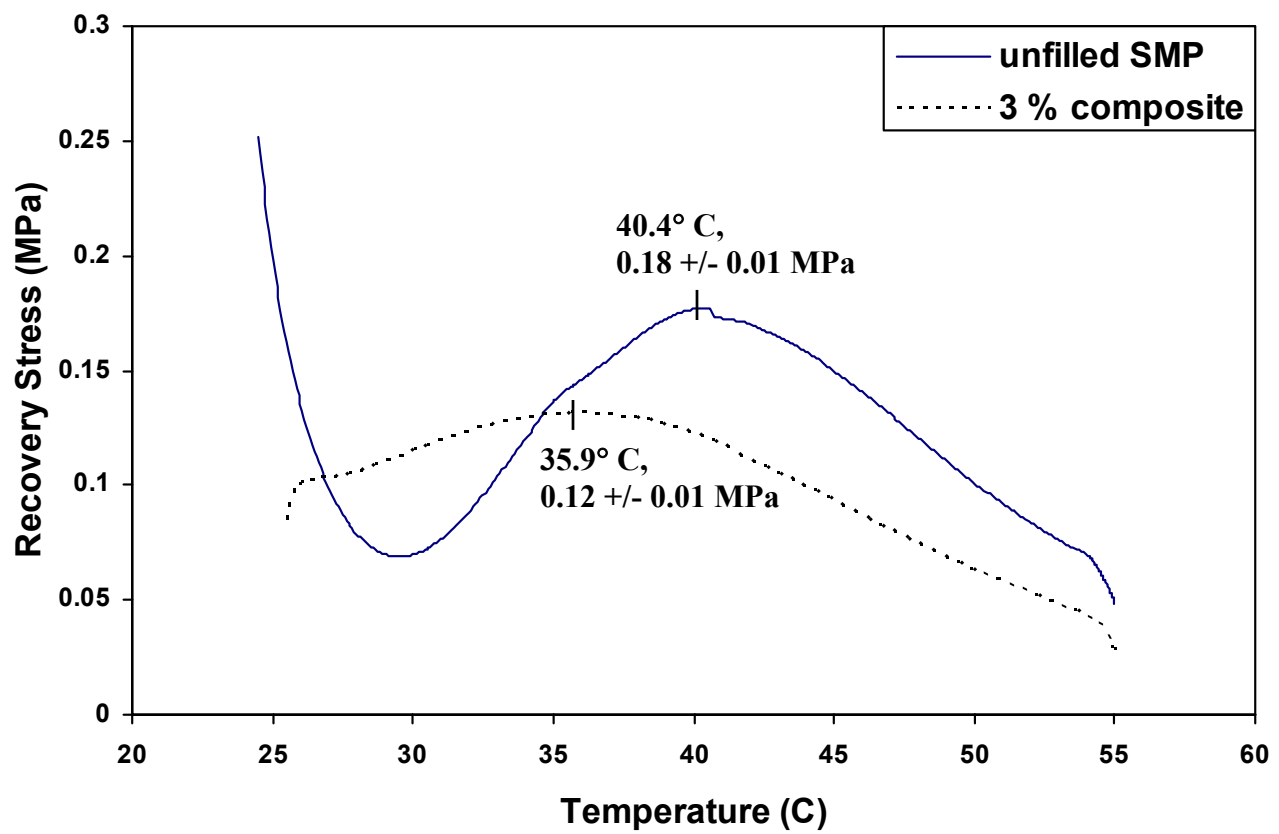
Figure 13. Recovery stress curves of the unfilled and composite SMP material.

Another notable finding is that the temperature at which the maximum recovery force temperature is lower in the composite than the unfilled material. Furthermore, the increase in the stress and the force begins around 27° C and continues over a wider temperature range than the unfilled material. The recovery in the composite specimen begins when the material has a higher modulus than the unfilled material. This may be explained by the idea that the metal particles linked to the hard segments in the polymer help the material recover internal strain at lower temperature and higher modulus. Metal particles linked to the soft segments do not offer much resistance to strain recovery once the soft segments become rubberized. This is a reasonable conclusion since the modulus test showed that the filler affects mechanical properties much more below T_g than in the rubber region.

In the modulus test, it was observed that the filler may either not affect or slightly increase the T_g of the material. The effect of the metal on the glass transition temperature of the SMP was investigated by DSC testing. If the filler causes T_g to shift lower, the recovery stress curve would also be shifted to lower temperatures.

DSC Testing

Figure 14 shows the results from DSC testing of the unfilled and composite material. A sudden drop in heat flow represents a molecular transition. At the glass transition temperature, polymer molecules become more mobile. This mobility can absorb extra heat from the environment. Therefore, the heat flow curves show a drop where molecular motion increases. Another transition point that shows up in the curves is at the melting point. The test data shows that the metal-filled material has a T_g which is approximately 3° C lower than the unfilled material. This result seems to validate the data from the recovery stress test. A separate molecular transition between T_g and T_{melt} was not observed. Thus, the temperature range at which shape programming occurs does not involve a noticeable change in heat flow.

An important result of the thermo-mechanical and DSC tests show that the processing procedure adopted in order to produce well-mixed composite specimens did not alter the shape recovery property or the molecular transitions of the SMP material. The modulus data observed during the modulus test was similar to the original, unprocessed material that has been published by the manufacturer. The magnitude of the recovery stress of the processed material was within the expected range. Also, the DSC test shows that the interaction of the SMP with solvent does not alter the molecular transition regions of T_g and the melting point.
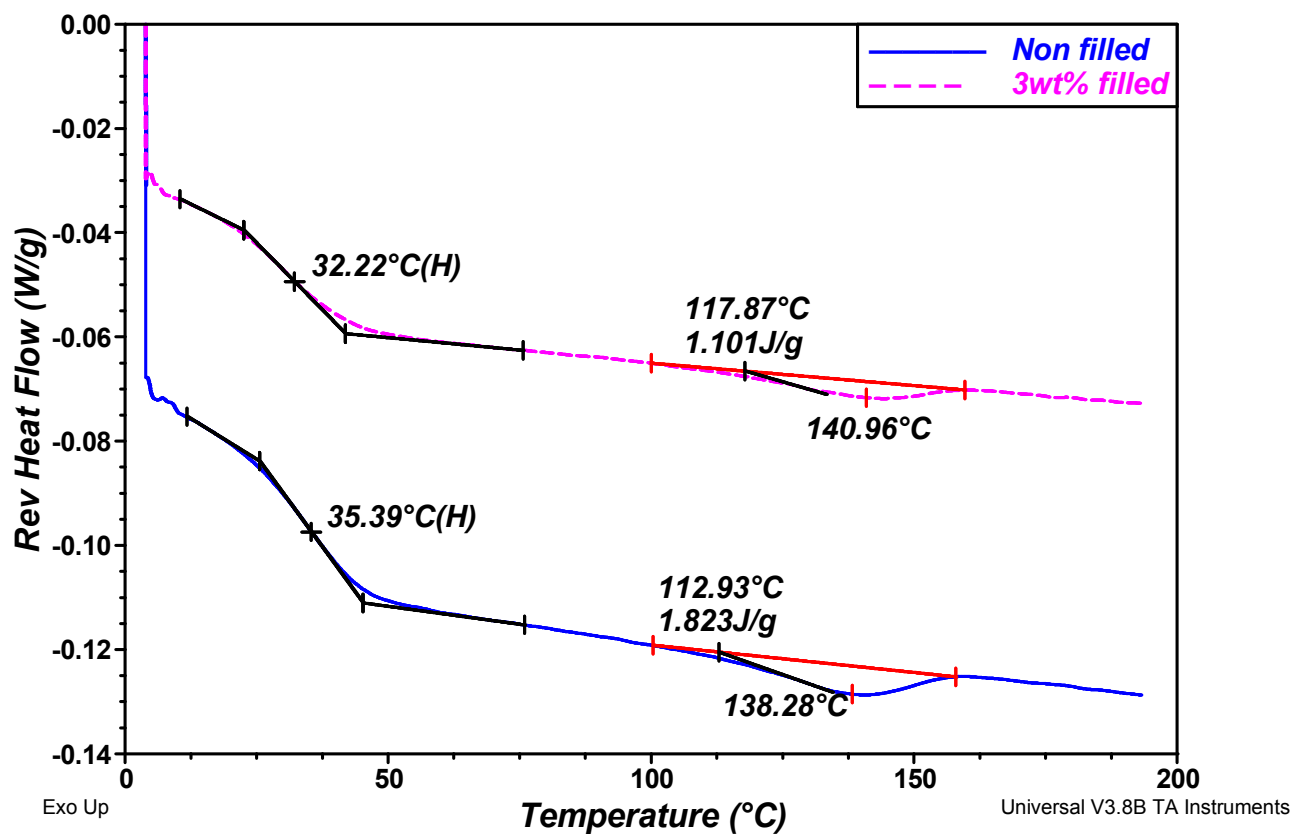
Figure 14. Reversible heat flow plots for unfilled and composite SMP material.

Simulated Aneurysm Experimental Model

A simulation of blood flow through a bifurcated artery with an aneurysm was created in an experimental model. The purpose of this experiment was to introduce shape-programmed SMP coils into a similar flow environment to in-vivo conditions, and observe the response of the material. To be a viable alternative to platinum coils, the SMP coils must behave in a predictable manner under hydrodynamic stress and confinement stress. The stress environment in an aneurysm is hard to predict. Every aneurysm has a different size and shape. The location of the aneurysm in the cerebral vasculature will affect the speed and pressure of the blood flow into the aneurysm cavity. Because of the variability of the external influences on an implanted coil, some generalizations were made to create an experimental model to simulate relatively extreme conditions. A typical bifurcation does not resemble a "T" shape; however, this arrangement was easier to fabricate, and it would allow higher fluid forces in the aneurysm cavity than would be expected. The velocity and pressure of the blood flow was maintained at 60 cm/s and 140 mm Hg.

The first criteria for successful deployment in the experimental model was that the coils would recover their programmed shape with fluid flow forces acting on the material. The second criteria for successful deployment were whether the coils would be stable in the aneurysm.

Two SMP coils were inserted into the aneurysm under simulated flow conditions. The first coil was inserted into the aneurysm cavity with no difficulty. As the straightened coil emerged from the catheter, it immediately began to recover the

programmed shape. Figures 15 and 16 show the first SMP coil inside the glass

aneurysm.

The second coil was inserted around the first coil. This coil exhibited the shape

recovery as expected, but a full recovery was not possible because of the space occupied

by the first coil. Figures 18 and 19 show the inter-twinning of the two coils.
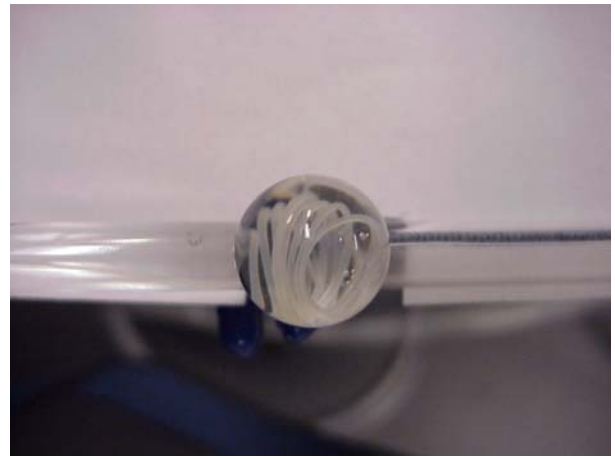
Figures 15 (left) and 16 (right). One SMP coil deployed in glass aneurysm under simulated blood flow conditions (top view and side view).
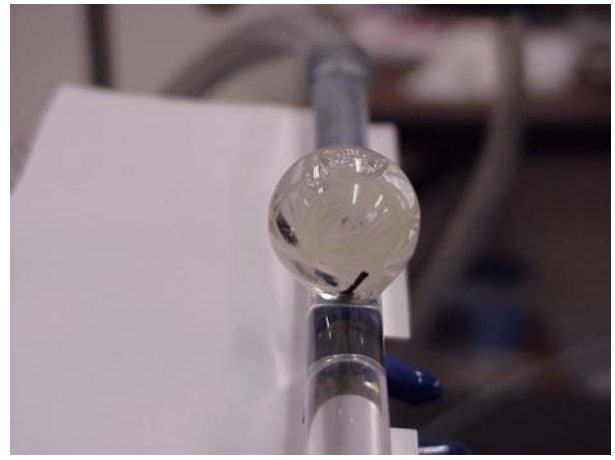
Figures 17 (left) and 18 (right). Two SMP coils deployed in glass aneurysm under simulatated blood flow conditions (side view and end view).

Both SMP coils achieved shape recovery, and no migration of the coils due to fluid pressure appeared to occur during the experiment. The first and second criteria for successful deployment were met.

In order to observe the effects of the coils on the flow environment, red dye was injected close to the neck of the aneurysm and within the cavity. Figures 19 and 21 show the response of the dye in each situation without coils. In Figures 20 and 22, dye was injected after the coils had been inserted. The flow pattern of the dye in Figures 19 and 20, and the retention of the dye inside the coiled aneurysm in Figure 22 seem to indicate that the coils help reduce flow velocity in the artificial aneurysm of this model.
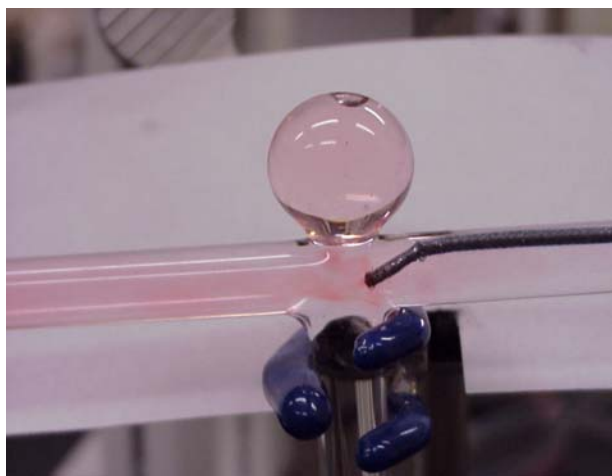
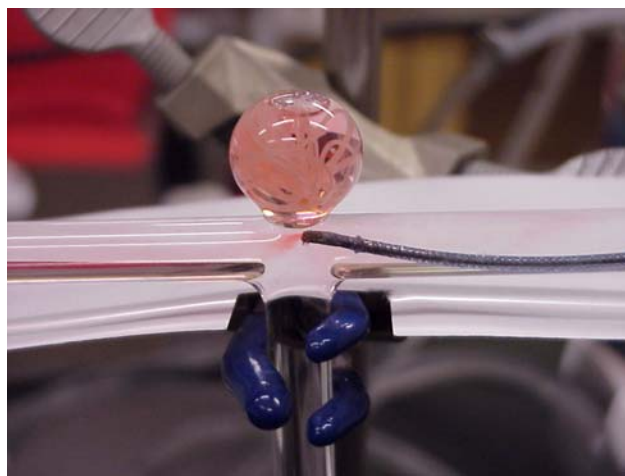Figure 19. Red dye injected near aneurysm neck without coils.

Figure 20. Red dye injected near aneurysm neck with coils partially blocking inflow.
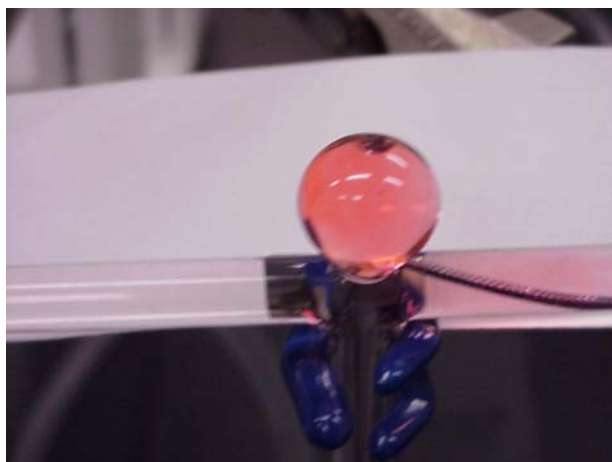

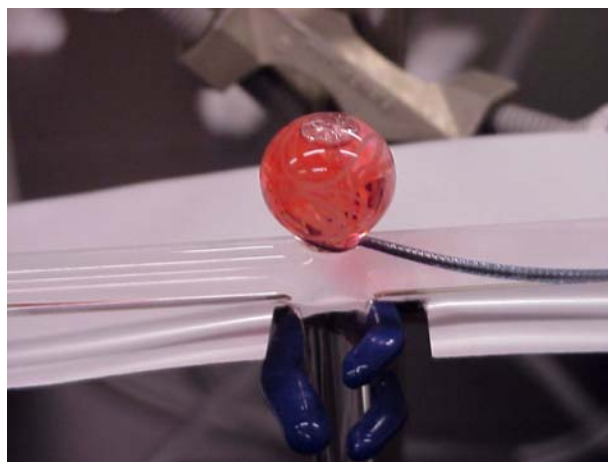Figure 21. Red dye injected inside aneurysm cavity without coils.

Figure 22. Red dye injected inside aneurysm cavity with coils restricting outflow.

Radio-Opacity Testing

Radio-opacity testing on the unfilled and metal-filled material was conducted on an x-ray diffractometer to observe the change in x-ray absorption of the material with the addition of tantalum powder. The diffractometer was set to scan at angles close to zero in order to measure photon absorption. The diffractometer generated characteristic Cu Kα_1 x-rays having a wavelength of 1.54 angstroms and energy of 8.04 keV. Three specimens were tested for x-ray opacity. Diffraction patterns for unfilled, 1%, and 3% tantalum (by volume) are shown in Figure 23. The patterns show that x-rays absorption increased with tantalum concentration. For the 1% tantalum composite, the intensity of x-rays received at the detector was 38% lower than the intensity for the unfilled material. For the 3% tantalum specimen, the x-ray transparency was reduced by 68%.

In clinical diagnostic imaging devices, the radiation source emits x-rays with higher energies and smaller wavelengths. Typically, the x-rays are generated from a tungsten target. The wavelength and energy of the characteristic radiation for tungsten is 0.209 angstroms and 58.87 keV, respectively (Cullity, 1978). At this photon energy, the mass absorption coefficient (μ/ρ) of tantalum is approximately 4.0 cm^2/g, while with Cu Kα_1 x-rays μ/ρ is approximately 160 cm^2/g (Hubbell and Seltzer, 1997). By comparison, the μ/ρ for human tissue with 60 keV medical x-rays is estimated at 0.2 cm^2/g, and the value is approximately 10.0 cm^2/g for 8 keV x-rays (Hubbell and Seltzer, 1997). The x-ray mass absorption coefficient of the metallic filler in the SMP matrix exposed to medical x-rays would be about 1/40 of the value obtained by diffractometry. It is difficult to compare the coefficients for the composite material because data for absorption of the SMP at various photon energies is not available. However, a review of

published absorption versus photon energy curves for various polymers shows that one would expect the mass absorption coefficient for the polymer in medical imaging would be about 1/20 of that in diffractometry (Hubbell and Seltzer, 1997). Considering the relatively similar coefficient ratios (1/40 for the filler and 1/20 for the polymer), it is expected that tantalum-filled SMP material would exhibit similar beam attenuation in medical imaging as in this work.

The mass absorption coefficient for a composite material could be theoretically predicted using the rule of mixtures. The equation for $\mu/\rho_{composite}$ is:

$$\mu/\rho_{composite} = \omega_1(\mu/\rho)_1 + \omega_2(\mu/\rho)_2 + \ldots \tag{1}$$

where the subscripts denote each phase in the composite (i.e. metal filler or polymer) (Cullity, 1978). The symbol ω denotes the weight percent of the particular phase.

Mass absorption coefficients at the photon energy of 8.04 keV can be calculated using equation 2 (Cullity, 1978).

$$I = I_0 e^{-(\mu/\rho)\rho x} \tag{2}$$

In equation 2, I is the maximum measured beam intensity, I_0 is the un-attenuated beam intensity, μ/ρ is the mass absorption coefficient, ρ is the density in g/cm^3, and x is the specimen thickness. It was assumed that μ/ρ for the shape memory polymer was approximately 4 cm^2/g, which is typical for most polymers at a photon energy of 8.04 keV (Hubbell and Seltzer, 1997). From the assumed value for the unfilled SMP, and the measured intensity values, a calculation was made to determine μ/ρ for the filled specimens (see Equation 3).

$$\ln I_{unfilled}/I_{composite} = -(\mu/\rho)_{unfilled}\rho_{unfilled}x + (\mu/\rho)_{composite}\rho_{composite}x \tag{3}$$

The value for specimen thickness, x, was 0.03 cm. The density of the unfilled polymer was 1.1%. For the 1% composition, the density of the composite was 3.4 g/cm^3. The density for the 3% composition was 8.6 g/cm^3.

A graph of μ/ρ versus metal volume percent is shown in Figure 24 along with the theoretical prediction. The experimental data from x-ray diffraction (XRD) does not follow the theoretical prediction of the rule of mixtures above a composition of 1%. It appears that the XRD line follows an asymptotic trend with the theoretical line as an upper bound. A reasonable conclusion for this behavior is that for a given particle size, there is a maximum number of particles that can span the thickness of the specimen. As volume fraction increases, the number of tantalum particles that the photon beam encounters approaches a limit which is based on the thickness of the specimen. Furthermore, the closer the particle size is to specimen dimensions (70 microns and 300 microns, in this case), it becomes less likely that a homogeneous distribution can be achieved. The rule of mixtures applies to a composite with a homogeneous special distribution of phases. In these tests, it seems that above 1% composition, there is a decreasing rate of increase of absorption for a given increase in metal filler. With the same specimen thickness, one may expect that a higher absorption would be achieved with smaller tantalum particles.

To determine if composite specimens having 3% tantalum by volume would be visible to clinical fluoroscopic imaging, metal-filled coils were produced and examined by fluoroscopy at Emory Hospital under the direction of Dr. Frank Tong. As shown in Figure 25, the coils were radio-opaque when submerged under approximately 50 cm of water. Water is similar to tissue in its ability to absorb x-rays. Therefore, the results of

42

this test show that the SMP composite containing a tantalum volume fraction of 3% is visible to clinical x-ray imaging.
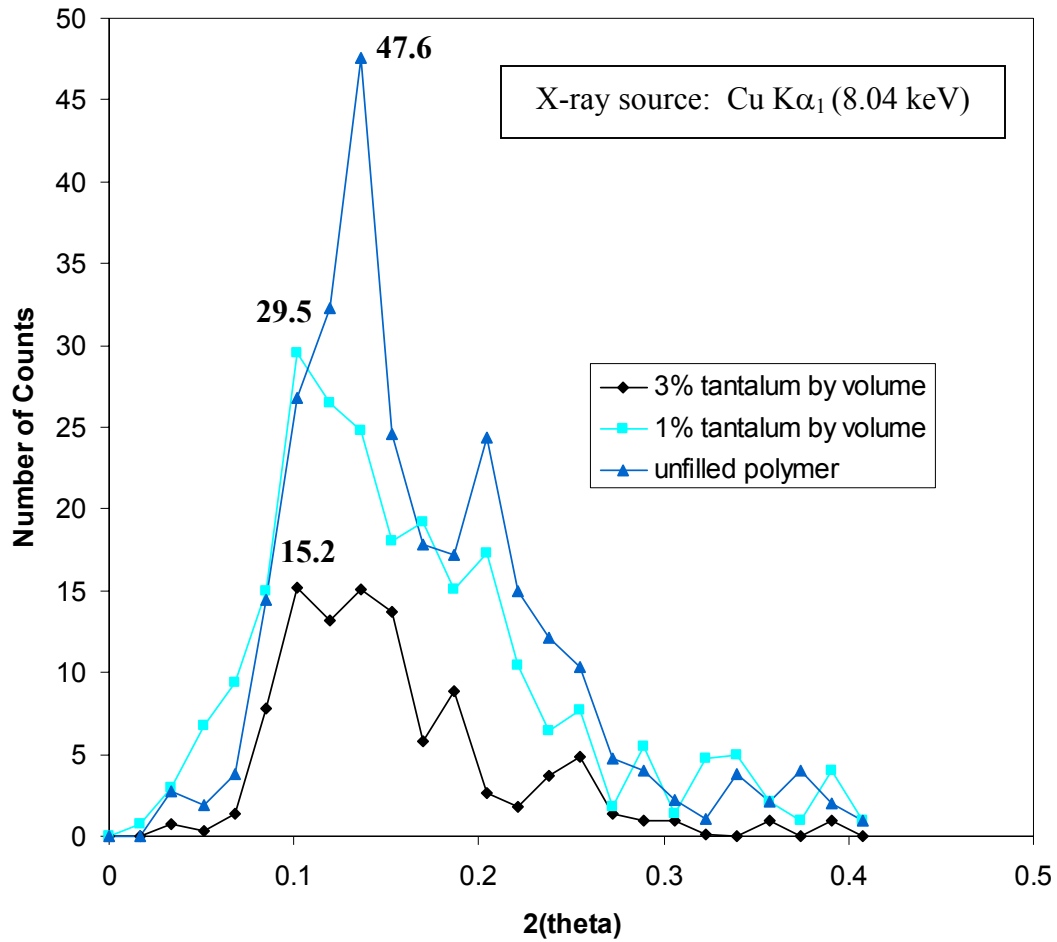

Figure 23. X-ray diffraction patterns for unfilled, 1%, and 3% (by volume) tantalum-filled SMP material.
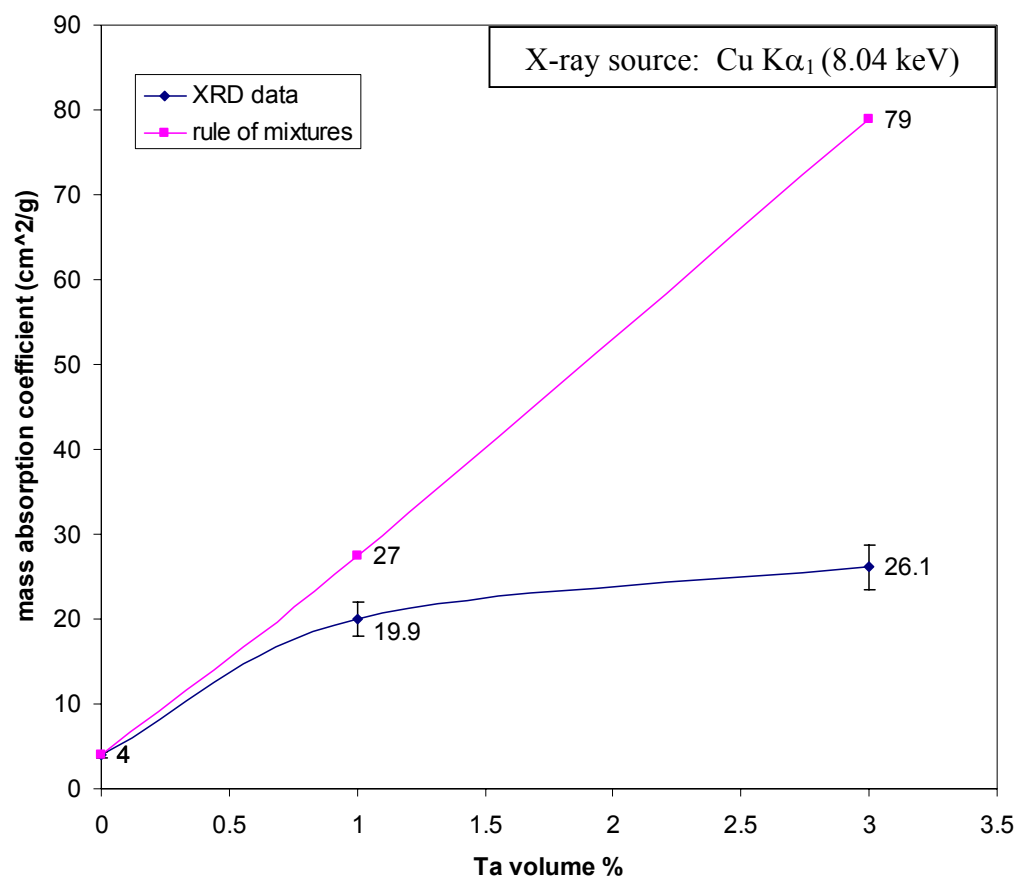
Figure 24. Theoretical and experiment composite mass absorption coefficient with varying tantalum fraction.
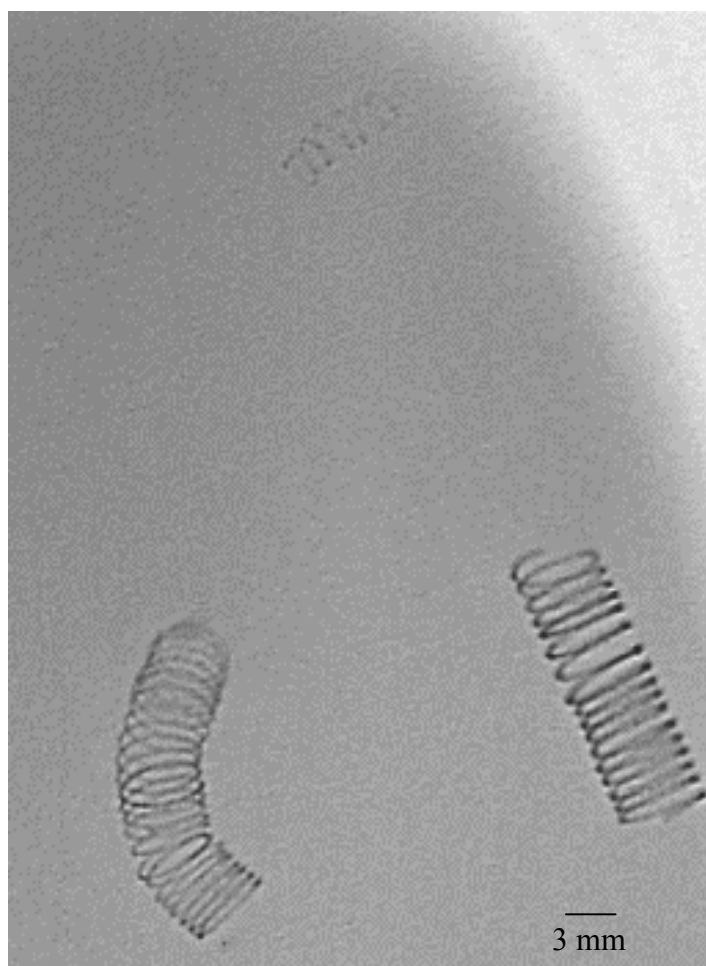
Figure 25. Fluoroscopic image of 3% tantulum-filled SMP coils with varying diameter immersed under 50 cm of water

CONCLUSIONS

The objective of this research was to investigate the mechanical and radiographic properties of a thermoplastic shape memory polymer material with and without metal filler for application in intracranial aneurysm coils. In this work, SMP material was successfully extruded into mechanical test specimens for thermo-mechanical testing. Also, prototype coils were produced to observe the response of the material under simulated hydrodynamic conditions. Additionally, composite specimens containing tantalum metal filler were successfully produced by a specialized mixing procedure that resulted in even distribution of metal particles in the specimen. The specialized processing procedure involved dissolving the polymer in toluene followed by drying of the solvent and casting of the SMP into sheets. The test data showed that the unique properties of the SMP were not affected by the radio-opaque filler.

The 3% metal-filled material showed an increase in modulus below T_g, but a similar modulus to the unfilled material's modulus above T_g. Both materials showed a steep decrease in modulus from 27° C to 55° C. Differential scanning calorimetry tests revealed that the T_g of the composite material was about 3° C lower than the unfilled material. In the modulus test, a measure of the T_g of the two materials gave similar results, however, in both cases it was higher than the DSC result.

A recovery stress test was performed with specimens to measure the available force which would be generated during shape recovery. Stress was measured at a constant strain as shape-programmed specimens were heated to the activation temperature. The magnitude of the maximum recovery stress was 0.12 MPa for the

composite material and 0.18 MPa for the unfilled material. A variation in the temperature in which the recovery stresses increase was seen. Maximum recovery stresses in the composite material occurred at a temperature of approximately 5° C lower than seen in the unfilled material. For the composite material, the maximum recovery stress is approximately 3° C above T_g as measured by DSC. The unfilled material exhibited maximum stress recovery 5° C above T_g.

The thermo-mechanical data shows that maximum recovery of composite and unfilled SMP material occurs in a range of 3° to 5° C above T_g. To achieve the highest recovery force from the material at body temperature, an SMP with a T_g between 32° and 35° C should be chosen. Adding metal filler does not affect the shape recovery behavior, but it does lower the T_g and maximum recovery stress.

An experimental model was created to simulate fluid forces on a SMP coil implanted into an intracranial aneurysm. Heated water was circulated at a flow velocity and pressure similar to in-vivo conditions. Coils were produced by shape-programming SMP fibers to have a helical coil configuration. These coils were deployed into a model aneurysm created in glass tubing as straightened fibers. Once introduced into the flowing heated water, the fibers quickly returned to the programmed coil shape inside the glass aneurysm. The hydrodynamic forces did not prevent the shape recovery from occurring. Also, coils were stable inside the aneurysm dome and did not compact or migrate within the cavity.

The x-ray diffractometer tests showed that tantalum filler increased the radio-opacity of the material, albeit under lower energy x-rays than would be used in medical imaging. The rule of mixtures formulation for calculation of composite mass absorption

coefficients did not agree with the experimental data above a 1% filler composition. The ratio of the particle size to the minimum specimen dimension may be a factor in predicting composite absorption coefficients. Examination of coils having 3% metal composition with clinical fluoroscopic x-rays did demonstrate that the composite material was radio-opaque at the higher energy radiation used in medical imaging

This research has shown that SMP material has acceptable mechanical properties for application in aneurysm treatment. The material has a low, tissue-friendly, modulus. Additionally, the shape recovery force is low enough to be acceptable in sensitive areas. Also, the polyurethane composition of the material is likely to be safe for use in the human body. Having shape memory allows the material to be introduced intravenously, and achieve a complex three-dimensional geometry inside the aneurysm. Achieving radio-opacity while maintaining the unique physical behavior does not appear to be an obstacle. The experimental model shows that extreme hydrodynamic conditions do not hinder shape recovery or coil implant stability.

Evaluating the mechanical and radiographic properties of SMP and SMP-metal composite materials is the first step toward determining whether they can improve the outcome of aneurysm treatment. The next step is to establish the biological response to this material.

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