Medical Applications of Shape Memory Polymers

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Abstract

Developed in last decade, the shape memory polymers (SMP) have been gaining widespread attention for new product innovation. They are lightweight, have a high strain/shape recovery ability, easy to process and required properties can be tailored for variety of different applications.

Recently a number of medical applications have been considered and investigated for polyurethane-based shape memory polymers. Two major unique properties are of particular interest to the medical world. One is that these materials were found to be biocompatible, non-toxic and non-mutagenic in human body. Another attractive aspect is the glass transition temperature Tg of these materials which can be tailored for shape restoration/self-deployment of different clinical devices when inserted in the human body. Recently developed shape memory polymer foams together with cold hibernated elastic memory (CHEM) processing further widen their potential biomedical applications. The CHEM technology provides a simple end-to-end process for stowing and deployment, and avoids the complexities associated with other methods for deployment of medical devices

Shape memory polymers are described here and major advantages in some applications are identified over other medical materials such as shape memory alloys (SMA). A number of medical applications are anticipated for shape memory polymers. Some simple applications are already utilized in medical world, others are in examination process. Lately, several important applications are being considered for CHEM foams for self-deployable vascular and coronary devices. One of these potential applications, the endovascular treatment of aneurysm was experimentally investigated with encouraging results and is described in this paper as well.

1. Introduction

One of the advanced high-performance smart materials for which development and study of practical use have progressed are shape memory materials. The practical applications of shape memory alloys (SMA) have been underway for some time in the past. However, developed in last decade, shape memory polymers (SMP) have been gaining widespread attention just recently for new product innovation.
A number of bio-medical applications have been considered and investigated for polyurethane-based shape memory polymers. These materials were found to be biocompatible, non-toxic and non-mutagenic in human body. Another attractive feature is the glass transition temperature can be tailored for shape restoration/self-deployment of different clinical devices when contacted or inserted in the human body. Most recently developed shape memory polymer foams together with cold hibernated elastic memory (CHEM) processing further widen their potential biomedical applications. CHEM biocompatible materials have appealing properties for the design of some medical devices. They can be miniaturized and deformed to be inserted in the human body through small catheters and then they can recover a larger predetermined shape once placed in satisfactory position.
In this review paper, shape memory polymers and their potential and investigated medical applications are described. Their major advantages in some applications are identified over other medical materials such as shape memory alloys (SMA). Also several important medical applications that are being considered and investigated for CHEM foams, are revealed in this paper as well.

2. Shape Memory Polymers (SMP)

The polyurethane-based shape memory polymers (SMP) materials have been under development by Mitsubishi Heavy Industries, Nagoya R & D Center, Japan in the last 15 years. They offer unique properties for a variety of applications. These materials are polyurethane-based thermoplastic polymers with wide glass transition temperature Tg range. They are unique because of exhibiting large changes in elastic modulus E above and below the Tg. Variations of elastic modulus with temperature is shown in Figure 1.

The material's shape memory function allows repeated shape changes and shape retention. At temperature above the Tg the material enters a rubbery elastic state where it can be quite easily deformed into any shape. When the material is cooled below its Tg, the deformation is fixed and shape remains stable. At this stage, the material lacks its rubbery elasticity and is rigid. However, the original shape can be recovered simply by heating the material once again to a temperature higher than Tg. This phenomenon is explained on the basis of molecular structure and molecular movements [2, 3, 4, 5].

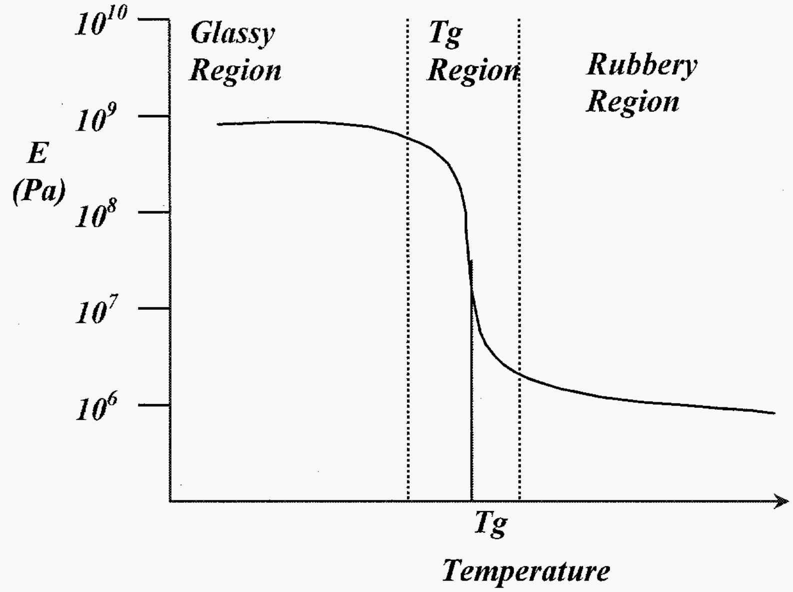

Figure 1 Variations of SMP's elastic modulus with temperature

The molecular chains can undergo micro-Brownian movement above the Tg (rubbery state) when the elastic modulus of the polymer material is low. In the rubbery state, the material can be easily deformed by application of external force, and the molecular chains can be oriented in the direction of the tension. When the temperature is lowered below the Tg and the deformation remains constant, the micro-Brownian motion will be frozen and the chain orientation and deformation will be fixed. When the material is heated above the Tg, the micro-Brownian movement starts again, the molecular chains lose their orientation and the material will recover its original shape. In this case, the shape-recovery function of the material requires crosslinking or partial crystallization. Despite the crosslinked structure, the polymer has the ability to melt and can be processed like conventional polyurethanes through injection molding or extrusion. Mechanical and chemical properties as well as durability are the same as in conventional polyurethanes. Figure 2 shows three major ingredients: diisocyanate (OCN-R-NCO), polyol (HO-R^{I}-OH) and chain extender (HO-R^{II}-OH) in the basic process of polyurethane formation. In order for the polyurethane to have an shape memory function, the required molar ratio should be as followed:

$$\text{mole of NCO group / total mole of OH group} \leq 1$$

The unique properties and major advantages of SMP materials over their "older cousins", shape memory alloys (SMA) are summarized below.

• SMP are lightweight. The density of these materials is about 1.13 through 1.25 g/cm^3 vs 6.4-6.5 g/cm^3 for NiTi.

• Wide range of the glass transition temperature Tg from -70^0C to $+70^0C$ allowing a wide variety of potential applications in different thermal environments.

• Shape recovery up to 400% of plastic strain vs 7-8% for SMA

• Large reversible changes of elastic modulus between the glassy and rubbery states of the polymers can be as high as 500 times.

• Excellent biocompatibility allowing a wide variety of potential biomedical applications

• Reversible changes from the moisture-permeable to waterproof barrier characteristics during transition from rubbery to glass state.

• Energy damping. At temperatures near the Tg, tan δ become large and is about 1. Tan δ, defined as the ratio of loss modulus G^{II} to storage modulus G^{I} is used to infer the amount of energy dissipated as heat during deformation.

• Easy processing. They are applicable to molding, extrusion and conventional or CNC machining.

• They are low cost materials; ~ 10% of existing shape memory alloys SMA.

• SMP materials are characterized by low recovery forces, i.e. low actuating forces and cannot be utilized in high power actuators.

The unique characteristics and properties of SMP make these materials very attractive to many commercial applications. Some of these applications are already utilized others are in examination process. Also, a number of biomedical applications are being considered and investigated for polyurethane-based SMP materials and are described in following section.

3. Medical Applications of SMP

A number of bio-medical applications have been considered and investigated for polyurethane-based shape memory polymers. Two of their properties are of particular interest to the medical world. One is that these materials were found to have excellent biocompatibility. Several independent standard cytoxicity and mutagenicity test have been conducted on SMP materials with excellent results 18. Another attractive feature is the glass transition temperature can be tailored for shape restoration/self-deployment of different clinical devices when contacted or inserted in the human body.
Hayashi et al. was investigating SMP for several different medical applications ( ). As a result of these investigations, SMP materials will soon be used to manufacture several types of catheters presently under development. These catheters will remain stiff externally for accurate manipulation by the physician, but they will become softer and

more comfortable inside the human body. The same group of investigators considered the manufacturing orthopedic braces and splints from SMP materials that can be custom fit to an individual's requirements. By heating the shape memory component above its Tg and deforming, a desired custom made fit can be obtain and than sustained after cooling. In one of the first applications, a polyurethane-based SMP was utilized for a specially designed spoon handle, designated for the physically handicapped. In this application, the spoon handle can be heated and deformed to individual shapes of hands and then its deformation is firmed at a room temperature to provide a comfortable and custom fit.

Using SMP materials in orthopedic and dental surgeries are under examination. Utilizing SMP and their properties such as moisture permeability and energy dissipation and storage for bandages and artificial skins are considered. The SMP loss tangent, tan δ in the transition region is very similar to than of human skin, providing a natural smooth feel in contact with or implanted in the human body.

Recently, Wache at al. has conducted a feasibility study and preliminary development on a polymer vascular stent with shape memory as a drug delivery system ( ). Samples from thermoplastic polyurethane-based SMP were manufactured by injection molding and the field of applications of a polymer stent was demonstrated in pre-trials. Presently, almost all commercially available stents are made of metallic materials. There are several designs of these minimally invasive implanted vascular stents for coronary applications among which are tubular mesh, slotted tubes and coils. A common after effect of stent implantation is restenosis. The use of the shape memory polymer stent as a drug delivery system leads to significant reduction of restonosis and thrombosis. An improved biological tolerance in general is expected when utilizing biocompatible SMP materials.

In another application, the shape memory polymer suture was investigated for wound closure ( ). A design of smart surgical suture was considered whose temporary shape is obtained by elongating the fiber with controlled stress. This suture is applied loosely in its temporary elongated shape. When the temperature is raised above Tg, the suture shrinks and tightens the knot, applying the optimum force.

SMP materials could be used in a variety of different medical devices and diagnostic products as deployable elements of implants from vascular grafts to components of cardiac pacemakers and artificial hearts. Present memory metals such as Ni-Ti are being used as components of different devices and provide a mean of inserting a thin, wirelike device, contained in a needle like casing, through a small incision. This device can regain a more complex shape once case is removed.

SMP materials with high shape recovery/packaging capability can be inserted through small incision or non-invasive way by catheters and subsequently regain their original shape/size by the body heat and then stay there to perform a desired function.

The SMP stent represents also an innovative alternative to the conventional stent due to less costly manufacturing compared to metal stents. The manufacturing of SMP stents by injection molding, extrusion or dip-coating technology from solution guarantees an economical production. Compared to the production of conventional metal stents, which are slotted by laser, the production costs are reduced by more than 50%.

4. CHEM Foam Structures

The concept called "cold hibernated elastic memory" or CHEM has been developed lately by Sokolowski et al. ( ) as a new, simple, ultra-light, self-deployable smart structure.
The CHEM technology utilizes polyurethane-based shape memory polymers (SMP) in open cellular (foam) structures or sandwich structures made of shape memory polymer foam cores and polymeric composite skins[1].
The CHEM foam technology takes advantage of the polymer's heat activated shape memory in addition to the foam's elastic recovery to deploy a compacted structure. The glass transition temperature T_g depending on the application is tailored to rigidize the structure in the fully deployed configuration[6,7]. The stages in utilization of a CHEM processing and foam structure (2) are illustrated in Figure 1 and are as follows.

1. Original Structure: The original structure is produced/assembled in a room held below T_g.

2. Compaction or Rolling: The structure is warmed above T_g to make it flexible and then compacted and/or rolled up for stowing.

3. Hibernation (storage): The compacted/rolled structure is cooled to ambient temperature to achieve the hibernated stowage. As long as the temperature is maintained below T_g, no external forces are needed to keep the structure compressed.

4. Deployment: The compacted/rolled structure is warmed above T_g in an unconstrained configuration. Memory forces and the foam's elastic recovery cause the structure to naturally deploy back to its original shape and size without external actuation.

If needed:

5. Rigidization: The deployed structure is cooled by ambient temperature to rigidize it, whereupon it is put into service.

The advantage of this technology is that structures when compressed and stored below Tg, are a small fraction of their original size and are lightweight (two orders of magnitude lighter than Al). Stowed and deployed CHEM structures are shown in Figure 2.
The foam configuration ensures higher speed of deployment, better precision of original shape restoration and higher full/stowed volume ratio when compared with solid SMP materials. Similar like in solid SMP, the wide range of T_g that can be selected for deployment and, if necessary, rigidization. The T_g of shape-memory polymers ranges from – 75°C to + 100°C, including a Tg slightly below the human body temperature of ~ 37°C . Thus allowing a wide variety of potential biomedical applications. Currently, the

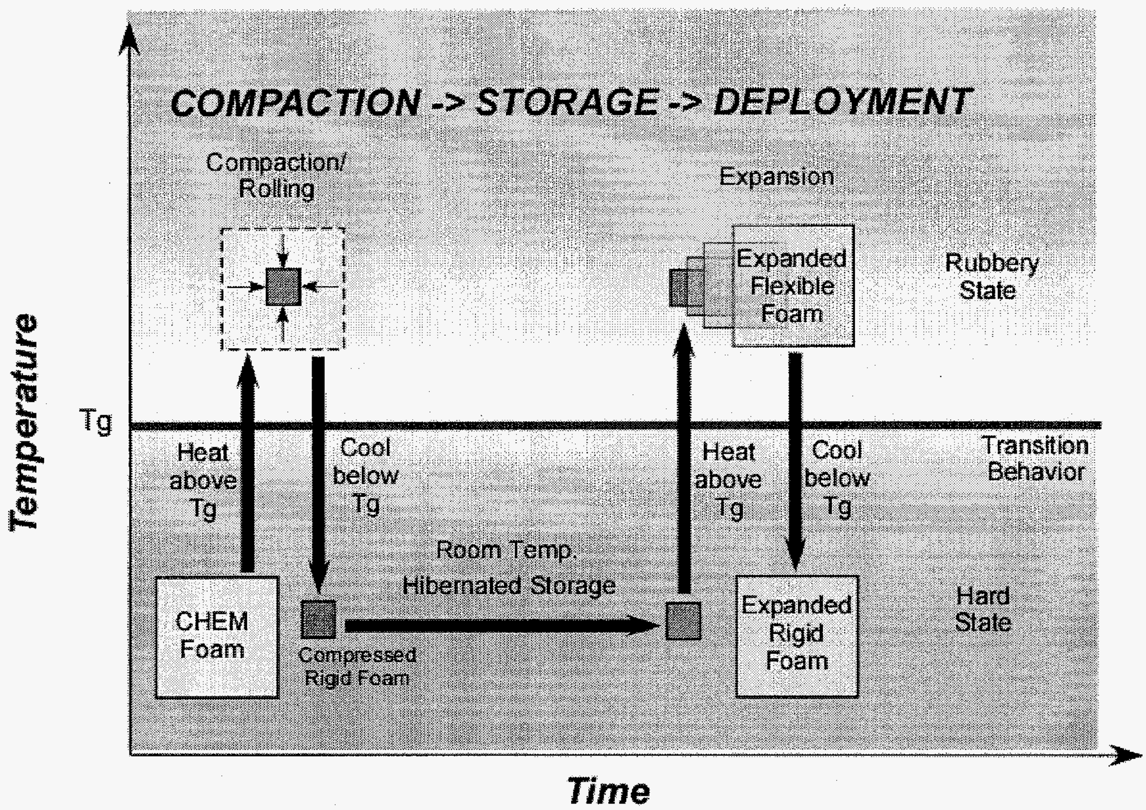

Figure 1: Cold hibernated elastic memory (CHEM) processing cycle

CHEM foam concept is well formulated and accumulated data indicate that the CHEM foams can perform robustly in the Earth and space environments as well as in human body. Some of biomedical applications that are being considered and investigated for CHEM materials are revealed in following section.

5. CHEM Medical Applications

Polyurethane-based CHEM foam materials have very unique and appealing properties for the design and manufacturing of self-deployable medical devices. Similar like solid SMP, they have an excellent biocompatibility and the glass transition temperature Tg can be tailored for shape restoration/self-deployment when inserted in the human body.

Combination of these properties plus natural CHEM foam porosity, lightweight, high full/stowed volume ratio and precision of original shape restoration suggest that it has potential to be utilized in deployable and functional elements of different clinical devices.

They can be miniaturized, deformed and inserted in the body through small catheters. Then, under the body heat, they can precisely deploy/recover a much larger predetermined required shape in satisfactory position. The CHEM part will self-expand when inserted in the body as it reaches a temperature of 37^0C. Also, a CHEM foam porosity can be adjusted to the needs of the application. In addition, the CHEM technology provides a simple end-to-end process for stowing and deployment, and avoids the complexities associated with other methods for deployment of medical devices

Consequently, a lot of potential CHEM medical applications are foreseen for vascular and coronary grafts, orthopedic braces and splints, medical prosthetics and implants, just to name a few.

Presently, several important CHEM applications are being considered for self-deployable vascular and coronary devices. One of these potential applications is the removal of a blood clot (thrombus) from the arterial network. Feasibility studies and preliminary in vitro demonstrations on SMP conducted by M. Metzger at al. were optimistic ( ) The formation or lodging of thrombus in the arterial network supplying the brain, typically causes the ischemic strokes. The stroke is the third leading cause of death and the principal cause of long-term disability in North America.

The strokes can by caused also by the intracranial aneurysm. However, present endovascular interventions on aneurysms have important drawbacks such as a significant incidence of residual lesion, deficient healing at the neck, recanalization or recurrences. Therefore, the search for new and more effective methods has been continued. The CHEM foam materials have appealing characteristics for the design of endvascular devices. Their unique properties suggest that they have a large potential to be used as an embolic agent and filling material to occlude aneurysms.

The CHEM foams were experimentally investigated for endovascular treatment of aneurysm at Ecole Polytechnique [18], Montreal with encouraging results. Lateral wall venous pouch aneurysms were constructed on both caroid arteries of 8 dogs. The aneurysms were occluded per-opertively with CHEM blocks. Internal maxillary arteries were occluded via a 6F transcatheter technique using compressed CHEM blocks. Angiography and pathology were used to study the evolution of the occlusion and neointimal formation at the neck of experimental aneurysms after 3 and 12 weeks [9]. The CHEM extract demonstrated no evidence of cell lysis or cytoxicity and no mutagenicity. The efficient vascular embolization was confirmed in the aneurysms and good neointimal formation over the neck of treated aneurysms was demonstrated at the CHEM interface. Maxillary arteries embolized with CHEM foam remained occluded during this experiment. The major conclusion of the investigation was that the foamy nature of this new embolic agent favors the ingrowth of cells involved in neointima formation and new embolic devices for endovascular interventions could be designed using CHEM's unique physical properties.

6. Summary

The unique attributes of shape memory effect, biocompatibility and other properties of shape memory polymers (SMP) materials make them a worthy technology for numerous potential self-deployable medical products. Presently, some SMP applications are already utilized in medical world, others are in examination process.

Recently developed shape memory polymer foams together with cold hibernated elastic memory (CHEM) processing further widen their potential biomedical applications. The CHEM foams can be miniaturized, deformed and inserted in the body through small catheters. Then, under the body heat, they can precisely self-deploy/recover a much larger predetermined required shape in satisfactory position. Currently, several important CHEM applications are being considered for self-deployable vascular and coronary devices. One of these applications, endovascular treatment of aneurysms was experimentally investigated with encouraging results. The major conclusion of this investigation was that new embolic devices for endovascular interventions could be designed and built using CHEM's unique physical properties.

The authors believe that SMP materials and CHEM foams will significantly and positively impact the medical device industry. They have unique characteristics that enable the manufacture of devices not possible with current materials, including shape memory alloys (SMA). Their application could enable a revolution in low-cost deployable medical devices which can be used in ways never before conceived. The SMP/CHEM stents represent an innovative alternative to the conventional stents due to less costly manufacturing compared to metal stents The authors feel the SMP/CHEM technology will gain widespread attention for new medical product innovation in near future. It will open a door to design and build novel, exciting and often, life-saving, medical products and devices.

Acknowledgement

The investigation described in this paper was carried out by the Jet Propulsion Laboratory, California Institute of Technology, under contract with the National Aeronautics and Space Administration.

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