

M^edical Applications of Titanium and Its Alloys

*The Material and
Biological Issues*

S. A. BROWN
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EDITORS



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Medical Applications of Titanium and Its Alloys: The Material and Biological Issues

Stanley A. Brown and Jack E. Lemons, Editors

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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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Contents

Overview—S. A. BROWN AND J. E. LEMONS	ix
--	----

PROCESSING AND Ti-6Al-4V

Titanium Alloys as Implant Materials—M. A. IMAM AND A. C. FRAKER	3
Manufacturing Processes for Semi-Finished Titanium Biomedical Alloys— R. M. DAVIS AND R. M. FORBES JONES	17
Taguchi Experiment on the Mechanical Properties of Sintered Titanium 6-4— R. R. PETERSON AND C. V. FRENCH	30

NEW ALLOYS

New Titanium Alloys to be Considered for Medical Implants—Y. OKAZAKI, Y. ITO, A. ITO, AND T. TATEISHI	45
Characterization of Ti-15Mo Beta Titanium Alloy for Orthopaedic Implant Applications—L. D. ZARDIACKAS, D. W. MITCHELL, AND J. A. DISEGI	60
Microstructure and Properties of a New Beta Titanium Alloy, Ti-12Mo-6Zr-2Fe, Developed for Surgical Implants—K. K. WANG, L. J. GUSTAVSON, AND J. H. DUMBLETON	76
Optimization of Properties of Ti-15Mo-2.8Nb-3Al-0.2Si and Ti-15Mo-2.8Nb-0.2Si- 0.260 Beta Titanium Alloys for Application in Prosthetic Implants— S. K. BHAMBRI, R. H. SHETTY, AND L. N. GILBERTSON	88
Mechanical and Tribological Properties and Biocompatibility of Diffusion Hardened Ti-13Nb-13Zr—A New Titanium Alloy for Surgical Implants— A. K. MISHRA, J. A. DAVIDSON, R. A. POGGIE, P. KOVACS, AND T. J. FITZGERALD	96

POROUS COATINGS

Methods of Detecting and Predicting Microfractures in Titanium—D. H. KOHN, C. C. KO, S. J. HOLLISTER, D. SNOEYINK, J. AWERBUCH, AND P. DUCHEYNE	117
Evaluation of the Corrosion Fatigue Behavior of Porous Coated Ti-6Al-4V— H. HAMPEL AND H. R. PIEHLER	136

A Novel Porous Coating Geometry to Improve the Fatigue Strength of Ti-6Al-4V Implant Alloy—D. WOLFARTH AND P. DUCHEYNE	150
---	-----

CORROSION, LABORATORY STUDIES

Chemical and Electrochemical Aspects of the Biocompatibility of Titanium and Its Alloys—P. KOVACS AND J. A. DAVIDSON	163
---	-----

Passive Dissolution of Titanium in Biological Environments—K. E. HEALY AND P. DUCHEYNE	179
---	-----

Corrosion Behavior of Dental Casting Alloys Coupled with Titanium—A. A. CHOHAEB, A. C. FRAKER, F. C. EICHMILLER, R. M. WATERSTRAT, AND J. BOYD	188
---	-----

Titanium Oxide Film Fracture and Repassivation: The Effect of Potential, pH, and Aeration—J. L. GILBERT, C. A. BUCKLEY, AND E. P. LAUTENSCHLAGER	199
---	-----

FRETTING AND WEAR TESTING

Transitional Behavior in Ti-6Al-4V Fretting Corrosion—B. J. SMITH AND P. DUCHEYNE	219
--	-----

Effects of Material Combination, Surface Treatment, and Environment of Fretting Corrosion of Ti-6Al-4V—S. A. BROWN, J. S. KAWALEC, A. C. MONTAGUE, K. MERRITT, AND J. H. PAYER	231
---	-----

Mechanical and Corrosion Properties of Nitrogen Diffusion Hardened Ti-6Al-4V Alloy—R. H. SHETTY	240
--	-----

Characterizing the Fretting Fatigue Behavior of Ti-6Al-4V in Modular Joints—D. W. HOEPPNER AND V. CHANDRASEKARAN	252
---	-----

Wear of Titanium 6-4 Alloy in Laboratory Tests and in Retrieved Human Joint Replacements—H. A. MCKELLOP, T. ROSTLUND, E. EBRAMZADEH, AND A. SARMIENTO	266
--	-----

BIOLOGICAL ISSUES

The In Vitro Response to Particulate Titanium Alloy—S. D. ROGERS, D. W. HOWIE, D. R. HAYNES, AND M. J. PEARCY	297
--	-----

Response of Titanium Surfaces to Simulated Biological Environments—J. L. ONG, L. C. LUCAS, AND C. W. PRINCE	306
--	-----

In Vitro Osteoblast Responses to cpTi and Ti-6Al-4V Alloy—J. C. KELLER, C. M. STANFORD, R. A. DRAUGHN, AND J. P. WIGHTMAN	319
--	-----

Induction of Bone Resorbing Agents by Titanium Particulates: Responses of Macrophages, Fibroblasts and Osteoblasts In Vitro—T. T. GLANT, J. YAU, AND J. J. JACOBS	333
--	-----

Determination of In Vivo Titanium Release from a Non-Articulating Commercially Pure Titanium Implant—P. D. BIANCO, P. DUCHEYNE, AND J. M. CUCKLER	346
Distribution of Titanium and Vanadium Salts and Corrosion Products in Cells, Fluids, and Organs in vivo and In Cell Culture in vitro—K. MERRITT AND S. A. BROWN	357
CLINICAL EXPERIENCE	
Clinical Studies on Titanium and Stainless Steel Plates (LC-DCP). A Comparative Evaluation—A. UNGERSBÖCK, O. E. M. POHLER, F. W. BAUMGART, B. RAHN, AND S. M. PERREN	371
Wear and Osteolysis in Relation to Prostheses Design and Materials—D. W. HOWIE AND M. A. MCGEE	388
A 3-Year Prospective Study of Serum Titanium Levels in Patients With Primary Total Hip Replacements—J. J. JACOBS, A. K. SKIPOR, J. BLACK, L. M. PATTERSON, W. P. PAPROSKY, AND J. O. GALANTE	400
Retrieval Analysis of Ti-6Al-4V Miller-Galante Total Knee Replacements—M. J. KRAAY, V. M. GOLDBERG, S. A. BROWN, AND K. MERRITT	409
Author Index	417
Subject Index	419

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 be 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. Hoepfner 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 PGE₂ 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 studies 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 PGE₂, 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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