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Ti based biomaterials, the ultimate choice for orthopaedic implants – A review

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A R T I C L E I N F O

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A B S T R A C T

The field of biomaterials has become a vital area, as these materials can enhance the quality and longevity of human life and the science and technology associated with this field has now led to multi-million dollar business. The paper focuses its attention mainly on titanium-based alloys, even though there exists biomaterials made up of ceramics, polymers and composite materials. The paper discusses the biomechanical compatibility of many metallic materials and it brings out the overall superiority of Ti based alloys, even though it is costlier. As it is well known that a good biomaterial should possess the fundamental properties such as better mechanical and biological compatibility and enhanced wear and corrosion resistance in biological environment, the paper discusses the influence of alloy chemistry, thermomechanical processing and surface condition on these properties. In addition, this paper also discusses in detail the various surface modification techniques to achieve superior biocompatibility, higher wear and corrosion resistance. Overall, an attempt has been made to bring out the current scenario of Ti based materials for biomedical applications.

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1. Introduction

The field of biomaterials gained its due recognition after the first meeting held on biomaterials at Clemson University, South Carolina in 1969 and continues to receive substantial attention since then. Biomaterials are artificial or natural materials, used to in the making of structures or implants, to replace the lost or diseased biological structure to restore form and function. Thus biomaterial helps in improving the quality of life and longevity of human beings and the field of biomaterials has shown rapid growth to keep with the demands of an aging population. Biomaterials are used in different parts of the human body as artificial valves in the heart, stents in blood vessels, replacement implants in shoulders, knees, hips, elbows, ears and orodental structures [1–3]. It is also used as cardiac simulator and for urinary tract reconstruction. Amongst all these, the number of implants used for spinal, hip and knee replacements are extremely high. Human joints suffer from degenerative diseases such as arthritis leading to pain or loss in function. The degenerative diseases lead to degradation of the

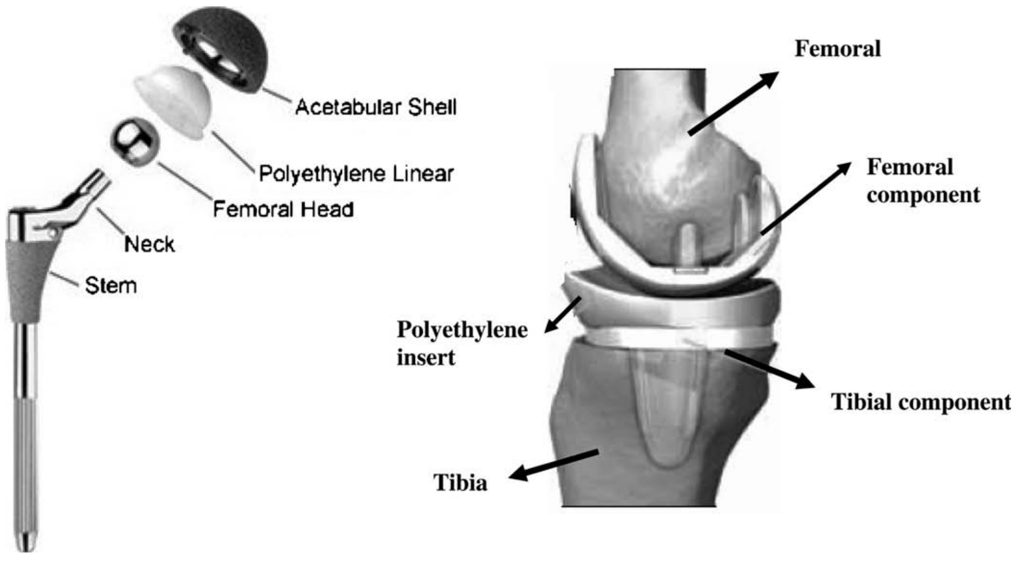

Fig. 1. Total hip and knee implants replacements (THR and TKR).

mechanical properties of the bone due to excessive loading or absence of normal biological self-healing process. It has been estimated that 90% of population over the age of 40 suffers from these kinds of degenerative diseases and the aged people population has increased tremendously in recent past and it is estimated there will be a seven times increase (from 4.9 million which was in 2002 to 39.7 million by 2010) [4]. Musculoskeletal disorders are most widespread human health problem which is costing around 254 billion dollars to the society [5]. Artificial biomaterials are the solutions for these problems, as surgical implantation of these artificial biomaterials of appropriate shapes help in restoring the function of the otherwise functionally compromised structures. Examples of an implant used in hip and knee joints are shown in Fig. 1. There is tremendous increase in the demand for the new long lasting implants, as the data collected on total joint replacements surgery it is estimated that by the end of 2030, the number of total hip replacements will rise by 174% (572,000 procedures) and total knee arthoplasties is projected to grow by 673% from the present rate (3.48 million procedures) [6]. The reason for joint replacements is attributed to diseases such as osteoporosis (weakening of the bones), osteoarthritis (inflammation in the bone joints) and trauma. Not only the replacement surgeries have increased, simultaneously the revision surgery of hip and knee implants have also increased.

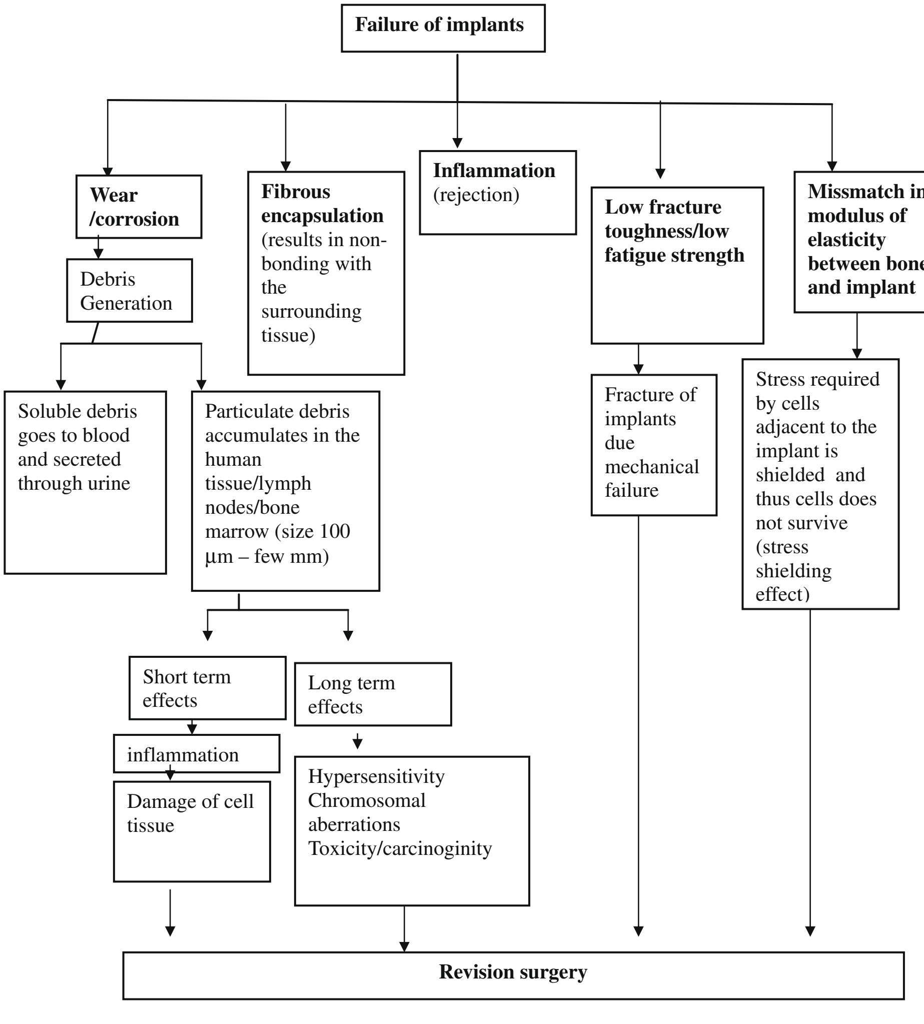

Fig. 2. Various causes for failure of implants that leads to revision surgery.

These revision surgeries which cause pain for the patient, is very expensive and also their success rate is rather small. The total number of hip revision surgery is expected to increase by 137% and knee revision surgery by 607% between the years 2005 and 2030 [6]. Thus a very high boom in implant manufacturing is expected in coming years. Ever-increasing demand for implants makes it imperative that development efforts on biomaterials have been accelerated. The materials used for orthopedic implants especially for load bearing applications should possess excellent biocompatibility, superior corrosion resistance in body environment, excellent combination of high strength and low modulus, high fatigue and wear resistance, high ductility and be without cytotoxicity [7,8]. Presently, the materials used for these applications are 316L stainless steel, cobalt chromium alloys, and titanium-based alloys. Unfortunately, these materials have exhibited tendencies to fail after long-term use due to various reasons such as high modulus compared to that of bone, low wear and corrosion resistance and lack of biocompatibility. The various causes for revision surgery are depicted in Fig. 2. Yet another acceptable reason for the increase in the number of revision surgeries is due to the higher life expectancy. Earlier, THR was performed for patients below the age of 65 and hence the expected longevity of orthopedic implants was considered only for about 15 years [9]. However, the scenario has changed now, due to the advancements in medical technology people live longer, in addition, the prognosis is better for those who are physically traumatized due to sports or incorrect or over exertive exercise habits or due to road traffic and other accidents. Thus, the implants are now expected to serve for much longer period or until lifetime without failure or revision surgery. Thus, development of appropriate material with high longevity and excellent biocompatibility is highly essential. While several materials are currently in use as biomaterials, titanium alloys are fast emerging as the first choice for majority of applications. This paper presents an overview of various aspects of titanium alloys that make this material an ideal choice for bio-applications. The article is divided into ten sections, starting with the requirements to be fulfilled by biomaterials, the status of the current biomedical materials and their limitations, classification of titanium alloys, structure property correlations, effect of heat treatment on modulus, wear and corrosion properties of biomedical alloys and their remedies, surface modifications required for high resistance to wear and corrosion and enhanced osseointegration and biocompatibility issues of titanium alloys and future biomaterials.

2. Requirements of a biomaterial

The design and selection of biomaterials depend on the intended medical application. Development of new biomaterials is an interdisciplinary effort and it often requires a collaborative effort between material scientists and engineers, biomedical engineers, pathologists and clinicians. In order to serve for longer period without rejection an implant should possess the following attributes:

2.1. Mechanical properties

The mechanical properties decide the type of material that will be selected for a specific application. Some of the properties that are of prime importance are hardness, tensile strength, modulus and elongation. The response of the material to the repeated cyclic loads or strains is determined by the fatigue strength of the material and this property determines the long-term success of the implant subjected to cyclic loading. If an implant fractures due to inadequate strength or mismatch in mechanical property between the bone and implant, then this is referred to as biomechanical incompatibility. The material replaced for bone is expected to have a modulus equivalent to that of bone. The bone modulus varies in the magnitude from 4 to 30 Gpa depending on the type of the bone and the direction of measurement [10,11]. The current implant materials which have higher stiffness than bone, prevent the needed stress being transferred to adjacent bone, resulting in bone resorption around the implant and consequently to implant loosening. This biomechanical incompatibility that leads to death of bone cells is called as “stress shielding effect” [12]. Thus a material with excellent combination of high strength and low modulus closer to bone has to be used for implantation to avoid loosening of implants and higher service period to avoid revision surgery.

Table 1
Classification of biomaterials based on its interaction with its surrounding tissue.

Classification	Response	Examples	Effect
Biotolerant materials	Formation of thin connective tissue capsules (0.1–10 μm) and the capsule does not adhere to the implant surface	Polymer-poly tetra fluorethylene (PTFE), polymethyl metha acralyte (PMMA), Ti, Co–Cr, etc.	Rejection of the implant leading to failure of the implant
Bioactive materials	Formation of bony tissue around the implant material and strongly integrates with the implant surface	Bioglass, synthetic calcium phosphate including hydroxyl apatite (HAP)	Acceptance of the implant leading to success of implantation
Bioreabsorbable materials	Replaced by the autologous tissue	Polylactic acid and polyglycolic polymers and processed bone grafts, composites of all tissue extracts or proteins and structural support system	Acceptance of the implant leading to success of implantation

2.2. Biocompatibility

The materials used as implants are expected to be highly non toxic and should not cause any inflammatory or allergic reactions in the human body. The success of the biomaterials is mainly dependent on the reaction of the human body to the implant, and this measures the biocompatibility of a material [13]. The two main factors that influence the biocompatibility of a material are the host response induced by the material and the materials degradation in the body environment. The classification of biomaterials based on the response by the human body is given in Table 1. Bioactive materials are highly preferred as they give rise to high integration with surrounding bone, however, biotolerant implants are also accepted for implant manufacturing. When implants are exposed to human tissues and fluids, several reactions take place between the host and the implant material and these reactions dictate the acceptability of these materials by our system. The issues with regard to biocompatibility are (1) thrombosis, which involves blood coagulation and adhesion of blood platelets to biomaterial surface, and (2) the fibrous tissue encapsulation of biomaterials that are implanted in soft tissues.

2.3. High corrosion and wear resistance

The low wear and corrosion resistance of the implants in the body fluid results in the release of non compatible metal ions by the implants into the body. The released ions are found to cause allergic and toxic reactions [14]. The service period of the material is mainly determined by its abrasion and wear resistance. The low wear resistance also results in implant loosening and wear debris are found to cause several reactions in the tissue in which they are deposited [15]. Thus development of implants with high corrosion and wear resistance is of prime importance for the longevity of the material in the human system.

2.4. Osseointegration

The inability of an implant surface to integrate with the adjacent bone and other tissues due to micromotions, results in implant loosening [16]. A fibrous tissue is formed between the bone and the implant, if the implant is not well integrated with the bone [16]. Hence, materials with an appropriate surface are highly essential for the implant to integrate well with the adjacent bone. Surface chemistry, surface roughness and surface topography all play a major role in the development of good osseointegration.

3. Currently used metallic biomedical materials and their limitations

The materials currently used for surgical implants include 316L stainless steel (316LSS), cobalt chromium (Co–Cr) alloys and titanium and its alloys. Elements such as Ni, Cr and Co are found to be released from the Stainless steel and cobalt chromium alloys due to the corrosion in the body environment [17]. The toxic effects of metals viz., Ni, Co and Cr released from prosthetic implants have been reviewed by Wapner [18]. Skin related diseases such as dermatitis due to Ni toxicity have been reported and numerous animal studies have shown carcinogenicity due to the presence of Co [19]. In addition, both 316L SS and Cr–Co alloys possess much higher modulus than bone, leading to insufficient stress transfer to bone leading to bone resorption and loosening of implant after some years of implantation. The high cycle fatigue failure of hip implants is also reported as the implants are subjected to cycles of loading and unloading over many years [20]. Amongst the materials available for implant applications, the natural selection of titanium-based materials for implantation, is due to the combination of its outstanding characteristics such as high strength, low density (high specific strength), high immunity to corrosion, complete inertness to body environment, enhanced biocompatibility, low modulus and high capacity to join with bone and other tissues [21] Coming to Ti alloys, their lower modulus varying from 110 to 55 GPa compared to 316 L stainless steel (210 GPa) and chromium cobalt alloys (240 GPa), which have been used for the past several years is a very positive factor. The modulus of elasticity of various biomedical alloys is compared with bone and shown in Fig. 3. Attempts to use titanium for implant fabrication dates back to the late 1930s when it was found that titanium was well tolerated in cat femurs, like other implant materials such as stainless steel and vitallium (a CoCrMo alloy). Commercially pure Ti and Ti–6Al–4V ELI (Ti64, Extra Low interstitial) are most commonly used titanium materials for implant applications. In spite of the fact that Ti64 was originally developed for aerospace applications, its high corrosion resistance and excellent biocompatibility led its entry into biomedical industry. Apart from the implant applications titanium alloys are used in healthcare goods such as wheel chairs, artificial limbs, artificial legs etc owing to their excellent compatibility and non-allergic nature. The alloys such as Ti–4.2Fe–6.9Cr (TFC) and Ti–4Fe–6.7Cr–3Al (TFCA) are being evaluated for making wheel chair frame as the weight of the chair made out of these alloys is calculated to be just 50% of pure titanium [22]. The strength of the titanium alloys is very close to that of 316 L SS, and its density is 55% less than steel, hence, when compared by specific strength (strength per density), the titanium alloys outperform any other implant material. Commercially pure (CP) titanium materials and some of its important alloys employed in the field of biomedical devices along with their mechanical properties are listed in Table 2. The range of application of titanium and its alloys in medical area is truly astonishing. The applications cover dental implants

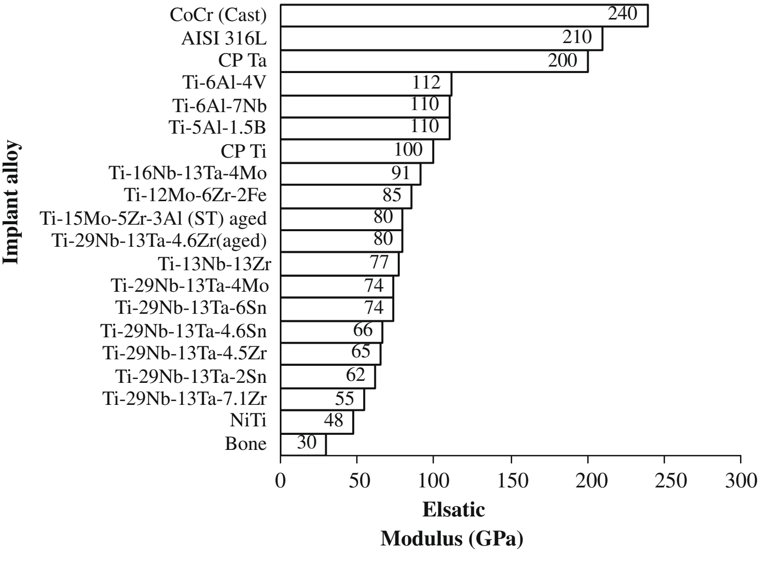

Fig. 3. Modulus of elasticity of biomedical alloys.

Table 2
Mechanical properties of biomedical titanium alloys.

Material	Standard	Modulus (GPa)	Tensile strength (Mpa)	Alloy type
First generation biomaterials (1950–1990)				
Commercially pure Ti (Cp grade 1–4)	ASTM 1341	100	240–550	α
Ti–6Al–4V ELI wrought	ASTM F136	110	860–965	α + β
Ti–6Al–4V ELI Standard grade	ASTM F1472	112	895–930	α + β
Ti–6Al–7Nb Wrought	ASTM F1295	110	900–1050	α + β
Ti–5Al–2.5Fe	–	110	1020	α + β
Second generation biomaterials (1990-till date)				
Ti–13Nb–13Zr Wrought	ASTM F1713	79–84	973–1037	Metastabe β
Ti–12Mo–6Zr–2Fe (TMZF)	ASTM F1813	74–85	1060–1100	β
Ti–35Nb–7Zr–5Ta (TNZT)		**55**	596	β
Ti–29Nb–13Ta–4.6Zr	–	65	911	β
Ti–35Nb–5Ta–7Zr–0.40 (TNZTO)		66	1010	β
Ti–15Mo–5Zr–3Al		82		β
Ti–Mo	ASTM F2066			β

and parts for orthodontic surgery, joint replacement parts for hip, knee, shoulder, spine, elbow and wrist, bone fixation materials like nails, screws, nuts and plates, housing device for the pacemakers and artificial heart valves, surgical instruments and components in high-speed blood centrifuges [23–25]. Although titanium and its alloys mainly Ti64 have an excellent reputation for corrosion resistance and biocompatibility, long-term performance of these alloys has raised some concerns due to release of aluminum and vanadium from Ti64 alloy. Both Al and V ions released from the Ti64 alloy are found to be associated with long-term health problems, such as Alzheimer disease, neuropathy and ostemomalacia [26]. In addition, vanadium is also toxic both in the elemental state and oxides V_2O_5, which are present at the surface [18,27] Further, titanium has poor shear strength, making it less desirable for bone screws, plates and similar applications. Titanium also tends to undergo severe wear when it is rubbed between itself or between other metals [28]. Titanium-based alloys that have a high coefficient of friction can lead to formation of wear debris that result in inflammatory reaction causing pain and loosening of implants due to osteolysis [29]. Owing to the above-mentioned limitations of the first generation materials listed in Table 2, the service period of the implants made out of them has been restricted to 10–15 years. This has stimulated biomedical researchers to develop an optimized prosthesis that mimics human bone. This has led to the development of low modulus beta titanium alloys that consist of compatible alloying additions and have modulus closer to that of bone which is discussed in detail in a later section. The low modulus alloys that are currently under research with great interest are given in Table 2. The mechanical, wear and corrosion properties of a material are largely dictated by its microstructure. Titanium alloys are privileged in a sense that a wide spectrum of microstructures is possible depending upon alloy chemistry and thermomechanical processing. This makes titanium alloys highly amenable to tailor its properties as per specific requirements. Though the structure property correlations have been well developed and critically addressed for structural titanium alloys, the role of microstructure is sparsely addressed in the case of alloys. Hence, the variations in properties of the implants alloys based on the microstructure is discussed in detail in the following section. A brief introduction to the physical metallurgy of the titanium alloys is provided as a background for better understanding.

4. Thermomechanical processing, microstructure and properties in titanium alloys

Titanium exists in two allotropic forms. At low temperatures it has a closed packed hexagonal crystal structure (cph), which is commonly known as α, whereas above 883 °C it has a body centered cubic structure (bcc) termed β. The α to β transformation temperature of pure titanium either increases or decreases based on the nature of the alloying elements. The alloying elements such as (Al, O, N, etc.) that tend to stabilize the α phase are called alpha stabilizers and the addition of these elements increase the beta transus temperature, while elements that stabilize β phase are known as beta stabilizers (V, Mo, Nb, Fe, Cr, etc.) and addition of these elements depress the β transus temperature. Some of the elements that do not have marked effect on the stability of either of the phase but form solid solutions with titanium are termed as neutral elements (Zr and Sn). However, work carried out by Geetha et al.[30]and Tang et al. [31] have shown that the addition of Zr stabilizes the β phase in Ti–Zr–Nb system.

The α and β phases also form the basis for normally accepted classification of titanium alloys. Alloys having only α stabilizers and consisting entirely of α phase are known as α alloys. Alloys containing 1–2% of β stabilizers and about 5–10% of β phase are termed as near α alloys. Alloys containing higher amounts of β stabilizers which results in 10–30% of β phase in the microstructure are known as α + β alloys. Alloys with still higher β stabilizers where β phase can be retained by fast cooling are known as metastable β alloys. These alloys decompose to α + β on aging. Most of the biomedical titanium alloys belong to α + β or metastable β class.

In all conventional titanium alloys, α to β transus temperature (known as β transus) plays a central role in evolution of microstructure and is of great technological importance in determining heat treatment and processing schedule. The various microstructures that are developed under different thermomechanical processing conditions are shown in Fig. 4. The alloys processed/heat treated above the β transus temperature result in acicular or lamellar structure and are typically known as β treated structure. When these alloys are mechanically processed below the β transus (α + β phase field) and heat treated in α + β phase region, the microstructure consists of a mixture of equiaxed α and β phases. Depending upon the alloy chemistry, heat treatment temperatures and cooling rate, volume fraction of equiaxed α and nature of β phases may change. In faster cooled structure, transformed β phase may constitute martensite or α laths along with the retained β, while on slow cooling the transformed β phase may entirely be retained β. In metastable β alloys, the β phase is usually retained on quenching from the β phase field and very fine α precipitates on aging at lower temperatures, which leads to extremely high strength in these alloys. The details of phase transformation and processing-microstructure-property relationships are reviewed in several papers and books [31–37].

The Ti–6Al–4V (Ti64) alloy is still the most commonly used α + β titanium biomedical alloy and is normally used in annealed condition. The metastable biomedical alloys are preferred in solution treated (ST) and, ST and aged conditions. The α + β treated structures have higher strength, higher ductility and higher low cycle fatigue while the β treated structures have higher fracture toughness. In general, strength of an alloy increases with increasing β stabilizer content. A typical example of the effect of oxygen on mechanical properties in Ti64 alloy is shown in Table 3. Representative properties for a few β alloys of biomedical interest along with their microstructures are presented in Table 4. Alloy chemistry and structural constituent appear to have significant influence also on elastic modulus of the alloys.

Since high modulus of α + β titanium alloys results in bone resorption and implant loosening, lower modulus alloys that retain a single phase β microstructure on rapidly cooling from high temperatures are attracting a great deal of interest. Further, theoretical studies of Song et al. [38] have shown that Nb, Zr, Mo, and Ta are the most suitable alloying elements that can be added to decrease the modulus of elasticity of bcc Ti without compromising the strength. It has been observed that addition of these alloying elements up to certain weight percentage decreases the modulus, beyond which increase in modulus is noted which is due to ω phase formation and precipitation of α on aging [33,39]. It is also interesting to note that these elements fall into the category of non-toxic elements, which make them more suitable for implant applications [40]. Based on these considerations the biomedical titanium alloys developed recently consist mainly of Ti, Nb, Ta and Zr. Alloys like Ti–29Nb–13Ta–4.6Zr, Ti–35Nb–7Zr–5Ta and several other compositions have now received considerable attention and investigated seriously [7,31,41,42]. Metastable beta alloys developed in the recent past include Ti–Mo–6Zr–2Fe (TMZF) [43], Ti–15Mo–5Zr–Al [44], Ti–15Mo–3Nb–3O TIMETAL 21SRx [45] and Ti–13Nb–13Zr [46].

Extensive research work is being currently pursued on beta alloys to understand the effect of alloying additions, processing parameters, and heat treatment procedures on the various aspects such as phase transformations and evaluation of microstructures, modulus of elasticity and deformation behavior, etc. The main objective of all these work is to develop a biomedical alloy with required properties that will increase the longevity of the implants.

The beta titanium alloys are generally solution treated in the beta phase field and aged to decompose the metastable phases and achieve high strength. In spite of the fact that variety of

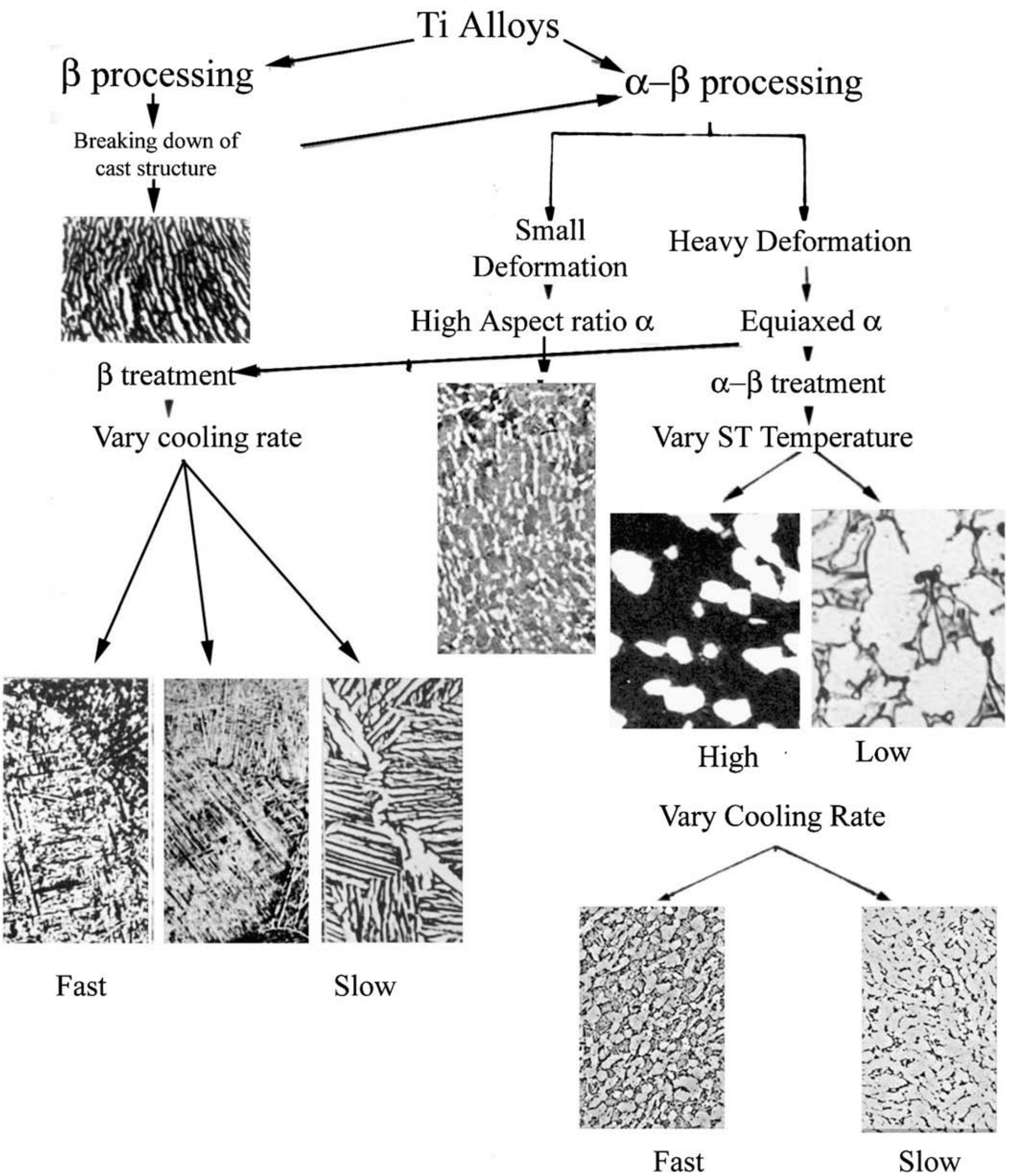

Fig. 4. Influence of thermomechanical processing on development of various microstructure in alpha beta titanium alloys.

Table 3
Mechanical properties of Ti–6Al–4V alloy with different oxygen content [20].

Oxygen content/microstructure	YS (MPa)	UTS (MPa)	EL (%)	RA (%)	K_{IC} (MPa/m ^{½})
0.15–0.2%, equiaxed	951	1020	15	35	61
0.15–0.2%, lamellar	884	949	13	23	78
0.13 Max equiaxed	830	903	17	44	91
0.18–0.2% equiaxed	1068	1096	15	40	54

Table 4
Phases formed in beta titanium alloys under different heat treatment.

Alloy composition	Heat treatment history	YS (MPa)	Modulus (GPa)	Microstructure
Ti–35Nb–7Zr–5Ta–(0.06–0.07) O	β ST/WQ + aging	530	–	β phase with average grain size ≈60 μm
	Low temperature aging (SA*)	630	–	Fine ω phase
	Double aging at low temperature(DA**)	1202	–	Fine α and ω phases
Ti–30Nb–10Ta–5Zr	HT/850 °C/30 min/AC	804	66.9	Equiaxed β phase with grain diameter of 62.3 μm
Ti–13Nb–13Zr	α + β ST/WQ	–	80	Primary alpha and transformed beta
Ti–29Nb–13Ta–4.6Zr	WQ from β field	–	65	Metastable β phase and orthorhombic martensite
	β ST/WQ	250	–	Metastable Orthorhombic martensite
	β ST at still lower temperature/WQ	400	–	Metastable Orthorhombic martensite
	Low temperature aging	1100	–	Metastable Orthorhombic martensite

* Single aging.
** Double aging.

microstructures can be formed in beta alloys by appropriate heat treatment, in particular, equiaxed structure in the beta alloys is tried with great interest, as equiaxed structure found to possess best combination of mechanical properties in the alpha beta alloys. It is important to note that thermomechanical processing of biomedical beta alloys has hardly received any attention and the first report on the effect of thermomechanical treatment on the development of equiaxed structure in Ti–13Nb–13Zr came out from the work of Geetha et al. [30]. In addition, their work consisted of development of equiaxed structure on two other new near β titanium alloys (Ti–13Nb–20Zr and Ti–20Nb–20Zr) obtained by appropriate thermomechanical procedures. The selection of appropriate processing window for Ti–13Nb–20Zr and Ti–20Nb–20Zr alloys resulted in fine equiaxed structure in these alloys, while a mixture of coarse equiaxed and elongated grains was observed in the case of Ti–13Zr–13Nb alloy. The presence of Nb in these alloys enabled working of these alloys at low temperatures, which led to the formation of fine equiaxed structure [30,32]. The concentrations of the alloying elements were selected to be less than 20 wt%, as further increase may lead to increase in the phase precipitation such as omega phase, which increases the strength and modulus of the alloy.

The modulus of elasticity of β alloys depends on the amount of beta phase present in the structure. Aging of beta alloys leads to increase in hardness and modulus due to precipitation of fine α phase. However, presence of fine α phase is not always associated with increases in strength and modulus. The origin of α and other microstructural features also decide these properties. For example, aging of Ti–34Nb–9Zr–8Ta (TNZT) results in low strength and modulus and this has been attributed to dissolution of the ordered B2 phase [26]. The B2 phase in homogenized conditions possesses higher hardness than the aged condition. In contrast to this, in TMZF (Ti–13Mo–7Zr–3Fe) alloy, both strength and modulus increase on aging due to precipitation of fine α from ω in the β native. Interestingly, in case of another alloy Ti–15Mo, the strength decreased and modulus increased [26] and this decrease in strength was due to the absence of nanometer scale ω phase on aging and increase in modulus was due to high volume fraction of fine α.

The low modulus β titanium alloy Ti–29Nb–13Ta–4.6Zr developed by the Japanese group [47] is reported to be an excellent candidate for biomedical applications whose modulus is 65 GPa. Extensive work performed on the effect of heat treatment on mechanical properties and biocompatibility has shown that β ST and aging at low temperature (below 400 °C) leads to high tensile strength and fatigue life in these alloys. This is attributed to the formation of fine α and ω phases on aging. The Young's modulus of this alloy can be reduced from 100 to 60 GPa by aging at approximate temperature of

400 °C [48]. In addition, biocompatibility studies of these alloys show good contact with bone and its cytotoxicity is found to be as good as pure titanium.

A systematic study on the deformation behavior of Ti–Nb–Ta–Zr alloy with varying composition of Nb and Ta was carried out by Nobuhito et al. [33] and it was shown that behavior of stress strain curve in these alloys depend upon Ta and Nb content [14]. The deformation mechanism in Ti–30Nb–XTa–5Zr alloys that contains less than 10 mass% of Ta is identified as SIM (Stress Induced Martensite) while above 10% it is identified as slip [35]. The concentration of Ta is very critical and has to be maintained within a limited range, because they tend to increase the modulus of elasticity if varied marginally. Nobuhito et al. have observed high modulus of elasticity of Ti alloys with 0 and 20 mass % of Ta and very low modulus for an alloy with 10 mass % of Ta addition [33]. This irregular variation viz., the high modulus of the alloy with 0 mass% of Ta was attributed to the presence of ω phase, while the low modulus of elasticity of the alloy with 10 mass % was ascribed to the presence of only β phase in the microstructure. Although, the alloy with 20 mass % Ta had only β phase, it exhibited high modulus because the high concentration in titanium alloy tends to behave like pure Ta metal rather than Ti alloy and exhibits modulus equivalent to that of Ta metal itself.. It was noted that the tensile strength for 0 and 5 wt% Ta additions were low in spite of the fact that the microstructure consisted of omega phase in beta matrix, possibly due to SIM in these alloys. Thus variation in the strength of the different alloys in Ti–Nb–Ta–Zr system with varying alloying concentrations could be attributed to various deformation mechanisms operating in these alloys. These variations in the strength and modulus due to alloying additions are shown in Figs. 5 and 6 and Table 5.

Rapid cooling from βST of the alloys Ti–(13–26) Nb–(23–38) Ta and Ti-(13–35.5) Nb–(5–22) Ta–(4–7.2) Zr leads to the formation of three phases viz., β + α″ + ω. The volume fraction of α″ is found to decrease with either increase in Nb + Ta or decrease in the cooling rate. In addition, the presence of Zr in the range (4.1–4.6 wt%) is also found to suppress α″ formation and only β + ω is formed on cooling [31]. The modulus of quaternary alloys was found to be highly sensitive to compositional variation and varies with Nb/Ta ratio. The quaternary alloy consisting Nb/Ta ratio of 12.0 at 5 at% Zr was found to exhibit minimum moduli on air cooling [31]. However, amongst all beta alloys developed, the alloy Ti–35Nb–7Zr–5Ta exhibits lowest elastic modulus of 55 GPa and good fatigue properties in the solution treated condition [49]. Duplex aging of this alloy (260 °C for 4 h plus 427 °C for 8 h) is found to result in optimum tensile yield and ultimate tensile strength compared to single aging treatment (260 °C for 4 h or 427 °C for 8 h). Further, extensive studies have been made on the effect of oxygen addition on the mechanical properties and phase transformations. Both increases oxygen content

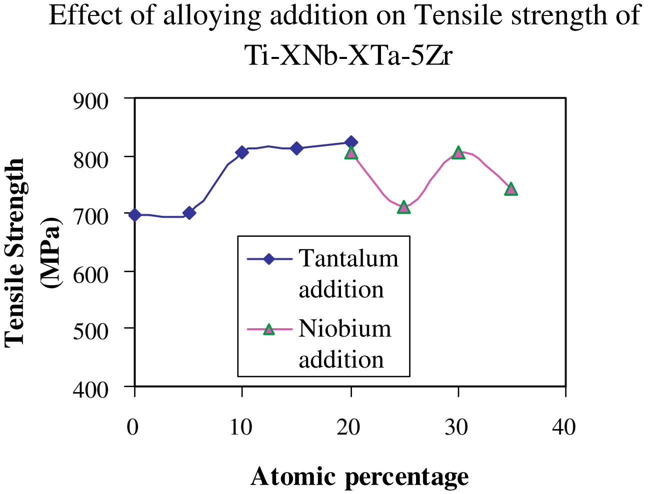

Fig. 5. Effect of alloying additions on tensile strength of Ti–XNb–XTa–5Zr alloy.

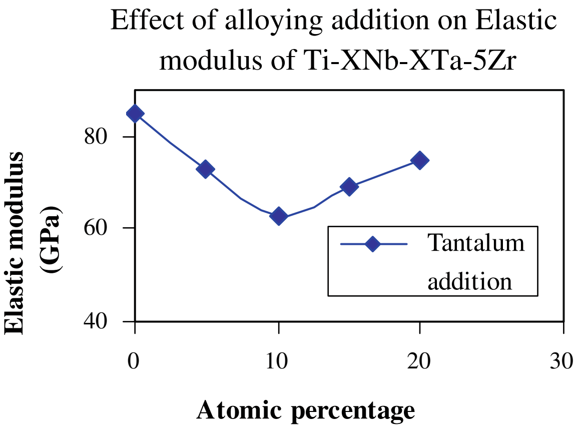

Fig. 6. Effect of the tantalum addition on the modulus Ti–Zr alloy.

Table 5
Effect of alloying addition on the mechanical properties of beta Ti alloys.

Alloying addition	Tensile strength (Mpa)	0.2% Proof stress (Mpa)	Elongation (%)	Reduction in area (%)	Elastic modulus (Gpa)
Ti–30Nb–XTa–5Zr					
0Ta–20Ta	698–823	572–798	19.3–43.8 (decreases with increase in Ta)	51.3–73.0 (decreases with increase in Ta)	74.8–85.2 (decreases with increase in Ta)
Ti–XNb–Ta–5Zr					
20Nb–35Nb	742–806 (decreases with increase in Nb)	704–779 (decreases with increase in Nb)	11.6–22.6	19.0–62.4	–
Ti–XNb–13Ta–4.6Zr					
29Nb–39Nb	715 612	590 600	15 22	– –	– –
Ti–35Nb–7Zr–5Ta–XO					
0.0 O–0.68	590–1074	–	21–27	47–69	

and duplex aging were found to increase the YS of this alloy on aging, due to ω and or α phase precipitation. The increase in the strength due to presence of ω phase in metastable β alloys is well understood. However, the influence of oxygen on ω phase formation and strengthening mechanism of the metastable alloys due to oxygen were not clear till recent past. Qazi et al. have recently carried out extensive studies on the influence of oxygen (ranging from 0.06 to 0.7 wt%) and duplex aging on the phase transformation behavior of the Ti–35Nb–7Zr–5Ta alloy [50]. They observed that 0.7 wt of O completely suppresses the ω phase formation and concluded that the high YS of the alloy with 0.7% O was due to the presence of the fine α precipitate only. Increasing oxygen above a certain (>0.46 wt%) level inhibits ω formation by oxygen occupying the interstitial sites within the beta and resisting atomic displacements that can lead to ω formation. In addition, increase in α precipitates in the absence of ω phase has been attributed to the formation of oxygen rich clusters within the prior β grain boundaries and these clusters act as nucleation sites for α precipitation [50].

Very recently, Taneichi et al., have intensively and extensively studied the cold workability of 38 different beta titanium alloys, which could be used in the form of fine wires and thin sheets for the fabrication of biomedical stents and electrodes for electrical stimulations. They varied the composition

Nb, Zr, Ta and Fe in the two base alloys; Ti –10Mo–2Fe and Ti–14Mo and evaluated the hardness at various solution treated conditions and rolling reduction ratio. Out of 38 compositions, they finally arrived at an optimum composition Ti–14Mo–3Nb–1.5Zr, as this alloy exhibited good cold workability and is also of low cost, as it is free from the alloying addition Ta. Excellent cold workability which was obtained, is attributed to the presence of stable beta phase at low temperature. In addition, the biocompatibility of this alloy was found to be equivalent to the other biomedical titanium alloys that are currently in use [51]. However, this alloy exhibited high passive current density than conventional biomedical titanium alloys due to the presence of Mo in solid solution state in the passive film. Further, the modulus (90 Gpa) of this alloy was found to be higher than the other beta biomedical titanium alloys.

Formation of nanostructured α phase from ω precursor is expected to enhance the biocompatibility of Ti–6Mo–3Fe–5Ta and Ti–4Mo–2Fe–5Ta and Ti–6Mo–3Fe–5Ta –5Zr systems as the bio molecules favor microstructure on nano scales for better cell attachment [52]. Fe is a low cost β stabilizing element and attempts have been made to develop the following β titanium alloys: Ti–8Fe–8Ta, Ti–8Fe–8Ta–4Zr and Ti–10Fe–10Ta–4Zr. While Ti–8Fe–8Ta and Ti–8Fe–8Ta–4Zr alloys exhibit higher tensile strengths in cold forged conditions, Ti–10Fe–10Ta–4Zr shows higher tensile strength than the other two alloys in solution treated condition. However, Ti–10Fe–10Ta–4Zr in solution treated condition has lower ductility than the other two alloys. These alloys are found to possess higher strengths than the conventional Ti–6Al–4V and Ti–13Nb–13Zr systems. Also, on aging, the rate of α precipitate is found to decrease with increase in Ta content [34].

Recently an alternative method called Equal Channel Angular Pressing (ECAP) has been attempted to develop fine grain structure in grade 2 CP Ti. This process resulted in enhanced hardness, higher Yield strength (increase by 140%) and higher fatigue strength (increase by 100%) compared to the coarse-grained materials [53]. The experiments carried out by He et al [54] also revealed that combination of high strength and low modulus can be obtained in titanium-based alloys by proper combination of composition design and production method. The alloy composition was developed using an empirical relationship and was melted using copper mold casting. The resultant material had a novel combination of bimodal microstructure that consisted of a micrometer-sized dendritic β-phase and a nano/ultrafine-structured matrix. This bimodal structure possessed high strength of the nano/ultrafine-structure and the good ductility of the bcc-structured dendrites.

Thus from the above discussions it is evident that proper selection of alloying elements with right compositions and an appropriate thermomechanical treatment are highly essential to have a material with high strength and low modulus. The effect of each alloying element on phase transformation and resultant microstructure should be well understood in designing an implant material to achieve optimum properties.

5. Wear in biomedical alloys

Loosening of total joint replacements made of metal head and polymer cup has been reported often and 10–20% of joints need to be replaced within 15–20 years and the aseptic loosening accounts for approximately 80% of the revisions [55–57]. Noteworthy is the fact that knee replacement surgery (TKR)is performed on more than 2.5 million people in USA alone annually, followed by total hip joint replacement (TJR) of more than 3.5 million and around 7 million spinal fusions [58]. As younger, more active patients are diagnosed with joint osteoarthritis, the restricted life span of artificial joints is becoming an increasing concern for the medical community. Improving the fixation and wear characteristics of total joint components is a major focus of orthopedic research. The reason for the failure of the implants is due to the release of wear debris from the implant into the surrounding tissue that results in bone resorption, which ultimately leads to loosening of the implant (Fig. 7). The consequences of this process lead to the implant loosening and hence the implant has to be replaced by a new one. The revision surgery is not only expensive, its success rate is less compared to the first implantation. Further, the presence of foreign particles such as cement particles, metal beads or hydroxyapatite derived from coating aggravates the production of wear debris at the interface. Post-mortem studies of the patients who have received total hip or knee replacements demonstrated that accumulation of

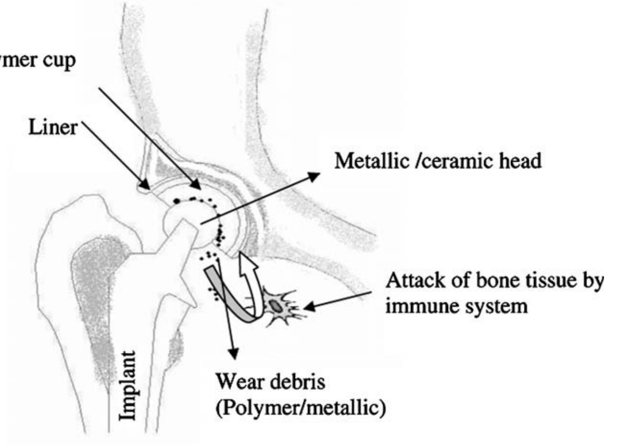

Fig. 7. Wear of implant.

wear particles in the liver, spleen or abdominal lymph nodes is a common occurrence in patients. Knee joints that operate as dynamically loaded bearing are subjected to 10^8 cycles of loading in 70 year lifetime. The average coefficient of friction of the load bearing synovial joints such as hip and knee is about 0.02 and the wear factor is about 10^6 mm^3/N. On the other hand the coefficient of friction for implant materials varies from 0.16 to 0.05 depending upon the materials that are in contact and the kind of lubricant used for testing. The most common type of hip joint comprises femoral head articulating against an ultra-high-molecular weight polyethylene (UHMWPE) accetabular cup. From the implant retrieval studies of femoral head of cobalt–chrome–molybdenum (Co–Cr– Mo), 316L stainless steel (SS) and titanium –aluminium –vanadium (Ti–6Al–4V) alloy that were loosened by aseptic loosening, it was noted that titanium alloy femoral heads consistently had the maximum wear averaging 74.3% against high molecular weight polyethylene acetabular component. Co–Cr alloy was found to wear the least and wear of SS was in between Co–Cr and Ti alloy. Further, high metal concentrations were found in tissue taken from the region around Ti alloy prostheses, while, the metals debris level were low in the tissues surrounding the CoCr and SS that were articulating against polyethylene [59]. In order to overcome this wear related and hence the revision surgery, there has been continuous effort to change the cup material from polymer to metal or ceramic Thus, the long-term problems associated with UHMWPE wear debris have led to explore the possibility of the use of metal on metal prostheses. Metal on metal prostheses is found to produce 20–100 times lower wear volumes compared to metal on polyethylene bearing [60]. The biological reaction to metal particles *in vivo* has been shown to be markedly different to that produced by UHMWPE wear debris and lower inflammatory reactions are found to be caused by metal [61]. However, it has also been observed that metal on metal prosthesis exhibits high frictional torques than the metal on polymer [48]. Though the metal on metal prosthesis produces low wear volume, there is concern for the effect of the metal particles released after long duration. Both the *in vivo* and *in vitro* studies have shown that CoCr particles have toxic effects on different cells and tissues. Ceramic on ceramic (Alumina) was introduced 20 years back as they exhibited much less wear than the metal (CoCr) on polymer and metal on metal. However, fracture of these implants and release of ceramic wear particles are also observed frequently. When the toxicity of CoCr wear particles of nanometre size was tested for its cytocompatibility, it showed high toxicity when compared to the ceramic wear particles that were obtained from the implant made of alumina [62]. The other ceramic material used for implant applications is zirconia, which was considered to be a better alternative for alumina as alumina is highly brittle. Zirconia exhibits best mechanical properties and have high resistance to crack propagation. Today more than 6,00,000 zirconia head implants have been fixed and it is more frequently used in USA and Europe than any other countries. However, there are few cases in which the implant failed early due to ageing phenomena; and these results are also not consistent with all the implants as different processing methods change the microstructure and hence the mechanical properties. There is a trend today to develop alumina–zirconia composites thus to utilize the toughness of alumina and zirconia transformation via toughening .Though various combinations are being tried, 80% zirconia and 20% alumina with high bending strength (2000 MPa) and implant made of 75% alumina and 25% zirconia with mechanical properties such as high strength (1150 MPa) and toughness of (8.5 MPa$\sqrt{}$m) seems to be very promising. However, the success of any new implant can be evaluated only after long period of implantation, and more studies are required for its final application. Thus there is continuing interest to develop a composite made of ceramic materials that will possess low friction of coefficient and low wear rate [63]. Though material choice is a major concern in the field of implant surgery, the other major problem in this area of research is related to the results obtained using in vitro wear testing. There is a wide variation between the wear rate determined *in vivo* (1–5 mm^3 per annum) and in vitro using hip motion simulating machines (0.01–0.1 mm^3/million cycles) [64]. The reason for the difference in the wear rate between *in vivo* and *in vitro* is attributed to several factors such as type of lubrication, angle of inclination of the actebalur cup and kind of motion between the mating pair. In actual motion of the patient with the implant, there is very small (micron level) separation between the ball and the socket during the swing phase of walking. When the microseparation was introduced in the in vitro wear testing, wear rate observed clinically was attained. Tipper et al introduced the harsh environment to produce the microseparation while testing the ceramic on ceramic and found that the wear rate of this combination was very less (2 mm^3 per million cycles) compared to the acetabular cup made of polyethylene (30–100 mm^3) for the same number of cycles. Some research findings have proved that there is no lubrication provided for the TJR in *in vivo* conditions [7,29–32]. A detailed study has been carried out to understand the difference in the lubrication modes and friction for a range of material combinations such as metal on polymer, metal on metal and ceramic on polymer. It was observed that the wear behaviour not only changes with the type of materials and also the mode of lubrication which was developed by the lubricant used for testing. Ceramic on ceramic, exhibited the lowest friction when tested in carboxy methyl cellulose (CMC) and highest when tested with the biological fluid (bovine serum). On the other hand metal on metal pair exhibited high friction coefficient when tested with CMC and lowest wear rate when tested in bovine serum. Though titanium and its alloys are materials of choice for implantation, due to their several favorable characteristics as enumerated earlier, its application in articulating surfaces remains somewhat limited owing to its poor tribological properties. The poor tribological property of titanium is due to its low resistance to plastic shearing and low protection induced by surface oxides [65]. Though Ti64/UHMWPE combination is used in TJR prosthesis, the wear rate of UHMWPE for Ti64 is found to be 35% greater than for Co–Cr–Mo in hip simulator testing. This high wear rate of UHMWPE is attributed to the mechanical instability of metal oxide layer. Further, wear of Ti64 femoral head is observed due to the presence of foreign bodies in UHMWPE counterpart component. Surface oxides, thus play an important role in influencing the wear behavior and optimization of surface oxide properties through bulk or surface chemical modification can ameliorate this problem. In addition to the surface characteristics, a high strain deformation occurring in near surface zone during wear is also of great importance. The process that occurs during wear is described in detail by Long et al. [66]. Fretting wear studies and sliding wear studies performed on Ti–35Nb–6Zr–5Ta by this group showed that mechanism of particle detachment is related to plastic deformation of superficial layers and formation of triboligically transformed layer (TTS) below the wear track. The formation of TTS was ascribed to deformation-induced transformation and this layer was formed of ultra fine grains of α-Ti with no β phases. Stress induced α'' and twinnings around wear scratches were also reported from their work. Fretting test performed on three other titanium alloys also had similar findings [66]. The fretting tests on two $\alpha + \beta$ alloys Ti64, Ti–5V–3Al–3Cr–3Sn and β alloy Ti–15V–3Al–3Cr in air resulted in the formation of particles and hard triboligically transformed structure that consisted of ultra fine grains α-Ti (20–50 nm diameter). The resultant wear particles were seen to quickly oxidize at interface leading to third body abrasive wear. Fretting wear studies of Ti64, Ti–5Al– 2.5Fe, Ti–13Nb–13Zr and Co–28Cr–6Mo alloys against steel ball in Hanks solution showed that coefficient of friction was lowest for Ti–5Al–2.5Fe and maximum for CP Ti [67]. Scanning electron microscopic investigation on the worn out surfaces suggested that wear was due to abrasion, plastic deformation and cracking. The wear behavior of a material is highly dependent on various factors such as load, velocity, type of displacement and the mating material. Reciprocating sliding wear resistance of Ti–35Nb–8Zr–5Ta against hardened steel was found to be superior than Ti64 at a low contact stress of 1.5 MPa, while the reverse was observed at higher contact stress of 5 MPa [68]. The subsurface deformation behavior is found to change with contact stress from twinning at low stress to slip at high stress. Wear surface investigations revealed three distinct zones, a chemically altered tribo-layer, a plastic shear zone and a plastic deformation zone. Further, when the wear surface was examined using Transmission Electron Microscope (TEM), slip bands intersections with other slip bands were found to increase with increasing strain. These regions of intersecting slip bands are not able to dissipate the strain energy associated with them and are found to become the sites for micro crack nucleation. Another, new low modulus alloy Ti15Mo–2.5Nb–0.3O also exhibits a similar trend at two different contact stresses. It possesses very low wear at high contract stresses which is due to inefficient way of dissipating strain energy at high contact stresses. Though the mode of wear is insensitive to heat treatment procedures, the presence of oxides at the surface is found to influence the wear behavior of a material and the repassivation characteristics. Titanium alloys with high Nb are found to be highly beneficial with respect to wear as Nb_2O_5 possesses very good lubricating properties [69–71] which is due to the fact that Nb repassivates more quickly and the passive film seems to stay longer than the low Nb alloy [7]. The enthalpy of formation of Nb element with oxygen is much higher than that of V or Al, hence, TNZT alloy is more wear resistant than Ti64. Development of nanograined materials is currently being pursued with vigorous interest as they exhibit superior tribological properties. Ultra fine-grained CP Ti is found to exhibit high wear resistance compared to the coarse-grained materials. However, the same trend is not observed in the case of fine-grained Ti–6Al–4V material processed via Equal Channel Angular Pressing (ECAP) where only a marginal increase in the wear resistance is observed.

6. Corrosion behavior of biomedical titanium alloys

All metals and alloys are subjected to corrosion when in contact with body fluid as the body environment is very aggressive owing to the presence of chloride ions and proteins. A variety of chemical reactions occur on the surface of a surgically implanted alloy. The metallic components of the alloy are oxidized to their ionic forms and dissolved oxygen is reduced to hydroxide ions. While there are many forms of corrosion damage, the rate of attack of general corrosion is very low due to the presence of passive surface films on most of the metallic implants that are presently used. Crevice attack refers to corrosion at shielded sites such as screw/plate interface and under washers. This is often observed in 316L stainless steel and other passive alloys in the presence of chlorides. Crevice corrosion is encountered beneath the heads of fixing screws made of 316L stainless steel and mechanically assisted crevice corrosion of modular total hip arthroplasty components has been associated with elevations in serum cobalt and urine chromium [72]. Pitting corrosion is a common problem with 304 SS implants. Pitting corrosion of the implants is more predominant in the oral cavity due to the greater availability of oxygen and acidic food stuffs in the environment. Introduction of ultra-high clean grades such as 316LVM and nitrogen additions have reduced the risk of pitting corrosion. Pitting corrosion of cobalt based alloys leads to the release of carcinogens into the body [73–75]. Though titanium and its alloys are highly resistant to pitting corrosion in different *in vivo* conditions encountered, they undergo corrosion in high fluoride solutions in dental cleaning procedures [76]. Most of the medical implants are subjected to low frequency loads that may lead to corrosion fatigue as even simple walking results in a hip implant being subjected to a cyclic loading at about 1 Hz. Fatigue corrosion resistance of titanium is almost independent of the pH value while the fatigue corrosion strength of stainless steel declines below pH 4. According to Yu et al. the pitting corrosion facilitates the initiation of corrosion fatigue in stainless steel [77]. These authors also report that the nitrogen implantation and heat treatment procedures enhance the corrosion fatigue of Ti64 alloy. Large plates are found to offer good resistance to corrosion fatigue than the small one and Ti64 is found to outperform the 316L SS alloys. Fretting corrosion is very common in all load bearing metallic orthopedic implants. Fretting occurs at the bone-stems interface, the stem–cement interface and on the interface of modular connection between implant components. The generation of ionic and particulate debris through fracture and abrasion of the metal oxide protective layers and their deposition in the local tissue has caused clinical concern.

The clinical concern is due to the known potential toxicities associated with the elements used in implant alloys and known pathologies such as particle induced inflammation and hyper sensitivity associated with metal implant degradation. Fretting corrosion, which takes place at modular junctions is due to relatively small scale (between 1 and 100 μm) motion between implant components induced by cyclic loading. In total hip implants, the conical inserts on femoral stems are made either from Co–Cr–Mo alloys or titanium alloys and the heads which fit on these femoral stems are made of either cobalt based alloys, ceramic alumina or zirconia. Though there is a perfect interlocking mechanism between the head and stem due to micromotions the body fluids do penetrate in this junction leading to fretting corrosion. The corrosion of an implant is considerably reduced by the formation of protective oxide layer. According to Cabrera and Mott [78] the oxide film growth depends on the magnitude of the electric field and if the potential across the interface is decreased the film thickness decreases. The oxide film becomes thermodynamically unstable if the interface potential is made negative or pH is made low and this results in the dissolution of the oxide layer. The corrosion characteristics of an alloy are greatly influenced by the passive film formed on the surface of the alloy and the presence of the alloying elements. The structural changes in the film or the variation in the ionic or electrical conductivity of the film alters the passive film resistance against corrosion. In the case of Ti64 alloy, the vanadium oxide in the passive film dissolves and results in the generation and diffusion of vacancies in the oxide layer of Ti64 [79]. On the other hand, addition of Nb as an alloying element has a stabilizing effect on the surface film of Ti based alloys [80]. The addition of Nb enhances passivation and also resistance to dissolution. The enhanced corrosion resistance is due to the formation of Nb rich oxide which is highly stable in the body environment. Further, Nb addition improves the passivation property of the surface film by decreasing the concentration of anion vacancies. A comparative study on the corrosion behavior of Ti–Ta and Ti64 alloys showed that the addition of Ta remarkably reduces the concentration of metal release because more stable Ta_2O_5 passive film strengthens the TiO_2 passive film and hence possesses better corrosion resistance than Ti–6Al–4V alloy. Ta that has chemical properties similar to glass is immune to all acid environments except HF [81]. Thus the corrosion resistance of the passive film is greatly dependent on the alloying element and their oxides formed. The corrosion behavior of various titanium alloys has been studied extensively in different environments. This is due to the fact that the pH of the body may vary from 3.5 to 9 depending upon the condition of the area around the implant, wounded or infected. Nakagawa et al. studied the corrosion behavior of Ti64, Ti–6Al–7Nb and Ti–0.2Pd alloys and, they observed of all the three alloys, the titanium alloy with Pd exhibited high resistance to corrosion over a wide range of pH due to enrichment of palladium on the surface [82]. The work of Khan et al on corrosive wear studies of titanium alloys demonstrated that the Ti–6Al–7Nb and Ti64 possessed best combination of corrosion and wear in *in vitro* accelerated corrosion test, although Cp Ti, Ti–Nb–Zr and Ti–Mo alloys all displayed excellent corrosion resistance [83]. The presence of proteins also either inhibits or accelerates the corrosion of the implants in the body. The corrosion behavior of three titanium alloys viz. Ti64, Ti–6Al–7Nb and Ti –13Nb–13Zr alloys in phosphate buffered solution revealed that amongst the three titanium alloys, the alloy Ti–13Nb–13Zr was least affected by the change in the pH level and the hardness reduction due to corrosion in protein solution was less for this alloy when compared to other two alloys, thereby exhibiting its superiority compared to the other two alloys. The repassivation behavior of a material after corroding in a given solution also plays a vital role in deciding the corrosion behavior of the alloy. Titanium alloys tend to repassivate faster than the stainless steel and other biomedical alloys. The repassivated layer is found to be different from the native oxide layer; the incorporation of ions in the repassivated layer plays a deciding factor for its corrosion resistance. Further, the passivated surface oxide film is in contact with the electrolytes and is found to undergo partial dissolution and reprecipitation. Hence, the composition of the surface film changes with environment in which it is existing [84]. The surface film on titanium metal that has been surgically implanted into human jaw is found to consist of calcium, phosphorous and sulfur [85,86]. In vitro corrosion studies in Hanks's solution have revealed the formation of calcium phosphate on Ti64 and Ti–56Ni, and formation of only phosphate without calcium on Ti–Zr alloys [84]. The research on the interactions between material and biological system is relatively new and not yet matured, hence a systematic study based on physical chemistry and life science is required to understand the formation of the oxide film and repassivated layer obtained under different environments. The corrosion resistance of an alloy is not only affected by its bulk composition but also by the microstructure developed. The redistribution of the alloying elements during heat treatment has been found to influence the corrosion resistance of an alloy. In Ti64, titanium is present in the form of TiO_2 and aluminum in more stable oxidation state 3 + corresponding to Al_2O_3. On comparing the corrosion resistance of the two alpha beta alloys Ti–6Al–7Nb and Ti64, it is found that the high corrosion resistance of the former alloy is due to the formation of Nb_2O_5, which is chemically more stable, less soluble and more biocompatible compared to V_2O_5 formed on Ti64 alloy. The presence of the β phase with elements such as Nb, Ta, etc. in the two phase alloys improves the corrosion resistance of the alloy. However, care should be taken to ensure even distribution of alloying elements in both the phases by appropriate heat treatment procedure so that no galvanic corrosion occurs between the two phases. Heat treatments that lead to uneven distribution of alloying elements in either of the phase are detrimental with respect to corrosion. It has been observed that the ST that led to a high amount of α phase and a low β phase resulted in higher corrosion of α phase, as more aluminum was present in the α phase while the (phase was protected by the presence of Nb in the Ti–6Al–7Nb alloy. Extensive heat treatment studies carried out on Ti–6Al–7Nb alloy clearly revealed, the alloy heat treated at 950 °C /air cooled and aged at 550 (C exhibited the best corrosion performance in Ringer's solution [87,88]. The superior corrosion resistance of this heat treated sample was attributed to the formation of duplex microstructure that led to even distribution of the alloying elements. Similar studies carried out by Geetha et al. [89,90] confirmed that the Ti–13Nb–13Zr alloy with sub transus heat treatment possessed superior corrosion resistance to that of the β ST samples. Moreover, the repassivation behavior for the equiaxed microstructure was much superior to other microstructures developed. The simultaneous increase and decrease in current in the stable region that is noted in most of the titanium alloys, was not observed in this heat treated sample. The stable current is attributed to the formation of strong oxide layer on the surface and its high corrosion resistance. The presence of beneficial alloying elements like zirconium and niobium and their even distribution in the three phases α, β and α'' phases have resulted in high corrosion resistance. From the above studies, it is evident that appropriate heat treatment procedure should be selected for each alloy to have enhanced corrosion performance. The above discussion clearly brings out the fact that the material developed for implant applications should be free from crevice, fretting and pitting corrosion. Moreover, the oxide formed on the surface should be highly stable in various environments, must not undergo dissolution, ought to be strong and adherent and its properties must not change with the change in the pH of the body fluid. Thus, it is highly essential to select appropriate alloying elements and heat treatment procedure to have high corrosion resistant surface for biomedical applications.

7. Surface modification of titanium alloys for biomedical applications

7.1. Coatings for enhanced wear and corrosion resistance

Long-term performance of surgical implants is often restricted by their surface properties. The poor tribological property of the titanium and its alloys, such as low wear resistance leads to the problem of reduced service life of the implants. This problem can be overcome to a large extent by suitable surface coatings. Surface engineering can play a significant role in extending the performance of orthopedic devices made of titanium several times beyond its natural capability. Various surface treatments have been exploded for improving the tribological properties of titanium and its alloys. Surface modification techniques such as physical deposition methods like ion implantation [91] and plasma spray coating [92], thermo chemical surface treatments such as nitriding [93], carburization and boriding have been used to improve the surface hardness of titanium alloys. However, the former techniques are prone to interfacial separation under repeated loading condition and the latter techniques operated at high temperatures usually cause a torsional or twist of the substrate. TiN coated hip and knee implants have been found to possess increased wear resistance and good compatibility [94]. In vitro studies of Sundarajan et al. have shown that nitrogen ion-implanted Ti- Modified 316SS exhibits threefold increase in corrosion resistance when implanted with a dose of $1 \times 10\,17$ ions/cm^2 [95]. In addition, their studies on Cp Ti and Ti64 have shown enhanced corrosion resistance in nitrogen ion-implanted materials in the Ringers solution. The enrichment of nitrogen in the passive film and formation of oxynitrides in the implanted and passivated layers have improved the corrosion resistance of these alloys. TiN is produced either by depositing N on the surface with techniques like PVD, CVD or plasma nitriding and ion nitriding. These techniques may also give rise to various nonstochiometric compounds with high hardness on the surface [96]. The corrosion work carried out by Thair et al. on ion-implanted Ti–6Al–7Nb has demonstrated that specimen's ion-implanted at 100 KeV with a dose of 2.5 × 1017 exhibit highest corrosion resistance in Ringer's solution when compared to other dose parameters [97]. Thair et al. have also noticed that while plasma nitrided Ti–6Al–7Nb alloy exhibited improved corrosion behavior, this treatment led to lower corrosion resistance as compared to the nitrogen ion-implanted Ti–6Al–7Nb due to formation of large size titanium nitride precipitates [98].The enrichment of nitrogen in the passive film and formation of oxynitrides in the implanted and passivated layers have improved the corrosion resistance of these alloys. Though the corrosion resistance of ion-implanted surface is very high the ion implant layer is often found to wear off with time [98]. To overcome these problems associated with nitriding, high-energy electron-beam irradiation was able to develop Ti-based surface composites, which improves hardness and enhanced wear resistance [65]. Oxygen diffusion hardening (ODH) is another technique that has been studied with considerable interest as it is found to improve the abrasive wear of titanium alloys such as Ti–6Al–7Nb and Ti–13Nb–13Zr. The abrasive wear of Ti–13Nb–13Zr was found to be similar to Co–Cr alloys when its surface is hardened by ODH treatment. The wear resistance of Ti–6Al–7Nb was also found to be drastically improved by the ODH treatment and Ti–5Al–2.5Fe which was thermally oxidized, displayed frictional properties similar to ceramic alumina balls. Thermal oxidation is also widely applied to improve the corrosive wear properties of Cp Ti and Ti64 alloys. The improved performance of this technique is due to the adherent surface modification by oxygen diffusion, which does not spall or delaminate like the overlay coatings [99]. The hardness value of 1000 Hv is attained when titanium is oxidized at 625 °C for 30 h. However, spallation of TiO2 layer formed is observed due to the presence of residual stress on the oxidized zone. Laser annealing is another innovative technique to harden the surface of the titanium alloys. Nano tailoring of $\alpha + \beta$ titanium alloy using laser leads to improved mechanical property that is capable of enhancing tribological behavior of such alloys. The hardness of the surface and depth of the modified zone is very high in the laser nitrided samples. The hardness ranges from 1000 VHN in nitrogen-containing argon atmosphere and 2000 HVN in pure nitrogen atmosphere. However, laser nitriding is associated with the cracks on the surface, number of cracks decreasing with decrease in the concentration of nitrogen. Surface modification studies carried out on Ti–Zr–Nb alloys in nitrogen atmosphere by Geetha et al. [100,101] using Nd:YAG laser have shown to produce high surface hardness without crack formation. In addition corrosion resistance of the laser nitrided samples in simulated body environment was found to be significantly better than the untreated alloy. However, further *in vitro* and *in vivo* studies of these laser nitrided specimens are essential to assess their suitability for biomedical applications. A process called low plasticity burnishing in which high modulus ball is rolled over the surface of a metal under high pressure is found to improve the fatigue life of Ti64 alloy [102]. However, its effect on other properties such as corrosion and wear remains to be investigated. Diamond-like carbon (DLC) coating has also emerged as a promising technique for orthopedic implants as it offers superior tribological properties by reducing friction and increased wear [103,104]. In addition, DLC coating possesses superior corrosion resistance, enhanced mechanical properties, and higher biocompatibility and hemocompatibility. Cells are seen to grow well on these films coated on titanium and other materials without any cytotoxicity and inflammation [105,106]. A considerable reduction in the polymer wear debris is noticed when UHMWPE is rubbed against metal coated with DLC. However, there are some contradictory results reported on DLC coatings, such as the poor adhesion of this coating on steel and titanium alloy substrates and instability of the coating due to high residual stress [105]. However, various coating techniques are under investigation to achieve good adhesion and other required properties [107,108]. Thus without compromising the advantageous properties of titanium alloys, suitable surface modification techniques have to be employed to enhance the wear and corrosion resistance of titanium alloys.

7.2. Coatings for high osseointegration

Osseointegration which is the process of bone healing and the formation of new bone is the clinical goal of implant surgery. As soon as the implant is fixed into a body, number of biological reactions occurs in various stages. Initially, there will be an adsorption of water molecules and proteins and then one of the following processes will take place:

1. Formation of new bone cells on the implant surface, bone cells proliferation and differentiation leading to osseointegration. When this sequence of events occurs, then the implant is said to be well accepted by the body in which it is inserted.
2. Inflammatory response by the human body to reject the implant.
3. Micromotions of the implant leading to the formation of a fibrous tissue instead of bony interface that impedes osseointegration.

The processes that will occur depend upon the surface properties such as surface chemistry, surface topography, surface roughness and mainly the surface energy which changes with all the said properties [109]. The classification of the biomaterials based on the tissue response is given in Table 1. The dependence of cellular interactions on surface energy is dictated by various surface properties as shown in Fig. 8. However, the influence of the surface energy on cell differentiation, matrix production and calcification is not well understood. In orthopedic and trauma surgery the success or failure of the implant surgery is based on the integration of implant with the surrounding bone. The higher the degree of osseointegration, the higher is the mechanical stability and the probability of implant loosening becomes smaller. To achieve this, fibrin adhesion, blood vessel growth and micromotions should be avoided. Enhanced cell adhesion and reduction of micromotions can be obtained by appropriately tailoring the surface of the implant. The development of required interface is not only highly influenced by surface chemistry, but also more specifically by nanometer and micrometer scale topographies. A variety of strategies have been experimented to improve bone integration of titanium-based materials. The surface roughness is found to influence the cell morphology and growth. Alteration in surface topography by physical placement of grooves and depressions changes the cell orientation and attachment [110,111]. Experimental work of Jayaraman et al. on the behavior of grooved and sand blasted and acid etched titanium surface revealed that the grooved surface offers better cell attachment and proliferation than rough surfaces [112]. Various methodologies have been adopted to achieve biomechanical compatibility such as development of porous surface, coating of nano ceramic particles, HAP coating, oxide coating and thermal heat treatment of surfaces to reduce the grain size. Surface grit blasting and polishing methods enhance cell growth, improve fixation through increase in interlocking surface area [110,113–116]. This surface treatment also changes the oxide thickness and hence the biocompatibility of titanium implants, which is associated with oxide on its surface. In addition, appropriate heat treatment in oxygen or in air will obviously change the composition of oxygen and the alloying elements present on the surface and modify the biocompatibility. Heat treatment

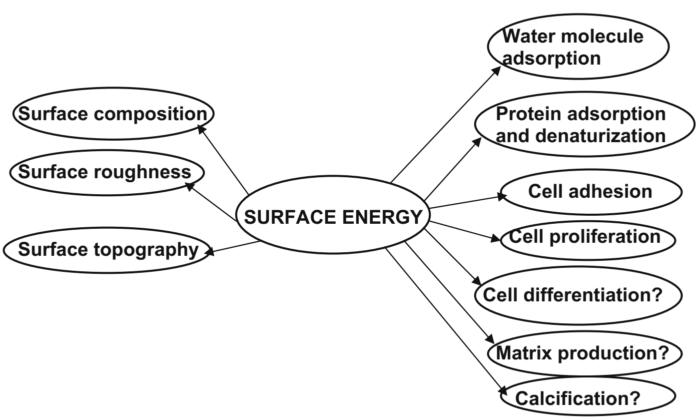

Fig. 8. The dependence of various reactions on surface energy.

experiments conducted on titanium alloy (Ti64) by MacDonald et al. revealed that the heat-treating at low temperature enriches the surface with Ti and Al and promotes the cell attachment [117]. In addition, waviness and porosity of the implant also plays a vital role in bone integration. Bone ingrowth into porous surface can cause strong interlocking of surrounding bone tissue with the implant, resulting in improved biomechanical compatibility and high resistance to fatigue loading [118–120]. Remodeling of bone on porous surface has also been investigated in great detail. From earlier studies it was noted, only 7% of porous-coated anatomic femoral components had to be replaced due to loosening or osteolysis after 15 years in contrast to 43% of stems that were cemented [121]. The work carried out by Zinger et al., showed that the cells need cavities on the implant surface equivalent or larger than their own size which is of the dimension $\approx$30 μm [102,119]. Cells cultured on Ti surface that was roughened by sand blasting with large grit and after acid etching occupied the shallow spaces existing in their rough topography which measured to 20–30 μm in diameter. WennerBerg et al. found on histology examination that optimal implant surface shows wavy structure with an average wavelength of 11.6 μm and with deviations in height by 1.4 μm [112]. From rabbit intermedullary implantation studies, it was found lamellar bone and bone remodeling highly favored 200 μm pores rather than 10–25 μm pores, which were created by laser [122]. Hulbert et al. also observed a similar relation between osteons and growth on porous surface. Studies carried out on ceramic implants revealed that osteons require mini pores whose diameters range from 150 to 200 μm [123]. The work of Li et al on transcortical model also showed that bone growth on 140 μm pore size yielded the best results among all [124]. A similar study carried out by Gotz et al. [125] on different laser textured surfaces, revealed that bone remodeling also occurs on the surface with different pore sizes. However, the bone growth on 300 μm pores was relatively slower than 200 μm in terms of total surface bone to implant contact after three weeks of implantation, suggesting the slow osseointegration process when big pores were present on the surface. Thus, from the detailed studies made by several authors lead us to conclude that the size of the pores should be in the range of 100–200 μm for better osseointegration.

In addition to porous coatings, development of porous biomaterials to enhance long-term fixation and bone growth have also been tried with great interest. The porous biomaterial is expected to lead to strong interface between the bone and the implant and also the modulus of such porous biomaterial is very low and thus these materials are expected to overcome the stress shielding effect and loosening of the implants. By using a technique called Laser Engineering Net Shaping (LENSTM), Vamsi et al. have demonstrated that the modulus of a material can be tailored to greater extent by varying its porosity. Their experimental results have shown that the modulus of porous titanium implant developed using LENSTM can be varied from 1.7 to 47.7 GPa by choosing appropriate laser processing parameters [126]. Modification of the implant surface that mimics the bone or designing a new implant similar to that of bone is a challenging problem in the field of biomaterials. Alloys developed for implants which will ensure a chemical bond with living bone is a problem, which has be tackled by physically forming a film of highly biocompatible calcium phosphate on the surface. The methods that have been used for coating Ca and phosphorous includes dip coating, electron-beam deposition, pulsed laser deposition and plasma spraying [127]. Surface coating of synthetic hydroxyapatite Ca10 $(PO_4)(OH)_2$ – a calcium phosphate compound that is similar to the bone promoted bone apposition to the surface. Enhanced osteoconductivity was observed by the introduction of femoral stem coated with plasma sprayed hydroxyapatite for a younger patient group for whom the service period of an implant is expected to be very high [128–131]. The coating, which helps in early fixation into bone, improves prosthesis life in spite of biomechanical mismatch [132,133]. Preliminary *in vivo* test on surface of titanium implant that was modified by micro arc oxidation treatment also showed improvement in osseointegration compared to the untreated surface. The improved osseointegration was attributed to rough porous oxide layer in which Ca and P ions were incorporated. Alkaline phosphate (ALP) activity was found to increase with increase in oxide layer thickness and increase in Ca and P ions in the layer [134]. Apart from the physical deposition methods, several chemical methods are recently being tried to form Ca–P coating on the surface as these methods are more economical and are able to produce uniform coating on complex shaped implants. HAP or mixture of HAP and TiO_2 is coated using sol–gel coating technique. The ceramics are either coated by dip coating or spin coating. In dip coating, the material is immersed in the Sol and then withdrawn with a well defined speed under a controlled temperature and atmospheric conditions. The coating thickness in this method depends on the withdrawal speed and by the solid content and the viscosity of the liquid. The atmosphere controls the evaporation of the solvent when pulled out and the subsequent destabilization of the Sols by solvent evaporation, which leads to gelation process and the formation of thin film of the ceramic. On the other hand, in spin coating, the material is made to spin around an axis that is perpendicular to the coating area. The samples after coating are usually dried for long time and heated at low temperature.

Li et al. developed a new methodology to achieve high osseointegration on highly oxidized material [127] wherein the alloys were initially heat treated at low temperature (400 °C) and later alkali treated with a method developed by Kim et al. [135]. The oxidized alkali treated titanium alloy was later immersed for 2–4 weeks in protein free body fluid (biomimetic solution) with ion concentrations nearly equal to that of human blood plasma. This two-step treatment increases the surface oxide and alkali level and enhances the formation of Ca–P onto the surface. This method seems to be very promising as it is seen to increase the wear resistance by forming TiO_2, ZrO_2 and Nb_2O_2 layers on the surface and also increases the bioconductivity by the alkali treatment. In addition to increase of the surface bioconductivity by forming Ca–P coating, development of nano surface topography is being studied with considerable interest as the nano surfaces mimic the human bone. Thomas et al. observed increased osteoblast adhesion on novel surface topography created by carbon fibers with nanometer dimensions [136]. It was understood that this type of nanometer surface roughness was imperative for osteoblast adhesion. Though, nanocrystalline titanium surface enhances cell growth and exhibits excellent wear resistance due to high hardness and strength, their effect on corrosion behavior remains uninvestigated [137]. The electrochemical behavior of nanocrystalline titanium surface has not yet been explored. However, cell compatibility studies on nano sized ceramic particles such as alumina and titania showed enhanced osteoblast function and hence large deposition of calcium minerals [138]. Further, wear particles generated from these nanophase ceramics are less detrimental on bone cells when compared to conventional ceramic wear particles [139].The above studies make us to conclude that a nanosurface seems to be advantageous from the biocompatibility and biomechanical compatibility points of view.

8. Biocompatibility of titanium and its alloys

The artificial implants, once implanted *in vivo*, induces a cascade of reactions in the biological micro-environment through interaction of the biomaterial with body fluid, proteins and various cells.

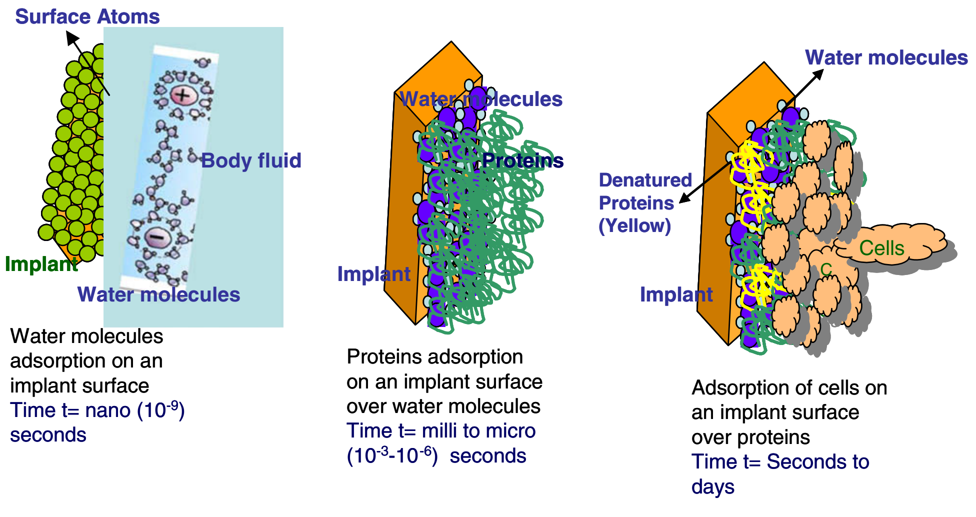

Fig. 9. Response of the human bone to an implant at different time intervals and the various reactions occurring during cell attachment on the implant.

Response of the human bone to an implant at different time intervals and the various reactions occurring on the surface is shown in Fig. 9.

The sequence of local events often leads to the classic foreign body response and the formation of a fibrous tissue capsule around an implant. It is clear that a major factor influencing this unfavorable reaction of the body is the biomaterial surface, since the first contact of the body is with the surface. The specific interactions determine the path and speed of the healing process and the long-term integration of the biomaterial-body interface. Both the chemical composition on the surface and the surface topography are believed to be important in bone contacting implants. They regulate the type and the degree of the interactions that take place at the interface like adsorption of ions and biomolecules such as proteins, formation of calcium phosphate layers, and interaction with different types of cells (macrophages, bone marrow cells and osteoblasts). Thus, the nature of the initial interface that is developed between an artificial material and the attached tissue determines the ultimate success or failure of the materials. Tissue compatibility is the most important issue to be considered for the implant success. No surgical study has ever shown to be completely free of adverse reactions in the human body. Titanium is found to be well tolerated and nearly an inert material in the human body environment. In an optimal situation titanium is capable of osseointegration with bone [140]. In addition, titanium forms a very stable passive layer of TiO_2 on its surface and provides superior biocompatibility. Even if the passive layer is damaged, the layer is immediately rebuilt. In the case of titanium, the nature of the oxide film that protects the metal substrate from corrosion is of particular importance and its physicochemical properties such as crystallinity, impurity segregation etc, have been found to be quite relevant. In vitro cytotoxicity tests are often conducted using L929 cells and osteoblast like MC3T3 E1 cells. The relative growth of these cells is estimated to test the cytotoxicity of the developed alloy. Titanium alloys show superior biocompatibility when compared to the stainless steel and Cr–Co alloys. In spite of the above stated merits, the question of the biocompatibility of titanium materials has been widely discussed and further studies are being made. Reservations have been expressed about the presence of long-term Ti64 implants, because elements such as vanadium are toxic in the elemental state. These concerns have led to the development of new beta titanium alloys with non toxic alloying elements like Ta, Nb, Zr. In fact, it is reported that the addition of Ta remarkably reduces the concentration of the metal release [17,141,142]. Studies performed by Okazaki et al [143] demonstrated that the relative growth of cells for the beta alloys such as Ti–15Zr–4Nb–4Ta, is much higher than that of the Ti64. Ninomi et al. [144] have shown that the cell viability of Ti–29Nb–13Ta–4.6Zr is much superior to the Ti64 alloy. The studies on the cell viability of Ti–*x*Ta revealed that the Ti–Ta alloys exhibit excellent biocompatibility in comparison to Ti–64 ELI alloy. In addition, the wear resistance of these Ti–Ta alloys is superior to Ti64 alloy. The grain size of metal implant influences the osteoblast adhesion. In vitro studies carried out using ultra fine-grained CP Ti (grade 2) and Ti64 alloy exhibited increased cell adhesion when compared to conventional materials. This increase in cell adhesion is attributed to the increase in surface energy at the grain boundaries. The above discussions, lead to a strong belief that the new β type titanium alloys are more promising from the wear, corrosion and biocompatibility aspects for biomaterial applications.

9. Nickel titanium (nitinol)

Nitinol is one of the most promising titanium implants that finds various applications as it possesses mixture of novel properties such as shape memory effect, enhanced biocompatibility, superplasticity and high damping properties [145]. Owing to these properties it finds wide applications in industries and medical field. Their medical applications include orthodontic wires for dental, intravascular stents, bone fracture fixtures, taples for foot surgery etc. Porous NiTi is used in making

Table 6
Elastic modulus of nitinol and bone.

Material	Nitinol	Stainless steel	Cortical bone	Cancellous bone
Elastic modulus (Gpa)	38–48	200	4.4–28.8	0.01–3.0

intramedullary nails and spinal implants. A comparison of the modulus of NiTi with bone and standard 316Lstainless steel is given in Table 6. It is important to note that the elastic modulus of the porous nitinol implants is closer to that of the bone. The porous nature of this biomaterial permits tissue/bone cell penetration and integration [146]. Studies made on the correlation between the superelasticity behavior, the different pore size and various heat treatment conditions of NiTi produced by gas expansion method revealed that the NiTi with 16% porosity exhibited excellent combination of mechanical properties such as high strength (1000 MPa), low young modulus (15 GPa), large compressive ductility (>7%), large recoverable strains (>6%) and high-energy absorption (>30 MJ/m^3) [147]. *In vivo* studies of NiTi implanted in soft tissues and *in vitro* experiments show excellent biocompatibility [148–150]. However, there are few reports on release of Ni from NiTi implant. The Ni that is released is seen to induce allergic reaction. Ni above certain concentrations leads to severe local tissue irritation, necrosis, and toxic reactions. However, the amount of nickel released from these implants has been found to be lower than the concentration required inducing such reactions [151]. Thus, from these observations it is concluded that NiTi is one of the suitable candidates for various biomedical applications.

10. Nanophase materials – the next generation biomaterials

Currently used biomaterials do not replicate the surface as well as the mechanical properties of the replaced bone, leading to failure due to insufficient bonding with juxtaposed bone, bone loss, implant loosening and fracture. Nanophase materials possess unique surface and mechanical properties similar to the bone and hence are considered to be the future generation orthopedic biomaterials [152].

Nanograined materials are materials in which the atoms are clustered in such a way that each grain consists of only few atoms with the grain size in nanometer range when compared to the conventional materials whose grain sizes are in micron range. It should be emphasized that in spite of the fact that nanograined materials have less number of atoms in each grain, the number of atoms on the surface is very high and hence possess large surface energy. Thus they exhibit entirely different behavior compared to the micron sized grains whose surface to volume ratio is less. The bone forming cells generally attach themselves to the surface whose roughness is of nanometer range. The nano roughness arises because of the fact that our bones consist of inorganic minerals of grain size varying from 20 to 80 nm long and 2 to 3 nm in diameter [153]. The variation in the surface energy due to the nanosurface roughness leads to desirable cellular responses on nanostructured titanium and other materials resulting in high osseointegration. [154]. Dongwoo et al. have investigated the cell adhesion behavior on submicron, nanometer structured titanium surface and compared their results with a flat smooth titanium surface [154]. Their study demonstrated that both nanometer and submicron surfaces have very high surface energy and adhesion of bone cells is very high on these surfaces. Apart from nanograined metals and alloys made of Cp Ti, Ti–6Al,4V and CoCr, nanoceramic biomaterials such as alumina, titania, hydroxyapatite also exhibit increased cell adhesion [155,156]. When the grain size was decreased from 167 to 24 nm, osteoblast adhesion got increased by 51% and fibroblast adhesion responsible for encapsulation was reduced by 235%. Proteins such as victronectin and fibronectin are the proteins responsible for cell adhesion and protein that inhibits cell adhesion is laminin. The protein victronectin has been identified for this increase in cell adhesion and increase in the unfolding of this protein was also observed. In addition, cell adhesion on proteins also depends on the biomolecules such as integrin and heparin sulphate proteoglycan [152]. The difference in the cell density between the conventional and nanomaterials is given in Table 7. It may be noted that, though different types of cells were utilized for cell culture studies on the alloys and ceramics, the cell density was observed to be relatively higher for the nanomaterials when compared to conventional counterpart. Apart from the roughness, the pore size on the surface also has an influence on the protein adhesion. The protein, victronectin, generally is adsorbed on pores of smaller sizes (0.69, 0.95 and 0.66 nm of Al_2O_3, TiO_2 and HAP), on the otherhand, the protein that decreases cell adhesion such as laminin, generally adsorbs to pore size 2.54, 2.33 and 3.1 μm corresponding to Al_2O_3, TiO_2 and HAP bioceramics. [157]. Thus it is understood that small pores enhance cell adhesion due to the protein that attaches to that surface when compared to the large pore size. Increased osteoblast adhesion was also observed on nano HAP coated Ti–13Nb–11Zr alloy and further bone ingrowth towards implant was noted indicating ceramic surface coatings leading to high osseoingtegration [158].

Table 7
Cell density on nano size (nanophase materials) and micron size (conventional materials) grains.

Material	Increase in surface area when compared to conventional materials	Roughness (nm)	Cell density[a] (cells/sq.cm.)
Ti (nano)	15%	11.9	2000[b]
Ti–6Al–4V (nano)	23%	15.2	1600[b]
Co–Cr–Mo (nano)	11%	35.6	1450[b]
Ti (conventional)			1400[b]
Ti–6Al–4V (conventional)			950[b]
Co–Cr–Mo (conventional)			600[b]
Alumina (24 nm) (nano)			6000[c]
Titania (39 nm) (nano)			8000[c]
Hydroxyapatite (67 nm) (nano)			9500[c]
Alumina (167 nm) (conventional)			5000[c]
Titania (4520 nm) (conventional)			7000[c]
Hydroxyapatite (179) (conventional)			7000[c]

[a] Rounded values.
[b] After 3 h.
[c] After 5 days

Apart from cell adhesion, nanophase materials also show high density of osteoclast adhesion, indicating bone remodeling and new bone formation, enhanced osteoblast proliferation and APT synthesis [152]. We conclude from the above studies that irrespective of the type of material used for an implant, the most important factor that decides the cell response and osseointegration is the size of the grains on the surface of the implant.

Apart from tissue compatibility, the mechanical properties also vary with grain size [152]. Further, nanocrystalline coatings on biomaterials with grains of nanosize will lead to novel and enhanced mechanical properties [159] Nanocoating of thickness in the range of 10–15 nm on Ti has been found to enhance fracture toughness and biocompatibility drastically. In addition, nano coatings exhibit greater ductility and high modulus than conventional ceramic coatings [160,161]. Also, nanograined materials have high superplasticity due to grain boundary sliding and enhanced plasticity both in compression and tension.

Thus, by modifying the surface one can elucidate specific reaction in the surrounding tissue and also tailor the mechanical properties. However, two issues have to be addressed and investigated. The first issue is to understand the mechanism by which nanosurface alters the cell adsorption behavior and the second is, if and how the enhanced mechanical properties of nanophase ceramic could be incorpated into the next generation biomaterials.

11. Summary

Titanium and its alloy Ti64 used since 1950s as implant biomaterial, are being continuously subjected to various modifications with respect to alloy composition and surface properties in order to meet the need for improved function and duration of an implant in the human body. Development of an appropriate microstructure with optimum mechanical properties is a challenging problem in the field of β titanium alloys. Hence, more studies on the effect of thermomechanical processing on the properties of these alloys are required to gain a better understanding. Secondly, though the modulus of Ti alloys is far less than the conventional alloys like Stainless steel and chromium cobalt, intense research are still being pursued in the development of new titanium alloys with modulus closer to bone. At present Ti–35Nb–% 7Zr–5Ta possesses the lowest modulus of 55 Gpa. In spite of the fact the newly developed titanium alloys have modulus closer to bone and consist of highly compatible alloying elements, their wear resistance under loading conditions are very poor. Extensive research is presently being carried out to improve the wear resistance of Ti-based materials. However, due to the lack of appropriate protocol for measurements of wear property of metallic biomedical materials at present, only comparative studies are carried out at different conditions of loading and environment. More research on development of an appropriate protocol for measuring the wear property should be performed for development of an alloy with better wear resistance. The performance of titanium and its alloys can be enhanced profoundly by developing an appropriate surface treatment procedure that will lead to increased wear resistance and osseointegration. Hence, it is suggested that in future, greater focus should be made on the areas of development of very hard nano surface of appropriate hardness on frictional parts and the formation of biomimetic surface in order to attain increased functional longevity of the implant in the human body.

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