TREATMENT OF MITRAL VALVE INSUFFICIENCY BY SHAPE MEMORY POLYMER BASED ACTIVE ANNULOPLASTY

Pilar Lafont Morgado, Andrés Díaz Lantada, Héctor Lorenzo-Yustos, Julio Muñoz-García
División de Ingeniería de Máquinas – E.T.S.I. Industriales – Universidad Politécnica de Madrid
C/ José Gutiérrez Abascal, nº 2. 28006 – Madrid, Spain

Ignacio Rada Martínez, Antonio Jiménez Ramos, José Luis Hernández Riesco
Hospital Gómez Ulla
Glorieta del Ejército s.n. 28047 – Madrid, Spain

Keywords: Shape Memory Polymers (SMP), Mitral valve Insufficiency, Annuloplasty ring, Laser Stereolithography, Silicone mould vacuum casting, Biomaterials.

Abstract: Active materials are capable of responding in a controlled way to different external physical or chemical stimuli by changing some of their properties. These materials can be used to design and develop sensors, actuators and multifunctional systems with a large number of applications for developing medical devices. (for both surgery and implants).

Shape memory polymers are active materials with thermo-mechanical coupling (changes in temperature induce shape changes) and a capacity to recover from high levels of distortion, (much greater than that shown by shape memory alloys), which combined with a lower density and cost has favoured the appearance of numerous applications. In many cases, these materials are of medical grade, which increases the chances of obtaining biocompatible devices.

This paper presents the design, manufacture, "shape memory" programming process and in vitro trials of an active annuloplasty ring for the treatment of mitral valve insufficiency, developed by using shape memory polymers. This has been done with the collaboration betweeen researchers from Universidad Politécnica de Madrid and doctors from the Hospital General Central de la Defensa.

1 MITRAL INSUFFICIENCY AND POSSIBLE IMPROVEMENTS IN ANNULOPLASTY TREATMENT

1.1 Mitral Valve Insufficiency

The mitral valve is made up of two components whose mission is to channel the blood from the left auricle to the left ventricle. Firstly, there is the so-called "mitral valve complex" comprising the mitral annulus, the valve leaflets, and the commissures joining both valves. Apart from the mitral valve complex itself, this valve has the so-called "tensor complex", which in turn comprises the chordae tendineae which continue with the papillary muscles attached to the left ventricle.

A failure of any of these elements leads to functional changes in the mitral apparatus, such as mitral insufficiency, explained below, and hemodynamic repercussions.

Mitral insufficiency (or regurgitation) is defined as the systolic regurgitation of blood from the left ventricle to the left auricle, due to incompetence in mitral valve closing. This can arise for three main reasons: a) primary disease of the mitral valve; b) an anatomic or functional alteration in the chordae tendineae or in the papillary muscles, and c) a disorder in the correct function of the left auricle and the left ventricle (Díaz Rubio, 1994).

Valve reconstruction is currently the preferred treatment for mitral insufficiency provided this is possible. With the aid of preoperative transesophagic echocardiography lesions can be located and their extent seen, so a surgeon can evaluate if valve repair is possible and thus design an exact plan for any

Lafont Morgado P., Díaz Lantada A., Lorenzo-Yustos H., Muñoz-García J., Rada Martínez I., Jiménez Ramos A. and Luis Hernández Riesco J. (2008).
TREATMENT OF MITRAL VALVE INSUFFICIENCY BY SHAPE MEMORY POLYMER BASED ACTIVE ANNULOPLASTY.
In *Proceedings of the First International Conference on Biomedical Electronics and Devices*, pages 17-22
DOI: 10.5220/0001046400170022

operation required. Nowadays, the object of this surgery is not simply limited to eliminating mitral insufficiency but in many cases to reconstructing the geometry of the entire mitral valve apparatus to ensure a durable repair.

Surgically restoring the geometry to normal conditions consists in: a) augmenting or reducing the abnormal leaflets; b) replacing broken or short chordae tendineae using "Goretex" type sutures, and c) annuloplasty.

1.2 Treating Mitral Insufficiency with Annuloplasty

Carpentier's description of a rigid prosthetic ring to allow a selective reduction of the entire mitral annulus opened the way to modern mitral repair. Annuloplasty consists in inserting the said ring-shaped device into the coronary sinus and after applying traction, retraction or heat, it reduces its perimeter, thereby reducing the mitral annulus and improving the contact between the valve leaflets, which leads to a reduction in the patient's degree of mitral insufficiency (Hernández, 2005).

Since then, a series of implants have been developed that can be basically classified as rigid or flexible and total or partial. Rigid monoplane implants have been displaced due to the large number of experimental and clinical works showing that the perimeter of the mitral annulus constantly changes in size and shape during the heart cycle. The recent findings showing that these changes are produced in a three-dimensional way with a hyperbolic paraboloid shaped ring has given rise to new rigid three-dimensional prosthesis. Duran proposes replacing the most conventional devices for other flexible or semi-rigid designs that reproduce the three-dimensional shape, such as the one marketed by Medtronic Inc..

1.3 Desirable Improvements Employing Progressive Procedures

However, inserting a device to close the mitral valve means making additional demands on the heart that may lead to postoperatory problems. It would be ideal to insert a ring with the same shape as the patient's mitral annulus and, when they have recovered from the operation, progressively act on this ring (in several stages) and remotely. This seeks to maintain a balanced situation and not excessively overload the patient's heart during the operation.

In this way, the progressive closing of the patient's mitral annulus can be controlled and, by using non-invasive inspection technologies, the improvement in the patient's mitral insufficiency can be evaluated after each stage of the ring actuation.

2 SOLVING MECHANICAL OPERATION USING SHAPE MEMORY POLYMER BASED DEVICES

2.1 Shape Memory Polymers in Medical Devices

Shape memory polymers (SMPs) are materials that give a mechanical response to temperature changes. When these materials are heated above their "activation" temperature, there is a radical change from rigid polymer to an elastic state that will allow deformations of up to 300%. If the material is cooled after manipulation it retains the imposed shape; it "freezes", the said structure returning to a rigid but "non-equilibrium" state. When the material is heated above its activation temperature, it recovers its initial undeformed state.

The cycle can be repeated numerous times without degrading the polymer and most suppliers can formulate different materials with activation temperatures ranging between –30 ºC and 260 ºC, depending on the application required.

They are therefore active materials that present thermomechanical coupling and a capacity to recover from high levels of distortion, (much greater than shown by shape memory alloys), which combined with a lower density and cost has favoured the appearance of numerous applications. Their properties allow applications for manufacturing sensors and actuators, especially for the aeronautic, automobile and medical industry (Lendlein, Kelch, 2002).

The main problem associated with the use of shape memory polymers is the lack of structured processes for developing devices based on these materials. The design process for these devices and the transformation processes for these materials need to be more thoroughly investigated.

The main advantages of shape memory polymers are:

- They are new materials with the ability to change their geometry from an initial deformed shape to a second shape predetermined during the manufacturing process.

- They are more economical than shape memory alloys.
- Different additives can be used to change their properties "a la carte", to better adapt them to the end application.
- The levels of deformation are much greater than those obtainable using shape memory alloys.
- They can also be more easily processed and allow the use of "Rapid Prototyping Technologies", which speeds up the production of devices.
- More complex geometries and actuators can be obtained than with developments based on shape memory alloy.

However, due to their recent appearance, in many cases their mechanical and thermomechanical properties are still not completely typified, which gives rise to doubts concerning how devices based on these materials will react. One of the basic aims of current research is to increase knowledge of the properties of these polymers by improving characterization processes.

Regarding the development of medical devices, both surgical and implantable ones, they have additional advantages to those mentioned above:

- They are frequently medical grade materials which increases the chances of obtaining biocompatible devices.
- The combined use of preoperative inspection technologies and CAD-CAE-CAM technologies means that prostheses and customised devices can be tailored for patients.
- Their activation temperature and properties can be adapted to the application, thanks to the amount of copolymers employed and the use of additives.

Among the medical devices developed that take benefit from the advantages of these polymers, the most notable are self-expanding stents, drug release devices, thrombectomy devices, intelligent sutures and active catheters (Lendlein, 2002, 2005, Wilson, 2006).

2.2 Shape Memory Polymers for Active Annuloplasty

Commercial annuloplasty rings based on shape memory polymers have been patented but not yet developed.

The Sorin Group's Memo 3D manages to reduce its shape by using a shape memory alloy (Nitinol type, similar to those used in the manufacture of self-expanding stents). However, the change of shape is produced during the operation itself on making contact with human body temperature, which means that no postoperative measures are possible.

Besides, the capacity of shape memory polymers to recover their shape against efforts of up to around 7 MPa means that a 3 mm thick annuloplasty ring, similar to devices currently in use, manufactured with these materials will be able to overcome a circumferential force of between 4 N to 12 N that is imposed by the patient's mitral annulus.

In accordance with the above, what is proposed is a ring made of shape memory polymer and electrical resistances or heaters distributed inside to activate the "shape memory effect" and therefore the required shape change.

Firstly, the ring adapts to the end size required (that needed to eliminate the mitral insufficiency) and with the resistances already in place. The ring is then uniformly heated to a temperature higher than the transition temperature (situated for the end product between 41 ºC and 43 ºC) and is forced to take on the expanded transitory shape (to do this cone-shaped tools can be used with a cross section similar to that of the mitral annulus), letting it cool down to room temperature. The device also consists of a battery to power the resistances and heat them. The rise in temperature of the resistances causes a local rise in temperature, which, if suitably controlled leads to a change in phase of the SMP and the associated size reduction.

Using an associated electronic control enables the resistances to be operated in pairs and at different times, in order to carryout the progressive or "step by step" operation required on the ring. Figure 1 shows a preliminary design.

Figure 1: Preliminary active annuloplasty ring design. SMP with internal resistances for heating.

A patent for this device was applied for by the authors under the title of "Active annuloplasty system for the progressive treatment of valve insufficiencies and other cardiovascular pathologies"

on 13 December 2006 with Application Number P200603149 and is currently being evaluated by the Spanish Patents and Trade Marks Office.

The following sections present the design alternatives and the prototypes obtained, as well as the first "in vitro" trials performed, the results, and future recommendations for optimising the results. The development has been carried out in collaboration between researchers from from Universidad Politécnica de Madrid and doctors from the Hospital General Central de la Defensa.

3 DESIGN AND MANUFACTURE OF PROTOTYPES

Computer aided design and calculation technologies, (CAD – Computer Aided Design and CAE – Computer Aided Engineering), have become an essential tool for developing medical devices. They enable alternative shapes and designs to be obtained quickly, as well as making it easier to evaluate their advantages by being able to analyse stress, deformations, ergonomics or dynamic response. They are also highly valuable for comparing and selecting the different materials that can be used. In addition, when combined with preoperative inspection techniques, they serve to design implantable devices tailored for the patient measurements and simulate their implantation.

Figure 2 shows alternative designs for annuloplasty rings made by using the "Solid Edge v.18" computer design package. With the help of these programmes it is very simple to change the parameters of a design, which enables a shape to be adapted to the size of a particular patient's mitral annulus or change the thickness of rings depending on how long the device is required to last.

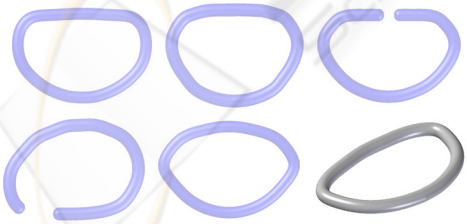

Figure 2: Alternative designs for annuloplasty rings produced with CAD technologies.

Bellow is explained how prototypes are manufactured from the designs shown and the advantages of using rapid prototyping and rapid tooling technologies.

Figure 3 shows the physical models obtained in epoxy resin by laser stereolithography using an SLA-350 machine available at the Product Development Laboratory of Universidad Politécnica de Madrid, from the designs shown in Figure 2. Together with the annuloplasty designs, also shown is a 3 mm thick, 30 mm outer diameter toroidal ring to give the image an idea of scale.

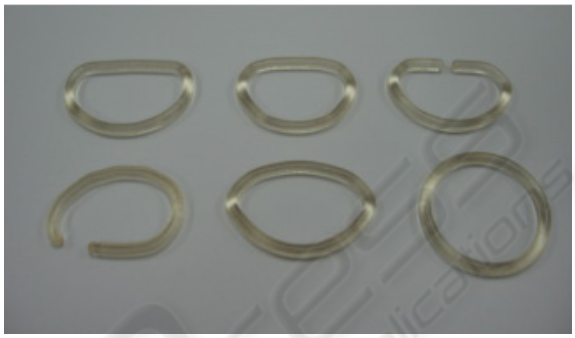

Figure 3: Models obtained by laser stereolithography from files containing the 3D part geometry.

The parts obtained by stereolithography are particularly suitable for checking sizes, shapes and appearance. They can also be used as models for obtaining silicone moulds, which are subsequently used to obtain polyurethane resin replicas, more resistant and suited to working trials, and which also possess shape memory properties. With the vacuum casting process different types of bicomponent resins can be used, with a wide range of properties, and the prototypes obtained reproduce the mould cavities with great precision (roughnesses of up to 50 μm) (Lafont, 2000).

The chosen material is a polyurethane resin from MCP Iberia company with reference 3174 which is supplied in bicomponent form, which means it can be cast (after mixing the two components) in silicone moulds to obtain the prototype shape required.

It must be pointed out that shape change temperature of the polyurethane resin used is not suited to the "in vivo" end trials, nor fits the initial specifications which required a range of 41 to 43 ºC to activate the shape memory effect.

However, this polyurethane resin has been used because it is easies to manipulate and cast in silicone moulds, which enables prototypes to be made in less than 5 days from computer file to end material.

Other mould manufacture technologies are currently being used for casting alternative shape memory polymers which do not attack the silicone moulds and whose transition temperature can be set from 4 to 6 ºC above that of the human body, suited to the "in vivo".

Figure 4 shows silicone moulds obtained from the physical epoxy resin models displayed in Figure 3. These moulds enable prototypes to be obtained from the material with shape memory properties.

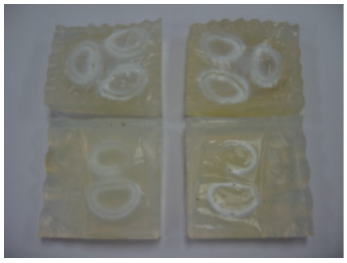

Figure 4: Silicone moulds obtained from laser stereolithographic models.

Enhanced design models have led to the construction of new silicone moulds and the obtaining of improved prototype annuloplasty rings, both solid ones and with circumferential grooves for housing the heating resistances. These are shown in Figure 5.

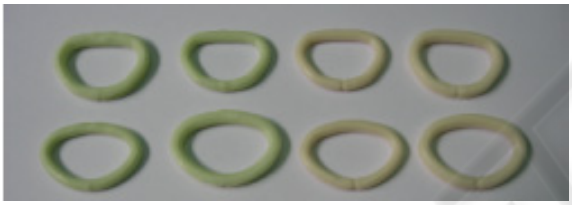

Figure 5: Different polyurethane resin prototypes obtained under vacuum casting in silicone moulds. Both open and closed rings were made to analyse alternative performances.

4 PROGRAMMING PROCESS OF THE SHAPE MEMORY

When the annuloplasty rings have been shaped to ensure the mitral valve closes properly, they need to undergo heat deformation at 80 ºC in the case of polyurethane resin, (higher temperature than that needed to activate the shape memory effect), to increase their cross section until it coincides with the patient's mitral valve annulus in the initial state of insufficiency.

By doing this, a temporary shape is obtained and the ring can be implanted without submitting the patient's heart to an additional overload due to a sudden reduction in the section of the mitral valve.

After the surgical operation the recovery effect of the original shape is activated, which produces a gradual, controllable closure of the valve and a controlled recovery of mitral regurgitation.

To perform this "shape memory programming process", tools were used that were obtained by laser stereolithography in the form of a cone base with a similar cross section to that of the patient´s mitral annulus.

Figures 6 shows the tool and deformations caused to ring prototypes thanks to the use of a counter-shape that acts as a press on the tool and the prototype.

Figure 6: Design and prototype of a tool for programming shape memory effect. Deformation caused at 80 ºC to obtain a temporary shape.

Figure 7 shows an annuloplasty ring with the temporary shape already applied and prepared for implant and the first "in vitro" trials. With the aid of a cone base a 15% increase in cross section was produced (maximum inner diameter ring size pass from 26 to 28 mm), which will be used to evaluate the subsequent shape memory recovery in "in vitro" trials.

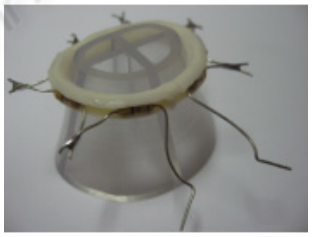

Figure 7: Active ring with heating resistances with the temporary shape already applied. It is ready to be implanted and subsequently activated.

5 RESULTS OF "IN VITRO" TRIALS

For performing the first "in vitro trials" two pig hearts were used because of their similarity to human ones, as is demonstrated by their being used for biological valve replacement operations.

Figure 8 shows the process for activating the shape memory process in the ring and reducing the associated mitral ring cross section.

The 4,7 Ω resistances (a total of 7 resistances with serial connection) were supplied with power by a 12 V transformer. Thus an intensity of 364 mA was obtained, similar to what can be supplied by

implantable commercial devices. The images (left to right) show a 10.7% reduction in cross section during an operating period of 150 seconds. This means a 71%, recovery compared to effort since the increase in cross section induced was 15%.

By interrupting heating the temperature decreases and the recovery process is halted, which means the required effect can be obtained step by step. By recommencing the heating process the recovery will continue, although in these first "in vitro" trials heating was done continuously in order to evaluate the maximum recovery that could be obtained and the duration of the entire process. Temperature was continuoustly measured using a thermocouple.

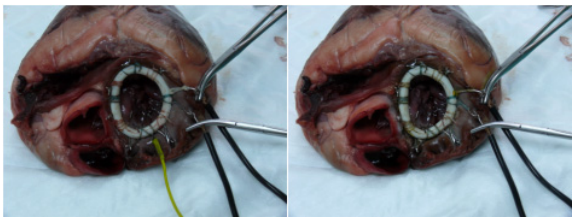

Figure 8: Activating the shape memory effect using heating resistances.

Despite it being desirable a cross section reduction of 15% to 20%, it is very important to point out the material's capacity for recovery while overcoming the forces imposed by the mitral annulus of the hearts used.

6 FUTURE IMPROVEMENTS AND CONCLUSIONS

For the postoperative and progressive treatment of mitral insufficiency the use of an annuloplasty device made of shape memory polymer has been proposed. It has electrical resistances distributed inside it to activate the "shape memory" effect, so that the required change in shape to reduce mitral regurgitation can be progressively induced. This provides an alternative to current devices, that do not permit any change of shape after implantation, and therefore any errors committed during the operation cannot be corrected.

The design, manufacturing, "shape memory" effect programming and "in vitro" trials of such an annuloplasty ring for treating mitral insufficiency, developed by using shape memory polymers, have been presented.

This has been done in collaboration between researchers from from Universidad Politécnica de Madrid and doctors from the Hospital General Central de la Defensa.

Using computer aided manufacture and design technologies has enabled different designs and prototypes to be produced in parallel, as well as rapid improvements to obtain the devices that were used in the in vitro trials.

Future actions regarding improvements in the shape memory programming process should lead to optimising the reduction in mitral ring cross section up to the required 15% to 20%. Using alternative shape memory polymers with a lower activation temperature will also result in more suitable devices, since they will require a smaller size heating system and will be easier to manufacture.

However, it is very important to point out the material's capacity for recovery against the forces imposed by the mitral annulus of the hearts used, which shows the feasibility of developing an active annuloplasty system based on the use of shape memory polymers.

REFERENCES

Díaz Rubio, M., Espinós, D., 1994. Tratado de Medicina Interna. *Editorial Médica Panamericana*.

Carpentier, A., 1983. Cardiac Valve Surgery – The French Correction. *Journal of Thoracic and Cardiovascular Surgery*.

Duran, C., 1992. Duran Flexible Annuloplasty Repair of the Mitral and Tricuspid Valves: Indications, Patient Selection, and Surgical Techniques Using the Duran Flexible Annuloplasty Ring. *Medtronic Inc.*.

Hernández, J.M., 2005. Manual de Cardiología Intervencionista. *Sociedad Española de Cardiología. Sección de Hemodinámica y Cardiología Intervencionista.*

Lendlein, A., S. Kelch, 2002. Shape-Memory Polymers. *Angewandte Chemie International*.

Lendlein, A., Langer, R., 2002. Biodegradable, elastic shape-memory polymers for potential biomedical applications. *Science*.

Lendlein, et al., 2005. Light-induced shape-memory polymers. *Nature*.

Wilson,T., et al., 2006. Shape Memory Polymer Therapeutic Devices for Stroke. *Lawrence Livermore National Laboratory*.

Lafont, P., Lorenzo, H. et al., 2000. Rapid Tooling: moldes rápidos a partir de estereolitografía. *Revista de plásticos modernos*.