## Original Article

# Ultrafine grained titanium for biomedical applications: An overview of performance

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### ARTICLE INFO

### ABSTRACT

Ultrafine grain sized titanium (UFG Ti) obtained by severe plastic deformation presents a bright potential for biomedical applications because it provides the strength of titanium alloys without toxic alloying elements, such as Al and V that, by dissolving away from the implant, may be harmful to human health. The most recent developments and challenges in this field are reviewed. UFG Ti mini-devices were implanted in rabbits and the removal torque was compared with that of conventional commercially pure (cp) grain sized Ti Grade 2 and Ti6Al4V alloy Grade 5. The osseointegration of the UFG Ti was slightly superior of that of cp Ti Grade 2. The microstructure and mechanical properties of the UFG Ti, with special emphasis on dental implant application are reviewed and some additional properties evaluated and presented.

## 1. Introduction

The area of human implants has undergone rapid and dramatic developments in the past years. This was greatly enabled by new materials with enhanced biocompatibility. Although implants have been used by humans since ancient times, there were many rejection problems and it is only recently that osseointegrated implants have become widely used. Materials for this purpose are known as biomaterials, which are not necessarily organic but must exhibit specific properties [1]. Biocompatibility is, obviously, their most desirable property. In addition, the corrosion resistance to body fluids as well as the mechanical strength, fatigue endurance, and impact toughness are also important requirements of a biomaterial, especially for implant applications. Biomaterials are usually classified [2], in terms of their interaction with the body, into:

- Biotolerant materials (e.g., stainless steel, CrCo alloy, and polymethyl-methacrylate) release substances in nontoxic concentrations, which may lead to the formation of a fibrous connective tissue capsule. Valiev [3] reported on several applications for the case of non-osseointegrated medical devices made with biotolerant materials. Plate implants for bone fixation and screws are the most common. However,

**Fig. 1 – Example of non-integrated medical devices. (A) Skull button closure; (B) bone sternum closure plate; (C) spine plate; (D) maxillofacial plate; and (E) reconstruction temporomandibular plate.**

there is also a cornucopia of devices used throughout the body. As an illustration, Fig. 1 shows examples of medical devices that are non-integrated.

- Bioinert materials (e.g., alumina and zirconia) exhibit minimal chemical interactions with adjacent tissue. A fibrous capsule can be formed around such materials.
- Bioactive materials (e.g., hydroxyapatite, bioglass) stimulate a biological response from the body, such as bonding to either a soft tissue, like cartilage, or hard like bone.

Hench and Jones [4] suggested that there are two classes of bioactive materials: osteoconductive and osteoproductive. Osteoconductive materials (e.g., synthetic hydroxyapatite and tricalcium phosphate) are able to bond to hard tissue. Osteoproductive materials stimulate the growth of new bone onto the biomaterial surface (unalloyed titanium and tantalum) and spontaneously bind to living bone cells, if they have been previously subjected to a surface treatment. Therefore, metals such as Ti and Ta may be called bioactive [5]. In Fig. 2(a), reproduced from Menezes et al. [6], attached osteoblast cells can be clearly seen bonded onto the metallic surface. Fig. 2(b) illustrates SEM details of a titanium dental implant removed 4 years after surgery. In fact, commercially pure titanium (cp Ti) is reported to be an effective bioactive material.

The main application of bioactive unalloyed cp Ti (ASTM grade 1–4) is for dental implants. This metal is not, however, used for orthopedic application owing to its low mechanical properties. This review focus on dental implants and in the introduction of ultrafine grained titanium (UFG Ti), obtained by severe plastic deformation (SPD) processing, for which recent properties were evaluated [7]. In particular, its strength was found to match that of Ti–6Al–4V alloy, commonly used in high strength structural implants.
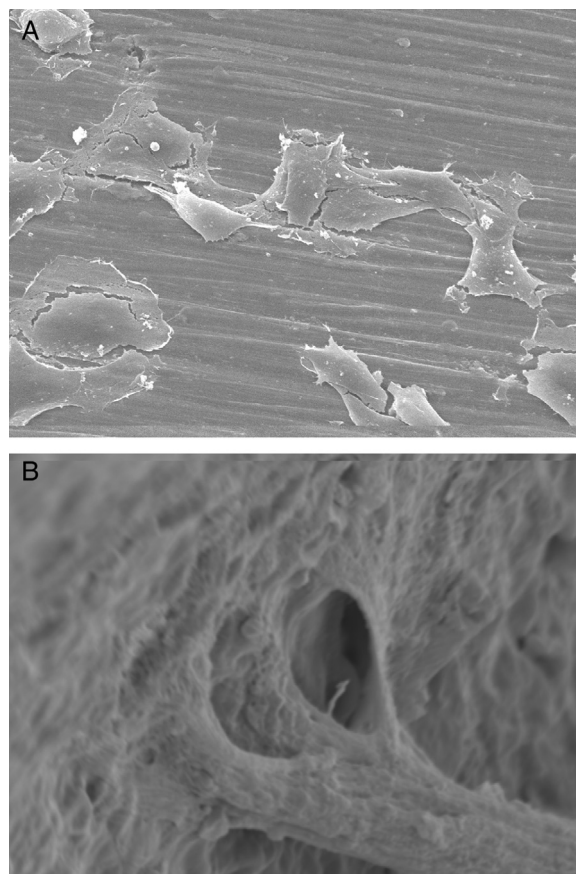


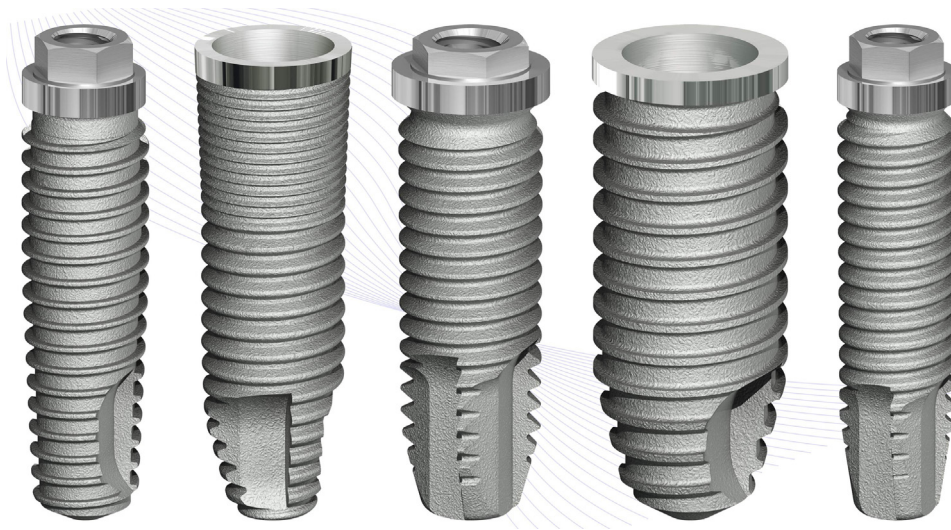**Fig. 2 – Titanium dental implant removed 4 years after surgery showing attached cell.**

**Fig. 3 – Examples of dental implants.**

## 2. Dental implants

### 2.1. Early achievements

When Brånemark [8], in the early 1960s, was studying blood flow in bone marrow, he never thought about the revolution that he was about to trigger. He used hollow metallic implants (chambers) that traversed the tibia of rabbits and enabled observation, through a glass window, of the marrow. Upon removing these implants at the end of the experiment, in order to reuse them, he observed that some of the implants were firmly attached to the bone and some even sheared off. The reader could imagine what an average researcher would have possibly done. Most probably use a few strong words and have the machine shop make new ones. That was not Brånemark reaction though. He realized that some of the stainless steel implants had been replaced by titanium, and these were the ones that were firmly bonded to the bone. He immediately abandoned his research and, in a stroke of genius, dedicated the next fifty years to the study of osseointegration. The emergence of titanium dental implants is the result of this discovery. In the United States of America, close to one million teeth are implanted each year, and a majority of dentists is qualified for the new field of implantology. In Brazil, the market of dental implant is close to 1.6 million a year. Even England, sometimes unjustly dubbed the "Land of Ugly Teeth", is adhering to the practice. Worldwide, over 250 million persons lack teeth. Beyond official statistic this number could be one billion. Hence, the potential of this technique is virtually limitless.

### 2.2. Osseointegration

Osseointegration occurs when a bioactive material like cp Ti becomes, when used as implant, firmly bonded to the bone. Dental implants will be given special attention in this overview, due to their association with a variety of procedures and implanted devices. There are different diameters

and designs of dental implants. Some of them are shown in Fig. 3, adapted from Elias et al. [9]. Although the majority is cylindrical with an external hexagon, there are also conical ones. The angles and designs of the screws threads also vary.

The dental implantation procedure should be conducted in two phases [9]. This is, in implantology terminology, called a protocol. Some of the reasons why titanium is as successful as a dental implant material will be described below jointly with illustrations of the implants insertion steps shown in Fig. 4.

- Once the anesthesia has taken effect, the dentist will make an incision in the gum.
- The jaw is exposed and the implant insertion site is pre-drilled, after X-rays are taken, which determine the direction and give an idea of the bone quality in terms of density and quantity.
- Pre-drilling is followed by drilling with the appropriate implant diameter, Fig. 4(a).
- The implant is attached into this hole with special torquing instrument, Fig. 4(b)
- With implants embedded into the bone, Fig. 4(c); reclosure of gum is done for 3–6 months in order to ensure tissue healing and osseointegration prior to loading.

After osseointegration, the top portion is attached to the implant. The prosthesis (ceramic or metal-ceramic) attachment corresponds to the final step shown in Fig. 4(d). In addition to delayed dental implants loading, one- and two-stages loading have also become commonplace.

(a) In one-stage dental implant treatment, the implant screw is inserted into the bone and the prosthesis is connected at the same time or at least 48 h after the surgery.
(b) In two-stage implant treatment, the implant screw is inserted into the gum and a wait time for tissue healing is needed. Then, a few months later (3–6 months) another small surgical procedure is necessary to attach the abutment.
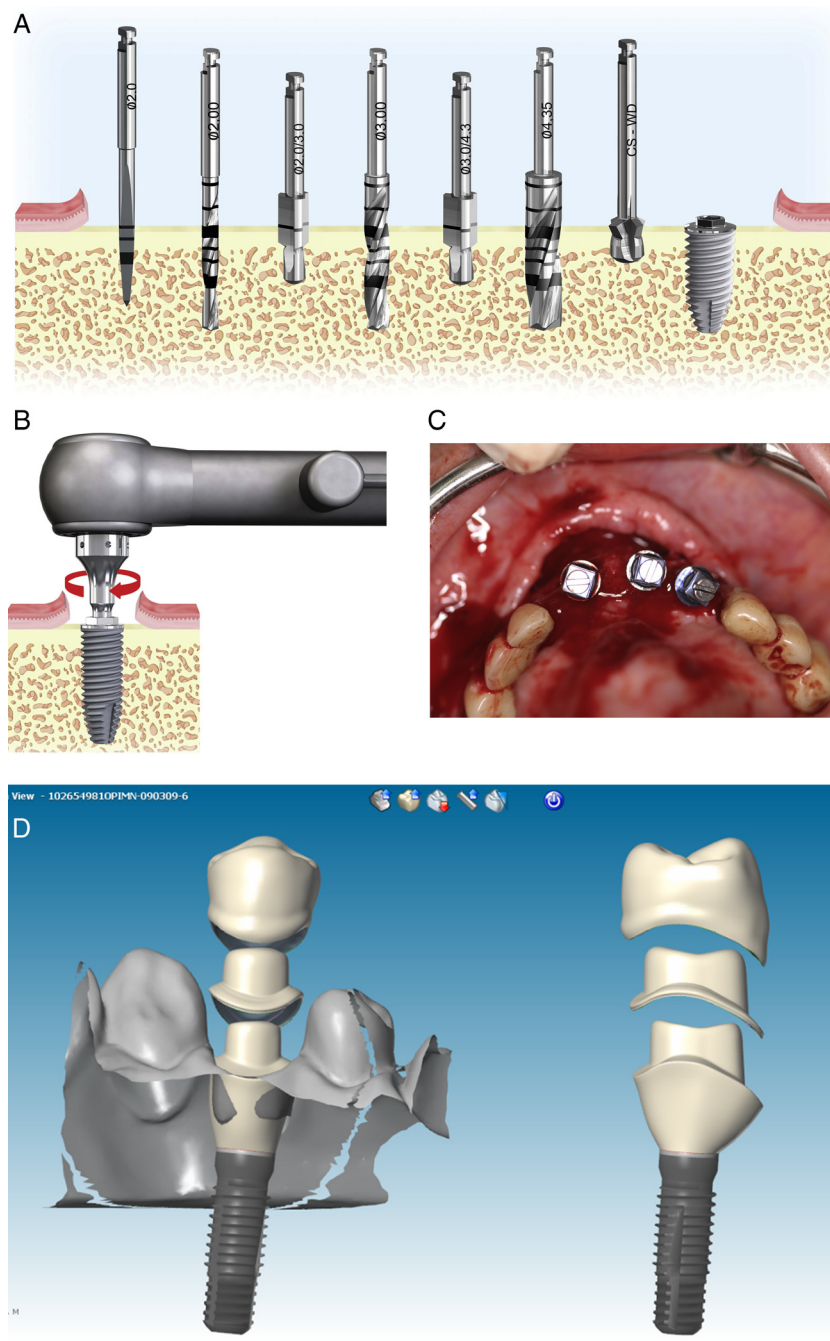
**Fig. 4 – Steps for dental implant surgery. (A) Selections of drilling with the appropriate implant diameter; (B) remove the dental implant from the box; (C) insertion the implant into the hole with special torquing instrument; and (D) insertion dental prosthesis.**

The term osseointegration, which occurs after bone healing, indicates the permanent attachment of the implant to the bone cells. The cp Ti is currently widely used for dental implants, owing to its recognized capacity of osseointegration. It has a surface that is indeed covered with an oxide layer. The exact nature of osseointegration is not well understood, but cells have to adhere to the titanium oxide implant surface. In vivo and in vitro experiments show that osteoblasts may completely and efficiently cover the cp Ti surface, as illustrated in Fig. 5. Actually, the osseointegration mechanisms involve two main types of cells, osteoblasts and osteoclasts. The first are related to the creation of new bone, and the second to the removal of necrotic bone produced during drilling. The cytoskeleton of the cells can be seen in Fig. 5 and fibers spreading out from them are attached. These cells are elongated along the machining groove orientation. It is clear that the roughness, chemical composition, energy, and wettability of the surface all play an important role in osseointegration.

The acid etching and anodizing of the surfaces has been shown to improve the strength of the bonds [10]. This strength,
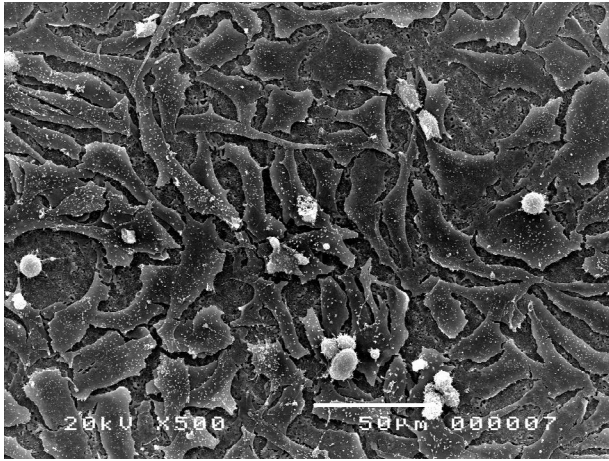
**Fig. 5 – Osteoblast cell on titanium surface.**

developed at the interface between the implant and the bone, can be measured by the removal torque, using an inverse procedure shown in Fig. 4(b). The removal torque is an effective measure of osseointegration and, experimentally, is usually done in rabbits after the animal is sacrificed. Removal torque values are shown in Fig. 6: as-machined, acid etched and anodized cp Ti implants are compared. In this figure, the measured torque is near 50 N cm for the as-machined implant and increases to 83 N cm for the anodized condition [10].

Fig. 7 shows the typical surface of cp Ti implants. The acid etched surface, Fig. 7(a), displays a microroughness of size ∼1 μm, which enhances platelet activation and aggregation as well as fibrin retention. A roughened surface like this plays an important role, not only in osteoblastic attachment, cell differentiation, and matrix production, but also as their growth factor and cytokine production. The anodized surface, seen in Fig. 7(b), shows an interesting pattern consisting of minivolcanoes and holes that assist the attachment of cells. This surface contains TiO$_2$ with crystalline structures in the form of rutile and anatase. Comparing results, Fig. 7 indicates that both types of roughened surfaces: (etched in Fig. 7(a) and anodized, in Fig. 7(b)), significantly enhance bone/implant contact and new bone formation around implant, as measured by removal
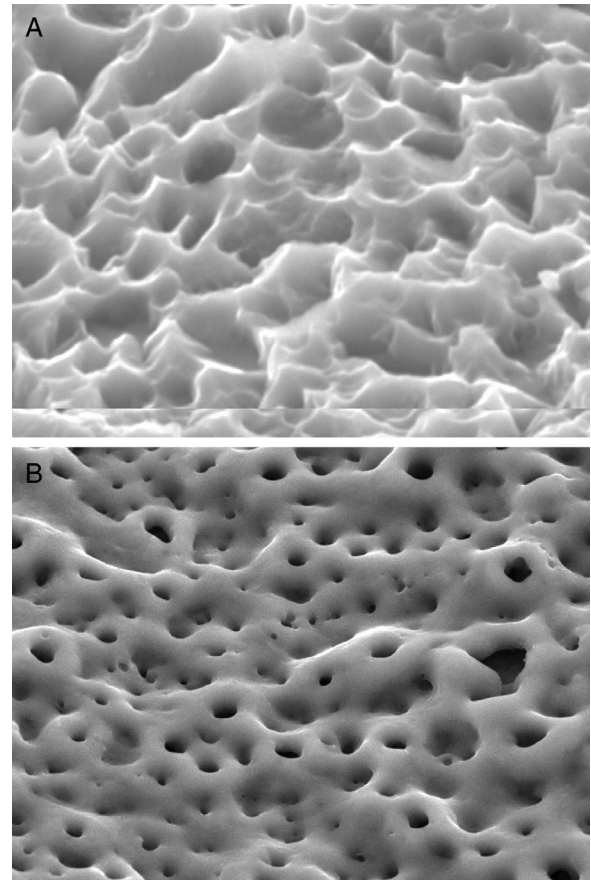


**Fig. 7 – Examples of commercially dental implant surface. (A) Acid etched and (B) anodized.**

torque, if compared with simply machined smooth surfaces [10].

### 2.3.    *Performance evaluation*

It is possible to correlate the removal torque [10,11], which is an external measurement dependent on the geometry of the implant, to the intrinsic shear strength of the interface bone/implant. This is done by the application of simple mechanics equations. The shear stress, $\tau$, acting on the interface is equal to the force divided by its area, $A$. This force, on its turn, is equal to the torque $T$ divided by the moment arm (half the diameter of the implant, $D/2$). Thus:

$$\tau = \frac{2T}{DA} \tag{1}$$

Fig. 8 shows a miniscrew for orthodontic anchorage example. The resisting area, $A$, can be obtained by summing the areas of the three sides of the screw: the flat bottom and the two angled sides:
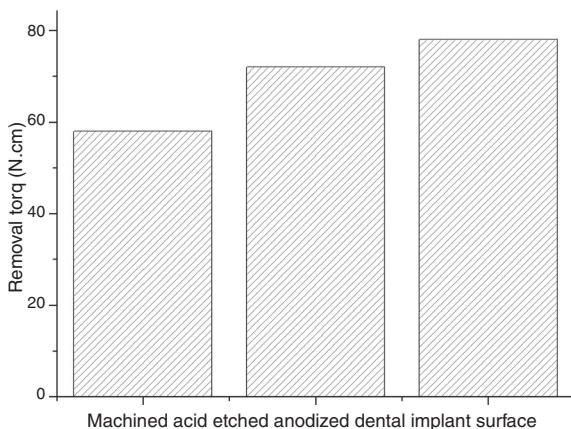
$$A = A_1 + A_2 + A_3 \tag{2}$$



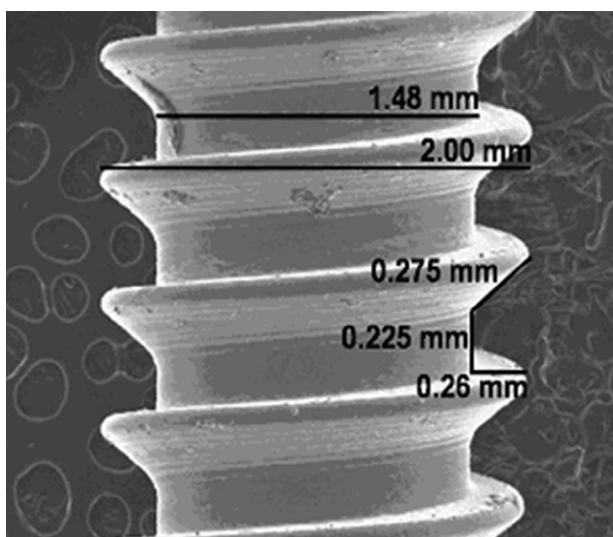**Fig. 6 – Dental implant removal torque from rabbit tibia.**

**Fig. 8 – Example of miniscrew for orthodontic anchorage.**

In Fig. 8, an unsymmetrical screw is shown, as an illustration. One has to compute the total area by making approximations and assuming lateral strips:

$$A = 2\pi(D_1L_1 + D_2L_2 + D_3L_3) \tag{3}$$

where $D_1$, $D_2$, and $D_3$ are average diameters and $L_1$, $L_2$, and $L_3$ are the lengths of the areas.

In order to increase the stability of the implant during the application of the force and reduce the stresses in the bone/implant interface, it is necessary to increase the implant surface. Increasing the diameter and length of an implant enhances bone/implant contact. But given the space constraints available and quantity of bone in the jaw, the surgeon has limitations to increase the diameter and length of the implant. To achieve the desired increase in surface, the implant design and thread shape are therefore optimized and implant surface treatment is carried out.

## 3.  Design of dental implants

The success of a dental implant is influenced by some factors such as loading time, micromotion, the quality and quantity of the bone available at the site of insertion, cortical bone thickness of the buccal plates, oral hygiene of the patient and load intensity. The strength and Young's modulus are very important factors for the long-term use of Ti and its alloys in implants for biomedical applications [12]. Table 1 presents the ASTM F67 mechanical requirement of Ti bars for implants. In this table, corresponding properties of grade 5 Ti, Ti–6Al–4V alloy as well as the different types of UFG Ti and bone are also presented.

Sometimes, the load transfer from the implant to the adjacent bone may result in bone reabsorption and eventual loosening of the medical device. According to Wolff' law, an excessive reduction or increase in tensile or compressive stress acting on a living bone causes a decrease in bone thickness as well as an increase in bone mass loss and osteoporosis. This is termed the stress-shielding effect, caused by the difference in the flexibility as well as the stiffness, which is partly dependent on the elastic modulus difference between the natural bone and the implant material [13]. Any reduction in the stiffness of the implant by using a lower-modulus material will definitely enhance the stress redistribution to the adjacent bone tissues, thus minimizing stress-shielding and eventually prolonging the device lifetime.

Morphologically, bone tissue is divided into two types: trabecular bone and compact bone. The differences are both structural and functional although both have the same matrix composition. Trabecular bone, also called cancellous or spongy bone, is composed of interconnecting plates and rods of tissue that form an interconnected, open-celled porous structure. Compact bone, also called cortical or osteonal bone, has a higher density and less porosity than cancellous bone. The type of bone available at the implant site is a very important factor in determining the success of dental implants. Misch [14] defined four types of bone quality in all regions of the human jaws, according to macroscopically observed differences in cortical and/or trabecular bones.

**Table 1 – Mechanical properties of different cp Ti, UFG Ti and Ti–6Al–4V alloy for implants and bone.**

| Types of titanium for implants | Yield strength (MPa) | Ultimate tensile strength (MPa) | Elongation (%) | Reference |
|---|---|---|---|---|
| cp Ti grade 1 | 170 | 240 | 24 | |
| cp Ti grade 2 | 275 | 345 | 20 | |
| cp Ti grade 3 | 380 | 450 | 18 | ASTM F 67 |
| cp Ti grade 4 | 483 | 550 | 15 | |
| Ti–6Al–4V grade 5 | 795 | 860 | 10 | |
| UFG Ti grade 2 4 XH + CR (70)(1) | 796 | 877 | 18 | [20,21] |
| UFG Ti grade 4 TMT + A (6h)(2) | 1110 | 1250 | 13 | [19] |
| UFG Ti grade 4 TMT + A (1h) + W(3) | 1200 | 1430 | 12 | [19] |
| Bone | 90–120 | 90–130 | 1–4 | [22] |

(1) 4 passes ECAP, 300 °C warm-deformed and 70% cold-rolling.
(2) 4 passes ECAP, 450 °C warm-deformed, forge-drawing plus 350 °C annealing for 6 h.
(3) 4 passes ECAP, 450 °C warm-deformed, forge-drawing plus 350 °C annealing for 1 h plus 450 °C isothermal straining.

Type I bone is composed of homogeneous compact bone; type II has a thick layer of compact bone that surrounds a core of dense trabecular bone; type III bone has a thin layer of cortical bone surrounding a core of dense trabecular bone; and type IV bone has a thin layer of cortical bone surrounding a core of low density trabecular bone of poor strength. In the jaws, an implant placed in poor-quality bone (type IV bone) has a higher chance of failure in confront with the other types of bones. When compared to the maxilla, clinical reports have indicated a higher survival rate for dental implants in the mandible, particularly in the anterior region of the mandible, which has been associated with better volume and density of the bone. Consequently, factors such as bone quality and quantity determine the procedure and the type of implant according to their design and surface treatment.

Unfortunately, the bone surrounding a dental implant is sometimes lost. For instance, if a dental implant is overloaded, this may cause loss of the bone surrounding the dental implant. In most cases, the bone loss starts at the top of the bone (crest) and progresses around the dental implant to form a saucer-type defect. It would be worthwhile to investigate possible factors that could reduce bone loading. To reduce the bone loss, the geometry of implant is an important factor to control. The standard ISO 14801 (Dentistry—Fatigue test for endosseous dental implants) is most useful for comparing endosseous dental implants of different designs or sizes. This test simulates the functional loading of an endosseous dental implant body and its pre-manufactured prosthetic components under "worst-case" conditions. The worst-case, shown in Fig. 9, has the lower implant clamped such that its axis makes a $30° \pm 1°$ angle with the loading direction of the testing machine.

In some cases, the surgeon must insert the implant in a region of the jaw with small thickness cortical bone. However, because of the limitation on the mechanical properties of cp Ti, the smallest implant needs to have a diameter equal to
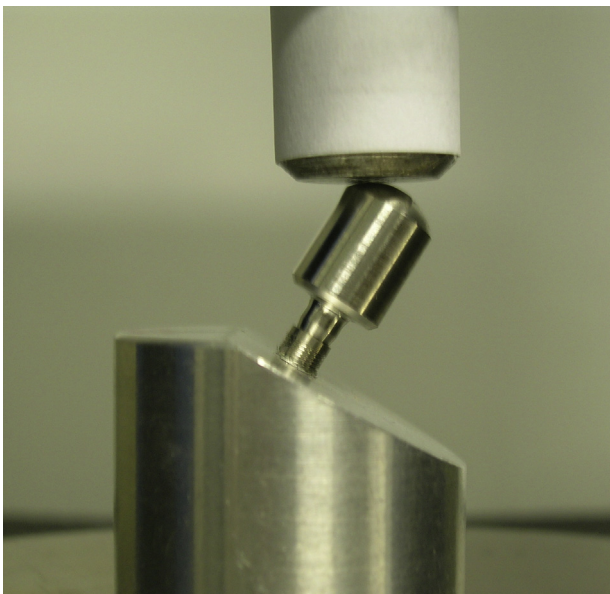


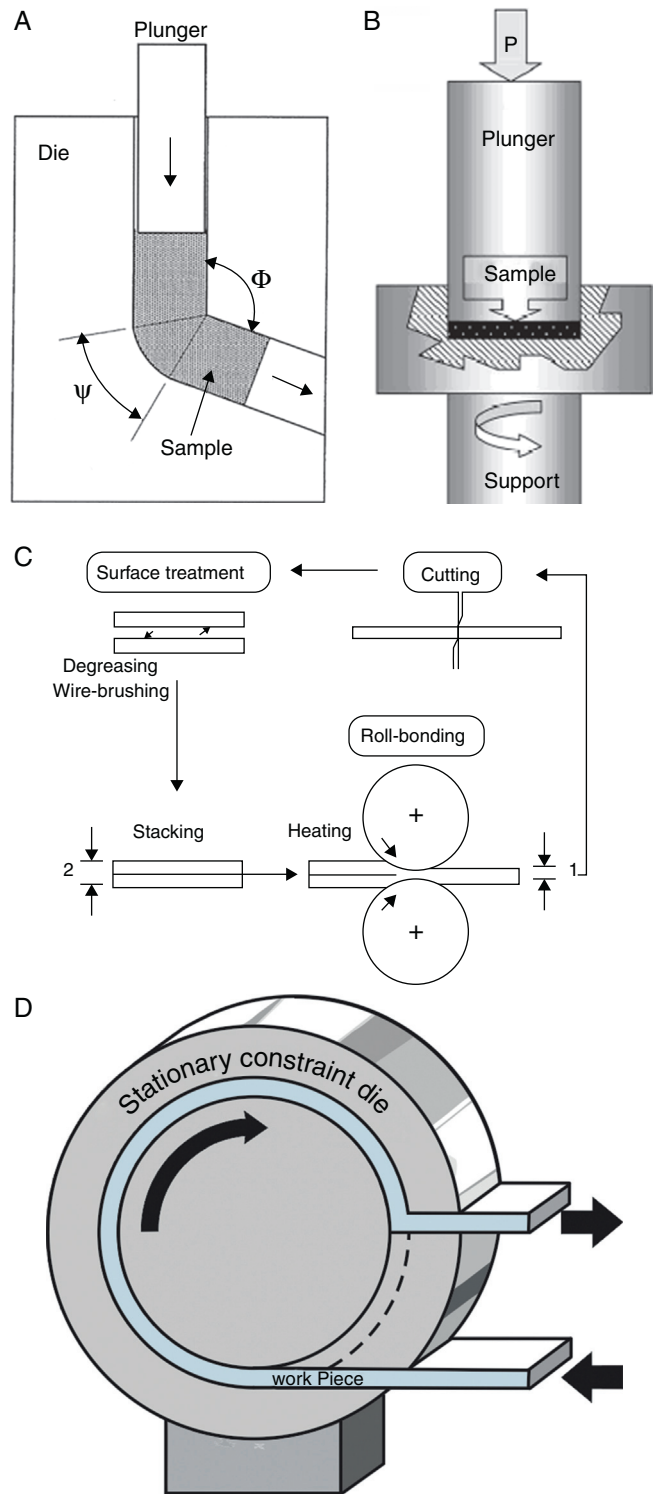**Fig. 9 – Setup for dental implant compression testing.**



**Fig. 10 – Processing routes for a strong grain size. (A) Equal-Channel Angular Pressing (ECAP); (B) high pressure torsion (HPT); (C) Accumulative roll bonding; and (D) ECAP-Conform.**
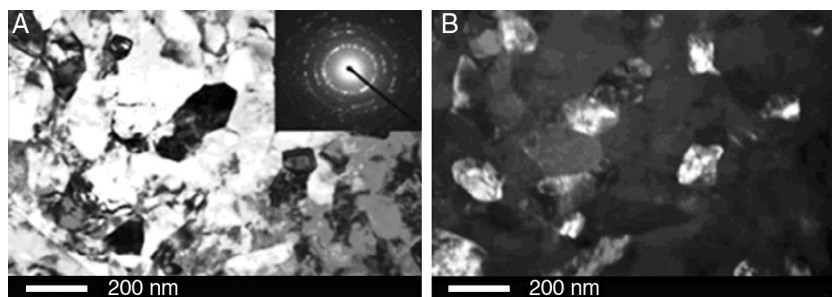
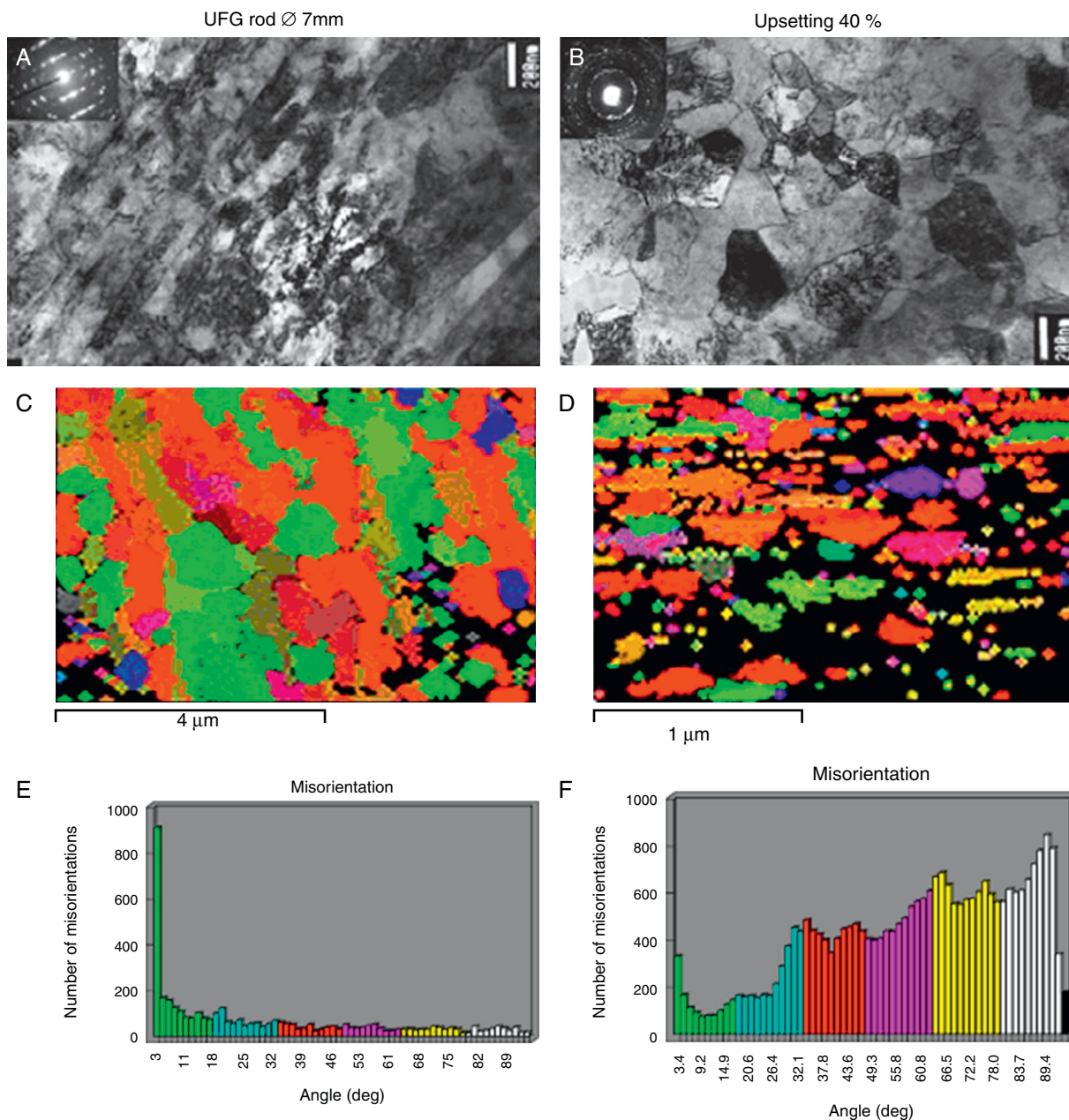**Fig. 11 – TEM micrograph of UFG Ti obtained by ECAP-Conform.**



**Fig. 12 – UFG Ti grade 4 produced by four passes ECAP and isothermal straining at 450 °C. Elongated grain after warm straining (A, C, E). Equiaxed grain after isothermal straining at 450 °C (B, D, F).**
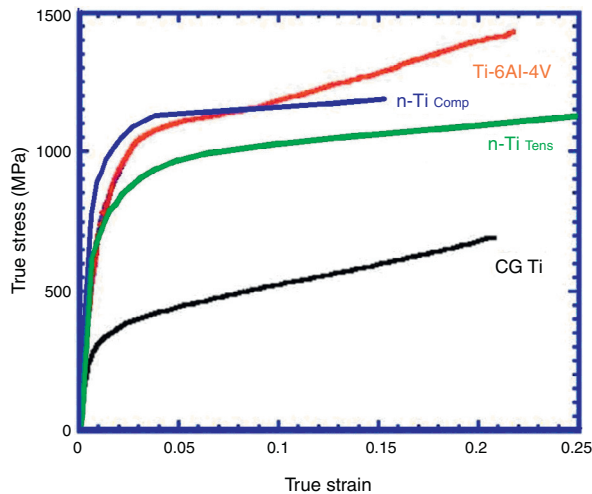
**Fig. 13 – Tensile mechanical properties of CG Ti (coarse grained), Ti6Al4V, and ultra-fine grained Ti (named nano-Ti).**

3.2 mm. In order to solve this undesirable situation, the manufacturers normally change the body shape of the implant and prosthetic connection. Examples are illustrated in Fig. 3 for conical (a) and cylindrical (b) implants. Miniscrews are also applied, Fig. 8, with a special threaded screw, to jaw bones with small thickness [11].

## 4. Ultrafine grained titanium

### 4.1. Relevance as a biomaterial

The reason for using Ti alloys has been their superior mechanical strength as compared to conventional cp Ti. One of the stimuli for the development of UFG Ti over conventional Ti alloys in dental implants is the presence of alloying elements in the latter that could present the potential toxicity when released into the system. The reduced grain size, which has now been achieved in the fabrication of UFG Ti by severe plastic deformation (SPD) made it possible to attain strength levels comparable to those of Ti alloys and thus justifying their substitution.

### 4.2. SPD processing

One of the most successful processing routes for a strong grain size reduction is by means of a special mechanical work named SPD [3,7]. Methods have been developed to subject metals to SPD as schematically shown in Fig. 10 [15,16]. The most common method shown in Fig. 10(a) is the Equal-Channel Angular Pressing (ECAP). The limitation of this technique is its batch nature. A sample has to be more than one time reinserted into the die and pressed. The reason is that shear strain per pass is only on the order of 1 and strains of 4–6 are required to generate equiaxed grains with submicrometer sizes. One way in which this can be overcome is by high pressure torsion (HPT), Fig. 10(b), which can generate strains as high as 15 in one single twisting operation. However,

**Table 2 – Dental implant removal torque after 8 weeks inserted in rabbit tibia [1].**

| Titanium implant | Removal torque (N cm) |
|---|---|
| cp Ti ASTM grade 2 | 17.0 ± 4.2 |
| UFG Ti grade 2 | 18.9 ± 1.9 |

the sizes and geometries of specimens prepared by this technique are limited and this technique has primarily been used as a research tool. Thus, efforts at developing a continuous processing method have been intense.

Two new approaches are nowadays gaining wide acceptance. The first is accumulative roll bonding, Fig. 10(c), in which a plate sample is rolled, then folded and re-rolled in successive stages until the total strain is sufficiently high. A second technique, developed by Valiev and Langdon [16], called ECAP-Conform, is shown in Fig. 10(d). It uses the principle of ECAP in a cylindrical roll for a continuous process. In this process, Fig. 10(d), a rod is inserted into the cylinder between guides, undergoing the ECAP process on its way out. In this manner, long rods can be produced. This technique is amenable to industrial scale production in rod geometry, well suited for dental implants.

For additional information on the above-mentioned as well as other SPD methods, the reader is referred to the work of Valiev and Langdon [16].

### 4.3. Microstructure

The SPD processing of cp Ti is an effective way to produce an UFG structure. As an illustration, Fig. 11 shows a TEM micrograph of UFG Ti obtained by ECAP-Conform [17]. In this figure, it is worth observing an almost equiaxed morphology with grain/subgrain sizes between 150 and 200 nm. This ultrafine structure is produced by the breakup of the original grain microstructure and by the successive rotation of the subgrains into new grains (nanosized) by the increase in angular misorientation between adjacent grains. The mechanism by which this occurs has been described and modeled by Mishra et al. [18].

In the case of a VT1-0 (Russian) cp Ti processed at room temperature by HPT under 5 GPa of pressure with (5 revolutions) strain of about 7, a ultrafine-grained structure with mean grain size of about 120 nm is formed. After annealing above 200 °C, a rearrangement of defects promotes high angle grain boundaries with very high dislocation densities, above $10^{14}/cm^2$, which indicates the non-equilibrium character of such grain boundaries after annealing [19].

In another case of UFG Ti grade 4 produced by four passes ECAP, which was then processed by forge-drawing at 300 °C (TMT), the ultimate strength significantly increase from 700 to 1240 MPa [20]. An additional isothermal straining at 450 °C of the previous (ECAP + TMT) UFG Ti, enhanced both the strength, up to 1420 MPa, and the ductility, up to 12% [20]. As shown in Fig. 12, the warm straining transforms the grains from elongated, Fig. 12(a, c, e), in the equiaxed with mainly high-angle boundaries, Fig. 12(b, d, f).
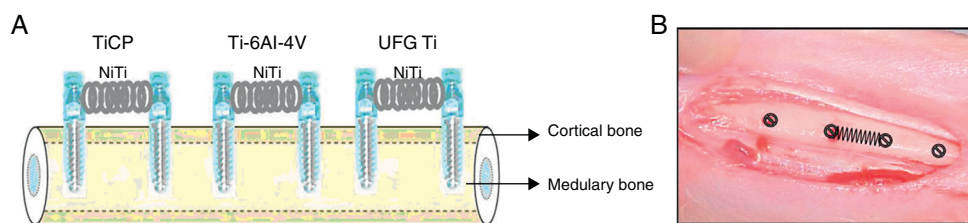
**Fig. 14 – Coarse grained cp Ti and UFG Ti mini-implants inserted in New Zealand rabbits.**

## 4.4. Mechanical properties

The primary effect of reducing the grain size is to increase the strength through the Hall–Petch equation:

$$\sigma_y = \sigma_0 + kd^{-1/2} \tag{4}$$

A reasonable value for the Hall–Petch slope parameter for titanium is $k = 6$ MPa mm$^{1/2}$ [21]. Thus, if one uses cp Ti Grade 4 as a guideline ($\sigma_y = 483$ MPa in Table 1), and considers a common grain size of 20 $\mu$m, one obtains the value of $\sigma_0$ as 441 MPa. For the case of UFG Ti with grain size of 200 nm, Fig. 11, by applying these values in Eq. (4) one obtains $\sigma_y = 865$ MPa, which is within the experimental results for UFG Ti shown in Table 1. Therefore, the main reason for the remarkable increase in strength of UFG Ti in comparison with cp Ti is the significant reduction in grain size to nanometric scale.

As far as the application of UFG Ti in dental implants is concerned, the most important properties are those related to the mechanical performance. As a result of the grain size reduction to nanometric values, see Figs. 11 and 12, the strength of the distinct grades, 1–4, of cp Ti is significantly improved by SPD processing as shown in Table 1 [20,22–24]. In this table, it should be noted that, in addition to the Hall–Petch effect, the marked increases in both the yield and the ultimate strength of cp Ti can also be attributed to the special processing involving not only multiple passes (ECAP) but also annealing and isothermal straining. Indeed, non-alloyed SPD titanium such as UFG Ti grade 4 TMT plus 350 °C annealing and 450 °C isothermal straining in Table 1, may reach a strength (1430 MPa), which is much superior than the traditional Ti–6Al–4V alloy (860 MPa) commonly used in dental implants.

Fig. 13 shows, as an illustration, the mechanical response of CG Ti (coarse grained), Ti6Al4V, and ultra-fine grained Ti (named nano-Ti). The Ti6Al4V alloy has strength over twice that of CG Ti. This difference in strength can also be accomplished by the grain size reduction. However, it should be noted that the work hardening beyond a strain of 0.05 is considerably lower.

In a recent review paper, Figueiredo and Langdon [25] presented general results on the association of crystallographic slip mechanisms with mechanical properties of ECAP processed metals and alloys. Among these results, the effect of the number of passes on the strength and the possibility of superplasticity were discussed. In the particular case of ECAPed cp Ti, the authors [25] emphasized the evolution reported by Mendes Filho et al. [22] on the hardness with the number of passes, as presented in Table 2.

| Table 3 – Dental implant removal torque after 8 weeks inserted in rabbit tibia. | |
|---|---|
| Titanium implant | Removal torque (N cm) |
| cp Ti ASTM grade 2 | 17.0 ± 4.2 |
| UFG Ti grade 2 | 18.9 ± 1.9 |
| Adapted from Elias et al. [1]. | |

## 5. In vivo experiments

In order to determine the degree of osseointegration, both cp Ti and UFG Ti machined mini-implants without surface treatment were inserted in New Zealand rabbits, Fig. 14, and loaded during the experiment to simulate the environment encountered in implants that undergo immediate loading. This was done by attaching two implants through a loaded NiTi spring and keeping the implants for 8 weeks. Subsequent to the sacrificing of the animals, the removal torque was measured. The results are given in Table 3. The ultrafine grained implants exhibited a removal torque of 18.9 N cm, which is slightly higher than cp Ti. Thus, the UFG structure resulted in a modest degree of osseointegration [1].

## 6. Concluding remarks

The exceptional properties of commercially pure titanium as a biomaterial for osseointegration in human implants have been improved to even higher levels of mechanical strength by severe plastic processing. The resulting ultrafine-grained titanium may present both yield and ultimate tensile strengths above 1000 MPa. This surpasses those of the commonly used Ti–6Al–4V alloy for structural implants. The main advantage is that it enables the use of pure titanium and avoids the toxicity of Al and V that have been shown to dissolve in the host tissue. The limited diameters of the ultrafine-grained processed Ti bars make them particularly convenient for dental mini-implant devices.

## Conflicts of Interest

The authors declare no conflicts of interest.

## Acknowledgements

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