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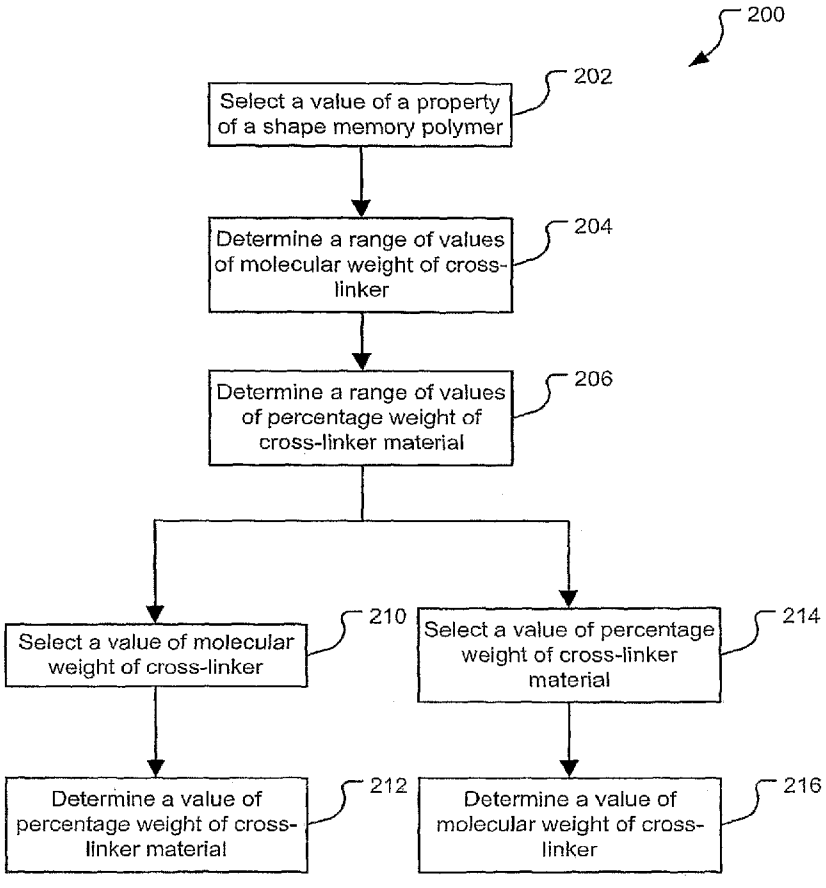

(57) Abstract: The thermomechanical response of shape memory polymer (SMP) materials can be controlled to predict and optimize shape-memory properties. Polymer systems may be designed and optimized to a high degree of tailorability that is capable of adapting and responding to patients needs for biomedical applications such as stenting or orthopedic fixation.

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The invention was sponsored by National Institute of Health Grant Nos. NIH-HL-067393 and NIH-EB-004481 and the government has certain rights to this invention.

Background

Shape memory polymer (SMP) materials offer the ability to activate with a mechanical force under the application of a stimulus. The stimulus may be light, heat, other types of energy, or other types of stimuli known in the art.

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. 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. In many operations, stents are the standard of care since they can be delivered via minimally invasive surgery resulting in rapid recovery time and less surgical risk.

Stents are used in part to reduce the rate of restenosis. Stenosis is defined as the constriction or narrowing of an artery often caused by arteriosclerosis, 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. However, restenosis occurs in 30-60% of all patients who undergo balloon angioplasty alone within the first 6 months of the procedure. Restenosis after balloon angioplasty follows a 3-stage response: acute elastic recoil, negative remodeling, and neointimal proliferation.

Stenting mitigates the responses of acute elastic recoil and negative remodeling and thus reduces the restenosis rate sometimes to as low as 10-40%. However, even in the presence of a stent, neointimal proliferation remains a contributing factor of restenosis and can be caused by the stretching and damaging of the wall during angioplasty, the body's response to the stent material, and a compliance mismatch between the stent and artery.

Metal stents have limited flexibility compared to the wall of some body lumens (e.g., 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

body lumen, local stiffness mismatch can cause tiny stent ribs to exert significant local pressure on the body lumen wall.

The feasibility and biocompatibility of polymer stents has been controversial especially after an early study showed an inflammation response to polymer coatings on stents. More recently, the biocompatibility of polymers has been demonstrated in cardiovascular applications.

The orthopedic fixation of tendons and ligaments to bone remains a central challenge in failed joint reconstruction and tissue engineering. Current techniques are based on traditional mechanical fasteners and devices that often provide inadequate strength, inefficient mechanobiological healing profiles, and excessive invasion.

Summary

The thermomechanical response of shape memory polymer (SMP) materials can be controlled to predict and optimize shape-memory properties. Polymer systems may be designed and optimized to a high degree of tailorability that is capable of adapting and responding to patients needs for biomedical applications such as stenting or orthopedic fixation.

One aspect is a method including selecting a transition temperature for a shape memory polymer network, and determining a first range of average molecular weights of cross-linker material and a second range of weight percentages of cross-linker material based on the selected transition temperature of the shape memory polymer network and based on a first relationship between transition temperature, weight percentage of cross-linker material and average molecular weight of cross-linker material. This aspect further includes determining a third range of rubbery moduli based on the first range of average molecular weights of cross-linker material and the second range of weight percentages of cross-linker material and based on a second relationship between rubbery modulus, weight percentage of cross-linker material and average molecular weight of cross-linker material. This aspect further includes selecting a rubbery modulus for the shape memory polymer network that is part of the third range of rubbery moduli, and determining an average molecular weight of cross-linker material and a weight percentage of cross-linker material based on the second relationship and the rubbery modulus selected.

In one embodiment, the method includes determining a mixing ratio of a first cross-linker material having a first average molecular weight and a second cross-linker material having a second average molecular weight such that a mixture of the first cross-linker material and the second cross-linker material in the mixing ratio would have

substantially the determined average molecular weight of cross-linker material. In another embodiment, the determining the second range of rubbery moduli is based on patient data.

In one embodiment, the selected rubbery modulus matches a value which is derived from patient data. In another embodiment, the selected transition temperature is derived from patient data. In another embodiment, the method includes making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material, and polymerizing the formulation to form the shape memory polymer network for use as at least part of a medical device.

In one embodiment, the method includes, installing the medical device within a patient, and heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus. In another embodiment, selecting the transition temperature includes receiving a desired value for the transition temperature.

Another aspect is a method including selecting a recovery time characteristic for a shape memory polymer network, determining a percentage weight of cross-linker material from the selected recovery time characteristic of the shape memory polymer network based on a first relationship between recovery time characteristics and the percentage weight of cross-linker material, and selecting a transition temperature for the shape memory polymer network. The aspect further includes determining an average molecular weight of the cross-linker material from the selected transition temperature of the shape memory polymer network based on the determined percentage weight of cross-linker material and based on a second relationship between transition temperature, percentage weight cross-linker material, and average molecular weight of the cross-linker material.

In one embodiment, the method includes determining a rubbery modulus of the shape memory polymer network based on a third relationship between rubbery modulus, percentage weight cross-linker material, and average molecular weight of the cross-linker material. In another embodiment, the method includes, if the rubbery modulus determined is incompatible with a desired application of the shape memory polymer network, selecting a different recovery time characteristic.

In one embodiment, the method includes determining a mixing ratio of a first cross-linker material having a first average molecular weight and a second cross-linker material having a second average molecular weight such that a mixture of the first cross-linker material and the second cross-linker material in the mixing ratio would have

substantially the determined average molecular weight of cross-linker material. In another embodiment, the selected transition temperature of the shape memory polymer network is derived from patient data.

In one embodiment, the method includes making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material, and polymerizing the formulation to form the shape memory polymer network for use as at least part of a medical device. In another embodiment, the method includes installing the medical device within a patient, and heating the medical device to about the selected transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

In one embodiment, selecting the recovery characteristic includes receiving a desired value for the recovery characteristic. In another embodiment, selecting the transition temperature includes receiving a desired value for the transition temperature.

Another aspect is a method including determining a percentage weight cross-linker material for a shape memory polymer network based on a first relationship between weight percentage of cross-linker, rubbery modulus, and transition temperature of the shape memory polymer network, based on a second relationship between average molecular weight of cross-linker material, rubbery modulus, and transition temperature of the shape memory polymer network, based on a desired rubbery modulus for the shape memory polymer network, and based on a desired transition temperature of the shape memory polymer network. The aspect further includes determining an average molecular weight of cross-linker material for the shape memory polymer network based on the first relationship, based on the second relationship, based on the desired rubbery modulus for the shape memory polymer network, and based on the desired transition temperature of the shape memory polymer network.

In one embodiment, the method includes determining a mixing ratio of a first cross-linker material having a first average molecular weight and a second cross-linker material having a second average molecular weight such that a mixture of the first cross-linker material and the second cross-linker material in the mixing ratio would have substantially the determined average molecular weight of cross-linker material. In another embodiment, determining the percentage weight cross-linker material and the determining the average molecular weight of cross-linker material are performed at about the same time.

In one embodiment, the desired rubbery modulus is derived from patient data. In another embodiment, the desired transition temperature is derived from patient data.

In another embodiment, the method includes making a formulation having substantially the determined average molecular weight of cross-linker material, substantially the determined weight percentage of cross-linker material, and polymerizing the formulation to form a shape memory polymer network for use as at least part of a medical device. In another embodiment, the method includes installing the medical device within a patient, and heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

In one embodiment, the formulation comprises a cross-linker material of poly-ethylene glycol di-methacrylate. In another embodiment, the formulation comprises a linear chain selected from methyl methacrylate, poly(methyl methacrylate), and tert-butyl acrylate.

Another aspect is a shape memory polymer network produced according to one or more of the methods described herein.

Another aspect is a method including determining a first relationship between transition temperature for a shape memory polymer network and percentage weight of cross-linker material based on an average molecular weight of the cross-linker material, determining a percentage weight of cross-linker material from a desired transition temperature of the shape memory polymer network based on the first relationship, and determining a second relationship between rubbery modulus for the shape memory polymer network and average molecular weight of the cross-linker material based on the percentage weight cross-linker. The aspect further includes determining the average molecular weight of the cross-linker material from a desired rubbery modulus of the shape memory polymer network based on the second relationship.

In one embodiment, determining the percentage weight of cross-linker material, determining the average molecular weight of the cross-linker material, determining the first relationship, and determining the second relationship are performed at about the same time. In another embodiment, the method includes determining a mixing ratio of a first cross-linker material having a first average molecular weight and a second cross-linker material having a second average molecular weight such that a mixture of the first cross-linker material and the second cross-linker material in the mixing ratio would have substantially the determined average molecular weight of cross-linker material.

In one embodiment, the desired rubbery modulus of the shape memory polymer network is derived from patient data. In another embodiment, the desired transition temperature of the shape memory polymer network is derived from patient data.

In one embodiment, the method includes making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material, and polymerizing the formulation to form a shape memory polymer network for use as at least part of a medical device.

In one embodiment, the method includes installing the medical device within a patient, and heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

Another aspect is a method including determining a first relationship between rubbery modulus and percentage weight of cross-linker material based on an average molecular weight of the cross-linker material for a shape memory polymer network, determining a percentage weight of cross-linker material from a desired rubbery modulus of the shape memory polymer network based on the first relationship, and determining a second relationship between transition temperature and average molecular weight of the cross-linker material based on the percentage weight cross-linker. The aspect further includes determining the average molecular weight of the cross-linker material from a desired transition temperature of the shape memory polymer network based on the second relationship.

In one embodiment, the method includes determining a mixing ratio of a first cross-linker material having a first average molecular weight and a second cross-linker material having a second average molecular weight such that a mixture of the first cross-linker material and the second cross-linker material in the mixing ratio would have substantially the determined average molecular weight of cross-linker material. In another embodiment, the determining the percentage weight cross-linker material and the determining the average molecular weight of cross-linker material are performed at about the same time.

In one embodiment, the desired rubbery modulus of the shape memory polymer network is derived from patient data. In another embodiment, the desired transition temperature of the shape memory polymer network is derived from patient data.

In one embodiment, the method includes making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material, and polymerizing the formulation to form a shape memory polymer network for use as at least part of a medical device. In another embodiment, the method includes installing the medical device within a patient, and heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

Another aspect is a method including selecting a desired value of a property of a shape memory polymer, determining a first range of values of average molecular weights of a cross-linker material based on the desired value of the property, and determining a second range of values of percentage weight of a cross-linker material based on the desired value of the property.

In one embodiment, the method includes selecting a desired first value of average molecular weight of the cross-linker, and determining a second value of percentage weight of cross-linker material. In another embodiment, the desired first value is within the first range of values, and the second value is within the second range of values.

In one embodiment, the method includes selecting a desired third value of percentage weight of cross-linker material, and determining a fourth value of average molecular weight of the cross-linker. In another embodiment, the fourth value is within the first range of values, and the desired third value is within the second range of values.

In one embodiment, the property is a transition temperature. In another embodiment, the transition temperature is the glass transition temperature. In another embodiment, the property is a rubbery modulus. In another embodiment, the property is a recovery characteristic. In another embodiment, the recovery characteristic is a recovery time. In another embodiment, the recovery time is a time to complete substantial recovery given a known set of constraints on the shape memory polymer.

In one embodiment, the method includes making a formulation having an average molecular weight of cross-linker within the first range, a weight percentage of cross-linker material within the second range, and polymerizing the formulation to form a shape memory polymer network for use as at least part of a medical device. In another embodiment, the method includes installing the medical device within a patient, and heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially

the selected rubbery modulus. In another embodiment, selecting the desired value of the property includes receiving the desired value for the property.

Another aspect is a method including selecting a first value of a compliance characteristic of a first body lumen in a patient, determining an average molecular weight of cross-linker material and a percentage weight of cross-linker material for a shape memory polymer network based on the first value, and producing a stent comprising the shape memory polymer network.

In one embodiment, a second body lumen in the patient is the intended insertion site of the stent. In another embodiment, the method includes estimating the compliance characteristic of the second body lumen in the patient based on the compliance characteristic of the first body lumen in the patient.

In one embodiment, the method includes estimating the compliance characteristic of first body lumen based on patient data. In another embodiment, the body lumen is an arterial blood vessel.

In one embodiment, producing a stent comprising the shape memory polymer network includes making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material, and polymerizing the formulation to form the shape memory polymer network for use as at least part of the stent. In another embodiment, the method includes installing the stent within a patient, and heating the shape memory polymer network to about a transition temperature of the shape memory polymer network thereby activating the shape memory polymer network thereby causing the shape memory polymer network to have substantially the selected rubbery modulus. In another embodiment, selecting the first value of the compliance characteristic includes receiving a desired value for the compliance characteristic.

Another aspect is a method including selecting a first value of a compliance characteristic of a first bone in a patient, determining an average molecular weight of cross-linker material and a percentage weight of cross-linker material for a shape memory polymer network based on the first value, and producing a graft fixation device comprising the shape memory polymer network.

In one embodiment, a second bone in the patient is the intended insertion site of the graft fixation device. In another embodiment, the method includes estimating the compliance characteristic of the second bone in the patient based on the compliance characteristic of the first bone in the patient. In another embodiment, the method includes

estimating the compliance characteristic of first bone based on information about the patient.

In one embodiment, producing a graft fixation device comprising the shape memory polymer network includes making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material, and polymerizing the formulation to form the shape memory polymer network for use as at least part of the graft fixation device.

In one embodiment, the method includes installing the graft fixation device within a patient, and heating the shape memory polymer network to about a transition temperature of the shape memory polymer network thereby activating the shape memory polymer network thereby causing the shape memory polymer network to have substantially the selected rubbery modulus. In another embodiment, selecting the recovery characteristic includes receiving a desired value for the recovery characteristic.

Another aspect is a method of including selecting a first value of a patient characteristic, determining a second value of a device characteristic based on the first value, determining a percentage weight of cross-linker material for the shape memory polymer network based on the second value, determining a molecular weight of cross-linker material for the shape memory polymer network based on the second value, and manufacturing the shape memory polymer network with the determined percentage weight of cross-linker and the determined molecular weight of cross-linker material.

In one embodiment, the method includes selecting a linear chain for the shape memory polymer network based on a required recovery force of the shape memory polymer network. In another embodiment, determining the percentage weight of cross-linker material is performed based on the selected linear chain for the shape memory polymer network.

Another aspect is a method including adding a dissolving material to a shape memory polymer formulation, polymerizing the shape memory polymer formulation to form a shape memory polymer network, and dissolving the dissolving material thereby altering a surface roughness of the shape memory polymer network.

In one embodiment, the method includes using the shape memory polymer network as at least part of a medical device. In another embodiment, the method includes exposing the shape memory polymer network to an environment which promotes the dissolving of the dissolving material thereby altering at least part of the surface roughness

of the shape memory polymer network of the medical device over time. In another embodiment, exposing includes implanting the shape memory polymer inside a patient.

In one embodiment, adding the dissolving material comprises embedding the dissolving material in a surface of the shape memory polymer network formulation prior to polymerization. In another embodiment, adding the dissolving material comprises including the dissolving material in the shape memory polymer formulation prior to polymerization.

Another aspect is a method including selecting a recovery characteristic of a shape memory polymer network, modifying the recovery characteristic through selecting a deformation temperature of the shape memory polymer network, causing the shape memory polymer network to be substantially at the deformation temperature, and deforming the shape memory polymer network.

In one embodiment, selecting a recovery characteristic is based on a weight percentage of cross-linker material and an average molecular weight of cross-linker material in the formulation of the shape memory polymer network. In another embodiment, the causing operation is performed through placing the shape memory polymer network in contact with a system that is substantially at the deformation temperature. In another embodiment, the material is selected from: a liquid bath, a deformation apparatus, a heating member, a cooling member.

In one embodiment, the method includes creating the shape memory polymer network with substantially the selected recovery characteristic for use as at least part of a medical device. In another embodiment, the method includes installing the medical device within a patient, and heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

Another aspect is a polymer exhibiting a shape memory effect, the polymer comprising a polymerization of a mixture of a first monomer selected from methyl methacrylate, poly(methyl methacrylate), and tert-butyl acrylate, and a second monomer with a first average molecular weight, wherein the second monomer is a multi-functional monomer. In the aspect, the second monomer comprises a combination of a first poly-ethylene glycol di-methacrylate material with a second average molecular weight different from the first average molecular weight and a second poly-ethylene glycol di-methacrylate material with a third average molecular weight different from both the first average

molecular weight and the second average molecular weight. In the aspect, the polymer has a rubbery modulus which substantially matches a first value derived from patient data.

In one embodiment, the polymer has a transition temperature which substantially matches a second value derived from patient data. In another embodiment, the polymer forms at least part of a medical device. In another embodiment, the medical device is a stent. In another embodiment, the medical device is a graft fixation device.

The following description of various embodiments is merely exemplary in nature and is in no way intended to limit the invention, its application, or uses.

A Brief Description of the Drawings

Fig. 1 shows a flow chart of an embodiment of a method of controlling SMP properties via variations in a cross-linker in the SMP formulation.

Fig. 2 shows a flow chart of an embodiment of a method of controlling a property of a SMP via variations in a molecular weight and percentage weight cross-linker in the SMP formulation.

Fig. 3 is an example of a computer program that implements some of the methods described herein.

Fig. 4 is a graph of relationships between glass transition temperature and percentage weight cross-linker for various average molecular weights (Mn) of cross-linker.

Fig. 5 is a graph of relationships between glass transition temperature and molecular weight of cross-linker for various percentage weights of cross-linker.

Fig. 6 is a graph of relationships between rubbery modulus and percentage weight of cross-linker.

Fig. 7 is a graph of rubbery modulus versus molecular weight of cross-linker for various percentage weights of cross-linker.

Fig. 8 is a graph of exemplary relationships between modulus and temperature illustrating the modulus transition of three different exemplary SMP networks as manufactured.

Fig. 9 is another graph of exemplary relationships between modulus and temperature illustrating the modulus transition of four different exemplary SMP networks.

Fig. 10 is a graph of recovery percentage versus time for various percentage weights of cross-linker.

Fig. 11 is a graph of modulus versus temperature illustrating the modulus transition of an exemplary SMP network.

Fig. 12 is a graph of recovery percentage versus time for three different SMP networks, each with a different percentage weight cross-linker and/or a different glass transition temperature.

Fig. 13 illustrates the distinction between recovery time characteristic and actual recovery time, by showing a number of SMP networks, each with different glass transition responding to similar recovery stimuli.

Fig. 14 shows a flow chart of a method of manufacturing SMP devices.

Fig. 15 shows a flow chart of an embodiment of a method of determining a recovery time.

Fig. 16 shows a flow chart of an embodiment of a method of determining a manufacturing parameter based on a patient characteristic.

Fig. 17 shows a smooth surface comprising a SMP network and heparin particles.

Fig. 18 shows a significant increase in surface variation after heparin has been removed both from the combined surface of a SMP network and heparin, and from the body of the SMP network.

Fig. 19 shows a flow chart of an embodiment of a method for achieving a peak stress in a SMP during the recovery phase of the SMP via variations in the deformation temperature of the SMP during manufacturing.

Fig. 20A is a graph of normalized strain versus time for a recovery temperature (Tr) = Tg.

Fig. 20B is a graph of normalized strain versus time for a recovery temperature, Tr = 0.875 * Tg.

Fig. 20C is a graph of normalized strain versus time for a recovery temperature, Tr = 0.75 * Tg.

Detailed Description of the Invention

The following description of various embodiments is merely exemplary in nature and is in no way intended to limit the invention, its application, or uses.

Shape memory polymer (SMP) materials may be used for a wide variety of applications. Their ability to recover strains imparted upon them, in a manner that is different than pure thermal expansion, due to an external stimulus, makes SMP materials well suited for many applications, such as biological (e.g., orthopedic, cardiac) and general

mechanical. The external stimulus that activates SMPs may be heat, light, or other stimuli known to those having skill in the art. SMPs which use heat as an external stimulus often have temperatures at which transition occurs.

A transition temperature can be a property of a material (e.g., SMP, thermoplastic, thermoset). A transition temperature may be defined through a number of methods/measurements and different embodiments may use any of these different methods/measurements. For example, a transition temperature may be defined by a temperature of a material at the onset of a transition (Tonset), the midpoint of a transition, or the completion of a transition. As another example, a transition temperature may be defined by a temperature of a material at which there is a peak in the ratio of a real modulus and an imaginary modulus of a material (e.g., peak tan-delta), as is illustrated in Fig. 11. It should be noted that the method of measuring the transition temperature of a material may vary, as may the definition of steps taken to measure the transition temperature (e.g., there may be other definitions of tan-delta) known to those with skill in the art.

A transition temperature may be related to a number of processes or properties. For example, a transition temperature may relate to a transition from a stiff (e.g., glassy) behavior to a rubbery behavior of a material. As another example, a transition temperature may relate to a melting of soft segments of a material. A transition temperature may be represented by a glass transition temperature (Tg), a melting point, or another temperature related to a change in a process in a material or another property of a material.

Supplemental heating during recovery of SMPs may not be desirable for in-vivo applications due to potential damage to cells from overheating (e.g., in cardiovascular applications where arterial scarring may have severe effects), though supplemental heating may be used in any application. For example, supplemental heating may be used for applications that have a strict recovery time priority that cannot be achieved through either polymer chemistry or thermomechanical processing.

The processes and properties relating to a transition temperature may be molecular, microscopic and/or macroscopic. For example, a transition temperature may relate to molecular mobility or microscopic material structure. As another example, a transition temperature may relate to the strength of molecular bonds. As yet another example, a transition temperature may relate to a modulus of the material or a change in the modulus of the material.

In addition, molecular and/or microscopic processes, including those processes around a transition temperature, may be related to the macroscopic properties of the material. Indeed, one method of determining whether a molecular and/or microscopic process is occurring (or has occurred) is to monitor macroscopic processes or properties. Molecular and/or microscopic properties are commonly related to macroscopic properties, and macroscopic characteristics are commonly monitored as a substitute for monitoring molecular and/or microscopic properties.

From a macroscopic viewpoint, as embodied in a modulus-temperature graph, a polymer's shape memory effect may possess a glass transition region, a modulus-temperature plateau in the rubbery state. A polymer's shape memory effect may include, as embodied in stress-strain graph, a difference between the maximum achievable strain, ε_{max}, during deformation and permanent plastic strain after recovery, ε_p. The difference $\varepsilon_{max} - \varepsilon_p$ may be considered the recoverable strain, $\varepsilon_{recover}$, while the recovery ratio (or recovery percentage) may be considered $\varepsilon_{recover}/\varepsilon_{max}$.

The properties of SMPs can be controlled by changing the formulation of the SMP, or by changing the treatment of the SMP through polymerization and/or handling after polymerization. The techniques of controlling SMP properties rely on an understanding of how SMP properties are affected by these changes and how some of these changes may affect more than one property. For example, changing the percentage weight of a cross-linker in a SMP formulation may change both a transition temperature of the SMP and a modulus of the SMP. In one embodiment, changing the percentage weight of a cross-linker will affect the glass transition temperature and the rubbery modulus of an SMP. In another embodiment, changing the percentage weight of cross-linker will affect a recovery time characteristic of the SMP.

Determining properties of SMPs may be performed before the SMP formulation is mixed or polymerized, and indeed, before any steps of SMP manufacturing are undertaken. Determining the properties and inputs of a SMP network, and therefore the formulation of the SMP, may be performed as described herein based on relationships and desired values of other properties. The determining may be performed based on empirically-derived data and theoretically-derived data to allow the values of a SMP's properties to be controlled before the manufacturing process has begun. The determining of the SMP formulation and the manufacturing process of the SMP network will be described in further detail below.

The properties of a SMP (e.g., transition temperature, rubbery modulus, recovery time characteristic) may be controlled independently, as will be described in further detail below. In one embodiment, changing the percentage weight of cross-linker changes the recovery time characteristic of the SMP as manufactured, but does not affect a transition temperature of the SMP or the rubbery modulus of the SMP. In one embodiment, independent control of SMP properties is achieved by changing more than one input or constituent part of the SMP formulation, as will be discussed in further detail below.

Some properties of a SMP may be interrelated such that controlling one property has a strong or determinative effect on another property, given certain assumed parameters. For example, the force exerted by a SMP against a constraint (e.g., a bony tunnel, a body lumen) after the SMP has been activated may be changed through control of the rubbery modulus of the SMP. Those skilled in the art will appreciate that several factors including a level of residual strain in the SMP enforced by the constraint will dictate the stress applied by the SMP, based on the modulus of the SMP. Those skilled in the art will also appreciate that the stress applied by the SMP is related to the force exerted on the constraint by known relationships.

Examples of constituent parts of the SMP formulation include monomers, multi-functional monomers, cross-linkers, initiators (e.g., photo-initiators), and dissolving materials (e.g., drugs, salts). Two commonly included constituent parts are a linear chain and a cross-linker, each of which are common organic compounds such as monomers, multi-functional monomers, and polymers.

A cross-linker (or "crosslinker"), as used herein, may mean any compound comprising two or more functional groups (e.g., acrylate, methacrylate), such as any poly-functional monomer. For example, a multi-functional monomer is a poly ethylene glycol (PEG) molecule comprising at least two functional groups, such as di-methacrylate (DMA), or the combined molecule of PEGDMA. The percentage weight of cross-linker indicates the amount of the poly-functional monomers placed in the mixture prior to polymerization (e.g., as a function of weight), and not necessarily any direct physical indication of the as-polymerized "crosslink density."

Average molecular weights of cross-linker material (Mn) may be referred to herein as simply molecular weight or weight of cross-linker. The term average molecular weight may refer to a cross-linker material that has a majority of molecules with that molecular weight. The term may also refer to a cross-linker material that contains substantially no molecules with that particular weight. For example, a mixture of PEG with a molecular

weight of 330 and PEG with a molecular weight of 500 may result in a mixture of PEG with an average molecular weight of 415. Other mixing ratios may be used to attain other average molecular weights.

A linear chain may be selected based on a requirement of a particular application, because of the ranges of rubbery moduli and recovery forces achieved by various compositions. In one embodiment, a high recovery force and rubbery modulus may be used in an orthopedic graft fixation device comprising a shape memory polymer made from a formulation with methyl-methacrylate (MMA) as the linear chain. In another embodiment, a lower recovery force and rubbery modulus may be used for a body lumen endoprosthesis (e.g. stent) comprising a shape memory polymer made from a formulation with tert-butyl acrylate (tBA) as the linear chain. In other embodiments, other linear chains may be selected based on desired properties such as recovery force and rubbery modulus.

Representative natural polymer blocks or polymers include proteins such as zein, modified zein, casein, gelatin, gluten, serum albumin, and collagen, and polysaccharides such as alginate, celluloses, dextrans, pullulane, and polyhyaluronic acid, as well as chitin, poly(3-hydroxyalkanoate)s, especially poly(.beta.-hydroxybutyrate), poly(3-hydroxyoctanoate) and poly(3-hydroxyfatty acids). Representative natural biodegradable polymer blocks or polymers include polysaccharides such as alginate, dextran, cellulose, collagen, and chemical derivatives thereof (substitutions, additions of chemical groups, for example, alkyl, alkylene, hydroxylations, oxidations, and other modifications routinely made by those skilled in the art), and proteins such as albumin, zein and copolymers and blends thereof, alone or in combination with synthetic polymers.

Representative synthetic polymer blocks or polymers include polyphosphazenes, poly(vinyl alcohols), polyamides, polyester amides, poly(amino acid)s, synthetic poly(amino acids), polyanhydrides, polycarbonates, polyacrylates, polyalkylenes, polyacrylamides, polyalkylene glycols, polyalkylene oxides, polyalkylene terephthalates, polyortho esters, polyvinyl ethers, polyvinyl esters, polyvinyl halides, polyvinylpyrrolidone, polyesters, polylactides, polyglycolides, polysiloxanes, polyurethanes and copolymers thereof. Examples of polyacrylates include poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate) and poly(octadecyl acrylate).

Synthetically modified natural polymers include cellulose derivatives such as alkyl celluloses, hydroxyalkyl celluloses, cellulose ethers, cellulose esters, nitrocelluloses, and chitosan. Examples of cellulose derivatives include methyl cellulose, ethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, hydroxybutyl methyl cellulose, cellulose acetate, cellulose propionate, cellulose acetate butyrate, cellulose acetate phthalate, carboxymethyl cellulose, cellulose triacetate and cellulose sulfate sodium salt. These are collectively referred to herein as "celluloses".

Representative synthetic degradable polymer segments include polyhydroxy acids, such as polylactides, polyglycolides and copolymers thereof; poly(ethylene terephthalate); polyanhydrides, poly(hydroxybutyric acid); poly(hydroxyvaleric acid); poly[lactide-co-(.epsilon.-caprolactone)]; poly[glycolide-co-(.epsilon.-caprolactone)]; polycarbonates, poly(pseudo amino acids); poly(amino acids); poly(hydroxyalkanoate)s; polyanhydrides; polyortho esters; and blends and copolymers thereof. Polymers containing labile bonds, such as polyanhydrides and polyesters, are well known for their hydrolytic reactivity. Hydrolytic degradation rates of these polymers may be altered by simple changes in the polymer backbone and the polymer's sequence structure.

Examples of non-biodegradable synthetic polymer segments include ethylene vinyl acetate, poly(meth)acrylic acid, polyamides, polyethylene, polypropylene, polystyrene, polyvinyl chloride, polyvinylphenol, and copolymers and mixtures thereof.

Hydrogels can be formed from polyethylene glycol, polyethylene oxide, polyvinyl alcohol, polyvinyl pyrrolidone, polyacrylates, poly (ethylene terephthalate), poly(vinyl acetate), and copolymers and blends thereof.

Either type of polymeric block can be used, depending on the desired application and conditions of use. For example, shape memory is observed for acrylic acid copolymers largely in the hydrogel state, because the acrylic acid units are substantially hydrated and behave like a soft elastomer with a very low glass transition temperature. The dry polymers do not exhibit significant shape memory effects. When dry, the acrylic acid units behave as a hard plastic even above the glass transition temperature and show little change in mechanical properties on heating. In another example, copolymers including methyl acrylate polymeric blocks as the soft segments show shape memory properties even when dry.

The polymers can be obtained from commercial sources such as Sigma Chemical Co., St. Louis, Mo.; Polysciences, Warrenton, Pa.; Aldrich Chemical Co., Milwaukee,

Wis.; Fluka, Ronkonkoma, N.Y.; and BioRad, Richmond, Calif. Alternately, the polymers can be synthesized from monomers obtained from commercial sources.

A functional group may refer to any reactive group. For example, a functional group may be an acrylate group. A mono-functional molecule refers to a molecule having one functional group (e.g., an acrylate group, a methacrylate group). A multi-functional molecule may have two or more functional groups.

Those with skill in the art will recognize that other polymerization techniques, such as thermal radical initiation, can be used for polymer fabrication.

The order of any method described herein may be varied in different embodiments as may be desirable depending on the applied use of the method. In some embodiments, selecting/receiving operations may become determining operations and determining operations may become selecting/receiving operations, depending on the order in which the operations are performed. Determining operations normally require some form of input upon which the determining is to be based, whereas selecting/receiving may not require input before the selecting/receiving is performed. Therefore, when an order of operations is modified in other embodiments, operations may also be modified as appropriate.

Any method described herein may also be performed iteratively, repeatedly, and/or in parts. In addition, many of the operations of the methods described herein may be performed simultaneously. In some embodiments, a determined value for a property of a SMP network may not match expectations or requirements of an application and part or all of a method may be repeated in order to create another value for that property. For example, a formulation may create a SMP formulation that, when polymerized into a SMP network, will have a rubbery modulus which is out of an acceptable range. In one embodiment, the formulation may then be partially or completely redesigned using one of the methods described herein. For example, a new transition temperature may be selected for the SMP network and a new formulation for creating such a network may be determined.

Fig. 1 shows a flow chart of an embodiment of a method 100 of controlling SMP properties via variations in a cross-linker in the SMP formulation. The embodiment shown of method 100 includes selecting a transition temperature 102. Selecting may be performed, in this embodiment and in others, in a number of manners suitable for receiving or otherwise obtaining information. In one embodiment, selecting may be performed as the result of a determination made based on measurements of patient

characteristics, calculations, tables, charts, or other sources of information. In another embodiment, selecting may be performed on information received from a computer program or from another communication.

The embodiment of the method 100 includes determining a range of average molecular weights 104 of cross-linker material for use in a SMP. A range is determined from the transition temperature selected in 102. The transition temperature may be a desired transition temperature for use in a human body. Such a transition temperature may be close to human body temperature. The transition temperature affects the range of possible average molecular weights of cross-linker material that may be used in the SMP because certain combinations of average molecular weights and of percentage weights of cross-linker produce certain transition temperatures and other combinations produce other transition temperatures.

The method 100 also includes determining a range of percentage weights 106 of cross-linker material for use in a SMP. This range is determined from the transition temperature selected in 102 in a similar manner to that described above for determining a range of average molecular weights. Certain combinations of average molecular weights of cross-linker and percentage weights of cross-linker may be used in the SMP formulation to achieve a certain transition temperature, as described above. These values of percentage weights constitute the range determined in 106.

Determining the range of percentage weight cross-linker 106 and the range of molecular weights 104 is performed based a relationship between transition temperature, molecular weight, and percentage weight cross-linker. The relationship is specific to the linear chain and cross-linker used. Other inputs or manufacturing techniques may also affect the relationship and eventual transition temperature of a SMP.

As characterized in the Figures and description herein, there are repeatable relationships which predict rubbery modulus and transition temperature from percentage weights and molecular weights. There are also described herein relationships between percentage weight cross-linker and recovery time.

In one embodiment, the method 100 uses empirically-derived relationships which relate molecular weight and weight percentage cross-linker to (a) the transition temperature, (b) the rubbery modulus, and/or (c) a recovery time characteristic. In another embodiment, the method 100 uses relationships which are derived from theoretical models. Theoretical models are available to those skilled in the art. Examples of

empirically-derived relationships are disclosed below and are included within the exemplary computer code in Fig. 3.

The terms recovery time characteristic and recovery time are used herein to describe a property of a SMP which relates to the recovery time of the SMP, but does not necessarily equal the time for complete recovery unless it is used in conjunction with other factors, or if other factors are assumed. For example, the other factors could include the magnitude of the recovery stimulus, the interface between the SMP and the stimulus, and the storage temperature of the SMP. The effect of these other factors will be discussed further below.

A number of relationships may be determined from the empirically-derived relationships described herein and from the theoretical models available. For example, a first relationship may describe rubbery modulus based on weight percentage of cross-linker which may be derived from empirical data. A second relationship may also be derived between rubbery modulus, molecular weight, and percentage weight cross-linker from empirical data. In addition, a third relationship may be derived from the second relationship based on a percentage weight cross-linker which may be advantageous.

In one embodiment, the percentage weight cross-linker is advantageous because a value of a particular property of the SMP, for example, a recovery time characteristic, is desired for an application. In another embodiment, a different third relationship may be derived from the second relationship based on a molecular weight of cross-linker material which may be advantageous for a particular application. Indeed, any number of relationships may be derived from advantageous properties based on relationships which control those properties, at least partially. Any of the relationships contained herein, in the description and/or in the Figures, may be used to control and determine properties of SMPs.

The method 100 includes determining a range of rubbery moduli 110 from the ranges of percentage weights and molecular weights. The range of rubbery moduli are determined 110 by evaluating a relationship between rubbery modulus, percentage weight of cross-linker and molecular weights for each of the combinations determined in operations 104 and 106. This results in a range of possible rubbery moduli for SMPs which would also have the transition temperature desired and used for operations 104 and 106.

A rubbery modulus is selected 112 from the range of rubbery moduli. A rubbery modulus may be desired for a SMP for any of the reasons described herein, including,

patient characteristics or particular requirements of the therapeutic use or insertion site. In one embodiment, selecting 112 may be performed in response to the range of moduli being determined 110 or before the range is determined, for example, as an initial goal value of rubbery modulus for the SMP. In another embodiment, the selecting 112 may be performed after another transition temperature is selected, producing another range of rubbery moduli. In other words, the method 100 may be performed, for example, iteratively, repeatedly, and/or in parts.

The method 100 also includes determining a molecular weight and percentage weight of cross-linker 114 based on the selected rubbery modulus. In one embodiment, the determining 114 is performed using the relationship between rubbery modulus, molecular weight and percentage weight of cross-linker to find the combination of molecular weight and percentage weight that corresponds to the rubbery modulus selected.

In one embodiment of method 100, a computer program is used to evaluate the relationships based on the transition temperature and the rubbery modulus. In one embodiment, the computer program can query a user for a desired glass transition temperature and a desired rubbery modulus simultaneously, and return an error if the desired combination is not available. In another embodiment, the computer program may display ranges of transition temperature and rubbery modulus that a user may vary to see which combinations of transition temperature and rubbery modulus are available. For example, if a user restricts a transition temperature range to 45-52 degrees Celsius, the computer program may calculate the values of rubbery moduli available and change the display of the range of rubbery moduli accordingly. As another example, the user may restrict a rubbery modulus range and the computer program may calculate and display a range of transition temperatures available based on the range of rubbery moduli.

The operations of determining a range of molecular weights and percentage weights of cross-linker (104, 106) may be performed at about the same time. In one embodiment, determining a range of molecular weights 104 may create relationships that may be used to determine a range of percentage weights of cross-linker 106. These two determinations (104, 106) may be performed with any time separation, at about the same time, at large time intervals, or simultaneously.

In another embodiment, determining a range of molecular weights and percentage weights of cross-linker (104, 106) may be performed by creating and/or selecting a table, graph, or chart corresponding to a desired transition temperature or a desired rubbery modulus among a plurality of tables, graphs, and/or charts. In this embodiment, the tables,

graphs, and/or charts include information from the relationships described above and outline ranges of molecular weights and percentage weights cross-linker that correspond to the desired value of the property (e.g., transition temperature).

In one embodiment, values of rubbery moduli may be presented in a table along with corresponding values of molecular weight and percentage weight cross-linker. The table in this embodiment may be tailored to a specific value of transition temperature. In another embodiment, values of transition temperatures may be presented in a table along with corresponding values of molecular weight and percentage weight cross-linker. The table in this embodiment may be tailored to a specific value of rubbery modulus.

Determining an average molecular weight 114 may also comprise determining a mixing ratio of a first cross-linker and a second cross-linker. As discussed further above, different cross-linkers can be used to create a wide range of average molecular weight cross-linker materials. For example, if a first cross-linker has a first average molecular weight and a second cross-linker has a second average molecular weight, different from the first, the average molecular weight of the cross-linker material may be varied between the first and the second average molecular weight.

Fig. 2 shows a flow chart of an embodiment of a method 200 of controlling a property of a SMP via variations in a molecular weight and percentage weight cross-linker in the SMP formulation. Method 200 includes selecting a value 202 of a property of a shape memory polymer. In this embodiment, only one value of a property (e.g., a desired value of the property for the SMP) is selected. A range of values of molecular weight of a cross-linker is determined 204. Also a range of values of percentage weight of cross-linker is determined 206. Each of these ranges are determined based on relationships which relate the inputs of molecular weight and percentage weight of cross-linker which would attain the value of the property selected in 202. For example, if a certain rubbery modulus is desired for a SMP, a range of percentage weights of cross-linker may be used, and a range of average molecular weights of cross-linker may be used. These ranges may be further understood in the form illustrated in Figs. 4-9.

The embodiment of the method 200 also includes the option of selecting a value 210 of an average molecular weight of a cross-linker, and determining a value 212 of percentage weight of the cross-linker. The embodiment of the method 200 also includes the option of selecting a value 214 of a percentage weight of a cross-linker, and determining a value 216 of average molecular weight of the cross-linker. Each of these options utilizes the selected value of the property (e.g., from 202) and the selected value of

one of the inputs (e.g., percentage weight from 210, average molecular weight from 214) to determine the value of the other input.

In one embodiment, the method 200 is a computer program that receives (e.g., in place of selecting) values from a user, such as in operations 202, 210, 214. In this embodiment, the computer program provides to the user (not shown) the ranges it determines in operations 204, 206 and provides to the user (not shown) the value it determines in either operation 212 or 216.

In one embodiment, the method 200 uses two values of one property, constituting a range of those values. For example, the method may provide a range of values of molecular weights and percentage weights of cross-linker that may achieve a range of rubbery moduli. In one embodiment, the method 200 may be embodied in tabular form, such as in printed tables, graphs or charts. In another embodiment, determining a range of values of molecular weight and percentage weight cross-linker (204, 206) may be performed by selecting a table, graph, or chart based on a desired value or range of values of a property.

Fig. 3 is an example of a computer program that implements some of the methods described herein. The computer program is written in a language compatible with Matlab by The Mathworks, Inc. of Natick MA. The program assumes a linear chain of MMA, a cross-linker species of PEGDMA, and average molecular weights of cross-linkers of 550, 875 and 1000. Each of the relationships used in the program were derived from data contained in Figs. 4-9 and discussed further below.

The program requests a desired glass transition temperature from a user, and receives it from the user's input. From this desired glass transition temperature, a range of possible values is given for percentage weight of cross-linker material. This range is calculated using the temperature coefficients of the "pure" monomers which denote the average molecular weights of some commercially available monomers (e.g., PEGDMA with molecular weights of 550, 875, 1000). Therefore, this range is limited by the limited number of monomers used for the calculation and a larger range may be possible if other monomer species and/or weights were used by the program (e.g., PEGDMA with a molecular weight of 330).

The program then requests user input regarding the desired percentage weight of cross-linker material within the range supplied. The program then iteratively tries a first group of two cross-linkers (e.g., with molecular weights 550 and 875). In other words, the program checks if an average molecular weight between 550 and 875 will provide the

desired glass transition temperature (e.g., a property of the SMP) and the desired percentage weight of cross-linker (e.g., an input value of the SMP network). If so, the mixing ratio of the two average molecular weights is provided along with the resultant rubbery modulus. If not, the program checks if an average molecular weight between 875 and 1000 will work. If that check fails, the program concludes that the desired combination of glass transition temperature and percentage weight cross-linker, given the constraints provided in the assumptions of the program.

Other inputs may allow more flexibility through either more potential mixtures of inputs or through more ranges of possible values of inputs. In one embodiment, if the program in Fig. 3 were able to freely choose average molecular weights of the cross-linker, there may be more possible determinations. In another embodiment, the program in Fig. 3 could have more possible determinations if the program were able vary other inputs, such as selecting a different species of cross-linker, selecting a different species of linear chain.

The program in Fig. 3 is one embodiment of a method that combines and modifies the methods illustrated in Figs. 1 and 2, and described above. Other programs, methods and techniques may use parts of the exemplary methods described above in useful combinations and modifications which will be readily apparent to those skilled in the art.

For reference the relationships used in Fig. 3 are:

$Tg = WT*(Tx - Tl) + Tl$

Tg = glass transition temperature

WT = percentage weight of cross-linker material

Tx = temperature characteristic of cross-linker

(Tx = 23.5 for PEGDMA 550; –16 for PEGDMA 875; – 32.5 for PEGDMA 1000)

Tl = temperature characteristic of linear chain (140.6 for MMA)

$RM(550) = 5.1347*\exp(.0268*WT*100)$

$RM(875) = 4.4355*\exp(.0208*WT*100)$

$RM(1000) = 3.93*\exp(.0181*WT*100)$

RM(average molecular weight) = rubbery modulus characteristic of cross-linker of that average molecular weight

Other relationships may be included and/or substituted as empirically or theoretically derived from experimentation with different linear chains and cross-linkers. Some of these other relationships are demonstrated in Figs. 4-9, which detail empirical

data derived for some of the linear chain and cross-linker networks described herein. Figs. 4-9 show molecular weights of cross-linker as PEGn(Mn) which may include several types of cross-linker molecule. In Figs. 4-9, PEGn(Mn) refers to PEGDMA of multiple varieties and configurations. For example, these cross-linkers may have included PEG molecules with multiple different molecular structures and configurations with di-methacrylate (DMA). In the experiments for Figs. 4-9, PEGDMA of the average molecular weight indicated in the graph was used and should be understood as PEGDMA of that molecular weight, rather than pure PEG of that molecular weight.

For example, PEGDMA 330 may be used in some applications, depending on desired requirements of the SMP being formulated. For example, PEGDMA 330 may allow for a lesser glass transition temperature dependence and a greater rubbery modulus dependence on the weight percentage of cross-linker used. Other molecular weights of cross-linker may be used to increase the range of average molecular weight available for tailoring in the formulation.

A relationship which may be used in code such as that described in Fig. 3 and used for other purposes using PEGDMA 330 is: RM(330) = 6.19 * exp(.036*WT*100). The temperature characteristic (e.g., as used in Fig. 3) for PEGDMA 330 is 125.45 degrees Celsius.

Fig. 4 is a graph of relationships between glass transition temperature and percentage weight cross-linker for various average molecular weights (Mn) of cross-linker. Each line is a fit of data taken from SMP networks using a single average molecular weight cross-linker. The difference in slope between the lines illustrates the difference in glass transition temperature that may be achieved for any given percentage weight cross-linker by varying the average molecular weight of the cross-linker. In addition, the difference in slope between the lines illustrates the ability to vary the percentage molecular weight of cross-linker for any given glass transition temperature, possibly to achieve values of other properties (e.g., recovery time characteristic of the SMP).

Fig. 5 is a graph of relationships between glass transition temperature and molecular weight of cross-linker for various percentage weights of cross-linker. Each line is a fit from data of a SMP networks with the same percentage weight of cross-linker, but including different molecular weights of the cross-linker. This graph shows another view of some of the same data shown in Fig. 4.

Fig. 6 is a graph of relationships between rubbery modulus and percentage weight of cross-linker. Each curve is a fit of data taken from SMP networks using a single average molecular weight cross-linker. The difference between the curves illustrates the difference in rubbery modulus that may be achieved for any given percentage weight cross-linker by varying the average molecular weight of the cross-linker. A single relationship between rubbery modulus, molecular weight and percentage weigh of cross-linker may be created using the different curves. In addition, the difference between the curves illustrates the ability to vary the percentage weight of cross-linker without varying the rubbery modulus, possibly to achieve values of other properties (e.g., recovery time characteristic of the SMP).

Fig. 7 is a graph of rubbery modulus versus molecular weight of cross-linker for various percentage weights of cross-linker. Each curve is a fit from data of a SMP networks with the same percentage weight of cross-linker, but including different molecular weights of the cross-linker. The curves show relationships between the average molecular weight of cross-linker and the rubbery modulus that may be used to determine other inputs to a formulation given certain desired properties of an SMP network. For example, a particular relationship or curve may be chosen by selecting a percentage weight cross-linker for the SMP network.

Fig. 8 is a graph of exemplary relationships between modulus and temperature illustrating the modulus transition of three different exemplary SMP networks as manufactured. The graph tracks the change in modulus of the SMP network as the network is cycled from a low temperature (e.g., the storage temperature) to a higher temperature. The change in modulus may indicate, for example, a shape change in the SMP network and/or a stress exerted by the SMP network on an environmental constraint. Any shape change of the SMP network may also be affected by environmental constraints surrounding the network while the network undergoes a modulus transition.

Fig. 8 illustrates the ability, using some of the techniques described herein, to change a glass transition temperature (e.g., from 56 degrees to 92 degrees Celsius) without changing the rubbery modulus of an SMP network (e.g., keeping it fixed at about 12.8 MPa). For example, the SMP network with a glass transition temperature of 56 degrees Celsius has substantially the same rubbery modulus as the SMP networks with glass transition temperatures of 72 degrees and 92 degrees Celsius. Thus, through using some of the techniques herein, glass transition temperature may be varied substantially independently from rubbery modulus.

Fig. 9 is another graph of exemplary relationships between modulus and temperature illustrating the modulus transition of four different exemplary SMP networks. Fig. 9 illustrates the ability, using some of the techniques described herein, to change a rubbery modulus (e.g., from 9.3 MPa to 12.8 MPa to 17.2 MPa to 23.0 MPa) without changing the glass transition temperature of a SMP network (e.g., keeping it fixed at about 76 degree Celsius). For example, the SMP network with a rubbery modulus of 12.8 MPa has substantially the same glass transition temperature as the SMP networks with rubbery moduli of 9.3 MPa and 23.0 MPa. Thus, through using some of the techniques herein, rubbery modulus may be varied substantially independently from glass transition temperature.

Fig. 10 is a graph of recovery percentage versus time for various percentage weights of cross-linker. Each curve is a fit of data taken from different SMP networks, and represents the time the network took to recover to a certain recovery percentage. Other curves may be derived from Fig. 12 as some of the same data is disclosed in that graph. The difference between the curves illustrates the differences in recovery time characteristics that may be achieved by changing the percentage weight cross-linker. For example, the time difference from 50% recovered to 90% recovered is significantly shorter for 40% weight of cross-linker networks than it is for 10% weight of cross-linker networks. In addition, the overall recovery time to 90% recovered is much shorter between those two networks. These differences in time are achieved despite recovering the networks under similar conditions (e.g., stimulus interface, stimulus magnitude) and are largely the result of the differences in the structure of the network rather than any differences in the recovery environment.

In another embodiment, a particular recovery time is selected and a percentage weight cross-linker is determined from that recovery time. As noted above, the particular recovery time may depend on other factors, such as recovery stimulus magnitude, but even if these other factors cannot be changed given the application, the recovery time characteristic may be changed through varying the percentage weight cross-linker.

The relationships described by the curves on the graph in Fig. 10 are:

50% Recovered

$T = 3.95 + 193.05 * \exp((- WT - 10)/9.06))$

90% Recovered

$T = 3.45 + 256.55 * \exp((- WT - 10)/9.40))$

The time (T) in these graphs and equations may be considered a recovery time characteristic. Thus, the time (T) equates to seconds based on other factors that were consistent between the experiments that produced these results, such as recovery stimulus magnitude (e.g., liquid bath temperature in which the SMPs were immersed) and stimulus interface (e.g., surface area and form factor). Other factors such as starting temperature of a SMP may be important for heat-activated SMPs.

In one embodiment, by including another input capable of modification, further flexibility may be attained for the SMP properties determinable from the formulation of the network. In the examples above, two inputs are available for modification (percent weight of cross-linker and average molecular weight of the cross-linker) and to a large extent two properties may be controlled (transition temperature and modulus).

If substantial control of a third property in tandem with two others is desired, a third input may be used, depending on the relationships between the inputs (e.g., molecular weight, percentage weight of cross-linker, manufacturing parameters, species of linear chains, species of cross-linkers) and SMP properties (e.g., transition temperature, rubbery modulus, recovery time characteristics). In other words, some combinations of properties and of certain values of those properties, such as a certain transition temperature, a certain modulus and a certain response time parameter, may not be attainable in a SMP network given a limited group of available inputs (e.g., the group of inputs of: percent weight of cross-linker and molecular weight). For example, there may be only one pair of property values of a transition temperature and a modulus if the only inputs available for modification are the percent weight of cross-linker and the average molecular weight of the cross-linker.

The above techniques could be modified to accommodate different real-world constraints, such as the desirability/availability (or lack thereof) of a particular cross-linker or linear chain species or a particular molecular weight of a cross-linker species. For example, many of the linear chain and cross-linker species used in the examples below were chosen based on their known biocompatibility from use in other applications. In addition, as will be discussed further below, other factors such as manufacturing processes or the inclusion of other materials in the formulation may affect the relationships between inputs such as cross-linker weight percentage and properties such as a transition temperature or a modulus.

Fig. 11 is a graph of modulus versus temperature illustrating the modulus transition of an exemplary SMP network. The graph also includes a tan-delta measurement of the

modulus change and illustrates a method of determining a transition temperature of the material. The method includes finding temperature for the peak tan-delta of the modulus of the material. The tan-delta measurement represents the ratio of the storage modulus (shown), or alternatively, the real part of the modulus of the SMP network under dynamic analysis, to the loss modulus (not shown), or alternatively, the imaginary part of the modulus of the SMP network similarly under dynamic analysis. The graph was produced using a standard three-point flexural test using a dynamic modulus analysis machine (DMA machine).

The recovery of a SMP network depends on many factors and the recovery may not have a definite time at which recovery is 100% completed (e.g., recovered strain = maximum strain). There may be several reasons for this including, deformation that is permanent or otherwise unrecoverable (e.g., plastic deformation), long-term recovery of the last few percent of strain, constraints imposed by the application/installation site impeding recovery to an unconstrained shape, and other interactions with the installation site (e.g., degradation, assimilation, absorption). In addition, the SMP network may integrate itself with the installation site in a manner that blurs the distinction between the network and the site, and rendering a measurement of recovered strain imprecise. Measurements of partial, but significant recoveries may be used in some instances as a proxy for full recovery, for comparison between SMP networks, or in determining a recovery time characteristic of a SMP network.

Fig. 12 is a graph of recovery percentage versus time for three different SMP networks, each with a different percentage weight cross-linker and/or a different glass transition temperature. The three different networks include a network with 20% weight cross-linker and Tg = 52 degrees Celsius, a network with 20% weight cross-linker and Tg = 55 degrees Celsius, and a network with 10% weight cross-linker and Tg = 55 degrees Celsius.

The lines showing different glass transition temperature illustrate the effects of a different Tg on actual recovery time. The networks were each recovered using the same magnitude of stimulus (in this instance, temperature of a liquid bath) and the networks also shared the same interface with that stimulus (in this instance, surface area in contact with the bath). The network with a lower Tg recovered more quickly than the other networks, in part because the transfer of heat to the lower-Tg network (presumably consistent between the networks) caused the lower-Tg network to get closer to its Tonset and closer to its Tg more quickly than the same transfer of heat did in the higher-Tg networks.

Fig. 12 also illustrates that recovery time can be affected by simple energy transfer. Energy transfer is related to the magnitude of a stimulus and the interface the SMP network shares with the stimulus. As introduced above, recovery time characteristics are independent from changes in energy transfer from a stimulus (e.g., heat, light). In other words, changes in Tg such as those between the networks in Fig. 12 are not part of a change in recovery time characteristic.

Fig. 12 also illustrates a change in recovery time characteristic between the two SMP networks with Tg = 55 degrees Celsius. The heat transfer from the stimulus to both of these networks was similar, as was their glass transition temperatures. However, the internal differences between the two networks due to the different percentage weight cross-linker in each of the networks, caused the 10% weight cross-linker network to recover more slowly than the 20% weight cross-linker network.

Fig. 13 illustrates the distinction between recovery time characteristic and actual recovery time, by showing a number of SMP networks, each with different glass transition responding to similar recovery stimuli. The lower Tg network (Tg = 56 degrees Celsius) clearly recovers faster than the higher Tg networks. These changes do not necessarily correspond to different recovery time characteristics separate from the different transition temperatures of the three networks. Instead, because the three networks were substantially the same apart from their different transition temperatures, the differences in recovery time between the three networks shows the effect of energy transfer to networks with similar recovery time characteristics, but different transition temperatures.

Fig. 14 shows a flow chart of a method 1400 of manufacturing SMP devices. The method 1400 includes shaping a polymer material 1402 into a post-implantation shape, deforming the polymer material 1404 into a pre-implantation shape, and cooling the polymer material 1406 to below a certain temperature.

The method 1400 includes cooling the polymer material 1406 to below a certain temperature. The certain temperature may be the glass transition temperature of the polymer material. In one embodiment, the cooling the polymer material operation 1406 is performed after the deforming the polymer material operation 1404. For example, the polymer material may be above the glass transition temperature while the deforming the polymer material operation 1404 is performed. In another embodiment, the cooling the polymer material operation 1406 is performed before the deforming the polymer material operation 1404.

The shaping the polymer material operation 1402 may be performed in many manners. In one embodiment, the polymer material may be polymerized from a solution into a solid body while in a mold. For example, the mold may define a post-implantation shape or a pre-implantation shape. In another embodiment, the polymer material may be shaped via cutting, milling, turning (e.g., using a lathe), or other techniques used for shaping materials. As another example, the mold may hold a solution and a cable member while the solution is polymerized around an end of the cable member.

Fig. 15 shows a flow chart of an embodiment of a method 1500 of determining a recovery time. Method 1500 includes selecting a recovery characteristic of a SMP 1502. The recovery characteristic, as described above, may not correspond to a recovery time or speed of recovery and the characteristic be of any dimension (e.g., seconds per unit surface area exposure to a liquid bath at 55 degrees Celsius). In one embodiment, the recovery characteristic selected in 1502 may be determined by any of the methods described herein or may be selected as an output from another operation. In another embodiment, the recovery characteristic may be a known property of a SMP network that has already been manufactured and the method 1500 may be used to determine a recovery time (1516) based on the application of a recovery stimulus.

The method 1500 includes selecting a stimulus magnitude 1504 and selecting a stimulus interface characteristic 1506. Stimulus magnitude is discussed above further, and can be, for example, the temperature of a liquid bath, the temperature of a heating implement, the intensity of radiation, and/or the wavelength of radiation. Stimulus interface characteristic is also discussed further above and can be, for example, a cross-section of the SMP adapted to receive light from a waveguide source while the SMP is implanted in a surgery site. The stimulus magnitude may be used in conjunction with the stimulus interface characteristic to determine a rate of stimulation received by the SMP. In one embodiment, the stimulus magnitude and the stimulus interface characteristic may be combined to determine a rate of heat transfer to the SMP. In another embodiment, the stimulus magnitude and the stimulus interface may be combined to determine a radiation flux into the SMP.

The method 1500 also includes selecting a glass transition temperature 1510 and selecting a storage temperature of the SMP 1512. These operations may be used for SMP networks which are heat activated as temperature properties and measurements may or may not be important in SMP applications using a stimulus other than heat (e.g., light or other radiation). A transition temperature and a storage temperature (or other temperature

at which the SMP will be held before being subjected to stimulus) may be utilized, through standard thermodynamic calculations, to determine a prediction of the recovery time (1514) of the SMP given the glass transition temperature and storage temperature selected (1510, 1512).

The method 1500 includes determining a recovery time 1514 based on the selected information. For example, calculations may be performed using the recovery time characteristic, the stimulus magnitude and/or the stimulus interface characteristic. In one embodiment, relationships may be used in determining a recovery time 1514 that take into account each of these pieces of information. In another embodiment, relationships may be used which presume certain information, such as a consistent stimulus interface characteristic or starting temperature of the SMP, and allow a recovery time to be determined without selecting or using such presumed information.

In one embodiment, a recovery time may be determined 1514 based on a recovery characteristic, the recovery stimulus magnitude, and the stimulus interface characteristic of the SMP. For example, an SMP may have a certain stimulus interface characteristic (e.g., a form factor with certain surface area, an end of a plug where heat or light is applied) that is known to provide a certain amount of interface with a stimulus. In one embodiment, the stimulus intensity may be varied to change the recovery time achieved based on the stimulus interface characteristic and recovery characteristic derived from the SMPs.

In other embodiments, not shown here, the method 1500 can be performed in different orders than described herein, including in reverse. For example, a desired recovery time may be selected and used to determine a desired recovery characteristic that relates to the recovery time and which may then be used to determine a desired weight percentage of cross-linker material to be used in a SMP formulation.

Fig. 16 shows a flow chart of an embodiment of a method 1600 of determining a manufacturing parameter based on a patient characteristic. Using some of the techniques described above, SMP devices may be designed to have properties which are specifically targeted for use with a particular patient. Method 1600 includes selecting a value of a patient characteristic 1602 that relates to a particular patient. Patients receiving therapeutic treatment including a SMP may benefit from specific values of some of the properties of the SMP.

The value of a patient characteristic selected 1602 may include any type of patient data that may be used in selecting a SMP device or material for use within the patient. For example, a patient's particular treatment may call for a fast recovery characteristic or a

low transition temperature of the SMP. The techniques described herein for determining properties or inputs of SMPs may then be used to select a SMP or design a SMP formulation (e.g., 1604, 1606). A patient characteristic may relate to age, height, weight, sex, general health, body fat percentage, physical activity level, incidents in medical history (e.g., cardiac problems), response to similar treatments in the past, goals of the treatment, and use of the effected area after the treatment.

The value of the patient characteristic may be selected (e.g., 1602) from any available source, including via observation of the patient, retrieval from a data store, or reference to a preferred or common value. The value of the patient characteristic may also be any type of patient data measured from a patient, including, for example, data measured by a physician in observing a patient, data recorded by an instrument, data recorded by hand, or observed but not recorded by a physician.

In one embodiment, a specific value of a SMP property or SMP formulation input may be determined for a patient based on the patient data (e.g., value of a patient characteristic). In another embodiment, a range of values for a SMP property or a range of values of a SMP formulation input may be determined for a patient. For example, a device formulated and manufactured for treatment of patients needing a SMP device with SMP properties in a certain range may be determined for the patient based on these data.

Method 1600 includes determining a value of a device characteristic 1604 based on the selected value of a patient characteristic. In one embodiment, determining a value of a device characteristic 1604 may be performed by matching the value of the device characteristic to the value of the patient characteristic. In another embodiment, determining a value of a device characteristic 1604 may be performed by correlating the value of the patient characteristic with a different value of a device characteristic based on other information (e.g., physician's experience, a correlation table).

In one embodiment, a SMP stent may be designed for use with that patient that matches the particular elasticity of a body lumen (e.g., blood vessel) within the patient. For example, the age of a patient may contribute to and may be used to estimate a particular elasticity of the patient's blood vessels which is different from the norm. In one embodiment, the elasticity of the body lumen of the treatment site may be measured. In another embodiment, another body lumen may be measured instead, and the elasticity of the body lumen of the treatment site may be estimated from the measured data. In another embodiment, the elasticity of a body lumen may be estimated from other data (e.g., age, blood pressure, cardiac history, imaging/scans of blood vessels).

In another embodiment, a SMP graft fixation device may be designed for use with a patient based on a particular bone density or modulus of the bone insertion site within the patient. For example, the patient may participate in a lot of weight-bearing activities and have a commensurately high bone density than normal and could accommodate/need an especially strong fixation of a soft-tissue graft. A SMP fixation device may be designed for use with that patient that provides an installment force that is sufficient for the patient, but would be excessive for another patient with lower bone density. In another example, a child patient may require an SMP device in an area that is softer or has a lower modulus than a normal bone density. In one embodiment, the density or modulus of the bone of the treatment site may be measured. In another embodiment, another bone density or the modulus of another bone may be measured instead, and the density or modulus of the bone of the treatment site may be estimated from the measured data. In another embodiment, the density or modulus of a bone may be estimated from other data (e.g., age, blood pressure, cardiac history, imaging/scans of blood vessels).

In one embodiment, a kit contains a variety of devices for selection of a device when and as needed for a particular patient based on the data measured, received or selected from the patient. For example, a surgeon may select a device during treatment and/or during surgery based on patient data observed or measured in the patient. As another example a surgeon may wait to decide between two or three devices until the surgery in which the device is to be used in is partially completed. The surgeon may then select from the kit of devices a device that suits the patient.

Method 1600 also includes determining a value of a manufacturing parameter 1606, which may be performed in any of the manners described above for determining a SMP formulation input based on a desired or selected SMP property. In one embodiment, other inputs of a SMP formulation may be determined using the SMP device characteristic selected (in 1604). In another embodiment, other device characteristics (e.g., other SMP properties) may be used in addition to the device characteristic selected (in 1604) to determine a SMP formulation, depending on, for example, available inputs or other manufacturing factors described above.

A SMP network may include dissolving materials which may include part of the network or may be included in the formulation of the network before the network is polymerized (e.g, as an aggregate, mixed into the formulation). Dissolving materials may include materials that disperse over time, even if the material or part of the material does not actually dissolve or enter into a solution with a solvent. In other words, a dissolving

material as used herein may be any material that may be broken down by an anticipated external environment of the polymer. In one embodiment, a dissolving material is a drug which elutes out of a SMP network. A dissolving material may be attached by chemical or physical bonds to the polymer network and may become disassociated with the polymer network over time.

Dissolving materials may be used to create surface roughness, for example, in order to increase biocompatibility of the network. In one embodiment, the dissolving material may initially form a part of the surface of the SMP network, and leave behind a rougher SMP surface after the dissolving material has dissolved. In another embodiment, the dissolving material may be placed within the body of the SMP network , and upon dissolving may create an impression in the surface of the SMP by allowing the SMP to collapse due to the dissolution of the dissolving material within the body of the SMP.

Figs. 17 and 18 show the roughening of a surface of a SMP due to dissolving materials within and on the surface of the SMP. Figs. 17 and 18 have been processed to show in black and white the surface variations that were in the original images as grey-scale variations. The images in Figs. 17 and 18 were similarly processed from scanning electron microscope images taken at 248X resolution, and showing a legend bar that is 100 micrometers long to given dimension to the Figures. The scales of the images in Figs. 17 and 18 are the same.

In Fig. 17, the dissolving material, particles of heparin (an anticoagulent drug), fills part of the body and surface of a SMP network. Fig. 17 shows a smooth surface comprising a SMP network and heparin particles. The scanning electron microscope on at the 248X resolution did not detect enough surface variation on the smooth combined surface to register significant grey scale variation.

Fig. 18 shows a significant increase in surface variation after heparin has been removed both from the combined surface of a SMP network and heparin, and from the body of the SMP network. After the heparin is removed (e.g., through dissolving), the SMP surface that is left contains significant surface variations. The surface variations are significant enough to obscure the resolution and length legend that appeared along the top of the image (similar to Fig. 18) before the image was processed. These surface variations may be used for different purposes. For example, purposes may include increasing biocompatability of the SMP in biological applications, or increasing surface area contact (over time, as a material leaves the SMP) thus affecting mechanical properties.

Dissolving materials, through their dissolution over time, may be used for many purposes. In one embodiment, the dissolution of a material may affect a dissolution or breaking up of a biomedical device over time. In another embodiment, the dissolution of a material may elute a drug, achieving a pharmacological purpose.

An initial surface of a device may be a rough surface. In one embodiment, an initial rough surface may include a dissolving material. In another embodiment, an initial rough surface may be created by including dissolving material inside a SMP network. Once the material has dissolved, a surface with a different roughness may be left behind. In one embodiment, a smooth surface is left after a dissolving material has dissolved. In another embodiment, a surface rougher than the initial is left behind after a dissolving material has dissolved. In another embodiment, a surface with a different type of roughness is left after a dissolving material has dissolved. For example, an initial surface may have roughness in a random pattern and a surface left after a dissolving material has dissolved may have a roughness that is ordered and repeating.

An initial surface of a device may be a surface of an unconstrained shape, a pre-implantation shape, or a post-implantation shape. In one embodiment, an initial surface roughness is the roughness of a surface of the device before it is implanted (pre-implantation shape), and the surface may have a different roughness after the SMP network of the device is activated. In another embodiment, the initial surface roughness is the surface roughness after the SMP network has activated and before the dissolving material has begun dissolving substantially. In yet another embodiment, an initial surface roughness is the roughness of the surface of the device with the SMP network in an unconstrained shape, and the surface of the device takes on another roughness after deformation of the device into the pre-implantation shape, and yet another roughness after activation of the SMP network. An unconstrained shape is the shape of a SMP network that would occur without after activation constraints. An implanted device with a SMP network may not achieve its unconstrained shape. A pre-implantation shape may be any shape which the device attains due to deformation, storage, or other preparation for implantation. A post-implantation shape may include any shape attained after a SMP network activates within an implantation environment (e.g., a body lumen, a boney recess), and before substantial degradation and/or dissolving has occurred.

Initial surface roughness may be set by manufacturing processes. Manufacturing processes are described herein and can include, for example, milling, forming in molds, and extrusion. In one embodiment, an initial surface roughness may be designed to take

into account an expected implantation environment and a desired post-implantation shape. For example, a dissolving material (included in the SMP network and forming part of the surface of the SMP) may not compress in the same manner as the SMP network, the implantation environment will compress the dissolving material differently than the SMP network, and the desired post-implantation shape will be affected by this different compression. In another embodiment, an initial surface roughness may be designed for an unconstrained shape and a deformation process may be used to create a substantially smooth pre-implantation shape. In yet another embodiment, a surface roughness of an unconstrained shape is determined from a desired post-implantation shape and the expected compression of both the deformation process and the implantation environment.

In addition to the above-described techniques of modifying the properties of a SMP through varying the formulation of the SMP, there are also techniques for modifying properties by varying the manufacturing processes of the SMP (e.g., the processes described in relation to Fig. 14) and through other processes (e.g., recovery process).

Deformation conditions can affect other properties of the SMP, for example thermomechanical manufacturing and handling processes can influence shape recovery. Figs. 20-22 show the effects of deformation temperature (Td) on shape recovery. The stent with a higher Td experienced a delay in recovery compared to its lower Td counterpart.

Shape memory is driven by a favorable increase in entropy, thus lowering the free energy of the system. Sometimes, SMP's are deformed 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 energy may be needed for deformation and the energy is stored in enthalpic internal energy wells. In this case, shape recovery is now driven by both a favorable increase in entropy and decrease in enthalpy, which may result in shape-memory activation at lower temperatures.

Fig. 19 shows a flow chart of an embodiment of a method 1900 for achieving a peak stress in a SMP during the recovery phase of the SMP via variations in the deformation temperature of the SMP during manufacturing.

The embodiment of the method 1900 includes selecting a recovery characteristic 1902 of a SMP network. In one embodiment, the selecting 1902 may be performed by calculating or otherwise predicting the recovery characteristic of the SMP network. For example, the recovery characteristic may be calculated from the weight percentage cross-

linker, the magnitude of stimulus (e.g., recovery temperature), comparisons with other SMP networks, and/or other factors. In another embodiment, the selecting 1902 may be performed by receiving the recovery characteristic of a SMP network. For example, the SMP network may have a recovery characteristic listed in a table or chart, and the receiving of the characteristic may be performed through looking up the characteristic in the table or chart. In one embodiment, the receiving may be from an application which determines insertion site characteristics from patient data. In another embodiment, the receiving may be from requirements of a therapeutic use of the SMP network. In another embodiment, selecting a recovery characteristic may be performed by observation of the recovery of an SMP network. For example, the recovery of a SMP network may be observed and the recovery characteristic of the SMP network may be calculated therefrom.

The recovery characteristic selected (in 1902) for the SMP network may be different from a desired recovery characteristic of the SMP network. For example, the SMP network may be pre-manufactured and its recovery characteristic may not be modifiable through modifying the SMP formulation through the techniques described herein. The recovery characteristic selected may cause an anticipated recovery time that is different from a desired recovery time. There are several reasons why a desired recovery time may not be attainable given a particular recovery characteristic. For example, the recovery conditions may have particular constrained conditions (e.g., certain recovery temperature), or there may be a therapeutic reason to have the recovery time be particularly long or particularly short. Therefore, modifying the recovery characteristic may be useful.

Modifying a recovery characteristic 1904 through selecting a deformation temperature of the shape memory polymer network may be performed based on the experimental results provided in and discussed with respect to Figs. 20-22. Modifying a recovery characteristic 1904 may include modifying a manufacturing process of a SMP network to achieve a different recovery characteristic. In one embodiment, a recovery characteristic creates, given a certain recovery environment, a recovery time that is not desirable, and the recovery time may be modified through modifying the recovery characteristic without changing the recovery environment. For example, with respect to Fig. 21, a recovery time may be too long for recovering to 20% strain at a recovery temperature (Tr) = 0.875 * Tg, based on a deformation temperature (Td) = 0.75 * Tg. A different Td may be selected, for example, Td = 1.25 * Tg, to create a different recovery characteristic and therefore a different recovery time in the same recovery environment.

Selecting a deformation temperature, and modifying a recovery characteristic thereby 1904, may use other deformation temperatures (Td) than 0.75 * Tg and 1.25 * Tg. Curves such as those in Figs. 20A-C may be created for other scenarios and formulations, and such curves are meant to serve as examples as well as substantive data. Modifying a recovery characteristic 1904 may also be performed based on other experimental results based on other SMP networks or other ranges of recovery temperatures, deformation temperatures and/or transition temperatures as appropriate.

Method 1900 also includes causing the SMP network to be substantially at the deformation temperature 1906. Some techniques of causing the SMP network to be at a specified temperature are discussed elsewhere herein (e.g., temperature controlled liquid bath, contact with a heating or cooling element), and some are known to those with skill in the art. The causing 1906 may be performed to any degree of certainty, as appropriate. In one embodiment, contact with a heating or cooling element for a sufficient amount of time is an appropriate method both of causing 1906 a SMP network to achieve a deformation temperature and of assuring that the SMP network is substantially at the deformation temperature. In another embodiment, placement of a SMP network in a temperature controlled environment for a sufficient amount of time both causes 1906 the SMP network to attain the desired temperature and assures that the SMP network is substantially at the temperature (e.g., Td).

The temperatures discussed herein with respect to SMP networks do not need to be temperatures for each segment of the SMP network. Minimal variations in temperature common to experimental practice may be present without substantial variations from the useful results discussed herein. For example, the entirety of the SMP network does not need to be at a particular temperature or at the same temperature, nor does each part of the SMP network need to be at exactly a particular temperature to achieve the results discussed herein.

The SMP network is deformed 1910 while at the deformation temperature. In one embodiment, the deformation temperature may be checked by any of the method described above (e.g., with respect to causing the SMP network to be substantially at the deformation temperature 1906). In another embodiment, the deformation may be performed without continuing to control or to check the temperature of the SMP network.

Figs. 20A-C are graphs of normalized strain versus time for different SMP networks. In other words, the graphs represent the recovery of stored strain in SMP networks as a function of time. In Figs. 20A-C, the SMP networks were formulated

similarly, yet they exhibit different recovery processes and times based on the deformation temperatures and recovery temperatures to which the networks were exposed.

Fig. 20A is a graph of normalized strain versus time for a recovery temperature (Tr) = Tg. The graph shows recoveries of SMP networks deformed at Td = 0.75 * Tg and Td = 1.25 * Tg. As shown in the graph, the SMP network deformed at the lower temperature recovered more quickly in the same recovery environment.

Fig. 20B is a graph of normalized strain versus time for a recovery temperature, Tr = 0.875 * Tg. The graph shows recoveries of SMP networks deformed at Td = 0.75 * Tg and Td = 1.25 * Tg. As shown in the graph, the SMP network deformed at the lower temperature recovered more quickly in the same recovery environment. Comparing the graphs in Fig. 20B to those in Fig. 20A, the recovery process of the SMP network is also affected by the lowering of the recovery temperature, though recovery may still be completed for recovery temperatures below Tg.

Fig. 20C is a graph of normalized strain versus time for a recovery temperature, Tr = 0.75 * Tg. The graph shows recoveries of SMP networks deformed at Td = 0.75 * Tg and Td = 1.25 * Tg. As shown in the graph, the SMP network deformed at the lower temperature recovered more quickly in the same recovery environment. Comparing the graphs in Fig. 20C to those in Fig. 20B, the recovery process of the SMP network is also affected by the lowering of the recovery temperature, though recovery may still be completed for recovery temperatures below Tg.

Examples

Example 1

Some of the properties of six examples of polymer networks are shown below.

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

Networks 1-3 exhibit a Tg ~ 52 degrees Celsius while varying the cross-linking over 10, 20, and 40 wt% while Networks 4-6 have a Tg ~ 55 degrees Celsius with cross-linking varied in the same range. In all networks, the onset of the glass transition is ~10 degrees Celsius 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 Tg has slightly different rubbery moduli with Network 1 at 1.5 MPa and Network 4 at 2.4 MPa.

Example 2

The shape-memory effect was examined in polymer stents intended for cardiovascular applications. Three polymer networks were synthesized from poly(ethylene glycol) di-methacrylate (PEGDMA) and tert-butyl acrylate (tBA) with 10 wt% and 20 wt% crosslinker, and with glass transition temperatures (Tg) of 52°C and 55°C (see Fig. 12). Solid stents were manufactured and tested for free strain recoverability at temperatures at or just above 37°C. Stents with lower glass transition temperatures and a higher degree of cross-linking recovered faster than their counterparts.

Tert-butyl acrylate (tBA), di(ethylene glycol) di-methacrylate (DEGDMA), poly(ethylene glycol) di-methacrylate (PEGDMA) with typical Mn=550 and Mn=875, and photoinitiator 2,2-dimethoxy-2-phenylacetephenone 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 1 wt% photoinitiator.

The solutions were either injected in between two glass slides separated with 1mm 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 21.4mm Teflon rod sheathed with a 22mm ID glass tube (Allen Scientific) to create polymer tubes with a wall thickness of 300μm and 22mm OD. A UV-Lamp (Model B100AP; Black-Ray) was used to photopolymerize the solutions for 10 minutes at an intensity of 10mW/cm2 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 ensure the complete conversion of monomers.

The amount of cross-linking was affected by the wt% of multi-functional cross-linking monomers (DEGDMA, PEGDMA) to the mono-functional linear tBA monomer. Also, ethyleneglycol, diethyleneglycol, and triethyleneglycol based acrylates are forms of polyethyleneglycol based acrylates with one, two, or three repeat units.

Three polymer networks were synthesized with 10 wt% and 20 wt% crosslinker, and with glass transition temperatures (Tg) 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 network. The percentage of crosslinker indicates the amount of the multi-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 15mm x 4mm x 1mm 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 were run on samples (n=3) of each polymer using a Perkin Elmer DMA-7 to obtain their glass transitions. The peak of the tan delta curve marks the glass transition temperature (Tg) whereas the onset of the glass transition (Tonset) defines the beginning of the transition. The rubbery and glassy moduli can be seen as the plateaus above and below Tg. Exact values for Tg were calculated from the maximum of a 2nd order polynomial fitted to the peak of the tan delta curve while Tonset was calculated using instrument software.

In DMA tests, samples were cycled at 1Hz with static and dynamic stresses of 100 kPa and 90 kPa across a 5mm 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 degrees Celsius/min to eliminate temperature gradients within the sample. Data was collected every 5 seconds.

Stents were compacted to fit into an 18 Fr. catheter (~6mm). Stents were packaged 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.

Fig. 12 shows a performance comparison of the solid stents recovering at body temperature (37°C) using image analysis of the stent recovery data as indicated in Figure 4. Fig. 12 shows the free recovery data of solid stents made from all three materials and compacted at room temperature. The first stents to unroll and recover were the 20 wt% crosslinked polymer with Tg of 52°C, followed by the 20 wt% crosslinked polymer with a Tg of 55°C, and the 10 wt% crosslinked polymer with a Tg of 55°C.

The techniques described above may also be used to design SMP devices and/or their properties to be useful to a majority of patients based on factors which are fairly consistent among patients or in areas where an exact match is not especially critical. One example of a property value designed to be useful for a majority of patients is picking a value of a glass transition temperature to be roughly body temperature, or about 37

degrees Celsius. Another example of a property value designed to be useful for a majority of patients, and depending on the application, is the choice of linear chain in the SMP formulation, for example, the choice between MMA or tBA, based on the range of values of rubbery moduli required for the intended application. For example, tBA is often used in low rubbery modulus applications (e.g., stents in blood vessels) and MMA is often used in high rubbery modulus applications (e.g., graft fixation in bone).

Example 3

For the experiments giving which produced data for Figs. 4-9, polymer networks were created by polymerizing different amounts of mono and multi-functional monomers. Methyl methacrylate (MMA) was copolymerized with poly-ethylene glycol dimethacrylate (PEGDMA) with various molecular weights (Mn) to form each example polymer network. In the experiments, MMA is a mono-functional monomer and forms the linear backbone of the network, whereas PEGDMA is multi-functional and serves as a cross-linking agent. 2,2-dimethoxy-2-phenylacetophenone was used as a photo-initiator.

In other embodiments, other mono-functional monomers such as tert-butyl acrylate (tBA) or 2-hydroxyethyl methacrylate (2-HEMA) may be used in place of MMA. In other embodiments, other monomers that are multi-functional and have various molecular weights such as di-EGDMA or tri-EGDMA, may be used in place of PEGDMA. In other embodiments, thermal-initiation may also used to polymerize the networks using peroxide initiators.

In the experiments, a 4x4 matrix of polymer networks was used for characterization using 25, 50, 75, and 100 wt% PEGDMA with Mn = 330, 550, 875, and 1000. Normally, .2 wt% photo-initiator was used. However, at low weight percentages of PEGDMA, .4 wt% was used to promote complete conversion. Dynamic mechanical analysis (DMA) was used to characterize the thermomechanics of the networks.

Figs. 4-9 show the Tg results of the 4x4 matrix of polymer systems created. An extra data point of 40 wt% PEGDMA (875) was added for verification, while only 2 data points are left out due to the difficulty of obtaining an accurate measurement. Fig. 4 shows the relationship of glass transition temperature to wt% cross-linking being linearly dependent. Even though a data point for MMA was not obtained due to the difficulty of photo-polymerizing MMA, all trends converge on the same value of ~140 degrees Celsius. Furthermore, by increasing the molecular weight of PEGDMA, the Tg will decrease for the same wt% cross-linking. However, the effect of decreasing Tg as a function of Mn of PEGDMA is not linear. Fig. 5 shows the effect of molecular weight (Mn) of PEGDMA

(noted as (PEG)n) some places) may be represented by a power function (e.g., y=A*exp(xb)).

While various embodiments have been described for purposes of this specification, various changes and modifications may be made which will readily suggest themselves to those skilled in the art and which are encompassed in the spirit of the invention both disclosed herein and as defined in the appended claims.

Unless otherwise indicated, all numbers expressing quantities of ingredients, properties such as molecular weight, reaction conditions, and so forth used in the specification and claims are to be understood as being modified in all instances by the term "about." Accordingly, unless indicated to the contrary, the numerical parameters set forth in the following specification and attached claims are approximations that may vary depending upon the desired properties sought to be obtained by the present invention. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of the claims, each numerical parameter should at least be construed in light of the number of reported significant digits and by applying ordinary rounding techniques.

Notwithstanding that the numerical ranges and parameters setting forth the broad scope of the invention are approximations, the numerical values set forth in the specific examples are reported as precisely as possible. Any numerical value, however, inherently contains certain errors necessarily resulting from the standard deviation found in their respective testing measurements.

What is claimed is:

1. A method comprising:

selecting a transition temperature for a shape memory polymer network;

determining a first range of average molecular weights of cross-linker material and a second range of weight percentages of cross-linker material based on the selected transition temperature of the shape memory polymer network and based on a first relationship between transition temperature, weight percentage of cross-linker material and average molecular weight of cross-linker material;

determining a third range of rubbery moduli based on the first range of average molecular weights of cross-linker material and the second range of weight percentages of cross-linker material and based on a second relationship between rubbery modulus, weight percentage of cross-linker material and average molecular weight of cross-linker material;

selecting a rubbery modulus for the shape memory polymer network that is part of the third range of rubbery moduli; and

determining an average molecular weight of cross-linker material and a weight percentage of cross-linker material based on the second relationship and the rubbery modulus selected.

2. The method of claim 1, further comprising:

determining a mixing ratio of a first cross-linker material having a first average molecular weight and a second cross-linker material having a second average molecular weight such that a mixture of the first cross-linker material and the second cross-linker material in the mixing ratio would have substantially the determined average molecular weight of cross-linker material.

3. The method of claim 1, wherein the determining the second range of rubbery moduli is further based on patient data.

4. The method of claim 3, wherein the selected rubbery modulus matches a value which is derived from patient data.

5. The method of claim 1, wherein the selected transition temperature is derived from patient data.

6. The method of claim 1, further comprising:

making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material; and

polymerizing the formulation to form the shape memory polymer network for use as at least part of a medical device.

7. The method of claim 6, further comprising:

installing the medical device within a patient; and

heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

8. The method of claim 1, wherein selecting the transition temperature comprises:

receiving a desired value for the transition temperature.

9. A method comprising:

selecting a recovery time characteristic for a shape memory polymer network;

determining a percentage weight of cross-linker material from the selected recovery time characteristic of the shape memory polymer network based on a first relationship between recovery time characteristics and the percentage weight of cross-linker material;

selecting a transition temperature for the shape memory polymer network; and

determining an average molecular weight of the cross-linker material from the selected transition temperature of the shape memory polymer network based on the determined percentage weight of cross-linker material and based on a second relationship between transition temperature, percentage weight cross-linker material, and average molecular weight of the cross-linker material.

10. The method of claim 9, further comprising:

determining a rubbery modulus of the shape memory polymer network based on a third relationship between rubbery modulus, percentage weight cross-linker material, and average molecular weight of the cross-linker material.

11. The method of claim 10, further comprising:

if the rubbery modulus determined is incompatible with a desired application of the shape memory polymer network, selecting a different recovery time characteristic.

12. The method of claim 9, further comprising:

determining a mixing ratio of a first cross-linker material having a first average molecular weight and a second cross-linker material having a second average molecular weight such that a mixture of the first cross-linker material and the second cross-linker material in the mixing ratio would have substantially the determined average molecular weight of cross-linker material.

13. The method of claim 9, wherein the selected transition temperature of the shape memory polymer network is derived from patient data.

14. The method of claim 9, further comprising:

making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material; and

polymerizing the formulation to form the shape memory polymer network for use as at least part of a medical device.

15. The method of claim 14, further comprising:

installing the medical device within a patient; and

heating the medical device to about the selected transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

16. The method of claim 9, wherein selecting the recovery characteristic comprises:

receiving a desired value for the recovery characteristic.

17. The method of claim 9, wherein selecting the transition temperature comprises:

receiving a desired value for the transition temperature.

18. A method comprising:

determining a percentage weight cross-linker material for a shape memory polymer network based on a first relationship between weight percentage of cross-linker, rubbery modulus, and transition temperature of the shape memory polymer network, based on a second relationship between average molecular weight of cross-linker material, rubbery modulus, and transition temperature of the shape memory polymer network, based on a desired rubbery modulus for the shape memory polymer network, and based on a desired transition temperature of the shape memory polymer network; and

determining an average molecular weight of cross-linker material for the shape memory polymer network based on the first relationship, based on the second relationship, based on the desired rubbery modulus for the shape memory polymer network, and based on the desired transition temperature of the shape memory polymer network.

19. The method of claim 18, further comprising:

determining a mixing ratio of a first cross-linker material having a first average molecular weight and a second cross-linker material having a second average molecular weight such that a mixture of the first cross-linker material and the second cross-linker material in the mixing ratio would have substantially the determined average molecular weight of cross-linker material.

20. The method of claim 18, wherein the determining the percentage weight cross-linker material and the determining the average molecular weight of cross-linker material are performed at about the same time.

21. The method of claim 18, wherein the desired rubbery modulus is derived from patient data.

22. The method of claim 18, wherein the desired transition temperature is derived from patient data.

23. The method of claim 18, further comprising:

making a formulation having substantially the determined average molecular weight of cross-linker material, substantially the determined weight percentage of cross-linker material; and

polymerizing the formulation to form a shape memory polymer network for use as at least part of a medical device.

24. The method of claim 23, further comprising:

installing the medical device within a patient; and

heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

25. The method of claim 23, wherein the formulation comprises a cross-linker material of poly-ethylene glycol di-methacrylate.

26. The method of claim 23, wherein the formulation comprises a linear chain selected from methyl methacrylate, poly(methyl methacrylate), and tert-butyl acrylate.

27. A shape memory polymer network produced according to the method of claim 18.

28. A method comprising:

determining a first relationship between transition temperature for a shape memory polymer network and percentage weight of cross-linker material based on an average molecular weight of the cross-linker material;

determining a percentage weight of cross-linker material from a desired transition temperature of the shape memory polymer network based on the first relationship;

determining a second relationship between rubbery modulus for the shape memory polymer network and average molecular weight of the cross-linker material based on the percentage weight cross-linker; and

determining the average molecular weight of the cross-linker material from a desired rubbery modulus of the shape memory polymer network based on the second relationship.

29. The method of claim 28, wherein determining the percentage weight of cross-linker material, determining the average molecular weight of the cross-linker material, determining the first relationship, and determining the second relationship are performed at about the same time.

30. The method of claim 28, further comprising:

determining a mixing ratio of a first cross-linker material having a first average molecular weight and a second cross-linker material having a second average molecular weight such that a mixture of the first cross-linker material and the second cross-linker material in the mixing ratio would have substantially the determined average molecular weight of cross-linker material.

31. The method of claim 28, wherein the desired rubbery modulus of the shape memory polymer network is derived from patient data.

32. The method of claim 28, wherein the desired transition temperature of the shape memory polymer network is derived from patient data.

33. The method of claim 28, further comprising:

making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material; and

polymerizing the formulation to form a shape memory polymer network for use as at least part of a medical device.

34. The method of claim 33, further comprising:

installing the medical device within a patient; and

heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

35. A method comprising:

determining a first relationship between rubbery modulus and percentage weight of cross-linker material based on an average molecular weight of the cross-linker material for a shape memory polymer network;

determining a percentage weight of cross-linker material from a desired rubbery modulus of the shape memory polymer network based on the first relationship;

determining a second relationship between transition temperature and average molecular weight of the cross-linker material based on the percentage weight cross-linker; and

determining the average molecular weight of the cross-linker material from a desired transition temperature of the shape memory polymer network based on the second relationship.

36. The method of claim 35, further comprising:

determining a mixing ratio of a first cross-linker material having a first average molecular weight and a second cross-linker material having a second average molecular weight such that a mixture of the first cross-linker material and the second cross-linker material in the mixing ratio would have substantially the determined average molecular weight of cross-linker material.

37. The method of claim 35, wherein the determining the percentage weight cross-linker material and the determining the average molecular weight of cross-linker material are performed at about the same time.

38. The method of claim 35, wherein the desired rubbery modulus of the shape memory polymer network is derived from patient data.

39. The method of claim 35, wherein the desired transition temperature of the shape memory polymer network is derived from patient data.

40. The method of claim 35, further comprising:

making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material; and

polymerizing the formulation to form a shape memory polymer network for use as at least part of a medical device.

41. The method of claim 35, further comprising:

installing the medical device within a patient; and

heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

42. A method comprising:

selecting a desired value of a property of a shape memory polymer;

determining a first range of values of average molecular weights of a cross-linker material based on the desired value of the property; and

determining a second range of values of percentage weight of a cross-linker material based on the desired value of the property.

43. The method of claim 42, further comprising:

selecting a desired first value of average molecular weight of the cross-linker; and

determining a second value of percentage weight of cross-linker material.

44. The method of claim 43, wherein the desired first value is within the first range of values, and the second value is within the second range of values.

45. The method of claim 42, further comprising:

selecting a desired third value of percentage weight of cross-linker material; and

determining a fourth value of average molecular weight of the cross-linker.

46. The method of claim 45, wherein the fourth value is within the first range of values, and the desired third value is within the second range of values.

47. The method of claim 42, wherein the property is a transition temperature.

48. The method of claim 47, wherein the transition temperature is the glass transition temperature.

49. The method of claim 42, wherein the property is a rubbery modulus.

50. The method of claim 42, wherein the property is a recovery characteristic.

51. The method of claim 50, wherein the recovery characteristic is a recovery time.

52. The method of claim 51, wherein the recovery time is a time to complete substantial recovery given a known set of constraints on the shape memory polymer.

53. The method of claim 42, further comprising:

making a formulation having an average molecular weight of cross-linker within the first range, a weight percentage of cross-linker material within the second range; and

polymerizing the formulation to form a shape memory polymer network for use as at least part of a medical device.

54. The method of claim 53, further comprising:

installing the medical device within a patient; and

heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

55. The method of claim 42, wherein selecting the desired value of the property comprises:

receiving the desired value for the property.

56. A method comprising:

selecting a first value of a compliance characteristic of a first body lumen in a patient;

determining an average molecular weight of cross-linker material and a percentage weight of cross-linker material for a shape memory polymer network based on the first value; and

producing a stent comprising the shape memory polymer network.

57. The method of claim 56, wherein a second body lumen in the patient is the intended insertion site of the stent.

58. The method of claim 57, further including:

estimating the compliance characteristic of the second body lumen in the patient based on the compliance characteristic of the first body lumen in the patient.

59. The method of claim 56, further including:

estimating the compliance characteristic of first body lumen based on patient data.

60. The method of claim 56, wherein the body lumen is an arterial blood vessel.

61. The method of claim 56, wherein producing a stent comprising the shape memory polymer network comprises:

making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material; and

polymerizing the formulation to form the shape memory polymer network for use as at least part of the stent.

62. The method of claim 61, further comprising:

installing the stent within a patient; and

heating the shape memory polymer network to about a transition temperature of the shape memory polymer network thereby activating the shape memory polymer network thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

63. The method of claim 62, wherein selecting the first value of the compliance characteristic comprises:

receiving a desired value for the compliance characteristic.

64. A method comprising:

selecting a first value of a compliance characteristic of a first bone in a patient;

determining an average molecular weight of cross-linker material and a percentage weight of cross-linker material for a shape memory polymer network based on the first value; and

producing a graft fixation device comprising the shape memory polymer network.

65. The method of claim 64, wherein a second bone in the patient is the intended insertion site of the graft fixation device.

66. The method of claim 65, further including:

estimating the compliance characteristic of the second bone in the patient based on the compliance characteristic of the first bone in the patient.

67. The method of claim 64, further including:

estimating the compliance characteristic of first bone based on information about the patient.

68. The method of claim 64, wherein producing a graft fixation device comprising the shape memory polymer network comprises:

making a formulation having substantially the determined average molecular weight of cross-linker material, and substantially the determined weight percentage of cross-linker material; and

polymerizing the formulation to form the shape memory polymer network for use as at least part of the graft fixation device.

69. The method of claim 68, further comprising:

installing the graft fixation device within a patient; and

heating the shape memory polymer network to about a transition temperature of the shape memory polymer network thereby activating the shape

memory polymer network thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

70. The method of claim 64, wherein selecting the recovery characteristic comprises:

receiving a desired value for the recovery characteristic.

71. A method of manufacturing a shape memory polymer network device for use within a patient, the method comprising:

selecting a first value of a patient characteristic;

determining a second value of a device characteristic based on the first value;

determining a percentage weight of cross-linker material for the shape memory polymer network based on the second value;

determining a molecular weight of cross-linker material for the shape memory polymer network based on the second value; and

manufacturing the shape memory polymer network with the determined percentage weight of cross-linker and the determined molecular weight of cross-linker material.

72. The method of claim 71, further comprising:

selecting a linear chain for the shape memory polymer network based on a required recovery force of the shape memory polymer network.

73. The method of claim 72, wherein determining the percentage weight of cross-linker material is performed based on the selected linear chain for the shape memory polymer network.

74. A method comprising:

adding a dissolving material to a shape memory polymer formulation;

polymerizing the shape memory polymer formulation to form a shape memory polymer network; and

dissolving the dissolving material thereby altering a surface roughness of the shape memory polymer network.

75. The method of claim 74, further comprising:

using the shape memory polymer network as at least part of a medical device.

76. The method of claim 75, further comprising:

exposing the shape memory polymer network to an environment which promotes the dissolving of the dissolving material thereby altering at least part of the surface roughness of the shape memory polymer network of the medical device over time.

77. The method of claim 76, wherein exposing includes implanting the shape memory polymer inside a patient.

78. The method of claim 74, wherein adding the dissolving material comprises embedding the dissolving material in a surface of the shape memory polymer network formulation prior to polymerization.

79. The method of claim 74, wherein adding the dissolving material comprises including the dissolving material in the shape memory polymer formulation prior to polymerization.

80. A method comprising:

selecting a recovery characteristic of a shape memory polymer network;

modifying the recovery characteristic through selecting a deformation temperature of the shape memory polymer network;

causing the shape memory polymer network to be substantially at the deformation temperature; and

deforming the shape memory polymer network.

81. The method of claim 80, wherein selecting a recovery characteristic is based on a weight percentage of cross-linker material and an average molecular weight of cross-linker material in the formulation of the shape memory polymer network.

82. The method of claim 80, wherein the causing operation is performed through placing the shape memory polymer network in contact with a system that is substantially at the deformation temperature.

83. The method of claim 82, wherein the material is selected from: a liquid bath, a deformation apparatus, a heating member, a cooling member.

84. The method of claim 80, further comprising:

creating the shape memory polymer network with substantially the selected recovery characteristic for use as at least part of a medical device.

85. The method of claim 84, further comprising:

installing the medical device within a patient; and

heating the medical device to about the transition temperature thereby activating the medical device thereby causing the shape memory polymer network to have substantially the selected rubbery modulus.

86. A polymer exhibiting a shape memory effect, the polymer comprising a polymerization of a mixture of:

a first monomer selected from methyl methacrylate, poly(methyl methacrylate), and tert-butyl acrylate; and

a second monomer with a first average molecular weight, wherein the second monomer is a multi-functional monomer;

wherein the second monomer comprises a combination of a first poly-ethylene glycol di-methacrylate material with a second average molecular weight different from the first average molecular weight and a second poly-ethylene glycol di-methacrylate material

with a third average molecular weight different from both the first average molecular weight and the second average molecular weight;

wherein the polymer has a rubbery modulus which substantially matches a first value derived from patient data.

87. The polymer of claim 86, wherein the polymer has a transition temperature which substantially matches a second value derived from patient data.

88. The polymer of claim 86, wherein the polymer forms at least part of a medical device.

89. The polymer of claim 88, wherein the medical device is a stent.

90. The polymer of claim 88, wherein the medical device is a graft fixation device.

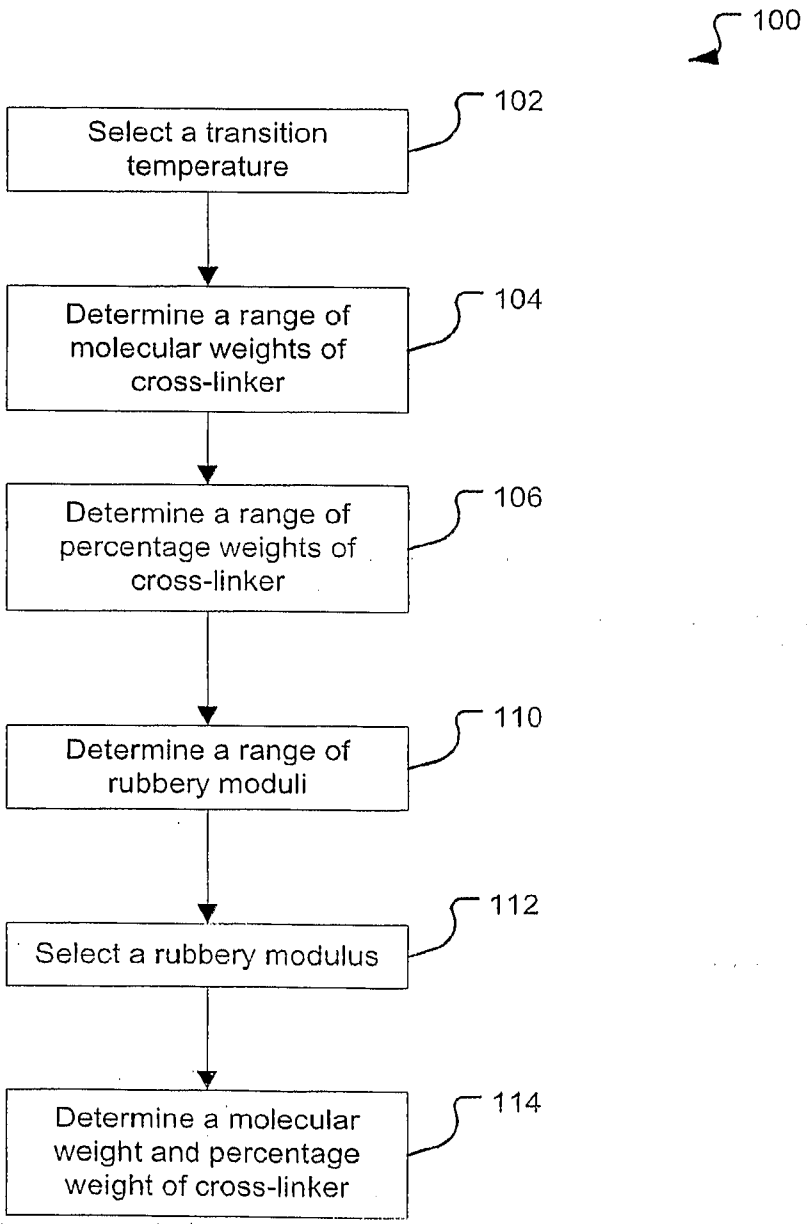
100
Select a transition temperature
102
Determine a range of molecular weights of cross-linker
104
Determine a range of percentage weights of cross-linker
106
Determine a range of rubbery moduli
110
Select a rubbery modulus
112
Determine a molecular weight and percentage weight of cross-linker
114

Fig. 1

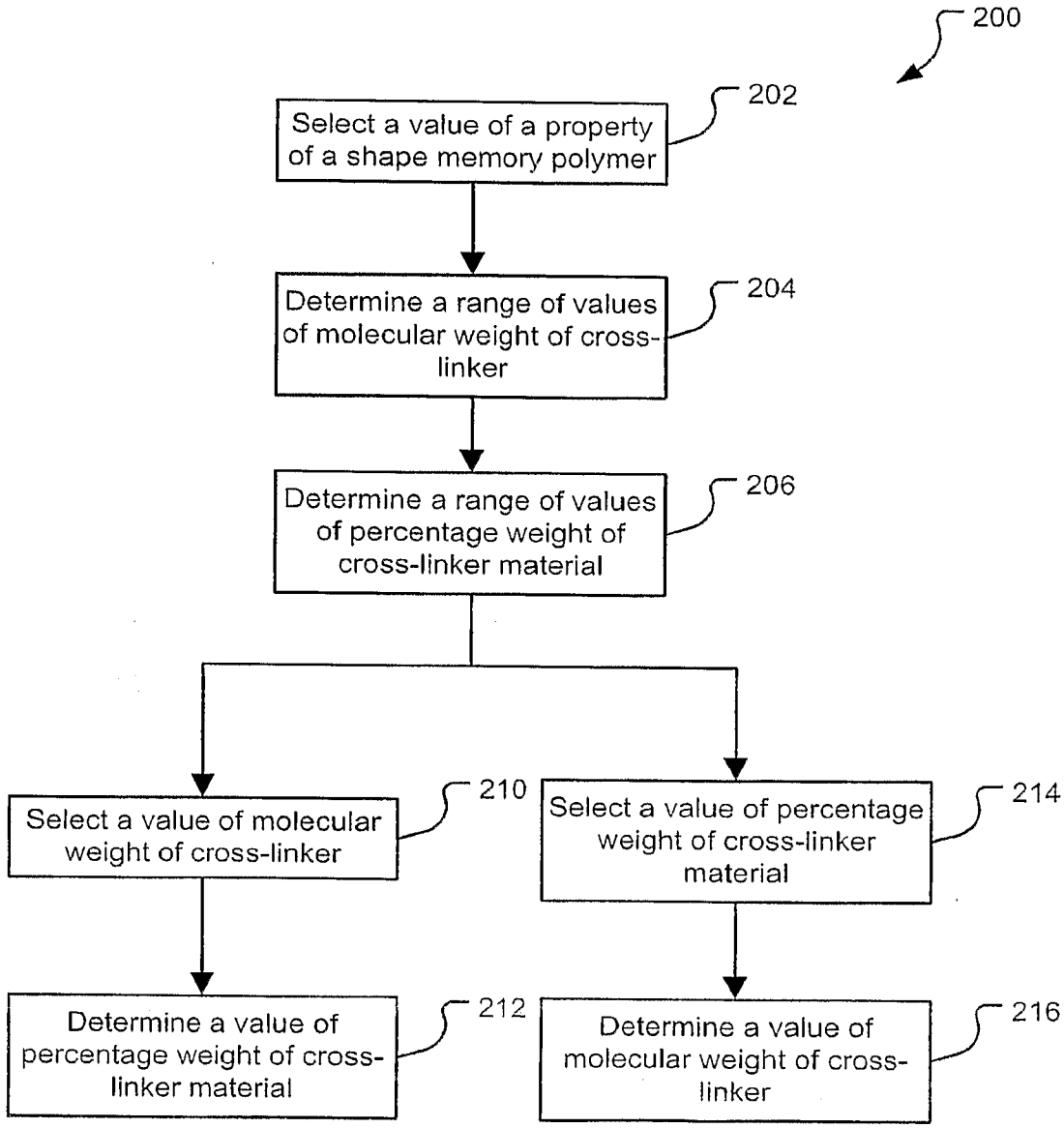
200
Select a value of a property of a shape memory polymer
202
Determine a range of values of molecular weight of cross-linker
204
Determine a range of values of percentage weight of cross-linker material
206
Select a value of molecular weight of cross-linker
210
Select a value of percentage weight of cross-linker material
214
Determine a value of percentage weight of cross-linker material
212
Determine a value of molecular weight of cross-linker
216

Fig. 2

```
%Assign T Values of Pure Monomers
T1 =  140.6;            %MMA
T2 =  23.5;             %PEGDMA 550
T3 = -16;               %PEGDMA 875
T4 = -32.5;             %PEGDMA 1000

%Input Tg and wt% Crosslinking
Tg = input('What Tg do you desire? (C) : ');
   min = (Tg-T1)*100/(T4-T1);       %Calculate minimum value of wt% crosslinking
   max = (Tg-T1)*100/(T2-T1);       %Calculate maximum value of wt% crosslinking
fprintf('\n');
fprintf('Minimum crosslinking is %0.4g wt percent \n', min);
fprintf('Maximum crosslinking is %0.4g wt percent \n', max);
wt = input('What wt% Crosslinking do you want? (%) : ');
wt = wt/100;            %Convert to fraction
g = input('How much solution do you want to make? (g) ');

%-------

%Assign Rubbery Modulus Values of wt% Pure Monomers in MMA
RM2 = 5.1347*exp(.0268*wt*100);
RM3 = 4.4355*exp(.0208*wt*100);
RM4 = 3.93*exp(.0161*wt*100);
%-------

%Try 1st iteration using PEGDMA 550 and 875
x=((T1-T3)*wt - T1 + Tg)/((T2-T3)*wt);  %Fraction of Lower Mn Monomer
if (x >= 0) & (x <= 1)          %Check to see if a real solution
   g1 = (1-wt)*g;
   g2 = wt*x*g;
   g3 = wt*(1-x)*g;

   RM = RM3 + (RM2-RM3)*x;

   fprintf('\n')
   fprintf('You will need:\n')
   fprintf('%0.4g grams of MMA \n', g1);
   fprintf('%0.4f grams of PEGDMA 550 \n', g2);
   fprintf('%0.4f grams of PEGDMA 875 \n', g3);
   fprintf('\n')
   fprintf('Your Rubbery Modulus is %0.4g MPa \n', RM);
   fprintf('\n')
   fprintf('Have a nice day \n')
   break
end
%---------
%Try 2nd iteration using PEGDMA 875 and 1000
x=((T1-T4)*wt - T1 + Tg)/((T3-T4)*wt);
if (x >= 0) & (x <= 1)          %Check to see if a real solution
   g1 = (1-wt)*g;
   g3 = wt*x*g;
   g4 = wt*(1-x)*g;

   RM = RM4 + (RM3-RM4)*x;

   fprintf('\n')
   fprintf('You will need:\n')
   fprintf('%0.4g grams of MMA \n', g1);
   fprintf('%0.4f grams of PEGDMA 875 \n', g3);
   fprintf('%0.4f grams of PEGDMA 1000 \n', g4);
   fprintf('\n')
   fprintf('Your Rubbery Modulus is %0.4g MPa \n', RM);
   fprintf('\n')
   fprintf('Have a nice day \n')
else                            %Case of impossible solution
   fprintf('\n')
   fprintf('Impossible solution')
   fprintf('\n')
   break
end
%--------
```

Fig. 3

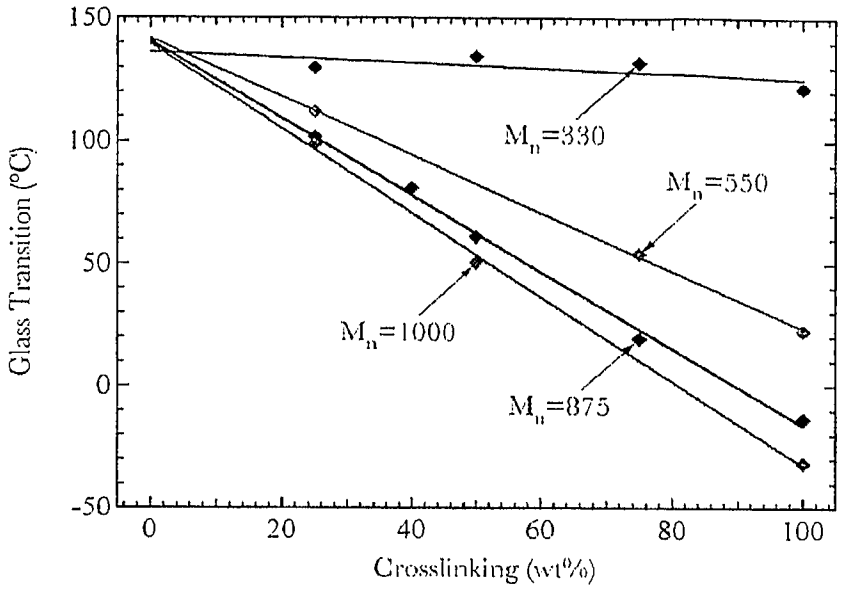
150
100
50
0
-50
0
20
40
60
80
100
Glass Transition (°C)
Crosslinking (wt%)
M_n=330
M_n=550
M_n=1000
M_n=875

Fig. 4

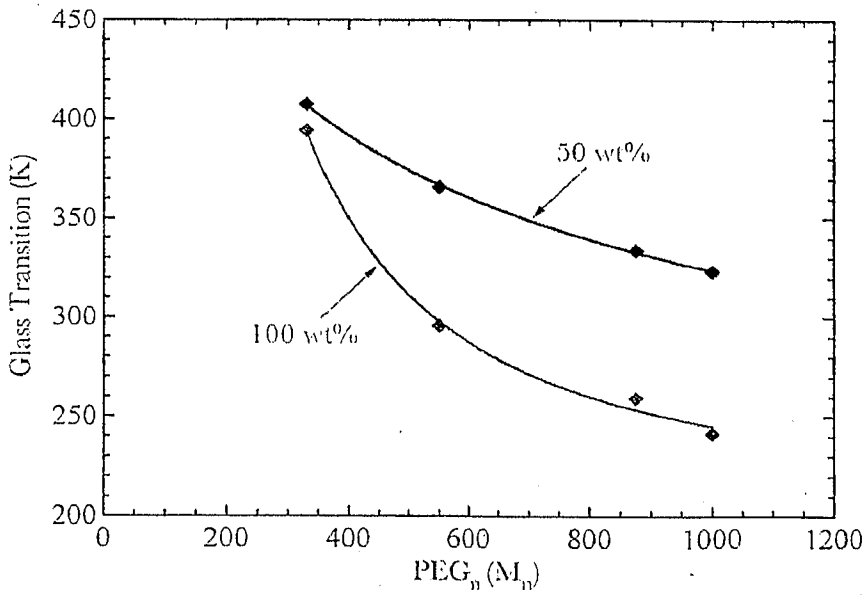
450
400
350
300
250
200
0
200
400
600
800
1000
1200
Glass Transition (K)
PEG_n (M_n)
50 wt%
100 wt%

Fig. 5

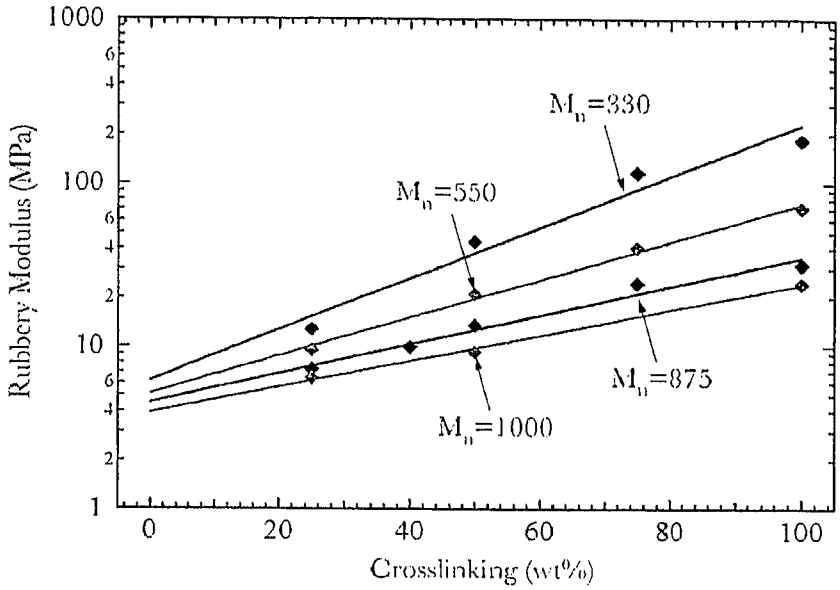
Rubbery Modulus (MPa)
Crosslinking (wt%)
M_n=330
M_n=550
M_n=875
M_n=1000

Fig. 6

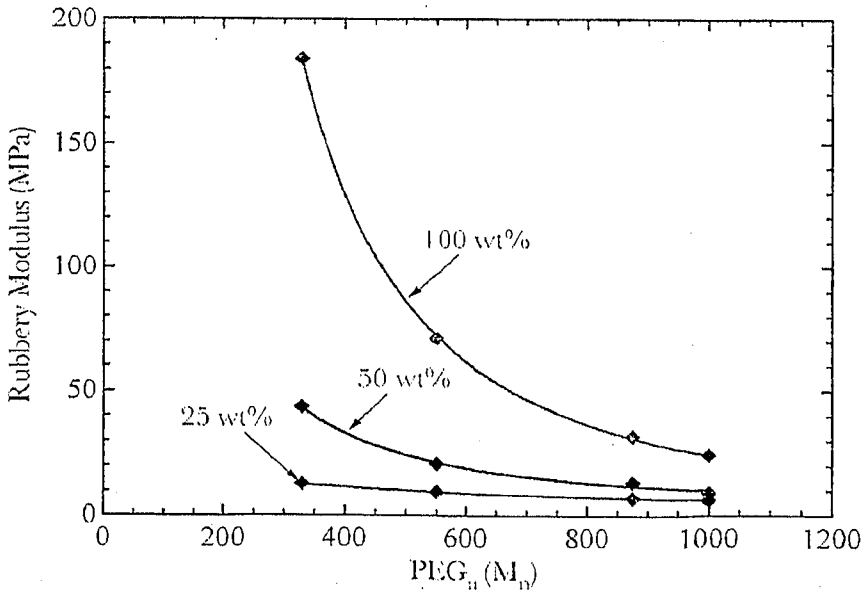
Rubbery Modulus (MPa)
PEG$_n$ (M_n)
100 wt%
50 wt%
25 wt%

Fig. 7

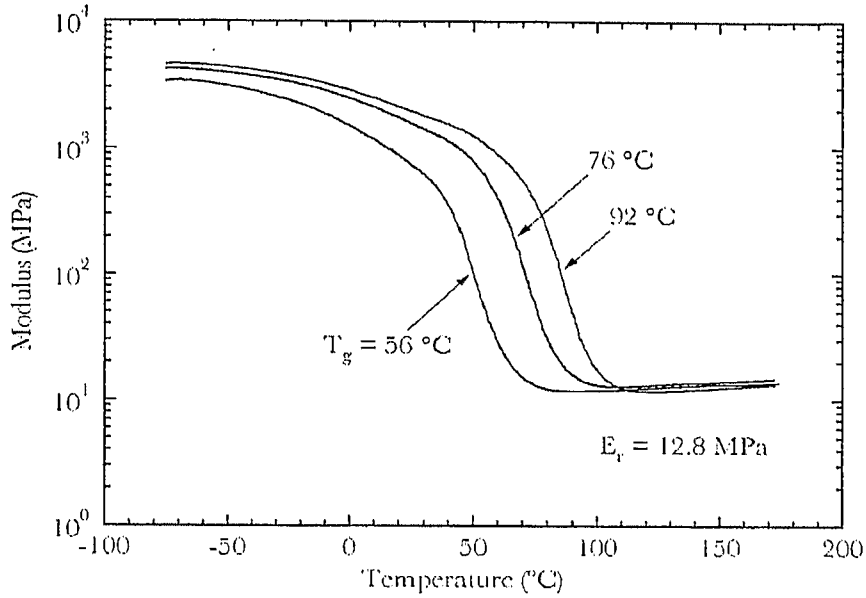
Modulus (MPa)
Temperature (°C)
76 °C
92 °C
T_g = 56 °C
E_r = 12.8 MPa

Fig. 8

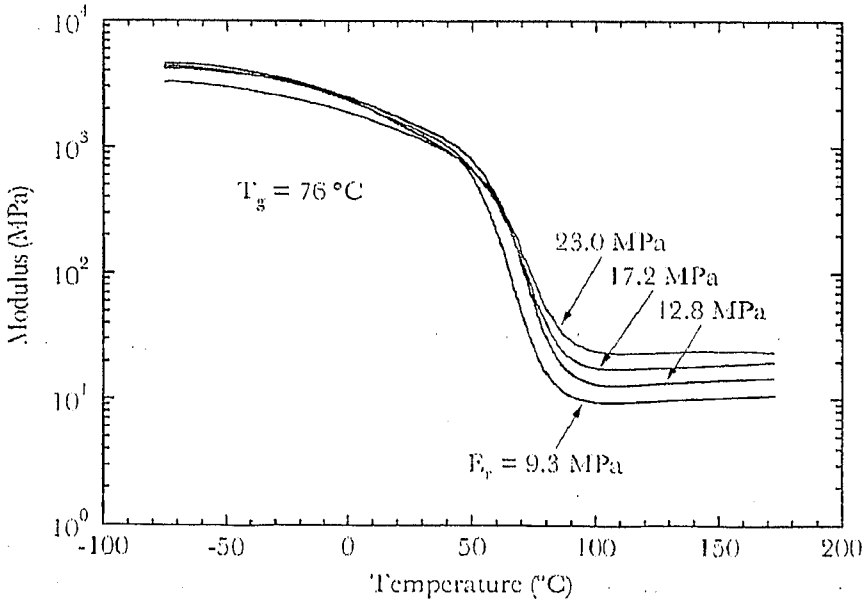
Modulus (MPa)
Temperature (°C)
T_g = 76 °C
23.0 MPa
17.2 MPa
12.8 MPa
E_r = 9.3 MPa

Fig. 9

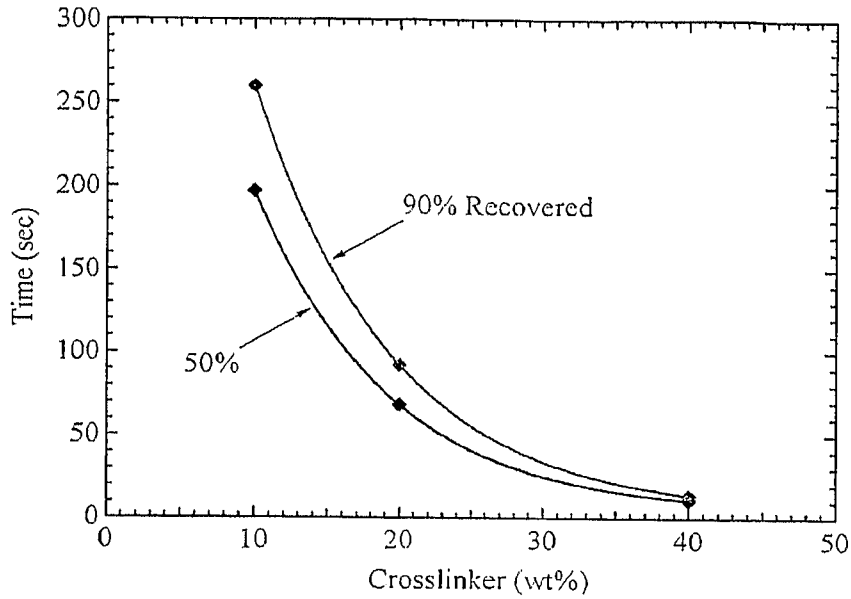
300
250
200
150
100
50
0
Time (sec)
90% Recovered
50%
0
10
20
30
40
50
Crosslinker (wt%)

Fig. 10

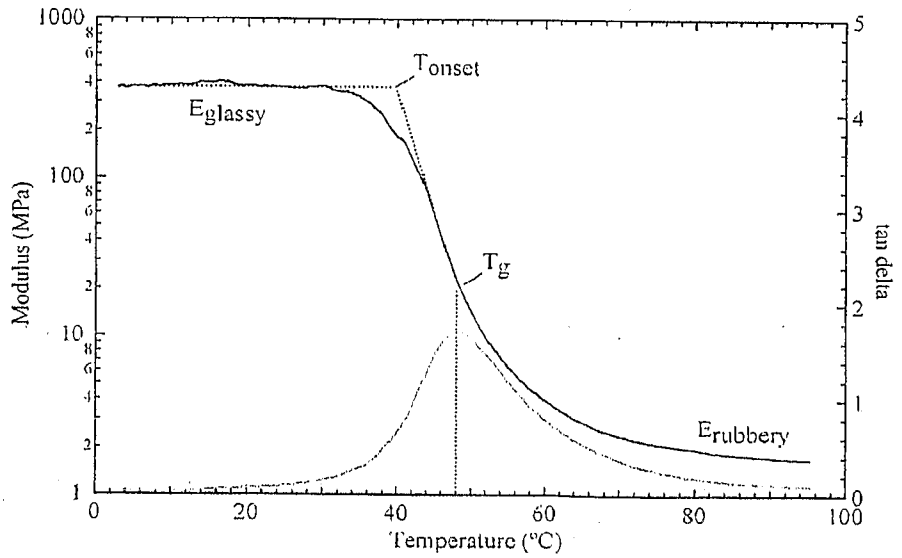
1000
100
10
1
Modulus (MPa)
Tonset
Eglassy
Tg
Erubbery
5
4
3
2
1
0
tan delta
0
20
40
60
80
100
Temperature (°C)

Fig. 11

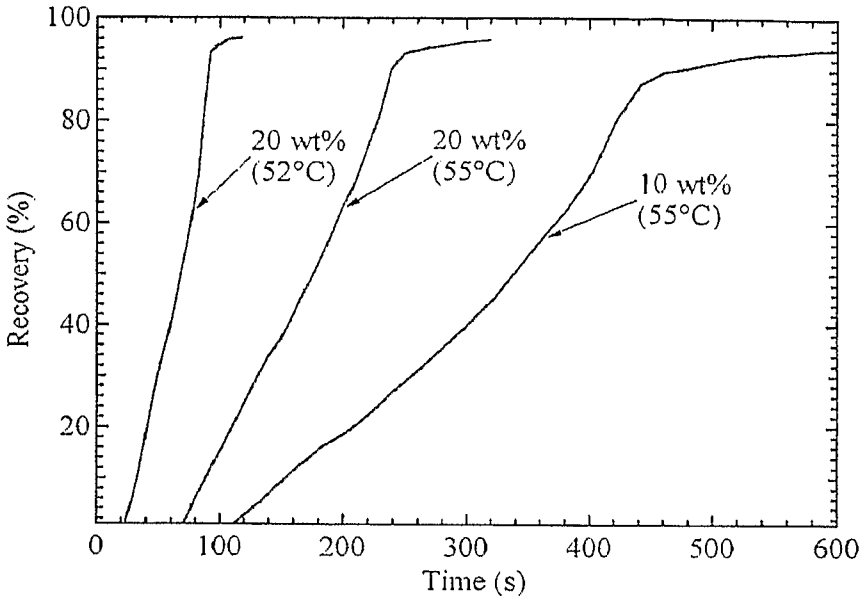
100
80
60
40
20
Recovery (%)
20 wt%
(52°C)
20 wt%
(55°C)
10 wt%
(55°C)
0
100
200
300
400
500
600
Time (s)

Fig. 12

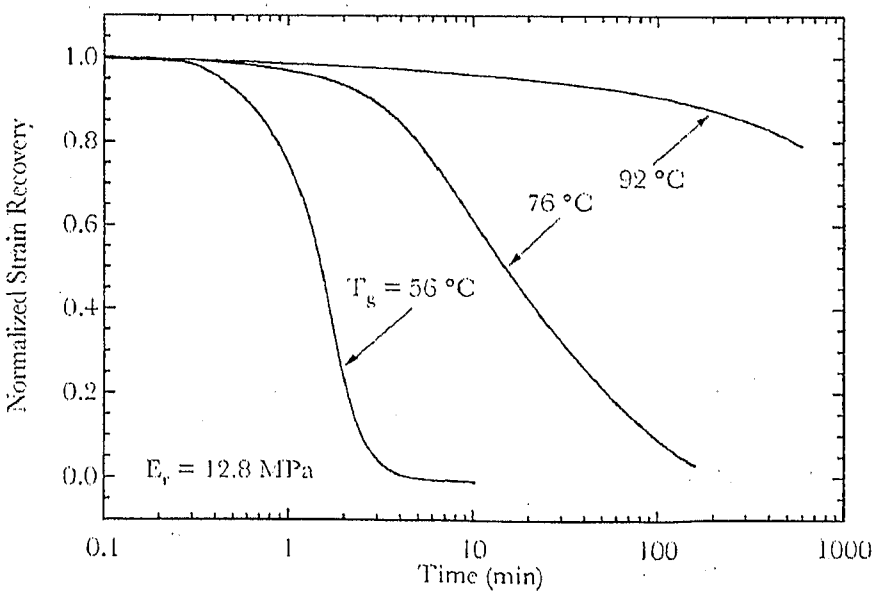
1.0
0.8
0.6
0.4
0.2
0.0
Normalized Strain Recovery
92 °C
76 °C
T_g = 56 °C
E_r = 12.8 MPa
0.1
1
10
100
1000
Time (min)

Fig. 13

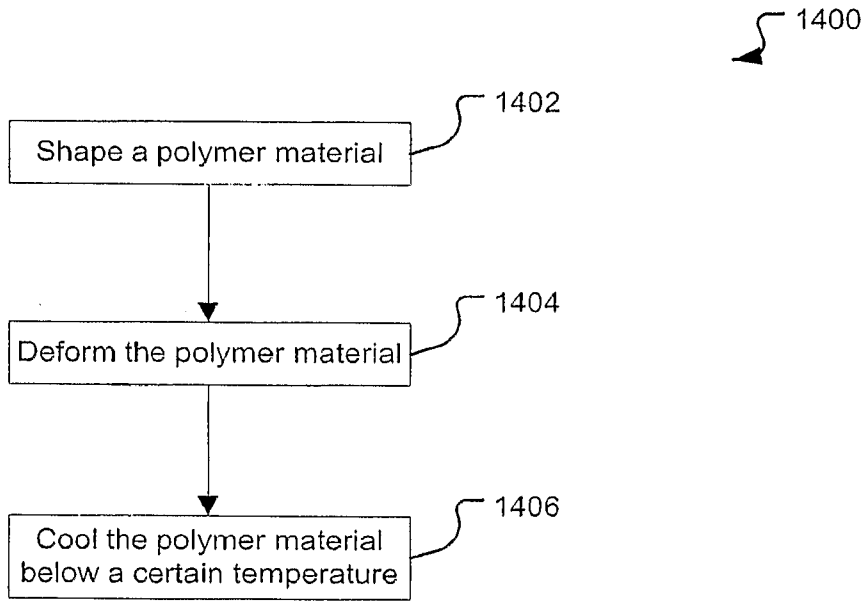
1400
1402
Shape a polymer material
1404
Deform the polymer material
1406
Cool the polymer material below a certain temperature

Fig. 14

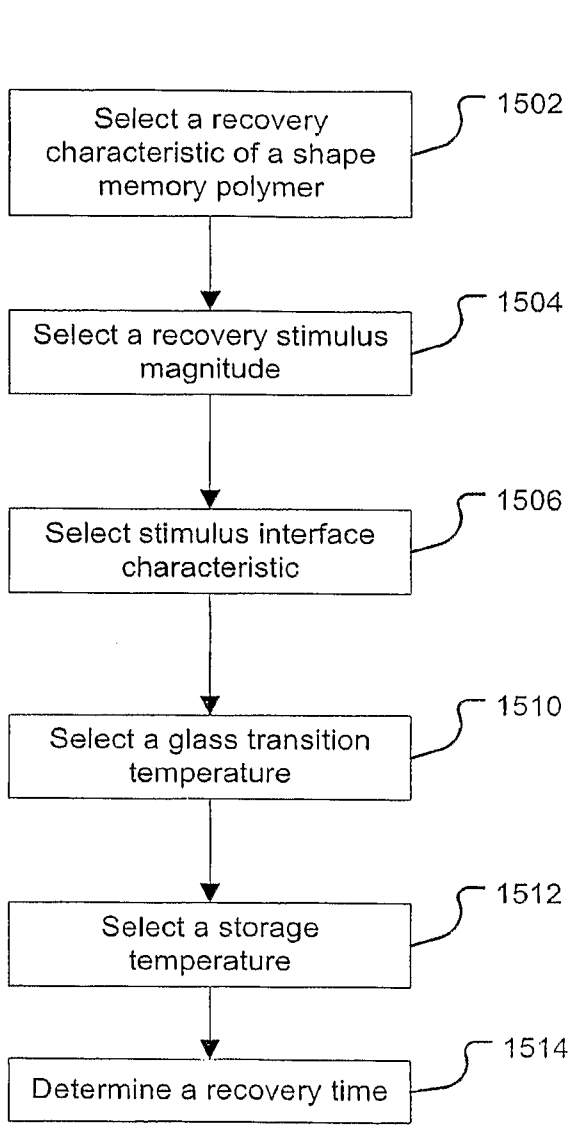
1500
Select a recovery characteristic of a shape memory polymer
1502
Select a recovery stimulus magnitude
1504
Select stimulus interface characteristic
1506
Select a glass transition temperature
1510
Select a storage temperature
1512
Determine a recovery time
1514

Fig. 15

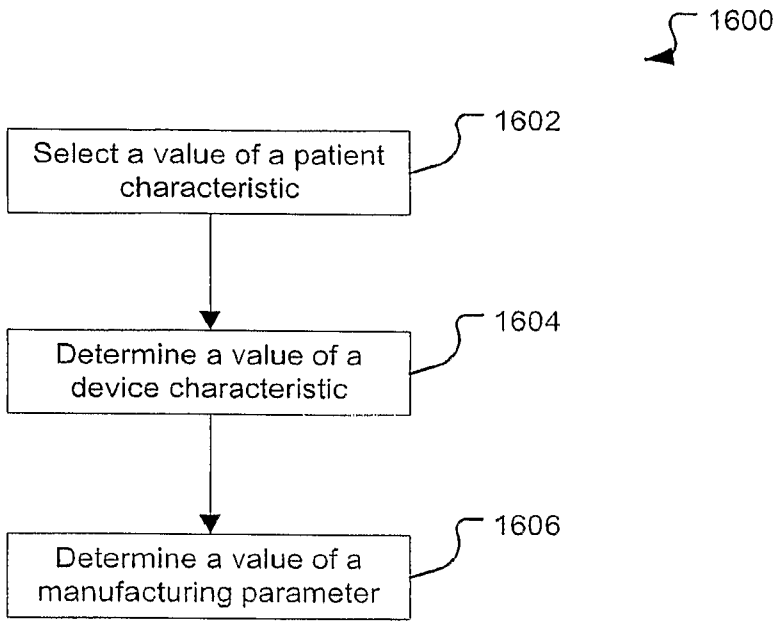
1600
Select a value of a patient characteristic
1602
Determine a value of a device characteristic
1604
Determine a value of a manufacturing parameter
1606

Fig. 16

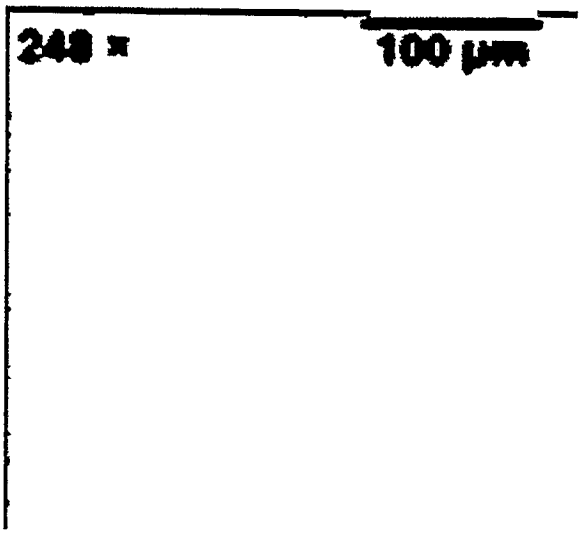

Fig. 17

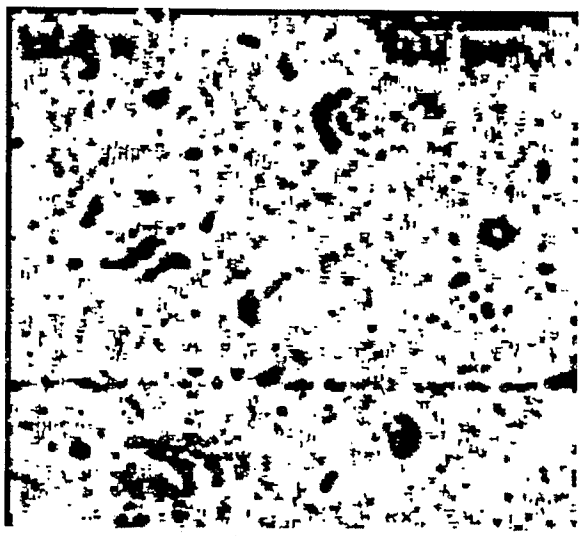

Fig. 18

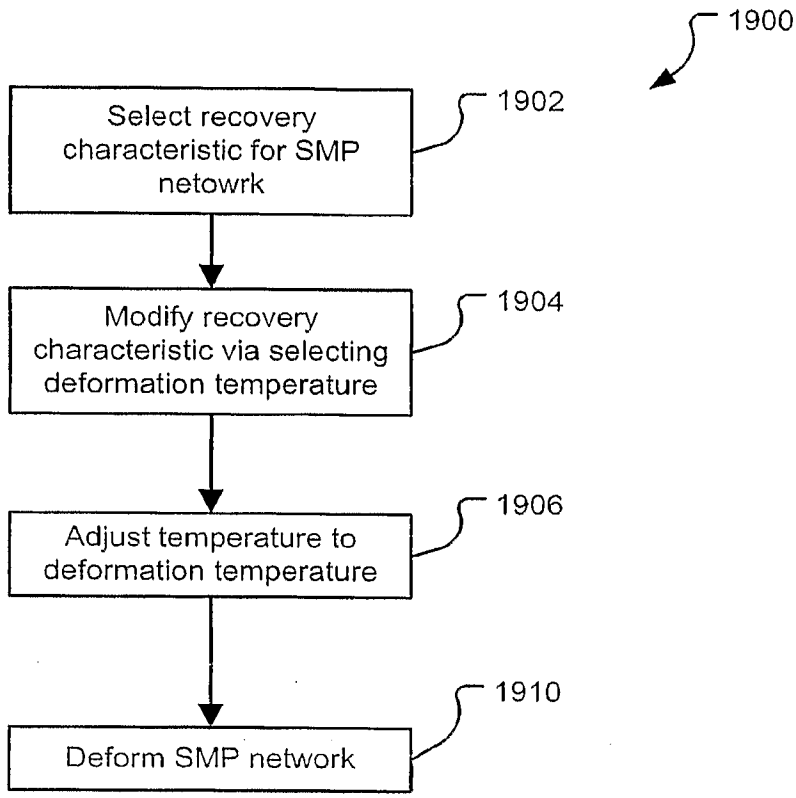
1900
Select recovery characteristic for SMP netowrk
1902
Modify recovery characteristic via selecting deformation temperature
1904
Adjust temperature to deformation temperature
1906
Deform SMP network
1910

Fig. 19

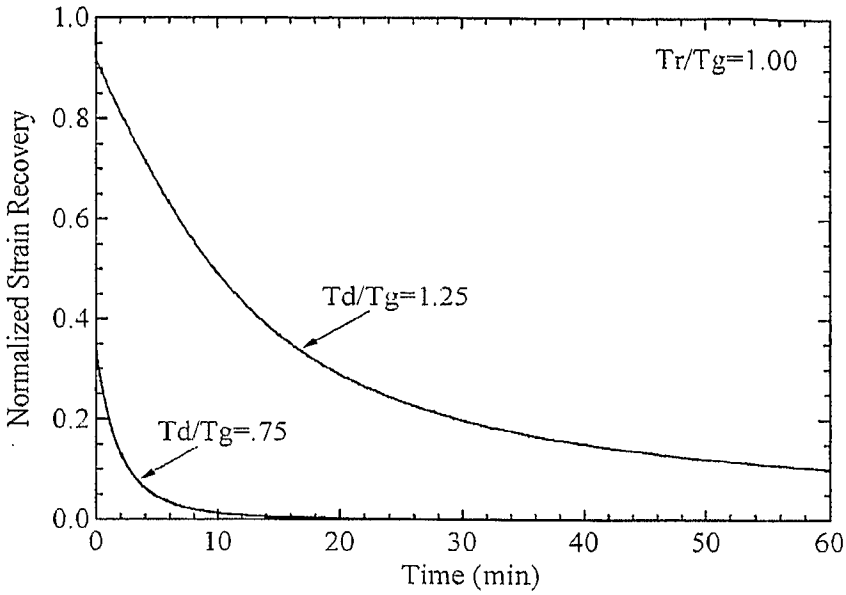

Fig. 20A

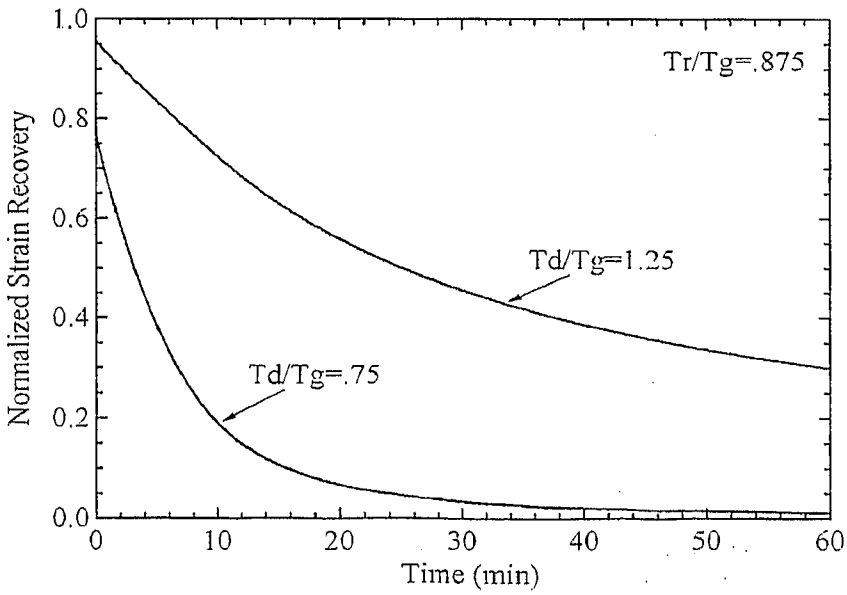

Fig. 20B

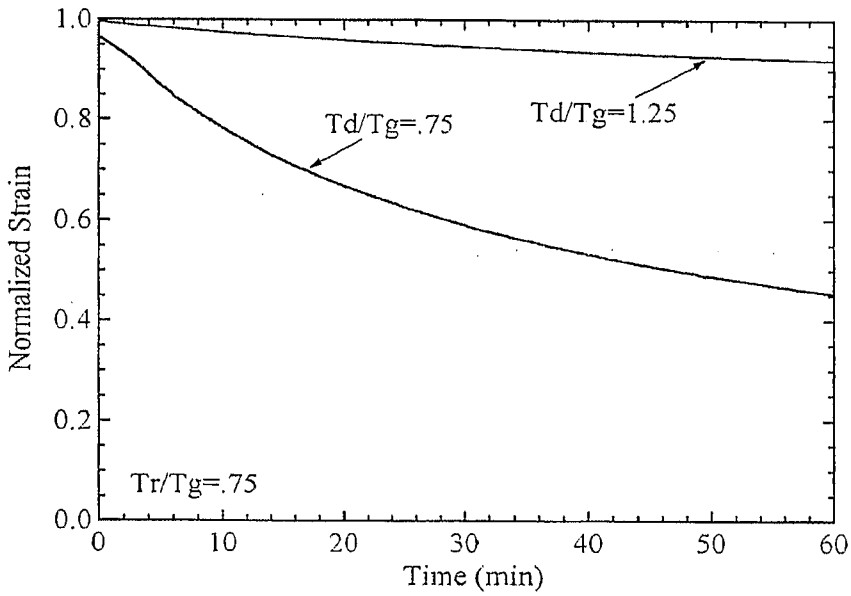
1.0
0.8
0.6
0.4
0.2
0.0
Normalized Strain
Td/Tg=.75
Td/Tg=1.25
Tr/Tg=.75
0
10
20
30
40
50
60
Time (min)

Fig. 20C

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 06/60297

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) -A61F 2/02 (2007.01)
USPC 623/11.11
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC 623/11.11 623/11.11, 900, 901, 911

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Google patents, Google scholar shape memory polymer, medical device
Medline shape memory polymer

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ------ Y	US 7,091,297 B2 (MATHER) 15 August 2006 (15.08.2006) (col. 2 In. 8)	9-11, 13, 16-17,28-29, 31-32 ---------- 12, 14-15, 21, 30, 33-34,49-52
X ------- Y	US 6,830,575B2 (STENZEL) 14 December 2004 (14.12.2004) (col. 2 In. 60)	56-61 ---------- 62-63
X	US 2005/0033295 A1 (WISNEWSKI) 10 February 2005 (10.02.2005) (para [0024])	64 - 70
X ----- Y	US 2006/0064170 A1 (SMITH) 23 March 2006 (23.03.2006) (para [0043]). (para [0050])	71-73 ---------- 1-8, 18-27,35-55, 86-90
X ------ Y	US 2004/0230309 A1 (DIMAURO) 18 November 2004 (18.11.2004) (para [0404]) (para [0289])	74-79 ---------- 25-26, 86-90
	SEE CONTINUATION	

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"E" earlier application or patent but published on or after the international filing date
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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 July 2007 (15.07.2007)	11 SEP 2007
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 06/60297

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --------- Y	US 6,160,084 A (LANGER) 12 December 2000 (12.12.2000) (col. 10 ln. 23) (col.6 ln.7)	80-85 ---------- 12,19-20,30,36-37
Y	US 6,720,402 B2 (LANGER) 13 April 2004 (13.05.2004) (col. 7 ln. 21)	1-8, 18-27,35-55
Y	US 6,388,043 B1 (LANGER) 14 May 2002 (14.05.2002) (col.16 ln. 23). (col.17 ln 48). (col. 16 ln.52)	6-7,14-15,33-34,40-41,53 -54,62-63
Y	J. Biomed Mater. Res.A. 2005 Jun 1;73(3):339-48 Gall et al.	25-26, 86-90