pg. 36



Shape Memory Alloys: Properties and **Biomedical Applications**

Diego Mantovani

Shape memory alloys provide new insights for the design of biomaterials in bioengineering for the design of artificial organs and advanced surgical instruments, since they have specific characteristics and unusual properties. This article will examine (a) the four properties of shape memory alloys, (b) medical applications with high potential for improving the present and future quality of life, and (c) concerns regarding the biocompatibility properties of nickel-titanium alloys. In particular, the long-term challenges of using shape memory alloys will be discussed, regarding corrosion and potential leakage of elements and ions that could be toxic to cells, tissues and organs.

INTRODUCTION

Shape memory alloys (SMA) possess certain original properties, particularly their ability to return to their memorized shape by a simple change of temperature. In 1938 Greninger and Mooradian¹ first observed the shape memory effect for copper-zinc alloys (Cu-Zn) and copper-tinalloys (Cu-Sn). Yet nearly 30 years elapsed until Buehler and his colleagues applied in 1965 for the first patent for a nickel-titanium alloy, called Nitinol,2,3 from the Naval Ordnance Laboratory.

Near the end of the 1960s, Raychem developed the first industrial SMA applications in aeronautics with the Cryofit connector for F-14 airplane hydraulic circuits.45 Meanwhile at the University of Iowa, Andreasen's interest in dental alloys led to the implantation of the first superelastic dental braces made from

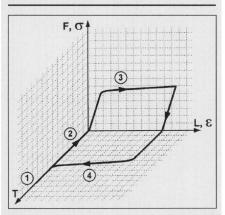


Figure 1. One-way shape memory effect after formation (1), and following a deformation (3) the specimen returns to its original shape by simple reheating.

nickel-titanium in 1975.6-8 Buehler suggested using SMA in dentistry for different implants that could retain the shape memory.5 Afterwards, industrial applications multiplied and entered the public domain for glasses frames, smoke detectors, bra underwires, and other

Since then the medical field tried to integrate SMA into new implantology design. Researchers focused on integrating advanced industrial materials (often developed for aeronautics, industrial, or military-specific applications) for use in human implantology. A critical concern was using SMA to improve physical and mechanical characteristics of implants while assuring that the devices improved the quality of life as unobtrusively as possible.

PROPERTIES AND PRINCIPLES

From a metallurgical perspective, the principal properties of SMA are explained by the solid state phase transition called martensitic thermoelastic transformation (from the austenitic phase to the martensitic phase and vice versa). These phase transformations result in different organizations of the material in the same state.15-18

The four temperatures that characterize this transition phase are (1) M_smartensite start, the temperature at which the martensite layer spontaneously appears; (2) $\rm M_{\rm f}$ —martensite finish, the temperature at which the entire specimen is transformed into martensite; (3) A_s —austenite start, the temperature at which the austenite layer spontaneously appears; and (4) A —austenite finish, the temperature at which the specimen is transformed into austenite.

When the SMA is placed in a singlephase situation (pure austenite or pure martensite) the effects are obvious. These effects require the presence of a specific phase, thus when the state is bi-phasal (austenite + martensite), the same effects occur but are of less significance.

Three parameters control the behavior of the material (see Table I): the stress, σ (where F is the force); the strain, ε (or the length L); and the temperature, T. The changes in these parameters were controlled by a class of thermomechanical cycles that allowed the SMA to show their specific characteristics.

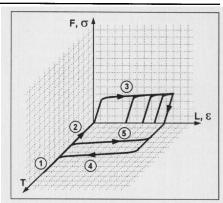


Figure 2. Two-way shape memory effect after formation (1), and following a learning by mechanical cyclage (3), the specimen passes alternately between the education shape and its original shape by simply changing the temperature (4, 5, 4, etc.).

These variations are represented by the following symbols:

- Parameter = k: indicates that the value of the parameter is constant.

 • Parameter ↑: indicates that the value
- of the parameter increases
- Parameter ↓: indicates that the value of the parameter decreases.

One-Way Shape Memory Effect

After deformation, the one-way shape memory effect allows a material to return to its original shape by simply increasing the temperature. This property allows the material to take a strain of up to eight percent, under an applied force of 800 MPa (equal to about 80 Kg per mm2), and under a maximum applied work of 5 J/Kg. The required thermodynamic cycle to obtain the one-way shape memory effect is as follows (Figure 1):

- The initial forming of a specimen in the austenitic state.
- The formation of martensite in the material without any visible macroscopic effect, (L = k), by a reduction of the temperature $(T\downarrow)$ and without the application of an external force (F = k = 0).
- Specimen strain (L↑) by the reorientation of different types of martensite present, an increase in the applied force on the material (F^{\uparrow}) at a constant temperature (T = k).
- Inverse cell strain occurred in the third step (L \uparrow), with a return of the initial shape (by a transformation of

JOM • October 2000

the martensite to the austenite), and an increase in temperature (T^{\uparrow}) without applying an external force on the material (F = k = 0).

Two-Way Shape Memory Effect

As in the one-way shape memory, the two-way shape memory effect allows the material to return to its original shape by simply increasing the temperature. In addition, it also permits the return of a second shape by cooling. This last effect must be memorized by the material through a learning process that consists of it storing the energy (for example, under internal shape constraints) that will be freed through cooling.

The required thermodynamic cycle to obtain the two-way shape memory effect is as follows (Figure 2):

- The initial forming of a specimen in the austenitic state.
- The formation of martensite in the material without any visible macroscopic effect, (L = k), by a reduction of the temperature (T↓) and without the application of an external force (F = k = 0).
- Education of the material by a mechanical process know as cycling (F[↑], then [↓], at least a dozen times) at a constant temperature (T = k), whereby the thermal process, or cycling, (T[↑], then [↓]) provides a constant force (F = k). The microstructural process in the two types of cycling is different, but the results are comparable because the role of the force and temperature are equivalent from a thermodynamic point of view. At this stage, the specimen has memorized its second shape (L[↑]) in the martensitic state.
- Specimen strain (L↓) for the second shape, acquired by step 3, toward the initial shape (by a phase transformation of the martensite to the austenite), with an increase in temperature (T↑) and with no external force on the material (F = k = 0).
- Inverse cell strain (L↑), from the initial shape to the second shape memorized in step 3 (by a phase transformation of the martensite to the austenite), with a decrease in the temperature (T↓), always without

applying an external force on the material (F = k = 0).

The repetition of the cycle (steps 4 and 5) allows the specimen to pass from the initial shape to the memorized shape repeatedly through the learning process by a simple modification of the temperature and without external force.

Superthermoelastic Effect

A material with elastic behavior is capable of recovering completely from a deformation. The superelasticity (or pseudoelasticity) allows the formation of a similar behavior but under a level of values more significant than those of the classic metals or alloys (the recoverable strain for a mono-crystalline sample of SMA can reach 10%). The term superthermoelasticity groups together three types of different behavior: the superelastic effect, the superthermic effect, and the rubber-like effect.

Superelastic Effect

The required thermomechanical cycle to obtain the superelastic effect (the temperature is constant throughout this process, T = k) can be described as follows (Figure 3):

- Initial forming of the specimen in austenitic state.
- Classic elastic deformation of the austenitic phase (L↑) by the application of a force (F↑).
- Large deformation of the specimen (L[↑]) by the formation of martensite in the interior of the austenitic phase of the material, with an increase in the applied force (F[↑]).
- Classic elastic deformation of the martensitic phase (L↑) by the accumulated force (F↑).
- Total recovery from all of the accumulated strain from steps 2, 3, and 4
 (L↓) through the release of the applied forces (F↓) (return to the original shape).

The superelastic behavior looks like that of elasticity but is more complex and of a different order of magnitude.

Superthermic Effect

The required thermomechanical cycle to obtain the superthermic effect (the applied force is constant and non-zero

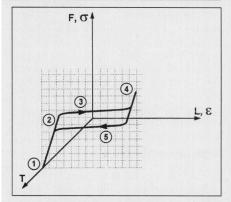


Figure 3. Superelastic effect after formation (1), and due to a phase change (3), the specimen can recover a larger total deformation than a classic alloy (4).

throughout this process, $F = k \neq 0$) can be described as follows (Figure 4):

- Initial forming of the specimen in austenitic state.
- Classic thermal contraction of the austenitic phase (L↓) produced by a reduction of the temperature (T↓).
- Large deformation of the specimen (L↓) by the formation of martensite in the interior of the austenitic phase of the material, with a continued reduction of the temperature (T↓).
- Classic thermal contraction of the martensitic phase (L↓) produced by the accumulated reduction of the temperature (T↓).
- Recovery from the accumulated strain of the preceding steps (L[↑]) with an increase in the temperature (T[↑]) (return to the original shape).

The superthermic behavior looks like that of thermal contraction but is more complex and of a different order of magnitude. From the thermodynamic perspective, this behavior is similar to the two-way shape memory effect, in which the external constraints $(F = k \neq 0)$ replace the internal constraints obtained through the learning process.

Rubber-like Effect

The required thermomechanical cycle to obtain the rubber-like effect (the temperature is constant throughout this process: T = k) can be described as follows (Figure 5):

- Initial forming of the specimen in martensitic state.
- Classic elastic deformation (L[↑]) by an applied force (F[↑]).
- Deformation of the specimen by the re-orientation of certain interior varieties of the martensite phase (L↑), with an increase in the applied force (F↑).
- Recovery from all of the accumulated strain from steps 2 and 3 (L↓) with the release of the applied force (F↓).

This behavior resembles elasticity but is more complex and of a different order of magnitude: it is the rubber-like effect

Parameters	Definition	Parameters Represented in the Text
Stress, (σ)	Ratio between the force, F,	Force, (F)
(Placed upon	and the surface, S,	
the material)	on which this force is applied:	
	$\sigma = F/S$	
Strain, (ϵ)	Observed relative	Length, (L)
	variation displacement, for	
	example a lengthening:	
	$\Delta L = L - L_0;$	
	$\varepsilon = \Delta L / L_0 = (L - L_0) / L_0$	
Temperature, (T)	Temperature that the material is placed under	Temperature, (T)

2000 October • JOM

(where superelasticity occurs by reorientation). The effect obtained is limited by the characteristics of the material (acceptable maximum value of the force). Therefore, the entire deformation is not recoverable. The accumulation of this unrecoverable damage during the fatigue mechanical cycle allows for the required learning for the two-way shape memory effect.

High-Damping Effect

The high-damping effect is the ability of a material to transform mechanical energy (provided by an applied force, for example) into thermal energy (in the form of heat dissipation). This irreversible energy transformation allows the material to resist shocks and absorb vibrations. The internal friction in the form of heat disperses the energy between the different phases or varieties of the same phase:

- For the dual phase domain (austenite + martensite), the internal friction determines the movement of the interfaces between austenite and martensite allowing the dispersal of a large amount of energy, resulting in an increased high-damping effect.
- For the martensite phase, the friction determines the reversible movement of the interfaces between varieties of martensite, allowing for a good dispersal of energy, but it is less significant than in the dual phase.
- În the case of the austenitic phase, the friction is weak, and is comparable to other metals or alloys.

Summary of Properties

The principal properties of the SMA are ruled by the phase transitions between the austenite ("high temperature" phase) and martensite ("low temperature" phase). The graphical representation of the transition of phases against temperature is particularly important for controlling the properties. Figure 6 shows

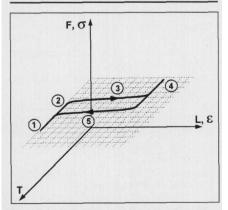


Figure 4. Superthermic effect after formation (1), and due to a phase change (3), the specimen can recover a larger total deformation than a classic alloy (4).

an integrated global overview of the different effects previously outlined:

- The one-way shape memory effect depicted in (1) and (2), where the changing of shape (L↓) is regulated by the transition from martensite to austenite.
- The two-way shape memory effect, with the learning process by mechanical cycles in (1) and the memory effect clearly described in (2), where the changes of shape (L↓ then ↑) are regulated by the phase transitions (martensite-austenite then austenite-martensite).
- The superelastic effect (3), where the deformations (L↓ then ↑) are regulated by the phase transitions (austenite-martensite then martensite-austenite).
- The superthermic effect is seen by displacing the Curve 2 from the plan (L, T, F=0) to the values of non-zero force. This returns to replace the accumulated internal constraints during the learning process by the external constraints.
- The rubber-like effect is seen in the repeated mechanical cycles of learning (1).

The interconnections between the three parameters are complex, making it difficult to predict the behavior of SMA for each application. Most of the applications use the alloys that allow the retention of two of three parameters, with the third fixed by the choice of alloy elements and thermomechanical treatment.

APPLICATIONS IN IMPLANTOLOGY

The unique properties of SMA allow the possibility of multiple applications in implantology. Some are still in the research stage (hip prostheses), but others are being developed into industrial products (synthetic bone plates, wire for the bone marrow cavity, dental implants, blood filters, and endovascular prostheses). In general, all materials used to make industrial products for implantation in the human body for short-, medium-, or long-term must be tested to prove their "biocompatibility." Before materials are authorized for human implantation the U.S. Food and Drug Administration (FDA) requires three successive tests of increasing level of scrutiny: in vitro, in vivo, and clinical studies. In this context, only a small part of the products developed by industrial R&D can be used effectively in implantology. Currently, the use of endovascular stents, orthopedic staples, and dental braces are acknowledged worldwide. However, intra-cranial staples are prohibited by the FDA in the United States. In the following sections, on-market and in-development applications will be presented, along with applications of historical interest.

Orthopedic Applications

Bone plates are used in the surgical treatment of broken bones. 19-21 They are fixed by an intermediate screw that allows the bone fracture to heal, orients the cellular regeneration, and maintains the original alignment of the bone. Plates that exert a constant, homogeneous pressure are more likely to promote rapid and complete healing of the broken bone.22 In this context, new plates based on the shape memory effect have been developed to allow a constant and uniform constraint on the two sections of the broken bone. After the broken bone parts are immobilized and aligned with the help of a screw, the SMA plate is implanted and heated to the transition temperature, controlled by a thermocouple. The resulting contraction (on the order of 5 mm) guarantees a snug fit between the two parts of the bone and imposes a permanent state of compression. This return to a continuous bone encourages rapid healing as well as a quick recovery of mobility compared to traditional surgical techniques. Today, synthetic bone plates made of SMA are available in most Western countries. However, because of their cost, their market share is small compared to plates made of traditional alloys.

Medical Staples

Like synthetic bone plates, compression staples are used to set broken bones and promote healing. They are implanted directly into the area of the break to compress the two parts of the bone.

The use of SMA appears to be sensible for such applications because they allow a constant torque to be applied between the two edges of the clip. The first clinical tests of SMA staples were undertaken in China in 1981:23,24 51 internal medical compressive staples made of nickel-titanium (44% nickel) were implanted over four years. The wires had a diameter of 1.5 mm, and the two arms of the staples formed a 60° angle. The staples were kept in the martensitic state at 5°C, and the transition to austenite-martensite occurred at 37°C. Of the 51 staples used, 10 were for dislocated ankles, 16 for broken leg bones, one for re-enforcing the knee ligament, and the others for treating jointed broken bones (hip, digits, and other bones). According to the authors the nickel-titanium alloy was excellent for these uses. The shape memory staples are now widely used in all Western countries.

Nails for Marrow Cavity

These implants stimulate the osteosynthesis where long bones, such as the femur, are broken.^{25,26} The current surgical procedure to treat this kind of break consists of hollowing out the bone marrow cavity of the two bone sections followed by the reconnection and insertion of a nail to allow the healing of the break. The nail is made of an SMA stem with soft polymer ends that completely fill the cavity and prevent relative movement of the bone. SMA are particularly adapted to this kind of operation because the setting of the bone is only a function of the deformation generated by the transition martensite-austenite. The following conditions must be taken into consideration when a cavity nail is designed (transition temperature, TTR):

- At low temperatures (T≤TTR) spacing must present a suitable shape for the installation and eventual removal
- At high temperatures (TTR ≤ T ≤ 37°C) the spacing must fill the marrow cavity of the broken bone without damaging the bone structure (necroses or bone absorption).
- The extremities of soft polymeric materials must be resistant enough to withstand a longitudinal state of compression between the two parts of the broken bone required for the healing process.

For optimal compression, the responsible elements of the fixation of one part and compression of the other part have different temperatures of transformation.

$$(A_F)_{\text{fixation element}} \le (A_S)_{\text{compression element}}$$

Where: A_s = temperature at the start of transformation, and A_F = temperature at the end of transformation. Additionally it is necessary that:

$$(A_F)_{compression element} < 20^{\circ}C$$

These two conditions assure that the compression state will not be activated before the nail fixation in the medullar cavity. Furthermore, the maximum compression state will only be reached at body temperature.

Medullar Spacing and the Treatment of Scoliosis

The insertion of a spacing disc between two vertebrae assures the local reinforcement of the spinal column and prevents all traumatic movement during the healing process. However, the bone integration and healing will not be possible if the total immobilization of the patient is not respected. Because they totally inhibit movement, SMA are of great interest for treating arthrodesis of the vertebrae (Figure 7).

Inserting an SMA spacing material between the two vertebrae allows the use of a constant force regardless of the position of the patient, who retains a certain degree of movement. For cervical vertebrae applications, Zhao suggested in 1986 an Ω -shaped, nickel-titanium SMA implant measuring 0.8 mm

wide and 8 mm long.²⁷ Thirty-two adult patients were successfully treated for cervical breaks or dislocations with symptoms of a compressed spinal column. Among the most obvious benefits were added patient mobility during recovery, simplified orthopedic and surgical procedures, shortened length of surgery, increased stability of the spacing in the medium- to long-term and easier installation. However, the long-term biostability of the implant remains unknown.

The SMA's are of great interest for treating scoliosis since they allow the application of a constraint that produces a traction-torsion force on the osseous environment, which restores spinal column alignment. Warious tests on cadavers have shown its feasibility. Nickeltitanium has remarkable advantages compared to other materials, including excellent flexibility during the surgery and easy post-operation treatment (the external heating of the dorsal zone is sufficient to retain the local state of constraint). However, these tests have not reached the clinical stage.

Hip Prostheses

SMA have been considered for the manufacture of hip prostheses.29 The total replacement of the acetabulum cavity of the hip joint by a double half-sphere, SMA prothesis represents a compromise between the friction resistance and mechanical resistance of the prosthetic joint. It is a question of fixing a half-sphere in the acetabulum cavity and a femoral stem in the medullar cavity of the femur. The femoral head of the prostheses is positioned in the half-sphere acetabulum while a second concentric halfsphere made of a material with a low coefficient of friction to limit the wear interposes between the components. Compared to classic materials used in operations, the use of SMA in this type of surgical operation would provide excellent resistance to wear caused by friction. Moreover, the dampening properties of SMA would constitute an important asset in this type of application.

Anterior Cruciate Ligament

The plethora of anterior cruciate ligament (ACL) prosthesis models represents an acceptance of impotence. Yet, reaching a consensus on its optimum design seems impossible. The ACL prosthesis replacement remains a debatable surgical procedure due to the material's technological limits.30 The use of nickeltitanium SMA in a ligament should be further explored.31 SMA could eventually answer the severe mechanical needs that are imposed on the ligament prosthesis. Concerning the resistance to rupture and the maximum elastic deformation, the nickel-titanium SMA approaches the behavior of a natural liga-

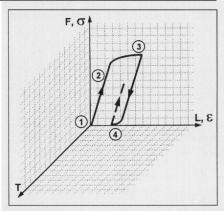


Figure 5. Rubber effect after a formation (1), and due to a reorientation of varieties of martensite (3), the specimen can recover a larger total deformation than a classic alloy (4)

ment. 32,33 However, the lack of fatigue resistance represents a weakness for applications in which the prosthesis is subject to repeated cyclic movements of the knee that can lead to failure. The problem appears to be difficult to solve unless our knowledge of the behavior and industrial implementation of mono-crystalline materials takes a great leap forward.

Dental Applications

Braces

The adjustments that the teeth are subjected to during an orthodontic treatment are due to remodeling of the bone by the force exerted by the braces.34 As a result, the mechanical stimulation allows the remodeling of the periodontal level.22 The strength of the force must be in a narrow range to permit a proper correction of the dental malformations. Too much force leads to the absorption of the bone, while too little force increases the possibility that the remodeling will not occur. Introduced in the 1940s, stainless-steel braces were an important advance in orthodontic treatments.34 However, the development of SMA resulted in a significant increase in correction forces,7 especially the homogeneous distribution of a constant force.^{35,36} The introduction in 1972 of nickel-titanium braces was significant because of the reduced length of the orthodontic treatment, easy and immediate placement, reduction of check-ups, and improved tolerance by the patients.3

Nickel-titanium braces are more comfortable for patients during the installation and throughout the treatment. The apparatus allows autonomous adjustment of the transmitted constraint, avoiding visits to the orthodontist to retighten it. The consumption of very cold or hot foods does not cause complications if the austenite-martensite transformation range is well chosen. Temperature swings can even prove to be beneficial for the orthodontic treatment if the transformation transport to the control of the control

sition temperatures are well chosen and fixed. Thus, the introduction of superelastic SMA allowed the application of the required force to remodel the bone. By choosing the suitable dimension of the wire adapted to the nature of the problem being treated, the SMA exerts a constant, homogeneous, and directed force on the teeth. For example, an SMA wire with a 0.41 mm diameter exerts a force of 7.4 Newtons with an elongation of 3 mm.

The use of SMA in orthodontics is recommended. However, careful attention is essential during the closing of the braces because the two ends of the wire must be welded. If the heat given out is excessive, the long-term viability of the braces may be compromised.

Dental Implants

Since 1985, Fukuyo has supported using SMA for endosseous dental implants. More than 15,000 clinical applications were reported in Japan from 1985 to 1988. SMA use in this type of operation assures a better fixation of the implant in the jaw due to shape memory. Among the other advantages he cited are the reliability of the implant fixation, easy operating technique, and greater homogeneity in the distribution of the constraint related to chewing.

Cardiovascular Applications

SMA were studied for cardiovascular applications because their insertion and deployment in the cardiovascular system does not necessarily require surgically "opening" the patient during an operation under total anesthesia. However, the exposure of SMA in the blood stream pose challenges such as agitating the arterial system to correct the stenosis and/or prevent stent restenosis, or to isolate the aneurysms (endo-prosthesis) of the venous system to prevent the release of embolus likely to move from the cava vein towards the lungs.

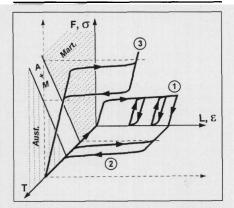


Figure 6. Review of principal properties of SMA: one-way memory (exterior line of (1) and (2)); two-way memory with learning (1) and the memory effect itself (2); pseudoelastic effect (3); superthermic effect, shifted (2) towards the values of non-zero force; rubber effect (Learning cyclage loops (1)).

Stents

The progress of atherosclerosis in the cardiovascular tree involves the formation of localized stenosis that reduces the width of the blood vessels. When they are wide, stenosis can quickly block blood flow in an artery. This pathology strikes at all levels — carotids, coronaries, renal arteries, abdominal aorta, iliac arteries, femoral, and lower arteries and must be treated. Bypasses and endarterectomies always receive a lot of surgical interest but they are not the only method of treatment. Dilations with or without arterectomy are frequently performed, mostly when the lesions are localized. The insertion of a stent permits the retention of the artery diameter and prevents the recurrence of the pathology in this area and the fibrous hyperplasia at the site of anastomoses. Such stents must be deployed up to their functional diameter by the expansion of a balloon made of stainless steel, tantalum or titanium. SMA stents can be deployed to the functional diameter by the heat of the blood stream, which prevents any initial mechanical damage. The use of stents in vascular endosurgery has expanded exponentially over the last 10 years,40-53 even if the scientific community has not reached a consensus yet. Although the clinical effectiveness of stents is well established, the superiority of the shape memory alloys or other materials must be considered. Researchers must study the disturbances of the blood flow, the blood compatibility of materials and their biostability in the long run, their biofunctionality, the need for eventual anti-coagulant treatments, and response of the patient to biological and immunological plans.

Endoprosthesis

The resection of unbroken aneurysms is a gratifying operation since the life expectancy of the patient returns to normal. The smaller, localized aneurysms in the abdominal aorta and iliaques arteries, as well as the aneurysms in the arteries, can now be isolated in the blood stream with the help of vascular endoprosthesis, or "covered" stents. This isolation allows the stents to be made of the same metals or alloys as before, on which a synthetic arterial graft is applied. The graft can be made of woven polyester, microporous Teflon®, or polyurethane.

The stent's role is more critical for this application than the previous one since it must maintain a constant diameter of the lumen while resisting the expansion in the initial stage and increasing pressure during the progressive healing process. With the establishment of the arterial prosthesis, blood loss is prevented and rapid healing is supposed to be promoted. The endoprosthesis made of shape memory alloy lattices and thin

woven polyester display a certain superiority over the other models because of their easy deployment and greater stability. Given the plethora of available designs, surgeons and radiologists launched large programs of clinical validation such as Eurostar.⁵⁴

Cava Filters

When the venous circulation is disturbed and pathology such as thrombophlebite appears, the release of embolus can occur. The thrombi in the venous system are then moved towards the cava vein. To prevent lung embolisms, the thrombi should be retained by a filter similar to that proposed by Homans in 1944.55 The installation of a cava vein filter is now widespread in Europe, 56,57 but its use creates controversy because the filters can degrade, completely thrombose, or migrate. As a result, interest in SMA should increase since they can be deployed with increased safety. However, the clinical tests have not demonstrated convincing advantages.

Intracranial Staples

Intracranial staples were first implanted in Japan in 1978 to isolate brain vessel. Different types of nickel-titanium staples and thermal processing were developed to treat the materials according to the specific application. The shape memory effect was exploited to facilitate the removal of the staples by simple heating. Despite interest in this area, these tests remain anecdotal.

Activation of an Experimental Artificial Heart

Energy requirements remain one of the key problems in developing an artificial heart that is completely implantable in humans. Since 1968, many ideas have been suggested, including nuclear batteries, magnetic energy transfer, and biological batteries. Sawyer proposed the use of shape memory in 1971.59 He suggested exploiting the ability of SMA to produce a constraint at the moment of transition martensite-austenite. In this model, ventricles would be made out of vinyl-ethylene acetate, the most bloodcompatible material at that time, and different sinusoidal elements made of six nickel-titanium wires replacing the cardiac muscles.

Different compositions of the elements were studied to optimize the output of the system. The required time to complete a thermal cycle represented a big technological limit, since the number of contractions was limited to 12 to 20 per minute. This preliminary study was quickly abandoned, even though the technology appeared attractive. The optimization of the output of the complete thermal cycle of nickel-titanium (toward a Carnot-cycle) might allow the feasibil-

ity of such a project to be re-evaluated.

Other Applications

Gynecological

In 1981, Xue introduced female sterilization in China using a cylindrical staple.⁶⁰ Measuring 15 mm to 17 mm in length and 2 mm in diameter, the staple was opened in iced water and closed again at body temperature, allowing the binding of the Fallopian tubes.

It was tested on 325 women, with a reported success rate of 98.77%. The operation lasted about 14 minutes, with no pain before, during, or after the implantation. The staples completely closed the tubes. The post-operation follow-up demonstrated the viability of this technique, but today this practice is of historic interest only.

Surgical Instruments

In 1988, Mitek Surgical Product Inc. (Dedham, MA), in collaboration with Tufts University (Medford, MA) suggested a breast cancer screening system⁶¹ designed to guarantee the location and isolation of the tumor during the surgical operation and to restrict the excision for aesthetic reasons.

A thin needle made of SMA was inserted into the tumor at body temperature to create a stable anchor, with the final shape of the needle resembling a "hook." During the operation, surgeons can quickly and precisely locate the tumor. This instrument has been used in over 300,000 surgical operations.

THE BIOCOMPATIBILITY OF NITINOL

The Problem

Since the early 1970s, the biocompatibility of nickel-titanium alloys for human implantation has been the focus of many studies. The works of Castleman and Motzkin showed that nickel-titanium orthopedic devices implanted in the femurs of rats, monkeys, and baboons for periods up to six months showed a strong encapsulation as a function of the implantation time, a moderate inflammation reaction, and an absence of giant cells. 62,63 These observations were considered sufficient to accept that the nickel-titanium SMA were biocompatible. Then in 1990, the accumulation of nickel in the fur of four dogs wearing subcutaneous nickel-titanium implants caused some worries. Spectroscopic analysis showed that the fur of animals wearing subcutaneous nickeltitanium discs in their backs contained nickel.64 However, neither the weight nor the shape of these discs had undergone any changes during the implanta-

In the mining industry nickel is seen as a potentially toxic metal for humans. However, the level of its toxicity remains difficult to assess because it appears to vary from person to person. In this context, it is easy to understand why doubts arise about the safety of nickel-titanium alloys. In 1981, Castleman and Motzkin published the results of a systematic of study the biocompatibility of the constituent elements of nickel-titanium based alloy.65 The following observations were presented: metallic debris of each constituent dispersed in the organism following corrosion caused by the biological environment, and metallic ions can be transported by the blood or

accumulate in the tissue surrounding the implant even if the alloy is highly resistant to corrosion. The authors also observed the following: the need for additional studies on nickel-titanium implants undergoing the austenite-martensite transformation in situ and designed to remain in the body for a long time; the risks represented by the preparation, storing, and sterilization processes; and the critical need to work on industrial alloys and not medical quality.

The question raised is not only that of knowing if the constituent elements are being leached out of the implant, but also of understanding its consequences. The temporary component of implantation makes the potential lifespan of the implant difficult to estimate. To date, the process of degradation caused by the body's environment on metal remains largely speculative: What level of risk is acceptable if the metal prosthesis degrades to a point where one or more elements in the alloy presents a known biological incompatibility?

Biocompatibility of Nickel

Nickel is an element with a potentially high level of toxicity to human health,66 70 even though it is an essential element for life.71 Despite many studies, a consensus has not been reached on the risks of nickel to the human body. The reactions of the human body after the installation of nickel implants seem unexpected.72 This can be explained by the multiple oxidation that nickel undergoes (Ni⁺, Ni²⁺, etc.) and the many nickel compounds in the human body (Ni₃S₂, NiO, Ni₂O₃, NiF₂, NiCl₃, etc.); and the subjectivity and variability of the response from person to person. This toxicity may manifest itself in humans in the following ways:73-77 acute pneumonia following the inhalation of nickel, chronic sinusitis and rhinitis, cancer of

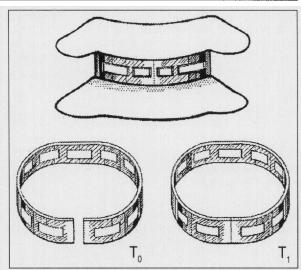


Figure 7. Principle function of the medullary spacing: the change in temperature (from $\rm T_0$ to $\rm T_1$) again closes the spacing ring that keeps the intervertebra distance even when posture changes.

the nostrils and lungs in nickel workers, and dermatitis and sensitivity caused by exposure to or physical contact with nickel.

The potential carcinogenicity, to animals as well as humans, of certain types of nickel was raised in several studies,78-88 but the role of nickel in the development of cancer remains fragmentary. Different nickel leakage products would be capable of causing irreversible damage to DNA and even impairing its production. However, the available data is insufficient to class nickel as a genotoxic element. Consequently, its role in the promotion or initiation of cancer has not yet been proved beyond reasonable doubt.89 As a result, the mechanisms of nickel must be understood and the eventual leaching out of nickel from an implant must be quantified because nickel is present in humans through food or other sources. As long as the natural ability to remove nickel exceeds that of accumulation, the risks are minimal.

Nickel is normally transported in the blood, particularly in the albumin, but also by the amino acids and plasma proteins. If the amount present in the body is too large, nickel first accumulates in the pulmonary alveoli and kidney glomerules. The speed of accumulation is proportional to the amount of nickel present. It can be removed by urine and feces. However, the speed of elimination is not only correlated to the concentration in the body, but also depends on personal metabolic factors. 90-97

Biocompatibility of Titanium

Unlike nickel, titanium and its alloys are considered to be biocompatible.98 They are frequently used in dentistry, orthopedy, and surgical applications. The biocompatibility of titanium is accepted because no toxicity was observed during animal experiments and human

2000 October • JOM 41

implants, except for a study which caused controversy in connection with the "undesirable irritation" caused by titanium; ⁹⁹⁻¹⁰¹ and titanium and Ti-Al-V alloys are known and highly trusted for their corrosion resistance in the human body. ^{102,103} These alloys have been adapted for human orthopedic prosthesis implants because of their excellent mechanical properties and safe biostability.

Biocompatibility of Nickel-Titanium Alloys

Inflammatory and immunological reactions caused by a prosthesis after installation do not go beyond the ability of a person to recover. The toxicity, which manifests itself by the leaching out of chemical elements, is capable of inducing one or more of the following reactions in a person: local tissue response, systematic toxic response, allergic response, and teratogenic, mutagenic, and carcinogenic response.

Among the many commercially available metallic alloys, only three are known to be biostable and biocompatible:104 austenitic stainless steel Fe-Cr-Ni (better known as 316L, which contains 12% to 14% nickel); Cr-Co alloy; and the titanium alloy Ti-Al-V. Compared to other metallic alloys or polymers, methodological studies on the biocompatibility of nickel-titanium alloys are rare. The tests in vivo of nickel-titanium elements were performed on dogs, rats, and monkeys, with the length of implantation lasting up to 17 months. The good behavior of nickel-titanium alloys leads to the scientific conclusion that the results were sufficiently safe to justify its implantation in humans. 62,63,65,105 Other studies, however, lead to the scientific conclusion that nickel leakage is likely to cause severe damage to patients. 106-109 What length of implantation of a nickeltitanium prosthesis might be expected in a person? What will be the influence of associated risk factors (tobacco, alcoholism, dyslipidemia, and hypertension)? How do we translate the results from animals to humans?

The nickel-titanium alloy is effectively the SMA with the best corrosion resistance compared to other shape memory alloys. But the corrosion resistance of nickel-titanium compared to other metallic alloys used in implantology (stainless steel 316L, Ti-6Al-4V, etc.) merits a profound study to reassure the potential patients of its long-term stability.

Biological Corrosion Tests

Nickel-titanium alloys, like all metallic alloys, are subject to in vivo degradation caused by corrosion from the biological environment. Different reaction products may appear during any corrosion process. In this context, the mere presence of nickel implies a risk for

person's health. The biostability, electrochemical potential, and corrosion rate should be studied in detail to set an acceptable threshold or reject the alloy.

In Vitro Studies

The corrosion of metals and metal alloys is a degradation process that is well understood. 110,111 It imposes severe limits on implant materials, particularly in orthopedy, since implant failure is possible. 112 The corrosion of metals and alloys is not yet entirely controlled. Different simulation methods have been developed in order to evaluate the resistance of different metallic implants, especially the nickel-titanium alloys.

The corrosion rate measured by loss of mass can be calculated by immersing the nickel-titanium alloy in a physiological solution. Shibi Lu observed a good resistance: after an immersion of 72 hours the corrosion rate reached a level equivalent to 0.001 mm per year.64 However, such a short experiment makes it difficult to predict the corrosion resistance in the long term. Oshida found that the corrosion rate increased with temperature (between 3°C and 60°C) and the acidity of the environment (pH varied from 3 to 11). For orthodontic wire, the corrosion rate increased from 0.02mm to 0.06 mm per year after seven days of incubation, which is not insignificant.113 Moreover, corrosion pitting appears when structures are not homogeneous, or in the case of imperfections in the surface. According to Schwaninger, corrosion of nickel-titanium will essentially be due to faults in the surface inherent in the manufacturing process of orthodontic wires.114 Nickel-titanium seems sensitive to pitting corrosion.

Chemical corrosion tests are essentially based on voltamperometric tests. 115-117 A potential is applied on a nickeltitanium electrode, resulting in the formation of an oxide film on the surface. In general, nickel-titanium has a better corrosion resistance than stainless steels and cobalt-chrome (Co-Cr) alloys, but corrosion resistance is localized and more random in nickel-titanium than in conventional alloys used in orthopedy. Rondelli proposed a scale to evaluate the localized corrosion resistance in different materials using damage tests on passivation films.118 In ascending order of corrosion resistance to localized corrosion, the results were

Ni-Ti < Ni-Ti-Fe < AISI 316L < Ti-6Al-4V

This weakness of nickel-titanium to localized corrosion confirmed that the re-passivation of the surface oxide film is a slow phenomenon. These results encourage prudence in the use of this alloy for long-term implantation. A surface treatment for further clinical use of

these alloys (for example, a re-enforcement of the passivation film) is recommended. However the schedule of conditions represents drastic needs. 119 All the electrochemical tests are carried out at a constant pH and temperature, whereas frequent changes in temperature and pH occur in the body and mouth. After surgery, the pH in the physiological milieu becomes acidic (pH = 5.5) before becoming neutral after 10 to 15 days. 120 Such an increase in acidity can damage the alloy's passive film.

Thus it is very important to choose well the corrosion environment for in vitro experiments. The extrapolation of in vivo results show a rule of behavior that must be weak. Among the different environments that have been suggested over the years, only Ringer's solution remains universally accepted.4 Randin tested the corrosion resistance of different nickel-based alloys used in jewelry in a highly corrosive milieu: sweat.75 This is composed of chlorides (0.3 g/l to 3 g/ l), urea (0.12 g/l to 0.57 g/l) and lactic acid (0.45 g/l to 5 g/l), with a variable pH between 3.8 and 6.5. Even if nickeltitanium alloys (55% and 45%, respectively) are in a passive state, they can be corroded by pitting. The pitting corrosion potential in the sweat is understood to be between 0.6 V and 1.05 V.

Considering the potential / pH balance diagrams, Pourbaix showed that nickel: 121,122

- Has only one stable thermodynamic region (pH > 7).
- Corrodes quickly in acidic solutions (pH < 7).
- Can passivate in precise conditions (9 < pH < 12).
- Corrodes in oxidizing alkaline solutions (pH > 12).

Randin found that titanium is highly stable in the sweat (pitting corrosion potential of 3 V). This result was confirmed in a sodium chloride solution (pitting corrosion potential of 10 V) and by the long-term biostability of titanium. ^{123,124} Extrapolating results obtained in vitro in predicting the behavior in vivo is risky, however.

In Vivo Studies

The corrosion resistance of nickel-titanium alloys has been widely reported^{29,64,125,126} since Castleman's study.⁶³ No signs of corrosions were reported in orthopedic implants (plaques and screws) that were installed in the femurs of 12 dogs for periods ranging from three to 17 months. The nickel-titanium rings that were implanted in the femurs of rabbits for four months by Cigada and his colleagues did not cause any interstitial corrosion. 126 Plates made of stainless steel and nickel-titanium also were implanted in a comparative study:29 The stainless steel plates were prone to pitting corrosion, whereas the nickel-titanium plates were not. Dental wire made of nickel-titanium, used in 22 patients, was not prone to corrosion, according to Edie and his colleagues.125

In a study of 1,120 hip prostheses of different models that were removed due to complications. Pohler studied the corrosion and degradation after different lengths of implantation.127 He also evaluated the tissue surrounding the prosthesis when the alloy contained nickel. Some 2 mm to 3 mm encapsulated tissue samples were taken to be studied microscopically by atomic absorption spectroscopic analysis and microanalysis. The concentrations of nickel in the surrounding tissue did not follow a homogeneous distribution since nickel was not detected in most specimens. However, moderate concentrations of nickel were found sporadically on the surface of material. It was often associated with other elements, such as Fe = 380 ppm, concentration of Cr below the detection level, and Ni = 50ppm. The nickel also has a tendency to migrate into the surrounding tissue, where it could then be transported in the body through metabolic interactions.

FUTURE CHALLENGES

The needs of biocompatibility represent a constraint that is not insurmountable but one that cannot be circumvented for the use of SMA in the field of medicine. The interactions between materials and the human environment must be better understood before the general use of SMA in implantology can be allowed. Degradation in vivo must be prevented and the possible toxicity and non-compatibility of SMA in the human tissues must be defined. Today, the advance of biomedical applications of SMA is important even though the level of knowledge in regard to its biocompatibility remains stagnant. A multidisciplinary approach is essential to study SMA with new, more efficient techniques. 128,129 New solutions must be found to solve the problems that arise. At the current level of scientific research, these problems can be tackled in two possible ways: the design and use of SMA without nickel and the use of surface treatments.

Shape Memory Alloys That Do Not Contain Nickel

The use of SMA is not obvious. Copper alloys 130,131 are less resistant to corrosion¹³² and less efficient; other shape memory alloys containing gold are not practical for commercial use because of the prohibitive cost. 133-135 As a result, the burgeoning technology of shape memory polymers will play an important role in the future of shape memory in the field of medicine. 136–139 For example, in cardiovascular applications, the low molecular weight of the polymers would undoubtedly have better compatibility and greater potential than metals. 140,141 Unfortunately, shape memory polymers technology has not been mastered, taking into account the complexity and variety of possible combinations. However, this technology could permit the development of new medical applications.

Surface Treatments and Coatings

The presence of nickel guarantees the mechanical performance of the alloy, but its biocompatibility has not been established beyond reasonable doubt. A surface treatment would perhaps make nickel-titanium SMA more tempting for human implantation since the presence of nickel in the alloy would be masked and corrosion resistance improved. 142,143 In effect, the surface treatment opens up unsuspected possibilities.144,145 The results of laser treatment are exciting,146 and other surface treatments and coatings may lead to improved sensitivity to corrosion resistance. The changes of shape and dimension associated with nickel-titanium during the austenitemartensite transition might cause the film to become detached.

The biocompatibility of SMA must be studied in a rigorous, orderly way to validate the long- term effects of the implant and eliminate the apprehensions of potential users. Orthopedy and the cardiovascular field remain the favorite fields for SMA use. However, they impose different constraints on the implant, and the validation studies require different approaches. The direction of studies of biocompatibility, biostability, and biofunctionality of SMA implants must follow from their specific functions.147

CONCLUSIONS

Even if the list of medical applications of SMA is seemingly endless, this article hopefully showed their obvious potential in the medical field. In the coming vears, a true revolution will occur in some medical specialties. The revolutionary advancements in endovascular surgery have already injected new challenges in the traditional vascular surgery. New horizons have been opened, and clinicians, scientists, and industrialists are starting to work together to master the complexity of a problem through a multidisciplinary approach. As a result, numerous applications have been considered, but many more are envisioned. Considering their revolutionary properties, these alloys were the stimulus for the most daring applications since the 1970s and have been used to break some scientific barriers and accomplish technological challenges. At that time, in the West, heart disease gained prominence as a major social concern. As a result, the development of an artificial heart was a strong point in the policy of U.S. National Institute of Health. Similarly, in the Far East the demographic explosion worried the authorities and

stimulated research, leading to the use of SMA in contraception. Today, a more rational and less emotional approach must be adopted. The potential applications must respond to the specific social requirements of our age: the medicalsurgical services must be assured at the lowest cost. The safety question of all material placed in the body requires particular attention, and all implants must have the required qualities of biocompatibility, biofunctionality, and biodurability. The applications now in development are more rational and have the potential to be more numerous.

ACKNOWLEDGEMENTS

The work benefited from the financial support of FCAR-Quebec and Quebec Biomaterials Institute. I would like to express my gratitude to Drs. R. Guidoin, G. Laroche, and M. Fiset for their help and guidance. I also thank Pierre Agard for creative contributions, and Oliver May for editing the final form of the manuscript.

References

- 1. A.B. Greninger and V.G. Mooradian, Trans. AIME, 128 (1938), pp. 337-341.
 2. W.J. Buehler and R.C. Wiley, U.S. patent 3,174, 851 (1965).
 3. C.A. Heisterkamp, W.J. Buehler, and F.E. Wang, (Paper presented at the 8th Int. Conf. on Medical and Biomedical Engineering, Chicago, IL 1969).
 4. W.J. Buehler and F.E. Wang, (Paper presented at the Ninth Navy Science Symposium, Washington, D.C., 1966).
 5. G.B. Kauffman and I. Mayo, Invention and Technology, Fall (1993), pp. 18-23.
- (1993), pp. 18–23. 6. G.F. Andreasen and T.B. Hilleman, J. Am. Dent. Assoc., 82
- (1971), pp. 1373–1375. 7. G.F. Andreasen and R.D. Barrett, *Angle Orthod.*, 42 (1972),

- 7. G.F. Andreasen and R.D. Barrett, Angle Orthod., 42 (1972), pp. 172–177.
 8. G.F. Andreasen and R.F. Morrow, Am. J. Orthod., 73 (1978), pp. 142–151.
 9. L.M. Schetky and R.B. Sims, Proc. ICOMAT 79 (Cambridge, MA: MIT Press, 1979), pp. 693–698.
 10. R. Kousbroek, Metal and Ceramic Biomaterials, vol. 2, ed. P. Ducheyne and G.W. Hastings (Boca Raton, FL: CRC Press, 1984), pp. 63–90.
 11. H.J. Wagner and C.M. Jackson, J. Mat. Eng., 70 (1969), pp. 28–31.
- 12. T.W. Duerig and K.N. Melton, Shape Memory Alloys 1986 (Guilin, China: China Academic Publishers, 1986), pp. 397–
- 13. S. Miyazaky and K. Otsuka, I. S. I. J. Internat., 29 (1989), pp.
- 353–377. 14. W.V. Moorleghem, Matériaux et Techniques, 6-7 (1993), pp.
- 14. W. Moorteghent, Materials & Lectinques, 6-7 (1993), pp. 87-91.
 15. C.M. Jackson, H.J. Wagner, and R.J. Wasilesky, 55-Niti-nol—The Alloy with a Memory: Its Physical Metallurgy, Properties and Applications, NASA Spec. Pub. 5110 (1972).
 16. G. Guenin and P.F. Gobin, Matériaux et Techniques, Oct./

- G. Guenin and P.F. Gobin, Matériaux et Techniques, Oct./ Nov. (1980), pp. 350-364.
 P. Rey, Colloque Matériaux Biomédicaux et Handicaps (Proceedings, University of Le Mans, France 1987), p. 199.
 S. Miyazaki et al., J. de Physique, C4, supplément au numéro 12 (1982), pp. 255-260.
 J. Haasters, G. Bensmann, and T. Baumgart, Current Concepts of Internal Fixation of Fractures, ed. H.K. Uhthoff (Berlin, Germany: Springer-Verlag, 1980), pp. 128-135.
 V. Brailovski and F. Trochu, Biomed. Mater. Eng., 6 (1996), pp. 291-298.
 F. Baumgart, G. Bensmann, and I. Hartwie, Tech. Mitt

- V. Braliovski and F. Irochu, Biomed. Mater. Eng., 6 (1996), pp. 291–298.
 F. Baumgart, G. Bensmann, and J. Hartwig, Tech. Mitt. Krupp Forse. Ber., 35 (1977), pp. 157–171.
 F. Pawels, Traduction de: Gesamelle Abhandlungen zur Funktionellen Anatomie des Beuvegengsapparates, ed. P.G. Maquet (Berlin, Germany: Springer-Verlag, 1979), pp. 131–178.
 F.J. Yang et al., in Ref. 12, pp. 438–443.
 K.R. Dai et al., in Ref. 12, pp. 430–432.
 J. Haasters, G.V. Salis-Solio, and G. Bensmann, Engineering Aspects of Shape Memory Alloys, ed. T.W. Duerig et al. (London, England: Butterworth-Heineman, 1990), pp. 426–444.
- 26. J. Haasters, J. Becker, and G. Bensmann, Praxis, 5 (1984), pp. 409–418. 27. D.L. Zhao et al., *Shape Memory Alloy 86*, in Ref. 12, pp. 433–
- 437. 28. M.A. Schmerling et al., J. Biomed. Mater. Res., 10 (1976), pp.
- M.A. Schmerling et al., J. biomea. Muter. Res., 10 (1976), pp. 879–892.
 Y. Sekiguchi, Shape Memory Alloys, ed. H. Funakabo (Amsterdam: Gordon and Breach Science Publishers, 1987), pp. 226–269.
 N. Poddevin and R. Guidoin, Polymers & Polymer Composition.
- site, 3 (1995), pp. 79-97. 31. N. Hagemeister, L' H. Yahia, and T. Lours, J. de Physique

IV, coll. C2, suppl. J. de Physique III, 5 (1995), pp. 403–408. 32. N. Hagemeister et al., First Intern. Conf. on Shape Memory and Superelastic Technologies (Santa Clara, CA: The International Organization on Shape Memory and Superelastic Technologies, 1994), pp. 395–400. 33. N. Hagemeister et al., *J. de Physique IV*, coll. C8, suppl. *J.*

de Physique III, 5 (1995), pp. 1223–1228.
34. C.J. Burstone, Current Concepts and Techniques, vol. 2, ed. T.M. Graber and C.V. Swain (St. Louis, MO: Mosby. 1985),

pp. 23–38. 35. S. Civjan, E.F. Huget, and L.B. De Simon, J. Dent. Res., 54

(1975), pp. 89–96. 36. G.F. Andreasen and R.D. Barrett, *Amer. J. Orthodont.*, 63

36. G.F. Andreasen and R.D. Darrett, Camer, J. Crimanant, 36 (1973), pp. 462–470.

37. R. Sachdeva and S. Miyazaki, Engineering Aspects of Shape Memory Alloys, ed. T.W. Duerig et al. (Stoneham, MA: Butterworth-Heineman, 1990), pp. 452–469.

38. R. Kousbroek et al., Biomaterials 1980, ed. G.D. Winter, D.F. Gibbons, and H. Plenk (London: John Wiley and Sons

D.F. Gibbons, and H. Pienk (London: joint whey also Solis Ltd., 1980), pp. 767-772.

39. S. Fukuyo et al., Engineering Aspects of Shape Memory Alloys, ed. T.W. Duerig et al. (Amsterdam: Butterworth-Heineman, 1990), pp. 470-476.

40. Y. Sugita et al., Trans. Amer. Soc. Art. Intern. Organs, 32

(1986), pp. 30-34. 41. T. Oku et al., Trans. Amer. Soc. Art. Intern. Organs, 14

(1988), pp. 399-403. 42. J.C. Palmaz, Am. J. Radiology, 150 (1988), pp. 1263–1269. 43. P.W. Serruys et al., J. Amer. Coll. Cardiol., 17 (1991), pp.

143-1345. 44. G.J. Becker, Circulation, 83 (1991), pp. 122-236. 45. R. Tominaga et al., Amer. Heart J., 123 (1992), pp. 21-27. 46. M.T. Rothman and S.W. Davies, British Heart J., 67 (1992),

pp. 425-429. 47. J.C. Palmaz, A*mer. J. Radiol.,* 160 (1993), pp. 613-618. 48. S.V. Lossef et al., *J. Vasc. Interv. Radiol.,* 5 (1994), PP. 341-

49. F. Flueckiger et al., J. Vasc. Interv. Radiol., 5 (1994), pp. 745-

750.
50. K.A. Hausegger et al., Radiology, 190 (1994), pp. 199–202.
51. F.J. Veith, J. Vasc, Surg., 20 (1994), pp. 855–860.
52. M.L. Marin et al., J. Vasc. Surg., 21 (1995), pp. 595–604.
53. K.H. Mak et al., J. Am. Coll. Cardiol., 27 (1996), pp. 494–503.
54. R. Guidoin et al., J. Endovasc. Ther., 7 (2000), pp. 105–122.
55. J. Homans, Surg. Gynecol. Obstet., 79 (1994), pp. 70–82.
56. M. Simon et al., Radiology, 125(1977), pp. 89–94.
57. M.R. Prince et al., Invest. Radiol., 23 (1988), pp. 294–300.
58. N. Netsu, T. Iwabuchi, and T. Honma, Bull. Res. Drest. Min. Dress. Met., Joko Ku Univ., 34 (1978), pp. 67–73.
59. P.N. Sawyer et al., Trans. Amer. Soc. Artif. Int. Organs, 17 (1971), pp. 470–473.

P.N. Sawyer et al., Trans. Amer. Soc. Artif. Int. Organs, 17 (1971), pp. 470–473.
 P. Xue, F. Yunyue, and Y. Danhua, Shape Memory Alloy '86, in Ref. 12, pp. 444–446.
 J.P. O'Leary, J.E. Nicholson, and R.F. Gatturna, Engineering Aspects of Shape Memory Alloys, ed. T.W. Duerig et al. (Amsterdam: Butterworth-Heineman, 1990), pp. 477–482.
 S.M. Motzkin et al., Proc. 4th New England Bioengineering Conference (New Haven Conp. 1984). Introopsity Proce. 1976.

Conference (New Haven, Conn.: Yale University Press, 1976), pp. 301-308.
63. L.S. Castleman et al., J. Biomed. Mater. Res., 16 (1976), pp.

695-731.
64. Y. Shibi Lu, Engineering Aspects of Shape Memory Alloys, ed. T.W. Duerig et al. (Amsterdam: Butterworth-Heineman, 1990), pp. 445-451.
65. L.S. Castleman and S.M. Motzkin, Biocompatibility of

65. L.S. Castleman and S.M. Motzkin, Biocompatibility of Clinical Implant Materials, ed. D.F. Williams (Boca Raton, FL: CRC Press, 1981), pp. 129–154.
66. T. Norseth and M. Piscator, Handbook on the Metal Toxicology, ed. L. Friberg, G.F. Nordberg, and V.B. Vouk (Amsterdam: Elsevier/North Holland Biomedical Press, 1979), pp. 541–553. 67. P. Camner et al., Nickel in the Human Environment, ed. F.W.

1979), pp. 541–553.
67. P. Camner et al., Nickel in the Human Environment, ed. F.W. Sunderman (Lyon, France: Int. Agency for Research on Cancer, 1984), pp. 267–276.
68. Nickel (Washington, D.C.: National Research Council, Division of Medical Sciences, 1975), pp. 97–128.
69. W.Z. Friend, Corrosion of Nickel and Nickel-Based Alloys (New York: John Wiley & Sons, 1980), pp. 32–94.
70. D.H.K. Lee, Metallic Contaminants and Human Health New York: (Academic Press, 1972), pp. 149–152.
71. M. Anke et al., Nickel in the Human Environment, ed. F.W. Sunderman (Lyon, France: Int. Agency for Research on Cancer, 1984), pp. 339–366.
72. K.S. Kasprzak, Genotoxic and Carcinogenic Metals: Environmental and Occupational Occurrence and Exposure, Advances in Modern Environmental Toxicology Vol. XI, ed. L. Fishbein, A. Furst, and M.A. Mehlman (Princeton, N.J.: Princeton Scientific Publishing Co., 1987), pp. 145–183.
73. E.J. Bernacki, G.E. Parsons, and F.W. Saundermann, Ann. Clin. Lab. Sci., 8 (1978), pp. 190–197.
74. L. Kreyberg, Brit. J. Ind. Med., 35 (1978), pp. 109–115.
75. J.P. Randin, J. Biomed. Mater. Res., 22 (1988), pp. 649–666.
76. S.L. Husain, Brit. Med. J., 2 (1977), pp. 998–1003.
77. A.A. Fisher, Cutis, 19 (1977), pp. 285–295.
78. J.P.W. Gilman, Cancer Res., 22 (1962), pp. 158–162.
79. T.J. Lau, R.L. Hackett, and F.W. Sunderman, Cancer Res., 32 (1972), pp. 2253–2258.

79. T.J. Lau, R.L. Hackett, and F.W. Sunderman, Cancer Res., 32 (1972), pp. 2253–2258.
80. A. Furst, Adv. Exp. Med. Biol., 91 (1977), pp. 1–29.
81. A. Gaechter et al., J. Bone Jt. Surg., 59 (1977), pp. 622–631.
82. G.F. Nordberg and O. Andersen, Environ. Health Perspect., 40 (1981), pp. 65–81.
83. A. Furst and S.B. Radding, J. Environ. Sci. Health, C2 (1984), pp. 103–133.
84. M. Gerin et al., Nickel in the Human Environment, ed. F.W. Sunderman (Lyon, France: Int. Agency for Research on Cancer, 1984), pp. 105–116.
85. J. Dunnick, C.W. Jameson, and J.M. Benson, Progress in Nickel Toxicology, ed. S.S. Brown and F.W. Sunderman (Oxford, U.K.: Blackwell Scientific Publications, 1985), pp. 49–

86. K.S. Kasprzak, Proc. Am. Assoc. Cancer Res., 28 (1987), p.

86. K.S. Kasprzak, Proc. Am. Assoc. Cancer Res., 28 (1987), p. 148.
87. G.S. Carvalho et al., Clinical Implant Materials, ed. G. Heimke, U. Soltesz, and A.J.C. Lee (New York: Elsevier Science Publishers, 1990), pp. 13–18.
88. F. Pott et al., Nickel and Human Health: Current Perspectives, ed. E. Nieboer and J.O. Nriagu (New York, NY: John Wiley & Sons Inc., 1992), pp. 491–502.
89. M.A. Cooke and R.A. Cooke, Nickel and the Skin: Immunology and Toxicology, ed. H.I. Maibach and T. Menné (Boca Raton, FL. CRC Press, 1989), pp. 35–44.
90. B. Sarkar, Coordination Chemistry, ed. J.P. Laurent (Tarrytown, NY: Pergamon Press, 1980), pp. 171–185.
91. C. Onkelinx, Nickel in the Human Environment, ed. J.O. Nriagu (New York, NY: Wiley-Interscience, 1980), pp. 526–545.

92. O.B. Christensen and V. Lagesson, Ann. Clin. Lab. Sci., 11

545.

92. O.B. Christensen and V. Lagesson, Ann. Clin. Lab. Sci., 11 (1981), pp. 119–125.

93. B. Sarkar, Nickel in the Human Environment, ed. F.W. Sunderman (Lyon, France: Int. Agency for Research on Cancer, 1984), pp. 367–384.

94. J. Swatek-Kozlowska, Cytotoxic, Mutagenic and Carcinogenic Potential of Heavy Metals Related to Human Environment, ed. N. Hadjiliadis and H. Kozlowski (Brussels, Belgium: NATO Advanced Study Institute, 1996), pp. 48–49.

95. H. Kozlowski, Cytotoxic, Mutagenic and Carcinogenic Potential of Heavy Metals Related to Human Environment, ed. N. Hadjiliadis (Brussels, Belgium: NATO Advanced Study Institute, 1996), pp. 549–558.

96. W. Bal and K.S. Kasprzak, Cytotoxic, Mutagenic and Carcinogenic Potential of Heavy Metals Related to Human Environment, ed. N. Hadjiliadis and H. Kozlowski (Brussels, Belgium: NATO Advanced Study Institute, 1996), pp. 52–53.

97. K.S. Kasprzak, Cytotoxic, Mutagenic and Carcinogenic Potential of Heavy Metals Related to Human Environment, ed. N. Hadjiliadis (Brussels, Belgium: NATO Advanced Study Institute, 1996), pp. 93–106.

98. S.A. Brown and M.B. Mayor, J. Biomed. Mat. Res., 12 (1978), pp. 67–78.

98. S.A. Brown and M.B. Mayor, J. Biomea. Mat. Kes., 12 (1978), pp. 67-78.

99. M. Berlin and C. Nordman, Handbook on the Metal Toxicology, ed. L. Friberg, G.F. Nordberg, and V.B. Vouk (Amsterdam: Elsevier/North Holland Biomedical Press, 1979), pp. 627-636.

100. S. Daum et al., Proc. R. Soc. Med., 70 (1977), pp. 31-44.

101. W.R. Parker, Proc. R. Soc. Med., 70 (1977), pp. 289-293.

102 G.B. Andersson et al., J. Bone Jt. Surg., 60 (1978), pp. 31-20.

103. D.S. Gordon and G.A.S. Blair, Br. Med. J., 2 (1974), pp.

104. J.B. Park, Biomaterials Science and Engineering (New York:

104.].B. Park, Biomaterials Science and Engineering (New YORK: Plenum Press, 1987), pp. 193–234.
105. M. Assad et al., Proc. First Intern. Conf. on Shape Memory and Superelastic Technologies, in Ref. 32, pp. 215–220.
106.].W. Harrison et al., Clin. Orthop., 116 (1976), pp. 253–258.
107. D.E. Cutright et al., Oral Surg. Oral Med. Oral Pathol., 35 (1973), pp. 578–586.
108. F.X. Gil., J.M. Manero, and J.A. Planell, J. Mat. Sci.: Mat. in Mad. 7 (1996) pp. 403–406.

F.A. Gil, J.M. Manero, and J.A. Planell, J. Mat. Sci.: Mat. in Med., 7 (1996), pp. 403–406.
 M. Webley, A. Kates, and M.L. Snaith, Ann. Rheum. Dis., 37 (1978), pp. 373–379.
 M.G. Fontana and N.D. Greene, Corrosion Engineering

(New York: McGraw-Hill Book Co., 1967).

(New York: McGraw-Hill Book Co., 1307). 111. M.G. Fontana and N.D. Greene, Corrosion Engineering (New York: McGraw-Hill Book Co., 1978). 112. R.J. Gray, Metallography in Failure Analysis, ed. J.L. McCall and P.M. French (New York: Plenum Press, 1977), pp. 231–

113. Y. Oshida, R. Sachdeva, and S. Myazaky, Biomed. Mat.

113. Y. Oshida, R. Sachdeva, and S. Myazaky, *Biomea. witt.* Eng., 2 (1992), pp. 51–69.
114. B. Schwaninger, N.K. Sarkar, and B.E. Foster, *Am. J. Orthod.*, 82 (1982), pp. 45–49.
115. K. Speck and A. Fraker, *J. Dent. Res.*, 59 (1980), pp. 1590–

116. H. Kimura and T. Sohmura, Dent. Mater. App., 6 (1987),

pp. 73-79. 117. Y. Nakayama et al., *Biomaterials*, 10 (1989), pp. 420–424. 118. G. Rondelli, B. Vicentini, and A. Cigada, *Corr. Sc.*, 30 (8/

9) (1990), pp. 805–812.
119. M.A. Barbosa, *Biomaterials Degradation, Fundamental*aspects and *Related Clinical Phenomena*, ed. M.A. Barbosa
(New York, NY: Elsevier Science Publishers, 1991), pp. 227–

257.

120. B.J. Edwards, Environmental Degradation of Engineering Materials, ed. M.R. Louthan, R.P. McNitt, and R.D. Sisson (University Park, Pa.,: the Pennsylvania State University Press, 1987), pp. 461–484.

121. M. Pourbaix, Atlas d'équilibres électrochimiques (Paris: Gauthier-Villars, 1963), pp. 330–342.

122. M. Pourbaix, Lectures on Electrochemical Corrosion (New York: Plenum Press, 1973).

York: Plenum Press, 1973).

123. C.D. Hall and N. Hackermann, J. Electrochem. Soc., 57 (1953), pp. 262-268.

124. S.G. Steinemann, Evaluation of Biomaterials, ed. G.D. Winter, J.L. Leray, and K. de Groot (New York, NY: John Wiley & Sons, 1980), pp. 1-34.

125. J.W. Edie, G.F. Andreasen, and P. Zaytoun, Angle Orthod., 51 (1981), pp. 319-324.

126. A. Cigada et al., Clinical Implants Materials, ed. G. Heimke, U. Schlese, and A.J.C. Leo (New York, NY: Eleguier Publishers.)

126. A. Ugadaetal, Alintui impianis vaiaci iais, ed. G. Hennick, U. Soltész, and A. J. C. Lee (New York, NY: Elsevier Publishers, 1990), pp. 51–56.

127. O.E.M. Pohler, Biomaterials in Reconstructive Surgery, ed.

127. O.E.M. Pohler, Biomaterials in Reconstructive Surgery, ed. L.R. Rubin (St. Louis, MO: Mosby, 1983), pp. 158–228.
128. S.A. Shabalovskaya and J.W. Anderegg, J. Vac. Sci. Technol. A, 13 (1995), pp. 2624–2632.
129. T.G. Bradley, W.A. Brantley, and B.M. Culbertson, Am. J. Orthod. Dentofac. Ortop., 109 (1996), pp. 589–597.
130. H. Pops, Metall. Trans., 1 (1970), pp. 251–256.
131. G. Barceló, R. Rapacioli, and M. Ahlers, Scr. Metall., 12

(1978), pp. 1069–1075. 132. M.H. Wu, Engineering Aspects of Shape Memory Alloys, ed. T.W. Duerig et al. (Stoneham, MA: Butterworth-Heineman,

1.W. Duerig et al. (Stonenam, MA: Dutterworui-Frememan, 1990), pp. 69-88.
133. G.B. Brooks, *Gold Bull.*, 6 (1973), pp. 8-12.
134. G.V. Raynor, *Gold Bull.*, 9 (1976), pp. 50-54.
135. M. Grimwade, *Interd. Sc. Rev.*, 17 (1992), pp. 371-381.
136. Y. Shirai and S. Hayashi, *Mitsubishi Heavy Industries Ltd.*

136. 1. Shirai and S. Hayasani, Mitsuoisin Feavy inaustries Lta. Technical Bullettin 184 (1988).
137. S. Echigo et al., ASAIO Trans., 36 (1990), pp. M195–198.
138. C. Liang, C.A. Rogers, and E. Malafeew, Smart Struct. Mater., 123 (1991), pp. 97–105.
139. S. Hayashi, Intern. Progr. in Urethanes. 6 (1993), pp. 90–113.

115. 140. P.N. Sawyer and S.R. Srinivasan, Bull. N.Y. Acad. Med.,

48 (2) (1972), pp. 235–286. 141. P.N. Sawyer et al., Trans. Amer. Soc. Int. Organs, 19 (1973),

pp. 195–199. 142. S. Lombardi, « Amélioration de la Résistance à la Corrosion de l'alliage à Mémoire de Forme Nickel-Titane par Modification de Surface, » Master Thesis, Institut de Génie Biomédical, Ecole Polytechnique, Montreal, Quebec, Ca-

nada, January 1995.
143. S. Lombardi et al., Proc. First Intern. Conf. on Shape Memory and Superelastic Technologies, in Ref. 32, pp. 221–226.
144. B.D. Ratner, A. Chikoti, and G.A. Lopez, Plasma Deposition, Treatment and Elching of Polymers, ed. R. D'Agostino (San Diego, CA: Academic Press, 1990), pp. 463–516.
145. Y.S. Yah et al., J. Biomed. Mater. Res., 22 (1988), pp. 795–818.

M. Tabrizian et al., (Paper presented at a seminar on shape memory alloys, Missisagua, Ontario, Canada, December 1996).
 J. Cederström and J. Van Humbeeck, J. de Physique IV, C2, suppl. J. de Physique III, 5 (1995), pp. 335–341.

Reference Books on SMA

1. L. Friberg, G.F. Nordberg, and V.B. Vouk, eds., Handbook on the Metal Toxicology (Amsterdam: Elsevier/North Holland

on the Metal Toxicology (Amsterdam: Elsevier/North Holland Biomedical Press, 1979), 2p. 541.

2. F.W. Sunderman, ed., Nickel In the Human Environment (Lyon, France: Int. Agency for Research on Cancer, 1984). Nickel (Washington, D.C.: National Research Council, Division of Medical Sciences, 1975).

3. W.Z. Friend ed., Corrosion of Nickel and Nickel-Based Alloys (New York, NY: John Wiley & Sons, 1980).

4. D.H.K. Lee, ed., Metallic Contaminants and Human Health New York: Academic Press, 1972).

5. H. Funakabo, ed., translated from Japanese by J.B. Kennedy, Shape Memory Alloys (Amsterdam, Holland: Gordon and Breach Science Publishers, 1987).

6. T.W. Duerig et al., eds., Engineering Aspects of Shape Memory

6. T.W. Duerig et al., eds., Engineering Aspects of Shape Memory Alloys (London: Butterworth-Heineman, 1990). 7. A. Patoor and M.Berveiller, eds., Technologie des Alliages à

7. A. Fator and M. Bervenier, eds., Technologie des Atlaiges u Mémoire de Forme: Comportement Mécanique et Mise en Oeuvre (Paris, France: Traité des nouvelles technologies, série maté-riaux. Édition Hermès, 1994). 8. R.E. Whan, ed., Metals Handbook, Volume 10: Metals Characterization, (Metals Park, OH: American Society for

Metals 1978)

Diego Mantovani is with the Department of Mining, Metallurgy and Materials Engineering at Laval Univer-

For more information, contact Diego Mantovani, Laval University, Department of Mining, Metal-lurgy and Materials Engineering, Pouliot Building, Room 1745-E, Quebec City, QC G1K 7P4, Canada; (418) 656-2131, ext. 6270; fax (418) 656-5343; e-mail: Diego. Mantovani@gmn.ulaval.ca

