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Recent Advances in Titanium Alloys for Biomedical Device Application

Replacement orthoplasticity made important advancements during the mid-20th century, primarily through the contributions of G. K. McKee and Sir John Charnley. For example, McKee introduced metal-on-metal hip prosthesis, originally fabricating these from stainless steel, this material being rapidly replaced by a Co-Cr-Mo alloy to mitigate the initially excessive friction and rapid loosening observed for the stainless steel pair. In the 1960s Charnley introduced low-friction arthoplasticity, this consisting of a small diameter metallic femoral head articulating against a polymeric, originally PTFE and now an ultra-high-molecular-weight polyethylene (UHMWPE) acetabular cup.

Until recently, the mainstream approach taken for the introduction of newer orthopaedic materials has involved adaptation of existing materials, as exemplified by the use of Ti-6Al-4V ELI, an alloy originally intended for aerospace applications. Indeed Ti-6Al-4V, because of its lower modulus, superior biocompatibility and corrosion resistance, has been increasingly preferred for orthopaedic devices. Other titanium alloys, principally Ti-6Al-7Nb, have found application primarily in response to concerns relating vanadium to potential cyclotoxicity and adverse reaction with body tissues. More recently newer alloys and processing techniques have begun to be introduced, these substitutions aimed at lowering modulus, enhancing biocompatibility and increasing fatigue performance.

The desire to reduce the elastic modulus of orthopaedic alloys has been largely driven by long-term experience which indicates that insufficient load transfer from the artificial implant to the adjacent remodeling bone may result in bone resorption and eventual loosening of the prosthetic device. Indeed, it has been shown that when the tension/compression load or bending moment to which living bone is exposed is reduced, decreased bone thickness, bone mass loss and increased osteoporosis may ensue. This phenomenon, termed stress shielding, has been related to the difference in flexibility or stiffness, dependent in part on elastic moduli, between natural bone and the implant material.

Minimization of stress shielding has resulted since the mid-1990s in the development of titanium alloys with moduli substantially lower than Ti-6Al-4V or Ti-6Al-7Nb. The mechanical performance of several of these materials is summarized in Exhibit 1. Thirty percent reductions in elastic moduli may be achieved through substitution of beta solution treated Ti-Mo base alloys for Ti-6Al-4V, with greater reductions being possible through substitution of Ti-Nb base alloys, although the latter substitution does come at some sacrifice in tensile and fatigue properties when compared to Ti-Mo based alloys. It should also be noted that increased tensile and fatigue performance can be gained in all the newer alloys shown in Exhibit 1 through aging; however, these enhancements also result in an increase in elastic moduli.

Exhibit 1 further suggests that cold reduction may enhance the strength of Ti-Nb base alloys, although the use of this procedure for restoring the high cycle fatigue performance of these materials has yet to be determined. Notably, this procedure has also been found to result in a further reduction of the elastic moduli of these alloys, wherein they are rapidly approaching those of bone. Finally, it should be noted that these newer alloys contain alloying additions that are generally considered to be biologically inert, eliminating not only vanadium but also aluminum, the latter having been suggested to be causal in osteolysis and neural disorder.

Application of these newer low moduli, enhanced biocompatibility titanium alloys has, however, remained limited. To some degree this may be traced to their having been developed by individual orthopaedic companies, for example Stryker Orthopedic holds patent rights for both TMZF and TNZT, having introduced the former for orthopaedic devices in the early 2000s. It is expected, however, that other systems will continue to be developed beyond those shown. Indeed, recent process developments have reduced the variability of product performance, and have thereby resulted in renewed interest in Ti-15Mo, this alloy system having been available for almost 20 years.

Exhibit 1: Advanced orthopaedic titanium alloys

Alloy Designation	Microstructure	Elastic Modulus (GPa)	Yield Strength (MPa)	Tensile Strength (MPa)	Fatigue Strength (MPa)R=0.1, 107 cycles, air
					600
Ti-6Al-4V	Annealed	115	850	960	
					325
Ti-15Mo	Beta	75	610	770	
					600
Ti-12Mo-6Zr-2Fe (TMZF)	Beta	75	1000	1060	
					325
Ti-29Nb-13Ta-4.6Zr (TNTZ)	Beta	63	600	650	350
	Cold rolled	63	755	830	
					275
Ti-35Nb-5Ta-7Zr (TNZT)	Beta	55	530	590	
					NA
Ti-Nb-Fe-Si	Extruded	81	866	1055	NA
	Cold rolled	39	900	1024	
Bone		Oct-30		150-400	

An alternative solution to increasing the performance of titanium alloys for orthopaedic applications is also being introduced to the market. This involves nanostructuring of existing alloys, with primary current attention being devoted to commercial purity titanium. Choice of commercial purity titanium completely eliminates any concerns about biocompatibility. Nanostructuring of commercial purity titanium combines dedundant severe plastic deformation (also known as SPD), as experienced through equal channel angular pressing, with subsequent thermo-mechanical processing, the former being designed to produce a nanostructured ultra-fine grained microstructure while the latter is intended to provide the product form and sizes required for modern mass production of orthopaedic devices. Indeed, the combination of these techniques for commercial purity grades 2 and 4 titanium results in a 100-fold decrease in the materials grain size from approximately 25 mm to 0.15mm (See Exhibit 2), while providing a two fold increase in the tensile and fatigue performance of commercial purity titanium, as seen in Exhibit 3.

Nanostructuring has also been found to speed the osteointegration of titanium within the human body. Exhibit 4 illustrates that adhesion of osteoblast cells to the surface of grade 2 commercial purity titanium may be substantially increased by nanostructuring. These results have been confirmed for nanostructured grade 4 commercial purity titanium, the occupation of mice fibroblast cells L929 after 24 hours exposure on a hydrofluoric acid etched surface increasing from 53 to 87.2 pct, as seen in Exhibit 5.

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Exhibit 2: Optical and electron micrographs illustrating microstructure of (a) conventionally processed and (b) nanostructured grade 4 commercial purity titanium.

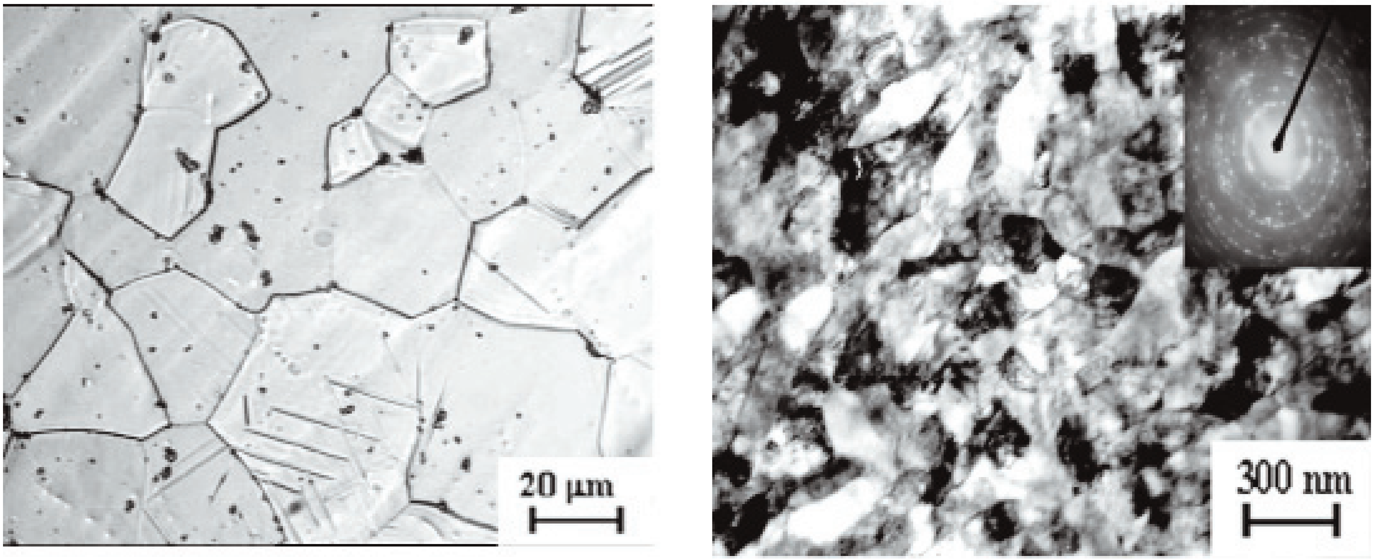

Exhibit 3: Mechanical Properties of Commercial Grade Titanium

	Yield Strength	Tensile Strength	Elongation	Fatigue Limit R=0.1, 10^7 cycles air
	MPa	MPa	Pct	MPa
Grade 2				
Annealed	370	420	25	225
SPD	900	1000	10	500
Grade 4				
Annealed	480	550	25	300
SPD	1050	1200	10	600

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Finally, ongoing clinical trials by Timplant® have also confirmed the benefits of nanostructuring. This involved redesign of a dental implant under standard EN ISO 13485:2003, the nanoimplant intraosseal diameter being reduced from 3.5 to 2.4 mm, Exhibit 6, while maintaining the load-carrying capacity of the older implant design. To date, over 250 Nanoimplants® have been implanted, with all results indicating the excellent primary stability of the Nanoimplants when compared to other implant types. For example, a male 55 years of age with edentulous mandible and maxilla was treated by insertion of conical implants laterally and Nanoimplants in the narrow anterior part. Primary retention of all implants was very good; on the day of surgery the patient received a complete provisional bridge. Healing of the operative wound passed without complications, with subsequent attachment of a definitive metalloceramic bridge completing treatment.

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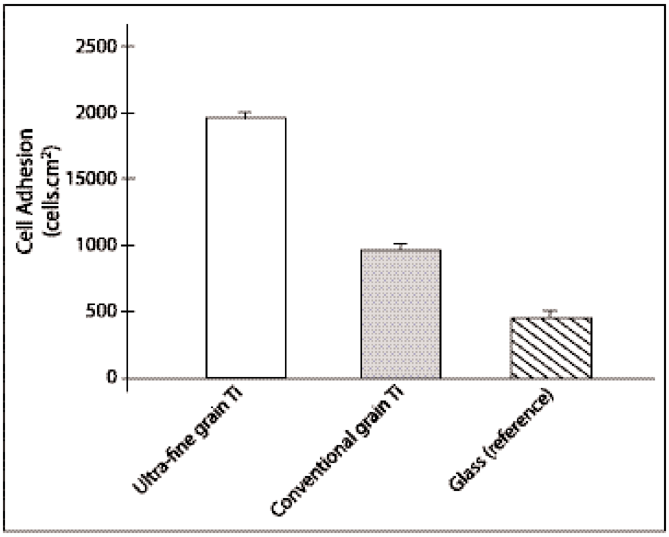
Exhibit 4: Osteoblast cellular response of grade 2 commercial purity titanium



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This short review has suggested that synthesis of new titanium alloy chemistries and processing techniques offer the opportunity of providing major enhancements in patient treatment through increased prosthetic device performance.

Dr. Rack has over 25 years of experience in advanced materials. He has published over 250 referred journal publications, is the inventor of several titanium and metal matrix composites and is a Fellow of ASM International having also been presented a Humboldt Research Prize in Metal Physics. Dr. Rack may be reached at rackh@exchange.clemson.edu.

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Exhibit 5: Occupation of the mice fibroblast cells L929 after 24 hours; nanostructured (ltop) and conventionally processed (bottom) CP Grade 4 titanium

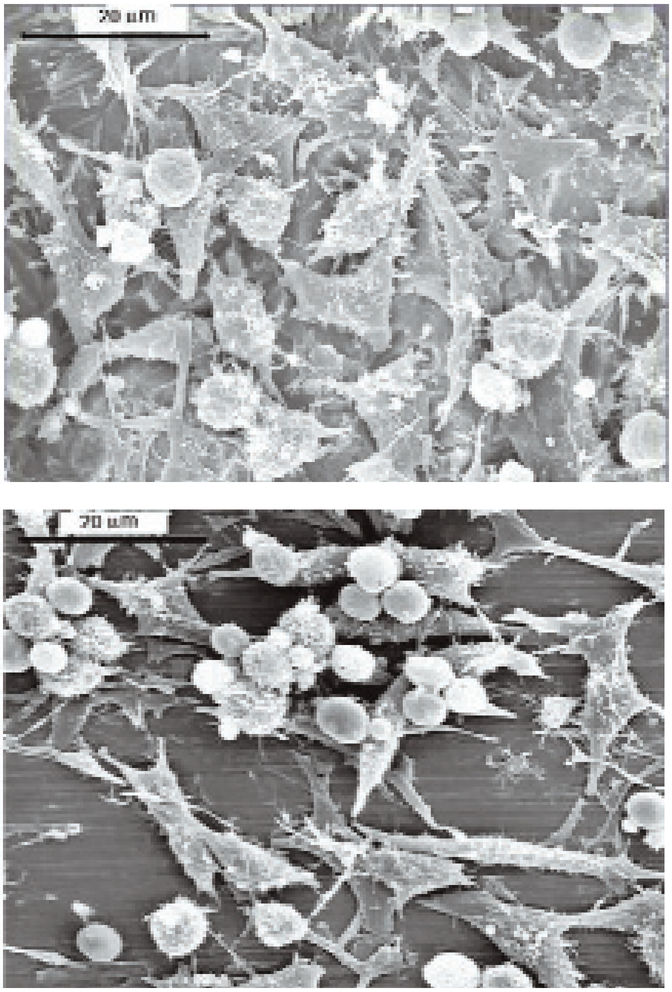

Exhibit 6: 3.5 mm diameter Timplant (above) and 2.4 mm diameter Nanoimplant (below)