Published in final edited form as:

Biomaterials. 2007 May ; 28(14): 2255–2263. doi:10.1016/j.biomaterials.2007.01.030.

Unconstrained Recovery Characterization of Shape-Memory Polymer Networks for Cardiovascular Applications

Christopher M. Yakacki¹, Robin Shandas^{1,*},², Craig Lanning², Bryan Rech¹, Alex Eckstein¹, and Ken Gall³

¹ Department of Mechanical Engineering, University of Colorado at Boulder, Boulder, CO 80309-0427

² Division of Cardiology, The Children's Hospital/University of Colorado Health Science Center Denver, CO 80218

³ School of Materials Science and Engineering/George Woodruff School of Mechanical Engineering Georgia Institute of Technology, Atlanta, GA 30332

Abstract

Shape-memory materials have been proposed in biomedical device design due to their ability to facilitate minimally invasive surgery and recover to a predetermined shape in-vivo. Use of the shape-memory effect in polymers is proposed for cardiovascular stent interventions to reduce the catheter size for delivery and offer highly controlled and tailored deployment at body temperature. Shape-memory polymer networks were synthesized via photopolymerization of tert-butyl acrylate and poly (ethylene glycol) dimethacrylate to provide precise control over the thermomechanical response of the system. The free recovery response of the polymer stents at body temperature was studied as a function of glass transition temperature (T_g), crosslink density, geometrical perforation, and deformation temperature, all of which can be independently controlled. Room temperature storage of the stents was shown to be highly dependent on T_g and crosslink density. The pressurized response of the stents is also demonstrated to depend on crosslink density. This polymer system exhibits a wide range of shape-memory and thermomechanical responses to adapt and meet specific needs of minimally invasive cardiovascular devices.

Keywords

Shape Memory; Polymer; Stent; Vascular Graft; Photopolymerization; Crosslinking

INTRODUCTION

Cardiovascular stents are synthetic material scaffolds used to expand and/or support blood-carrying vessels. The first clinical application of a metallic stent was performed in 1986 by Sigwart et. al.[1]. Since this pioneering surgery, approximately 650,000 – 1,000,000 percutaneous coronary interventions (PCI) are performed each year with nearly 80% of procedures involving stents [2,3]. In many conditions, stents are the standard of care since they

*Corresponding Author: E-mail: Shandas.Robin@tchden.org.

Corresponding Author for Submission: Christopher M. Yakacki, University of Colorado at Boulder, 427 UCB – Dept. of Mech. Eng., Boulder, CO 80309, chris.yakacki@colorado.edu, (303) 579-4624

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

can be delivered via minimally invasive surgery resulting in rapid recovery time and less surgical risk. Each year, advancements are made in stent design to reduce restenosis rates. Stenosis is defined as the constriction or narrowing of an artery often caused by atherosclerosis, in which cholesterol plaque builds on the inner walls of the artery. Angioplasty was developed in the 1970's to expand the walls of a stenosed artery using the inflation of a small balloon [4,5]. However, restenosis occurs in 30–60% of all patients who undergo balloon angioplasty alone within the first 6 months of the procedure [5]. Restenosis after balloon angioplasty follows a 3-stage response: acute elastic recoil, negative remodeling, and neo-intimal proliferation [3,6,7].

Stenting minimizes the responses of acute elastic recoil and negative remodeling [8] and thus reduces the restenosis rate to 10–40% [2,6,7]. However, even in the presence of a stent, cellular proliferation remains a contributing factor of restenosis and can be caused by the stretching and damaging of the wall during angioplasty [6], the body's response to the stent material [9], and a compliance mismatch between the stent and artery [9–11]. Drug-eluting stents (DES) are the most recent breakthrough in stent technology. Since their first clinical use in 2001 [12] and US commercial availability in 2003, DES's efficacy, demand, and cost have been growing exponentially [13]. Current DES's are polymer coated metal stents with anti-proliferative agents embedded within the polymer matrix. Drugs such as paclitaxel, sirolimus (rapamycin), and dexamethasone reduce restenosis by inhibiting proliferation, migration, and growth of smooth-muscle cells (SMC) [3,14,15]. This in turn reduces the SMC hyperplasia that forms a layer on the intimal wall of the vessel [3,7].

Even though polymer-coated metallic DES's further reduce the rate of in-stent restenosis, they do not represent an optimal solution. Metal stents have limited flexibility compared to the surrounding arterial wall, and thus induce a significant compliance mismatch. Even when the overall structural compliance of the metallic stent is matched to the compliance of the artery, local stiffness mismatch can cause the tiny stent ribs to exert significant localized stress on the artery wall [10]. Furthermore, given the miniaturized ribs required to lower overall stent compliance, only a limited amount of drug loading can be achieved in the thin polymer coating on a metallic stent [9].

Various researchers have proposed the use of pure polymer stents in place of metal stents [9, 16–18]. The feasibility and biocompatibility of polymer stents has been controversial especially after an early study showed an inflammation response to polymer coatings on stents [19,20]. More recently, the biocompatibility of polymers has been demonstrated in cardiovascular applications [16,21]. The Igaki-Tamai PLLA polymer stent was the first to be implanted in humans in 1999 [17]. The obvious advantages of polymer stents are the dramatic increase of drug-loading and biodegradation capabilities [9,18,22]. Additional potential advantages include improved compliance matching, ease and cost of fabrication, use of stereolithography for patient specific devices [23,24], molecular surface engineering [18], and the use of the shape-memory effect for minimally invasive deployment [9,25].

Shape-memory polymers (SMP) have gained increased attention over the last several years as a proposed biomaterial for minimally invasive surgical devices [26–32]. SMP's are defined by their capacity to recover large deformations from a stored packaged state in response to an environmental stimulus [32–34]. Shape-memory activation in polymers is most commonly induced by heat, but can also be triggered by light [35,36] or local chemical environment. To create a temporary compacted state, the polymer is heated above its glass transition temperature (T_g) to a soft rubbery state. The polymer is then deformed and cooled under constraint to set the material into a temporary packaged state. Shape-memory activation occurs when the polymer is reheated to the vicinity of T_g and returns to its original permanent shape. The fixing of the shape is due to restriction of micro-Brownian movement below T_g [37] whereas the

shape recovery is driven by favored entropic and internal energy states [27,31,38]. A useful shape-memory effect is observed in thermoset polymers with a distinct glass transition at an appropriate temperature.

Utilizing the shape-memory effect is an elegant and reliable way to deliver a large polymer scaffold in a minimally invasive manner. The stents can be pre-programmed to activate at body temperature, resulting in natural deployment without need for auxiliary devices (Figure 1). Strains up to 400% can be recovered in SMP's [39] without the adverse strain hardening effects encountered in metal stent expansion, facilitating delivery of larger devices through smaller delivery vehicles. Another area polymers may prove useful is the realm of pediatric stenting, in which metal stents cannot be sufficiently expanded throughout the growth of the patient [40–42]. Although various researchers have proposed the use of polymer stents, and even suggested deployment using shape-memory properties, very little work has been published on the design and performance of SMP's for cardiovascular stenting applications. The aim of this paper is to explore the storage, deployment, and subsequent deformation characteristics of several SMP stents with respect to their glass transition, crosslinking density, and mechanical design.

MATERIALS AND METHODS

Tert-butyl acrylate (tBA), di(ethylene glycol) dimethacrylate (DEGDMA), poly(ethylene glycol)_n dimethacrylate (PEGDMA) with typical molecular weights of $M_n=550$ and $M_n=875$, and photoinitiator 2,2-dimethoxy-2-phenylacetophenone were ordered from Aldrich and used in their as received conditions without any further purification. Solutions were made by manually mixing the functionalized monomers at different mass fractions in a glass vial with 0.1 wt% photoinitiator. The solutions were either injected in between two glass slides separated with 1 mm spacers for dynamic mechanical analysis (DMA) samples or in a thin-walled-tube mold to manufacture stents. The thin-walled tube mold consisted of a 21.4 mm Teflon rod sheathed with a 22 mm ID glass tube (Allen Scientific) to create polymer tubes with a wall thickness of 300 μm and 22 mm OD. A UV-Lamp (Model B100AP; Black-Ray) was used to photopolymerize the solutions at an intensity of $\sim 10 \text{ mW/cm}^2$ for 10 minutes for the DMA samples. Exact conditions for the polymer tubes are unknown because the mold was constantly rotating during photopolymerization. After processing of all materials, polymers were heat treated at 90°C for 1 hour to assist the complete conversion of monomers.

Polymer systems are defined by their glass transition temperature (T_g) and relative amount of crosslinking driven by the weight percent (wt%) of *di*-functional crosslinking monomers (DEGDMA, PEGDMA) contained within the entire solution. Six polymer networks were synthesized with 10 wt%, 20 wt%, and 40 wt% crosslinker, and with T_g 's of 52°C and 55°C. These chemistries were selected to systematically, and independently vary the rubbery modulus and glass transition temperature of the polymer. We note that the percentage of crosslinker indicates the amount of the *di*-functional monomers placed in the mixture prior to polymerization, and not necessarily any direct physical indication of the as-polymerized "crosslink density" which can be ascertained from rubbery modulus measurements.

Samples for DMA testing were cut to $15 \times 4 \times 1 \text{ mm}$ using a laser cutter. The edges of the samples were polished using 600-grit silicon-carbide paper to remove any localized edge effects caused by the laser. Dynamic flexural temperature scans (Figure 2) were run on samples ($n=3$) of each polymer using a Perkin Elmer DMA-7 to obtain the storage modulus through the glass transition. The peak of the tan delta curve marks the glass transition temperature (T_g) whereas the onset of the glass transition (T_{onset}) defines the beginning of the transition. The rubbery and glassy moduli can be seen as the plateaus above and below T_g . Exact values for T_g were calculated from the maximum of a 2nd order polynomial fitted to the peak of the

tan delta curve while T_{onset} was calculated using the intersecting line method. The breadth of T_g is defined as the twice the difference of T_g and T_{onset} .

In all DMA tests, samples were cycled at 1 Hz with static and dynamic stresses of 100 kPa and 90 kPa across a 5 mm span. These stresses were chosen to provide sample stability against collapse in the rubbery state while allowing measurable readings in the glassy state. Heating was performed at a rate of 2.5°C/min to eliminate temperature gradients within the sample. Data was collected every 5 seconds.

SMP stents were CNC machined from the polymer tubes previously defined. Solid stents and stents with 50% perforation (Figure 3) were compacted to fit into an 18 Fr. catheter (~6 mm). The perforation of the stent was created by drilling 1/8" holes in a close packed arrangement. Images of free recovery were taken using a digital camera at a frequency of 1 Hz and measurements were made using Image J once the stents had unrolled and started to unfurl (Figure 4).

Storage results were obtained by packaging stents to fit an 18 Fr. catheter at body temperature. Stents were cooled, pushed out of the catheter, and stored at room temperature, in which recovery measurements were taken over time. In this case, measurements correlated to the maximum diameter of the rolled stents before unfurling.

Lastly, stents were tested for pressurized response at body temperature. Stents were submerged into a body temperature bath and connected to a hose line with a variable pressure head. The pressure was gradually cycled twice from 55–160 mm·Hg with incremental steps of 15 mm·Hg. Digital images were taken at every step and diameter measurements were made using Image J.

RESULTS

The glass transition curves and parameters of the six networks are shown in Table 1 and Figure 5. Networks 1–3 exhibit a $T_g \sim 52^\circ\text{C}$ while varying the crosslinking over 10, 20, and 40 wt% while Networks 4–6 have a $T_g \sim 55^\circ\text{C}$ with crosslinking varied in the same range. In all networks, the onset of the glass transition is $\sim 10^\circ\text{C}$ lower than the glass transition temperature marked by the peak of tan delta. The rubbery moduli of the 20 wt% pair and the 40 wt% pair of crosslinked networks with different glass transitions are in strong agreement, measuring 5.6 MPa and 11.5 MPa. The pair of 10 wt% crosslinked networks with different T_g has slightly different rubbery moduli with Network 1 at 1.5 MPa and Network 4 at 2.4 MPa. Figure 5a illustrates independent variation in rubbery modulus through changes in crosslink density for Networks 1–3, which have $T_g \sim 52^\circ\text{C}$. The glassy regions for all three samples are essentially similar while the rubbery regions are significantly different. Figure 5b shows independent control of T_g for the 20 wt% crosslinked networks (Networks 2 and 5). Network 5 mimics Network 2's response, shifted $\sim 3\text{--}4^\circ\text{C}$ to the right.

Figure 6 shows a performance comparison of the solid stents recovering at body temperature (37°C) using image analysis of the stent recovery data as defined in Figure 4. Figure 6a shows the free recovery data of solid stents made from all 6 networks and compacted at room temperature. The first stents to fully recover in each group were the 40 wt% crosslinked stents, followed by the 20 wt% and the 10 wt%. The fastest recovery time was achieved in ~ 10 seconds (40 wt% crosslinked: $T_g = 52^\circ\text{C}$) whereas the slowest recovery time was ~ 10 minutes (10 wt% crosslinked: $T_g = 55^\circ\text{C}$). Figure 6b demonstrates the effect of deformation temperature (T_d) on the recovery characteristics of the stents. In this case, a 10 wt% crosslinked stent with a $T_g = 52^\circ\text{C}$ was deformed (packaged in the catheter) at both room temperature and body temperature. The stent deformed at a lower temperature experienced accelerated recovery compared to the stent deformed at body temperature. Figure 6c shows the effect of raising the

recovery temperature. In this case, a 10 wt% crosslinked stent with a $T_g=52^\circ\text{C}$ was deformed and recovered with $T_d=T_r$ at 37°C and 42.5°C . The stent with $T_d=T_r=42.5^\circ\text{C}$ recovered in approximately 100 seconds while the stent with $T_d=T_r=37^\circ\text{C}$ recovered in approximately 400 seconds.

The performance of the solid stents vs. the 50% perforated stents can be seen in Figure 7. Figure 7a compares the two designs of the 10 wt% crosslinked polymer with a $T_g=52^\circ\text{C}$. It is observed that the perforated stent design initiates recovery earlier than the solid stent. However, after approximately 50% recovery, the solid stent matches the recovery of the perforated stent. From ~50% recovery onward, both stents reform at the same rate. This trend has also been observed in the other networks. Figure 7b showcases this trend in stents made from Networks 2, 4, and 5. In all cases, the perforated stents initiate recovery earlier than the solid stent, but after some margin of time the solid stent recovery behavior closely matches the recovery of the perforated stent. The only exception to this is the 10 wt% crosslinked polymer with a T_g of 55°C . In this case, the solid stent recovers faster than the perforated stent after 20% recovery.

The ability to store packaged stents at room temperature *without constraint* is shown in Figure 8. During the course of 1 month, the average room temperature was 22.9°C with a minimum and maximum of 21°C and 25.8°C on days 10 and 4 respectively. Figure 8a shows the solid stents with a T_g of 52°C recovering significant strains with recovered strain proportionate to the crosslinking. The highest crosslinked stent, 40 wt%, fully recovered within 1 day and is marked by a circle. However, the 10 wt% and 20 wt% crosslinked stents gradually recover strains over 1 month and show a spurt of recovery at day 4, which corresponds to the hottest day of the month. In Figure 8b, the stents with a T_g of 55°C show a slower response, with the 10 wt% crosslinked stent maintaining its packaged state.

Stent performance under pressurized conditions is demonstrated at body temperature in Figure 9. Figure 9 shows the diameter change for solid stent tubes made from Networks 1–3. The 10 wt% crosslinked stent diameter shows a dramatic increase from its original 22 mm starting diameter. Furthermore, it shows a large hysteresis loop and permanent strain after the first cycle. The 20 wt% crosslinked sample displays a much smaller strain and hysteresis loop while the 40 wt% crosslink sample responds elastically with no hysteresis.

DISCUSSION

It is important that the thermomechanical response of SMP's be highly controlled to predict and optimize shape-memory properties. As of now, there is no definitive answer to how fast or how strong the shape-memory effect must be for deployment in cardiovascular vessels. Furthermore, there has been little work to evaluate the necessary thermomechanics of polymers for stenting. Therefore, we have chosen to work with a thermomechanically adjustable polymer system that is capable of adapting and responding to future research that will answer these fundamental questions.

Thermomechanical tailoring of this system is achieved by varying the concentration and molecular weight of the PEG crosslinker. Table 1 displays the thermomechanical values of the 6 polymer systems while Figure 5 illustrates the ability to independently control rubbery modulus and glass transition temperature. Two sets of polymers were manufactured with 10 wt%, 20 wt%, and 40 wt% crosslinking with glass transitions of $\sim 52^\circ\text{C}$ and $\sim 55^\circ\text{C}$. By measuring equal differences in the onset of glass transition and the glass transition itself ($T_g - T_{\text{onset}}$), we show the second set of polymers ($T_g=55^\circ\text{C}$) has the same thermomechanical response of the first set ($T_g=52^\circ\text{C}$) shifted several degrees to the right. Within each set, T_g can be held constant while the rubbery modulus is varied. The rubbery modulus is a direct indication of the crosslink density within the polymer matrix and highly influences the recovery rate and

induced forces during shape recovery. These formulations and temperatures were chosen to show the ability to create polymer networks that can fully activate the shape-memory effect at body temperature, thus eliminating the need for supplemental heating, while offering the ability to be stored at room temperature under constraint without permanent strain.

Additionally, these networks illustrate the effect of crosslinking density and T_g on free recovery properties critical for the delivery of cardiovascular stents. Figure 6a shows that networks with higher crosslinking densities will recover faster than their less dense counterparts even when both materials have a similar glass transition behavior. This is due to the fact that the crosslinking dictates the mechanism of shape memory in polymers [43]. Furthermore, Figure 6a shows that the polymers with a glass transition closer to body temperature will reform faster than polymers with a glass transition farther from body temperature. This occurs because chain motion becomes less restricted as the temperature approaches T_g . Figure 6a shows the fastest recovering stent has the highest degree of crosslinking and lowest T_g , while the slowest stent had the lowest degree of crosslinking and highest T_g . However, there is considerable overlap between these two extremes. Samples 2 and 6 (20 wt%: $T_g=52^\circ\text{C}$ and 40 wt%: $T_g=55^\circ\text{C}$) and Samples 1 and 5 (10 wt%: $T_g=52^\circ\text{C}$ and 20 wt%: $T_g=55^\circ\text{C}$) show very similar recovery characteristics. These results indicate that the recovery time is influenced by the glass transition and crosslink density, something that has not been previously demonstrated for shape memory polymers, and something that is critical for the design of cardiovascular stents. It is also important to note that in the present system, T_g and crosslinking can be varied independently of recovery time, which allows the stents to be designed to recover in a specific timeframe and have a range of mechanical properties.

The recovery time of a SMP stent is not strictly dictated by its chemical composition and network structure. Thermomechanical storage processes also influence shape recovery. Figure 6b shows the effect of deformation temperature (T_d) on shape recovery. One stent was packaged into a catheter at room temperature while the other was packaged at body temperature. The stent with a higher T_d experienced a delay in recovery compared to its lower T_d counterpart. This phenomenon was also observed in SMP coupon samples [34] and can simply be explained based on Gibbs Free Energy. Shape memory is driven by a favorable increase in entropy, thus lowering the free energy of the system. However, SMP's are typically packaged at temperatures well above their glass transitions, thus requiring relatively little mechanical energy for deformation. When a polymer is deformed below its glass transition a significant amount of mechanical force is needed for deformation and the energy is stored in enthalpic internal energy wells. In this case, shape recovery is driven by both a favorable increase in entropy and decrease in enthalpy, which results in shape-memory activation at lower temperatures. Figures 6a and 6b show that the recovery time for shape memory can be controlled independently by the glass transition, crosslink density, and temperature of deformation.

Although the primary goal of this paper was to examine SMP stents that recovered at body temperature, the influence of supplemental heating was also briefly examined. Though supplemental heating is not desirable in-vivo, especially for cardiovascular applications, it is important to understand its influence on shape recovery. Supplemental heating may be required for applications that have a strict recovery time priority that cannot be achieved through either polymer chemistry or thermomechanical processing. Figure 6c emphasizes this point by deforming and recovering a 10 wt% crosslinked stent with a T_g of 52°C at both body temperature (37°C) and 42.5°C . At 42.5°C , the stent is slightly above its T_{onset} and is less restricted by chain motion to reform. As a result, even with a higher T_d it recovers much faster ($\sim 4\times$) than the same stent at body temperature.

It was important to study the effect of perforation on stent recovery since cardiovascular stents on the market today have highly meshed designs. Aside from the biological arguments of

whether or not perforation is needed, it is a simple and effective way to optimize the overall structural compliance of the stent. Figure 7 indicates a unique trend of the 50% perforated stents initiating recovery sooner than the solid stents. This trend was seen in all of the polymer samples, though it was most pronounced in the stents with slower recovery times. This behavior however did not persist throughout the entire recovery process and was either matched or surpassed by the solid stent. This trend may be explained by an increase of local stored stress in the polymer due to the stress concentrations associated with the holes in the stent. To the best of the authors' knowledge, no work has been published to characterize whether or not stress concentrations will influence the shape-memory effect in polymers.

A robust understanding of SMP's ability to be stored at a given temperature must be developed to ensure a SMP medical device does not activate prior to implantation. An optimal choice for a shape-memory medical device is one that stores at room temperature and activates at body temperature. However, a narrow window separates the two temperatures by $\sim 15^{\circ}\text{C}$ with the added complication that room temperature is a relative and variable value. Figure 8a shows that packaged stents with a T_g of 52°C show significant recovery at room temperature and are highly dependent on the degree of crosslinking within the polymer. These networks appear to respond to thermal variations when a spurt of recovery is experienced from days 3–7 with an increase in room temperature. However, by raising the T_g of the polymers by 3°C , the shape-memory effect is more stable at room temperature as shown in Figure 8b. The only network that could be stored unconstrained at room temperature and activated at body temperature had 10 wt% crosslinking with a T_g of 55°C . This can be explained by the onset of glass transition and restorative forces due to crosslinking. If room temperature is too close to T_{onset} , then chain mobility in the network will be slightly increased. If the shape-memory restorative forces are high enough, the polymer will take advantage of the increased chain mobility and visco-elastically return to its original shape. Since crosslinking is directly related to a polymer's rubbery modulus, which governs the restorative stresses during shape recovery, an increase in crosslinking will provide more restorative forces and may enable accelerated visco-elastic recovery. The results indicate that the stents would require physical constraint during long-term storage (e.g. a catheter), especially for higher crosslinked materials.

The shape-memory effect is an acute phenomenon that will only occur over the first several seconds to minutes of implantation. After deployment, the stent ceases to be a shape-memory polymer and is simply a polymer stent. Therefore, it is important to understand the polymer's response after deployment to better tailor the thermomechanics of the stent. Figure 9 represents the response of a pressurized polymer stent. A maximum pressure of 160 mm·Hg was used to help accelerate any visco-plasticity that may be experienced by the stents. The 10 wt% crosslinked polymer showed very high initial strain and permanent strain after the first cycle. Furthermore, the diameter of the stent continues to increase during the initial portions of unloading and forms a large hysteresis loop, which indicates that the stent has a slight degree of viscous behavior. A very small amount of permanent strain is seen after the first cycle of the 20 wt% crosslinked polymer, which also displays a much tighter hysteresis loop. The 40 wt% polymer shows no permanent strains or hysteresis. This indicates that the system displays more linear elasticity with an increase in crosslinking.

This pressure supporting SMP stent system may be a useful solution to treating various pathologies including vascular aneurysms. The stent systems discussed were 22 mm in diameter with a wall thickness of 300 μm and fit into an 18 Fr catheter. Ongoing work shows the SMP stent can be packaged into a 14 Fr catheter when the wall thickness is reduced to 200 μm . Such a reduction in catheter insertion size would minimize the invasiveness of interventional procedures aimed at treating larger vessels. Furthermore, we can offer tight control over the thermomechanics of our polymer and optimize the shape-memory effect for implantation. The present work introduces a foundation to understand the storage and recovery

of shape memory polymer stents as a function of chemistry, polymer structure, and thermal transition behavior. Future work will investigate the factors that influence the pressure-diameter relationships of the stents to validate their performance and durability.

The stent system presented is one of preliminary and prototype nature. A clinical design of a SMP stent system would have to take into account the compliance, surface area, roughness, radio opacity, delivery mechanisms, and more with greater consideration than the scope of this paper could entail. However, this paper aims to cover how the thermomechanical properties, perforations, and packaging temperatures of the stent would influence shape recovery. This study was performed on stents designed for repair of larger vessels like the abdominal aorta, which can range from 4–5 cm during an aneurysm. Concurrently, our group is making efforts to reduce the size of the prototype system to fit vessels as small as 3–4 mm. Lastly, biocompatibility testing of our group's shape-memory networks is currently underway in an effort to advance SMP's as a biomaterial.

CONCLUSIONS

The glass transition and rubbery modulus of the SMP can be varied independently of each other and thus provide a platform for independently varying recovery properties and mechanical properties once implanted. The time for full shape recovery is highly dependent on glass transition temperature, T_g , crosslink density, and deformation (storage) temperature, T_d . Stents manufactured with a high amount of perforation initiated shape recovery sooner than their solid counterparts despite similar times to complete recovery. A SMP stent can be fabricated to maintain shape storage at room temperature and fully activate at body temperature.

Acknowledgments

The authors would like to acknowledge support from NIH (HL 067393, EB 004481), and NSF (DMI-0200495). Also, thanks to Don Geering for his expert machining of the perforated stents, Kendall Hunter for his help on ultrasound imaging analysis, and Alicia M. Ortega and Michael B. Lyons for their related work.

References

1. Sigwart U, Puel J, Mirkovitch V, Joffre F, Kappenberger L. Intravascular Stents to Prevent Occlusion and Restenosis after Trans-Luminal Angioplasty. *New England Journal of Medicine* 1987;316:701–706. [PubMed: 2950322]
2. Lemos PA, Serruys PW, Sousa JE. Drug-eluting stents - Cost versus clinical benefit. *Circulation* 2003;107:3003–3007. [PubMed: 12821586]
3. Winslow RD, Sharma SK, Kim MC. Restenosis and drug-eluting stents. *Mount Sinai Journal of Medicine* 2005;72:81–89. [PubMed: 15770337]
4. Zollkofer CL, Antonucci F, Stuckmann G, Mattias P, Salomonowitz EK. Historical Overview on the Development and Characteristics of Stents and Future Outlooks. *Cardiovascular and Interventional Radiology* 1992;15:272–278. [PubMed: 1423386]
5. Landau C, Lange RA, Hillis LD. Medical Progress - Percutaneous Transluminal Coronary Angioplasty. *New England Journal of Medicine* 1994;330:981–993. [PubMed: 8121462]
6. Lowe HC, Oesterle SN, Khachigian LM. Coronary in-stent restenosis: Current status and future strategies. *Journal of the American College of Cardiology* 2002;39:183–193. [PubMed: 11788206]
7. van der Hoeven BL, Pires NMM, Warda HM, Oemrawsingh PV, van Vlijmen BJM, Quax PHA, et al. Drug-eluting stents: results, promises and problems. *International Journal of Cardiology* 2005;99:9–17. [PubMed: 15721493]
8. Hoffmann R, Mintz GS, Dussaillant GR, Popma JJ, Pichard AD, Satler LF, et al. Patterns and mechanisms of in-stent restenosis - A serial intravascular ultrasound study. *Circulation* 1996;94:1247–1254. [PubMed: 8822976]

9. Eberhart RC, Su SH, Nguyen KT, Zilberman M, Tang LP, Nelson KD, et al. Bioresorbable polymeric stents: current status and future promise. *Journal of Biomaterials Science-Polymer Edition* 2003;14:299–312. [PubMed: 12747671]
10. Berry JL, Manoach E, Mekkaoui C, Rolland PH, Moore JE, Rachev A. Hemodynamics and wall mechanics of a compliance matching stent: In vitro and in vivo analysis. *Journal of Vascular and Interventional Radiology* 2002;13:97–105. [PubMed: 11788701]
11. Rogers C, Edelman ER. Endovascular Stent Design Dictates Experimental Restenosis and Thrombosis. *Circulation* 1995;91:2995–3001. [PubMed: 7796511]
12. Liistro F, Stankovic G, Chieffo A, Di Mario C, Montorfano M, Carlino M, et al. First clinical experience with a paclitaxel-derivate eluting polymer-stent system implantation for ISR: immediate and long-term outcome. *European Heart Journal* 2002;23:141.
13. Hodgson JM, Bottner RK, Klein LW, Walpole HT, Cohen DJ, Cutlip DE, et al. Drug-Eluting Stent Task Force: Final report and recommendations of the working committees on cost-effectiveness/economics, access to care, and medicolegal issues. *Catheterization and Cardiovascular Interventions* 2004;62:1–17. [PubMed: 15103593]
14. Fattori R, Piva T. Drug-eluting stents in vascular intervention. *Lancet* 2003;361:247–249. [PubMed: 12547552]
15. Radke PW, Weber C, Kaiser A, Schober A, Hoffmann R. Dexamethasone and restenosis after coronary stent implantation: new indication for an old drug? *Curr Pharm Des* 2004;10:349–355. [PubMed: 14965196]
16. Vogt F, Stein A, Rettemeier G, Krott N, Hoffmann R, vom Dahl J, et al. Long-term assessment of a novel biodegradable paclitaxel-eluting coronary polylactide stent. *European Heart Journal* 2004;25:1330–1340. [PubMed: 15288161]
17. Tamai H, Igaki K, Kyo E, Kosuga K, Kawashima A, Matsui S, et al. Initial and 6-month results of biodegradable poly-L-lactic acid coronary stents in humans. *Circulation* 2000;102:399–404. [PubMed: 10908211]
18. Palmaz JC. Intravascular stents in the last and the next 10 years. *Journal of Endovascular Therapy* 2004;11:200–206.
19. vanderGiessen WJ, Lincoff AM, Schwartz RS, vanBeusekom HMM, Serruys PW, Holmes DR, et al. Marked inflammatory sequelae to implantation of biodegradable and nonbiodegradable polymers in porcine coronary arteries. *Circulation* 1996;94:1690–1697. [PubMed: 8840862]
20. Fischell TA. Polymer coatings for stents - Can we judge a stent by its cover? *Circulation* 1996;94:1494–1495. [PubMed: 8840833]
21. Lincoff AM, Furst JG, Ellis SG, Tuch RJ, Topol EJ. Sustained local delivery of dexamethasone by a novel intravascular eluting stent to prevent restenosis in the porcine coronary injury model. *Journal of the American College of Cardiology* 1997;29:808–816. [PubMed: 9091528]
22. Colombo A, Karvouni E. Biodegradable stents - “Fulfilling the mission and stepping away”. *Circulation* 2000;102:371–373. [PubMed: 10908206]
23. Cooke MN, Fisher JP, Dean D, Rimnac C, Mikos AG. Use of stereolithography to manufacture critical-sized 3D biodegradable scaffolds for bone ingrowth. *Journal of Biomedical Materials Research Part B-Applied Biomaterials* 2003;64B:65–69.
24. Sodian R, Loebe M, Hein A, Martin DP, Hoerstrup SP, Potapov EV, et al. Application of stereolithography for scaffold fabrication for tissue engineered heart valves. *Asaio Journal* 2002;48:12–16. [PubMed: 11814091]
25. Wache HM, Tartakowska DJ, Hentrich A, Wagner MH. Development of a polymer stent with shape memory effect as a drug delivery system. *Journal of Materials Science-Materials in Medicine* 2003;14:109–112. [PubMed: 15348481]
26. Shmulewitz A, Langer R, Patton J. Convergence in biomedical technology. *Nature Biotechnology* 2006;24:277–280.
27. Lendlein A, Kelch S. Shape-memory polymers as stimuli-sensitive implant materials. *Clinical Hemorheology and Microcirculation* 2005;32:105–116. [PubMed: 15764819]
28. Lendlein A, Langer R. Biodegradable, elastic shape-memory polymers for potential biomedical applications. *Science* 2002;296:1673–1676. [PubMed: 11976407]

29. El Feninat F, Laroche G, Fiset M, Mantovani D. Shape memory materials for biomedical applications. *Advanced Engineering Materials* 2002;4:91–104.
30. Metcalfe A, Desfaits AC, Salazkin I, Yahia L, Sokolowski WM, Raymond J. Cold hibernated elastic memory foams for endovascular interventions. *Biomaterials* 2003;24:491–497. [PubMed: 12423604]
31. Liu C, Mather PT. Thermomechanical characterization of a tailored series of shape memory polymers. *Journal of Applied Medical Polymers* 2002;6:47–52.
32. Gall K, Yakacki CM, Liu YP, Shandas R, Willett N, Anseth KS. Thermomechanics of the shape memory effect in polymers for biomedical applications. *Journal of Biomedical Materials Research Part A* 2005;73A:339–348. [PubMed: 15806564]
33. Liu YP, Gall K, Dunn ML, Greenberg AR, Diani J. Thermomechanics of shape memory polymers: Uniaxial experiments and constitutive modeling. *International Journal of Plasticity* 2006;22:279–313.
34. Liu YP, Gall K, Dunn ML, McCluskey P. Thermomechanical recovery couplings of shape memory polymers in flexure. *Smart Materials & Structures* 2003;12:947–954.
35. Maitland DJ, Metzger MF, Schumann D, Lee A, Wilson TS. Photothermal properties of shape memory polymer micro-actuators for treating stroke. *Lasers in Surgery and Medicine* 2002;30:1–11. [PubMed: 11857597]
36. Lendlein A, Jiang HY, Junger O, Langer R. Light-induced shape-memory polymers. *Nature* 2005;434:879–882. [PubMed: 15829960]
37. Hayashi S, Kondo S, Kapadia P, Ushioda E. Room-Temperature-Functional Shape-Memory Polymers. *Plastics Engineering* 1995;51:29–31.
38. Metzger MF, Wilson TS, Schumann D, Matthews DL, Maitland DJ. Mechanical properties of mechanical actuator for treating ischemic stroke. *Biomedical Microdevices* 2002;4:89–96.
39. Wei ZG, Sandstrom R, Miyazaki S. Shape-memory materials and hybrid composites for smart systems - Part I Shape-memory materials. *Journal of Materials Science* 1998;33:3743–3762.
40. Ewert P, Riesenkampff E, Neuss M, Kretschmar O, Nagdyman N, Lange PE. Novel growth Stent for the permanent treatment of vessel stenosis in growing children: An experimental study. *Catheterization and Cardiovascular Interventions* 2004;62:506–510. [PubMed: 15274161]
41. Epstein ML. Does a “split” stent make sense? *Catheterization and Cardiovascular Interventions* 2004;62:511. [PubMed: 15274162]
42. Rao PS. Interventional pediatric cardiology: State of the art and future directions. *Pediatric Cardiology* 1998;19:107–124. [PubMed: 9396855]
43. Lendlein A, Kelch S. Shape-memory polymers. *Angewandte Chemie-International Edition* 2002;41:2034–2057.

Figure 1. Recovery of a 20 wt% crosslinked SMP stent with $T_g=52^\circ\text{C}$ delivered via an 18Fr. catheter into a 22 mm ID glass tube containing body temperature water at 37°C . Black rings were drawn to facilitate deployment visualization.

Figure 2.
Example of a glass transition curve measured by DMA with thermomechanical properties labeled on the curve. The DMA 3-point bending setup is also shown.

Figure 3.
Design of solid and 50% perforated shape-memory polymer stents.

Figure 4.
Example of free recovery measurements of a shape-memory polymer stent.

Figure 5.

a). Glass transition curves of materials with $T_g \approx 52^\circ\text{C}$ and differing amounts of wt% crosslinker.

b). Glass transition curves of materials with 20 wt% crosslinker and different T_g 's.

Figure 6.

Performance of solid stents. **a).** Recovery of stents deformed at room temperature and recovered at body temperature. **b).** Recovery of a 10 wt% crosslinked stent with a T_g of 52°C deformed at room and body temperature and recovered at body temperature. **c).** Recovery of a 10 wt% crosslinked stent with a T_g of 52°C deformed and recovered at both body temperature and ~5°C above body temperature.

Figure 7. Comparison of solid vs. perforated stents for a recovery temperature of 37 °C. **a).** Stents made from the 10 wt% crosslinked polymer with a T_g of 52°C. **b).** Stents made from Networks 2, 4, and 5.

Figure 8. Storage diameter of packaged stents as a function of time. **a).** Crosslinked stents with a T_g of 52°C. **b).** Crosslinked stents with a T_g of 55°C.

Figure 9.
Stents with a $T_g=52^{\circ}\text{C}$ gradually cycled twice between 55–160 mm·Hg

Table 1

Characteristics of 6 polymer networks used to make shape-memory polymer stents.

Network	Cross-Linking (wt%)	T _g (°C)	T _{onset} (°C)	Rubbery Modulus (MPa)
1	10	52.2 ± 0.3	41.3 ± 1.0	1.50 ± 0.03
2	20	51.4 ± 0.6	42.3 ± 0.6	5.62 ± 0.71
3	40	49.9 ± 0.8	40.5 ± 1.2	11.51 ± 1.19
4	10	54.8 ± 0.8	45.2 ± 0.6	2.42 ± 0.31
5	20	55.4 ± 0.7	44.6 ± 1.0	5.55 ± 1.42
6	40	53.5 ± 0.4	42.1 ± 0.7	11.54 ± 1.67