Medical Applications of Titanium and Its Alloys

The Material and Biological Issues

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Peer Review Policy

Each paper published in this volume was evaluated by three peer reviewers. The authors addressed all of the reviewers' comments to the satisfaction of both the technical editor(s) and the ASTM Committee on Publications.

To make technical information available as quickly as possible, the peer-reviewed papers in this publication were prepared "camera-ready" as submitted by the authors.

The quality of the papers in this publication reflects not only the obvious efforts of the authors and the technical editor(s), but also the work of these peer reviewers. The ASTM Committee on Publications acknowledges with appreciation their dedication and contribution to time and effort on behalf of ASTM.

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Foreword

This publication, *Medical Applications of Titanium and Its Alloys: The Material and Biological Issues,* contains 30 papers presented at the symposium of the same name, held on 15 and 16 Nov. 1994, in Phoenix, Arizona. The symposium was sponsored by ASTM Committee F-4 on Medical and Surgical Materials and Devices, as a joint effort with the Medical Applications Committee of the International Titanium Association (ITA), formerly the Titanium Development Association, and the Bioengineering Committee of the American Academy of Orthopaedic Surgeons (AAOS). Stanley A. Brown from the FDA Center for Devices and Radiological Health, in Rockville, Maryland and Jack E. Lemons of the University of Alabama at Birmingham, Alabama presided as symposium chairmen and are editors of the resulting publication.

The scope of the symposium was to cover the basic materials science issues pertaining to the processing of titanium alloys and the manufacturing of medical devices, the material and biological factors that make titanium alloys attractive for medical applications, as well as the problems that medical applications present. The scope was intended to include orthopaedic, dental, and cardiovascular applications. The major portion of the publication is focused primarily at the issues pertaining to orthopaedic applications.

The editors would like to express their appreciation for the help provided by their steering committee: Howard Freese from Teledyne Allvac (ITA), Thomas O'Connell from Timet (ITA), Bernie Stulberg, M.D. from the Cleveland Center for Joint Replacement (AAOS), Joshua Jacobs, M.D. from Rush Medical College (AAOS), Ken St. John from the University of Mississippi, Jim Davidson from Smith & Nephew Richards, Les Gilbertson from Zimmer, and Hugh Luckey from Materials Engineering, Inc.

We would also like to express our thanks to the ASTM staff that helped make the symposium and publication possible, most notably: D. Savini for her help with the symposium planning and K. Dernoga and R. Hippensteel for the handling of manuscript submission and review. We are also indebted to the many reviewers for their prompt and careful reviews.

As a final note, we would like to pay special tribute to Hugh E. Luckey, P. E. Hugh was active for many years in the materials and test method standards activities of ASTM Committee F-4. Due to his long-standing interest in medical applications of titanium, Hugh was actively involved in the planning of this symposium. Unfortunately, his illness had progressed to the point that he could not be actively involved in the meeting and review process, and did not survive to see publication of this STP. We will all miss Hugh Luckey.

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Overview

Titanium alloys are used extensively in medicine. The alloys provide many advantages over other alloy systems. However, there is controversy regarding their use. The objectives of this symposium and publication were to have both (all) sides of these issues need to presented in a complete and scientific way. To be complete, the symposium covered basic materials science issues pertaining to the processing of titanium alloys and the manufacturing of medical devices, the material and biological factors that make titanium alloys attractive for medical applications, as well as the problems that medical applications present. The scope included, but was not limited to, orthopaedic, dental, and cardiovascular applications. As with any meeting, there were scheduling conflicts that limited participation of representatives from some specialties.

The symposium and publication were divided into seven major categories. These are (1) processing and Ti 6Al 4V, (2) new alloys, (3) porous coatings, (4) corrosion, laboratory studies, (5) fretting and wear testing, (6) biological issues, and (7) clinical experience.

Processing and Ti 6Al 4V

The three papers in this section dealt primarily with the effects of manufacturing and processing, on titanium in general, and with Ti 6Al 4V in particular. The opening paper by Imam and Fraker discusses the different microstructures of titanium alloys. They present a review of the influence of composition, heat treatment and microstructure on the mechanical and corrosion behavior of titanium alloys. The effects of melting and working practices on properties is further developed by Davis and Forbes Jones. Key processes discussed included vacuum arc and cold hearth melting, rotary forging, continuous rolling and various finishing operations. Peterson and French used Taguchi experimental design to determine the effects of surface finish, test bar diameter, and material grade on the mechanical properties of Ti 6Al 4V. They demonstrated a strong correlation between smaller diameter and lower yield strength, and a minor correlation between surface finish and percent elongation.

New Alloys

The five papers in this section discussed the properties and advantages of several new titanium alloys. Okazaki *et al.*, examined a number of alloys with Zr, Sn, Nb Ta and Pd, instead of Al and V. They were evaluated mechanically and by corrosion testing. The alloy Ti 15Sn 4Nb 2Ta 0.2Pd had higher tensile strength and elongation compared with Ti 6Al 4V. Increasing concentration of these 4 elements resulted in decreases in corrosion currents. Zardiackas *et al.*, present the alloy Ti 15 Mo as a fine grained β-microstructure. Compared to CPTi grade 4, Ti 6Al 7Nb, Ti 6Al 4V and 316L stainless steel, the alloy has excellent corrosion resistance, lower strength but superior notch tensile properties, and satisfactory biological responses in *in vitro* and 2 year *in vivo* studies. Wang *et al.* present a new low modulus β-titanium Ti 12Mo 6Zr 2Fe (TMZF). Their analysis demonstrates the desirable low elastic modulus, excellent mechanical strength and corrosion resistance, and good formability and *in vitro* wear resistance. Bhambri *et al.* presented two β-titanium alloys developed as National Aerospace plane materials: 21S and 21S Rx. These alloys of Ti 15Mo 2.8Nb 0.2Si (plus 3% Al or 0.26% O, respectively) were studied in a number of heat treatments to identify optimum properties to exceed those of Ti 6Al 4V. Fretting fatigue of a simulated modular head/taper showed performance similar to Ti 6Al 4V. Mishra *et al.* present the mechanical, wear and biological testing on another β-titanium alloy Ti 13Nb 13Zr, with and without diffusion hardening. Compared to Ti 6Al 4V, the alloy has 30% lower elastic modulus, higher notched fatigue limit and other mechanical properties. They report lower inflammation and superior osseointegration compared to CP Ti.

Porous Coatings

The three papers address issues pertaining to the mechanical properties of porous coatings. Kohn *et al.* extended their studies on fatigue damage of coatings by the application of acoustic emission (AE) to detect crack initiation. They used finite element analysis to determine the local stresses. Hampel and Piehler examined the fatigue behavior of specimens with surfaces textured by etching and compared these to plasma sprayed coatings and smooth samples. Fractures of the etched specimens occurred at asperities, whereas fracture of the plasma sprayed samples occurred at a lower stress and was associated with delamination. Wolfarth and Ducheyne examined a novel method of producing a porous coating with porous nodules. Modeling by FEA and fatigue testing showed significant improvement in the fatigue strength compared to conventional beaded coatings.

Corrosion, Laboratory Studies

Four papers in this section address basic principles of corrosion of titanium and its alloys. Kovacs and Davidson discuss the physical chemistry and electrochemical issues regarding the solubility and passivity of titanium alloys. These principles led to identification of Ti, Nb, Zr, and Ta as appropriate elements, and the Ti 13Nb 13Zr alloy in particular. Healy and Ducheyne examined the passive dissolution kinetics of CPTi fibers in simulated interstitial electrolyte (SIE), SIE plus serum, and SIE plus EDTA. They identified a two phase model, with the first being dictated by equilibrium of the surface, and the second by mass diffusion. Chohayeb *et al.* studied the corrosion behavior of titanium coupled to several dental casting alloys (Ni-Cr, Co-Cr, Au-Pd-Ag, and Pd-Ag) in artificial saliva. The couple with Ni-Cr demonstrated sensitivity to localized corrosion, while the other couples showed only slight increases in corrosion. Gilbert *et al.* used a scratch repassivation technique to study the repassivation kinetics of titanium 6Al 4V. They found that aeration had minimal effect, whereas low pH and high applied potentials were associated with higher peak currents.

Fretting and Wear Testing

Laboratory studies on fretting corrosion and wear of titanium are presented in the five papers in this section. Smith and Ducheyne used a pin-on-disk to demonstrate a transition in corrosion rate during fretting corrosion experiments. Increasing amplitude increased the number of cycles to the transition. They concluded that the accumulation of fretting debris provided a protective mechanism, suggesting that minimization of relative motion between components would reduce corrosion. Brown *et al.* used a screw and plate fretting device as per F897 to study mixed metal fretting corrosion and the effects of environment. Titanium 6Al 4V fretting against itself suffered significantly more damage than did Ti 6Al 4V against stainless steel, cobalt alloy, or nitrided titanium. Fretting corrosion rates were higher in cell culture growth media with high levels of calcium or hydrogen peroxide. The paper by Shetty presents the results with a nitrogen diffusion hardened Ti 6Al 4V. While the tensile, fatigue and corrosion properties were unchanged, the surface treated specimens were harder and more wear resistant. Hoeppner and Chandrasekaran examined the effects of fretting on the fatigue strength of specimens tested under conditions simulating testing of hip prostheses. Their results demonstrated that the surface damage produced numerous crack nucleation sites, and significantly reduced the endurance limit of Ti 6Al 4V. In the final paper in this section, McKellop *et al.* present an overview of their extensive studies on wear testing of hip simulators and hip prostheses.

In the absence of 3rd-body abrasive contaminants, titanium alloy performs as well or better than the other surgical alloys. However, self-perpetuating wear was sometimes seen with acrylic particles, and always with metallic particles. Surface modification provided additional protection against cement particles, but did not prevent severe abrasion by entrapped metallic particles.

Biological Issues

Laboratory studies on the biological response to titanium are presented in the six papers in this section. *In vitro* studies by Rogers *et al.*, using human peripheral blood monocytes showed that Ti 6Al 4V particles were nontoxic, but did stimulate release of PGE_2 and several cytokines in a dose response manner. Thus, bone resorption could be in response to mediators released by macrophages stimulated by titanium wear debris. The paper by Ong *et al.* addresses both the effects of growth media and bone marrow cells on the titanium surface, as well as the effects of titanium on the cells. Surface analysis revealed a CaP deposit on the surfaces, similar to brushite. While there was no difference in the protein content in cell layers on Ti and polystyrene, 6 day studies indicated fewer cells on the titanium surfaces. Keller *et al.* examined the response of osteoblasts cultured on CPTi and Ti 6Al 4V surfaces. Their long term studies confirmed previous short term results demonstrating no difference in phenotypic expression. Glant *et al.* report on the response of macrophages, fibroblasts and osteoblasts to CPTi particles in cell and organ culture. Mediators released from cells could stimulate bone resorption and inhibit bone matrix formation. Bianco *et al.* used CPTi felt implanted in rabbits to examine the transport of degradation products in the absence of mechanical stress. They found that titanium accumulated locally, but there was limited systemic transport. Merritt and Brown studied transport of titanium and vanadium in hamsters and in cell culture. Salt injection studies demonstrated rapid excretion of vanadium, and local accumulation of titanium, with slight elevation in liver, spleen, kidney, and plasma. Cell culture studied confirmed these results with cell association of titanium, but no cell association of vanadium.

Clinical Experience

The final four papers report on biological responses issues seen in clinical studies. Ungersbock *et al.* compared the soft tissue response to fracture fixation plates made of stainless steel versus that to CP Titanium. At an average of 18 months, evidence of fretting corrosion was seen with stainless steel, but not titanium. Histologically, the fibrous capsules were thinner with CP titanium plates. Howie and McGee present a clinical overview of the issues relating to wear and particle release from titanium and cobalt chromium alloy implants. A rat model was used to quantify some of the observations. At clinical levels, Ti 6Al 4V particles were not toxic, but did have a stimulatory effect on the release of PGE_2, whereas the cobalt alloy particles were toxic. Jacobs *et al.* report on a 3 year, prospective study of total hip patients with uncemented CP Ti backed acetabular components and either cemented cobalt alloy or uncemented Ti 6Al 4V femoral components. Serum elevation of titanium was seen in both groups compared to controls, but no correlation was observed between serum titanium levels and clinical function. Kraay *et al.* report on 29 retrieved total knee prostheses with Ti6Al 4V femoral components. In these cases where failure of the metal backed patellar component occurred, significant metal-metal wear was observed. In the absence of significant wear, they have not observed significant problems at follow-ups of 7 years.

Significance and Future Work

The properties that guide the selection of materials process for one application, are often very different for another. With its low modulus of elasticity, especially in the β-form, titanium provides an advantage in some applications. In selected situations, titanium may present a concern regarding wear or fretting resistance. On the other hand, its corrosion resistance is superb. Thus, one can not say categorically that a particular material is good or bad for medical applications.

As with so many issues within the biomaterials arena, interpretation of the publications in this volume is not cut and dry. Problems such as the appropriateness of controls or uniformity of methods makes many of the studies difficult to compare and relate. As materials science and medical technology continue to advance, more applications of titanium and its alloys will become manifest. Clearly there is a need for further standardization of the methods used for study of materials for biological applications.

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Contents

Processing and Ti-6Al-4V

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TITANIUM ALLOYS AS IMPLANT MATERIALS

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ABSTRACT: Titanium alloys are prominent as dental and orthopedic materials because of their high strength-to-weight ratio, lower elastic modulus, excellent corrosion resistance and apparent biocompatibility. Based on microstructures that can be produced by alloying, titanium alloys are grouped as alpha, alpha-beta and beta alloys. Alpha titanium and alpha-beta alloys have been used for dental and orthopedic purposes. Beta titanium alloys are being considered as candidate materials for implant applications because of their ease of formability, increased strength and lower elastic modulus, in spite of increased cost. Studies show the presence of the omega phase in the beta alloy, Ti-15Mo-2.8Nb, in the unaged condition. Comparison of corrosion behavior of this alloy with the alloy Ti-6Al-4V shows the two alloys have comparable corrosion resistance in simulated physiological solution. A review and data are presented along with a discussion of the influence of composition, heat treatment and microstructure on mechanical properties and corrosion behavior of titanium alloys, in general, and of beta alloys, in particular.

KEY WORDS: titanium, titanium alloys, beta titanium alloys, heat treatment, mechanical properties, microstructures, corrosion, implant metals

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The need to find more reliable materials to replace broken or deteriorating parts of the human body is increasing with the increase in the number of both younger and older recipients. Modern surgery and dentistry need metals and alloys of extreme chemical inertness and adequate mechanical strength. Metals and alloys in use include stainless steels, Co-Ni-Cr alloy, cast and wrought Co-Cr-Mo alloy, commercially pure titanium, Ti-6Al-4V alloy and other titanium alloys. Commercially pure titanium

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is a material of choice as an implant because of its biocompatibility resulting in no allergic reaction with the surrounding tissue and also no thrombotic reaction with the blood of the human body. The average yield strength of commercially pure titanium is approximately 480 MPa. If a higher strength of the implant is necessary, for example, in hip prostheses, titanium alloys have to be used. The most widely used alloy, Ti-6Al-4V, reaches a yield strength almost double the yield strength of commercially pure titanium. Prostheses fabricated from wrought Ti-6Al-4V show almost double the load bearing capacity when compared to cast cobalt alloys [1]. The results of an investigation in rabbitt tissue on the toxic behavior of the element, vanadium, resulted in some hestiancy to use this material due to potential toxicological problems of the alloying constituents [2]. Toxicological effects associated with the alloying constituents have not been observed with titanium alloys. The toxicology question and the need to improve mechanical properties have led to the development of other titanium alloys.

Surface treatment variations such as porous coatings, ion implantation and oxidation are made to the titanium implant devices for various reasons; all directed to improving performance and biocompatibility. The use of "new" alloys and associated heat treatments and surface variations may result in changes in the mechanical and chemical behavior that ultimately affect the strength, durability and biocompatibility of the implant. This paper reviews the influence of titanium alloy compositions, and heat treatments on mechanical properties and electrochemical behavior, and presents data on microstructures and corrosion behavior.

BACKGROUND

Titanium was discovered in 1794 [3] and is the ninth most common element in the earth's crust, occurring as rutile, TiO_2, and ilmenite, $FeO{\cdot}TiO_2$. Extraction of titanium in amounts that were large enough for commercialization came about with the development of the Kroll process in 1936 [4]. Titanium has a high strength-to-weight ratio that makes it attractive for many applications.

Titanium has an hexagonal closed packed (hcp) crystal structure referred to as alpha phase, that undergoes an allotropic modification at 883 °C (1621 °F) to a body centered cubic (bcc) crystal structure known as beta phase. The manipulation of these crystallographic variations through alloying additions and thermomechanical processing results in a wide range of alloys and properties. These crystallographic variations help to categorize the titanium alloys. Based on the phase that can be produced by alloying additions, titanium alloys are grouped as alpha, alpha-beta and beta alloys. Some alloying elements stabilize the alpha phase whereas others stabilize the beta phase. Alloying elements that stabilize alpha titanium include aluminum, tin and zirconium, and alloying elements that act as beta stabilizers include vanadium, molybdenum, niobium, chromium, iron and manganese. Interstitial elements, B, C, N, and O are alpha stabilizers and will stimulate alpha phase formation at cell boundaries and defects [3].

The use of titanium for surgical implants has been the subject of a previous ASTM Symposium [5], and numerous other reviews [6]. Titanium, (alpha) and the Ti-6Al-4V alloy, (alpha-beta), are used for dental and orthopedic purposes. Pure titanium is used for dental implants and as material for porous coatings for other titanium alloy implants. Pure metals are not strong enough for use as orthopedic implants, and are not used for skeletal devices. Other titanium alloys, including beta titanium alloys, are being used and introduced for use as surgical implants, where strength requirements are higher than those of pure titanium. Among the titanium alloys, beta titanium alloys offer more potential for implant application because of their ease of formability, biocompatible chemical composition and wide range of mechanical properties.

The wide range of mechanical properties is based on the transformation characteristics of the beta phase (metastable). Although the stable phase at room temperature is alpha, the metastable beta is retained even after slow cooling from above the beta transus temperature. The beta phase is relatively ductile compared to the hexagonal close packed alpha phase. The transformation of beta phase is sluggish and can be controlled to produce desired properties. The structure of the transformed products and their distribution depend on the composition of the alloy and thermomechanical treatments. During aging at high temperatures, alpha is precipitated directly from beta by heterogeneous nucleation along grain boundaries and dislocations. At low temperatures, the transformation product is beta prime in solute-rich alloys, whereas, in less rich alloys, the transformation product has been found to be omega phase [7,8]. The precipitation of beta prime as well as omega is homogeneous. The low temperature precipitate particles are fine and the precipitation is intense; hence the alloy hardens rapidly, and it becomes brittle. Control of precipitation at the early stages of low temperature aging to achieve acceptable strength and toughness is of prime importance. Different methods to achieve desirable properties have been suggested including two step aging and a combination of cold work and high temperature aging [9,10].

ALLOY COMPOSITION

Commercially pure titanium and the workhorse titanium alloy, Ti-6Al-4V, have been in use as implant materials for a shorter time compared to stainless steel and cast or wrought cobalt base alloys. To attain higher strength, in commercially pure titanium, alloying elements are added. Alloy design criteria are not based only on alloying elements contribution to strength but on the biocompatibility of the resulting alloy. Alloying additions and thermomechanical processing dictate the microstructure of the implant material, and control of microstructure is a means to attain desirable properties.

The alloying elements, vanadium and aluminum, in alloy, Ti-6Al-4V, have been found in surrounding tissues under conditions of high wear but no toxic effect has been connected to this debris, whch also includes titanium [11]. Due to the perceived safety concern and possible toxic effect, different new alloys have been designed with no vanadium[11] and in some cases, with no aluminum [12]. There are safety concerns regarding other alloying elements such as molybdenum.

New titanium alloys are being introduced to change the chemical composition and the mechanical properties. Some titanium alloys that are in use today or are being considered for use as implant materials are listed in Table 1 along with their mechanical properties. The properties in Table 1 result from specific heat treatments and will vary depending on their processing parameters. Information in this table permits a comparison of mechanical properties of pure titanium, some alpha/beta titanium alloys and some beta titanium alloys.

Nominal compositions of major constituents are given in Table 1. Table 2 gives compositions of minor constituents for selected alloys. Minor constituents play an important role in affecting the mechanical properties as shown in Table 3 for different grades of titanium [13]. Table 3 shows that the ultimate tensile strength and the yield strength increase with increasing oxygen. Elongation would be expected to decrease,

Table 1. Mechanical Properties of Selected Titanium Alloys

Type, Alloy, Nominal Wt.%	E GPa	UTS MPa*	YS(0.2%) MPa	% El	% Red. Area	Ref.
Alpha						
Ti	105	240-617	165-520	12-27		[13]
Alpha/Beta						
Ti-6Al-4V	88-116	990-1184	789-1013	2-30	2-41	[14]
Ti-5Al-2.5Fe	110	943-1050	818-892	13-16	33-42	[2]
Ti-6Al-7Nb	108	900-1100	910-970	11-14		[15]
Beta						
Ti-13Nb-13Zr	79	550-1035	345-932	8-15	15-30	[16]
Ti-11.5Mo-6Zr-2Fe	74-85	1060-1100	1000-1060	18-22	64-73	[17]
Ti-15Mo-5Zr-3Al	15-113	882-1312	870-1284	11-20	43-83	[18]
Ti-15Mo-3Nb	79	1035	993	15	60	[12]

* 1 MPa = 0.145 ksi

Table 2. Maximum Chemical Composition of Minor Constituents of Selected Materials in Table 1.

Alloy	N	O	C	H	other
Ti-6Al-4V	0.05	0.13	0.08	0.012	0.25 Fe
Ti-6Al-7Nb	0.05	0.20	0.08	0.009	0.25 Fe
Ti-15Mo-2.8Nb	0.06	0.30	0.05	0.06	0.25 Si

but this effect is not as striking as it should be in this table. Studies keeping the composition and impurities constant would illustrate these effects more clearly.