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A Review of Titanium Based Orthopaedic Implants (Part-I): Physical Characteristics, Problems and the need for Surface Modification

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This paper reviews existing literature on basic titanium properties, applications and addresses the requirement for surface modifications to produce better implants. There is a significant demand for artificial implants, due to an ageing population that is a major driver of their growth. The use of titanium and its alloys as implant materials are widely common due to the excellent mechanical and biological properties and its manufacturability. It majorly reviews titanium and its alloy employed as orthopaedic implants. The basic mechanical properties, biocompatibility, corrosion and wear resistance of Ti-based biomaterial are also summarized. Furthermore, it is necessary for implants to comprise of necessary mechanical properties and physical characteristics to enable them to maintain their strength for a significant period of time by surface modifications. Therefore, comprehensive surface modification techniques for titanium alloys are discussed herein. This includes work on biocompatible properties of titanium implants enhanced by contact and non-contact surface roughening or coating biocompatible materials. Such techniques not only satisfy the end-users, but also improve the standard of their living. This paper also illustrates the current trend of titanium-based alloys and surface modification techniques, which contributes to the end-user to understand the pros and cons of titanium based implants.

Keywords: Titanium, implants, surface modification

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1 INTRODUCTION

Orthopaedic implants play an important role in medicine. The orthopaedic implant is a medical device designed and manufactured to support a damaged joint or to replace a fractured part of the bone. Specifically, orthopaedic implants are able to alleviate issues the bones and joints inside the human body when the original "human parts" are damaged, worn and unable to function on their own. They are subject to replacement due to various reasons, namely, bone fractures, osteoarthritis, scoliosis, spinal stenosis, and chronic pain. For example, pins, rods, screws and plates are used to anchor fractured bones while the bones are in the self-healing stage. [1].

The orthopaedic implants are made from alloys of different kinds of materials such as traditional materials (gold, silver, aluminium, iron steel, copper, etc.), stainless steel, titanium alloys and magnesium. For now, the traditional orthopaedic materials were no longer employed as their mechanical properties and releasing toxic ion when the implants are degraded inside the human body [2]. Nowadays, most of the materials employed for medical replacements are stainless [3] and titanium alloys [4]. Since the 1900s, the application of orthopaedic devices made from stainless steel has been continued to to-date. Especially, one of the most used stainless types is 316L stainless. Due to its capability of anti-corrosion, mechanical properties and cheap cost, it has been widely used in surgical procedures to replace biological tissue or help stabilize a biological structure, such as cranial plates, orthopaedic fracture plates, dental implants, spinal rods, joint replacement etc.[5]

However, due to the complex human body environment, the Stainless steel will be subject to the electrochemical mechanism. Once the metallic implants start to be corroded, the metal ion will be released from the surface materials into to human body thereby causing ion toxic. Compared with stainless steel, titanium and its alloys exhibit better performance in corrosion[6]. Thus, since 1962, titanium alloys have continuously received substantial attention.

1.2 The need for orthopaedic implants

If the need to have an orthopaedic implant is a thought that comes to mind for the end-user when it becomes an absolute requirement. The use of prosthetic implants for replacing and restoring tissues is continuously increased. It has been estimated that 90% of the world population over the age of 40 suffers from the degenerative diseases that are caused by the absence of normal biological self-healing ability or excessive and pre-longed loading [7-9]. For instance, for musculoskeletal conditions, such as arthritis, (disorders of the joints, bones and muscles) affect around 10 million people across the UK and cost around £5 billion to the National Health Service (NHS) programme in the U.K.to treat new and existing patients [10, 11].

Besides that, broken bones are also a main reason why one would require an artificial implant. The braking of bones occurs through fractures which are often very painful for patients. There are many types of bone fractures, including the complete, incomplete, simple and complex type of failures that a bone may undergo. A total of over 1 million bone fractures are reported each year in the UK, around 21% of fractures occurred as a result of road traffic accidents[12]. Bone fractures can happen in people of any age. However, Children and elderly people tend to sustain the most fractures. In children, a broken forearm is the most common fracture, with boys sustaining fractures more than girls have. Teenagers tend to be the most active age group, which increases their risk of injury, and their bones are more prone to breaking following the period of rapid growth during adolescence. What is more, in the elderly age group a combination of Osteoporosis (decreased bone density) and increased incidence of falls means that the number of broken bones naturally increases with age[13]. Thus, the recovery period is also likely to increase with age.

What is more, a hip fracture is the most common for elderly people, occupying over 4,000 hospital beds in any day each year and costs the NHS roughly a £1 billion per annual [14]. Moreover, the age and frailty of hip fracture patients mean that nearly a third of people die within a year of the injury due to different reasons, namely; osteoarthritis, as reported by National Joint Research (NJR) [14]. There are 2055687 procedures between 2003 to 2015.

The number of primary surgery is shown in Table 1, This includes 800,686 total hip replacements, 875,585 knee replacements, 17,300 shoulder replacements, 3,185 ankle replacements 1,639 elbow replacements. What is more, 146220 of the 1698395 surgeries had a revision surgery, due to the complicated human physical environment.

The need for implant products is not only for the initial replacement surgeries, but also, also for the revision of the second procedure due to the implant failure. For example, total hip revision (THR) is one of the highest numbers of surgeries in the UK. There are many reasons for a revision surgery. The THR may become painful, because it has been in place for many years and the components have begun to wear and loosen, moving a little in the bone. This type of loosening usually causes some bone loss and damage, and this bone loss needs to be dealt with at the time of revision surgery. THRs can dislocate on repeated occasions and revision surgery is needed to stop this distressing complication from happening.

TABLE 1
Shows the statistics of primaries (first) and revisions surgeries in the UK [14].

Body parts	**Knees**	**Hips**	**Shoulders**	**Ankles**	**Elbows**	**Total**
Primary	875,585	800,686	17,300	3,185	1,639	1698395
Revision	54,287	89,023	2,045	358	507	146220

In summary, according to a published report by BIS Research, the global market for orthopaedic implant products in 2016 was $40.20 billion [15]. The industry sees annual growth of 6.1% compared with last year, which means the market is expected to reach $ 61.02 billion by 2023. Therefore, the need for implant products is significant and the quality of implant products should be strictly controlled and supervised for the health of people all over the world.

1.3 Reasons for Failures in Orthopaedic implants

As we mentioned in Table 1, there are nearly 150 thousand procedures done in 2016 [14]. Since there are many reasons for failures for orthopaedic implants as shown in Figure 1, the primary reasons for the revision are as follow aseptic loosening (5,073 surgeries); pain (4,078); wear (3,548 surgeries); and infection (2,889 surgeries). It can be seen that aseptic loosening is the most reason, followed by pain (26%), wear (22%) and infection (19%)

1.3.1 Loosening of Implants

Implants loosening, which is a mode of failure resulting from implant movement or migration in the bone or cement according to Havelin *et al.* [16]. In 1993, implant loosening accounted for 64% among the revision procedures from 1987 to 1990 in Norway. Also, Malchau *et al*. [17], found that 79% of revisions were due to implant loosening in Sweden from 1987 to 1990. Additionally, a report by the national joint research, UK (2016), stated that implant

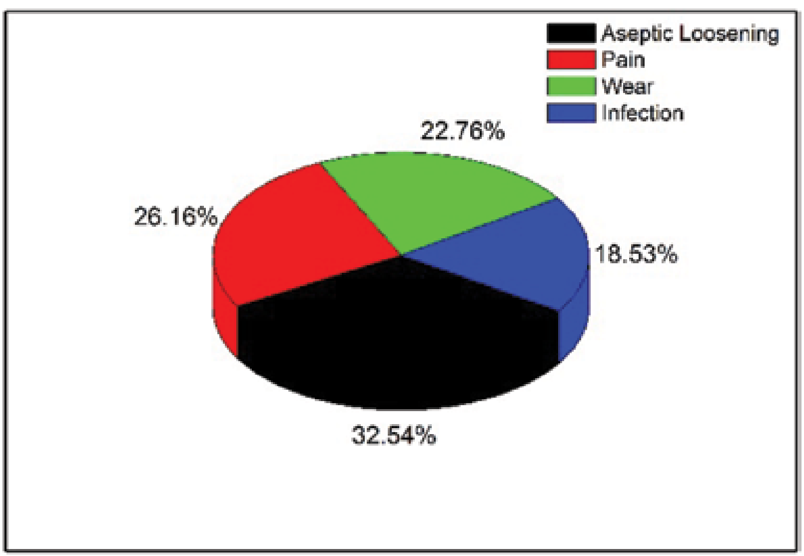

FIGURE 1
The main reason for revision procedures: aseptic loosening; pain; wear and infection.

loosening was still the highest failure reason corresponding to 32.6%. Stress shielding was one of the reasons that leading to implant loosening. Stress shielding refers to the osteopenia as a result of the removal of typical stresses from the bone by an implant. This is because by Wolff`s law, bone in a healthy person or animal will remodel in response to the loads it is placed under[18]. Therefore, if the loading on a bone decrease, the bone will become less dense and weaker because there is no stimulus for continued remodelling that is required to maintain bone mass [19-22].

Shown in Figure 2, when the artificial femoral and Proximal Femur were implanted in the body, it shared the load from the body instead of the bone. In a healthy body environment, the load should be born by bone, otherwise, the upper femoral subjected to reduced stress could cause a loss of bone mass (osteopenia) through the biological process called "resorption"[23]. In the contact, in the lower femoral, the bone is overloaded which causes dense skeleton.

According to Wolff's law, a bone will remodel itself to become stronger to resist the load acting upon it. In order to investigate the schematic of this remodelling, many researchers have worked on calculating the stresses in the bone. Especially, with Finite Element Analysis, conducted by Joshi *et al.*[24], explored a hypothesis that a total hip prosthesis can be developed to substantially reduce

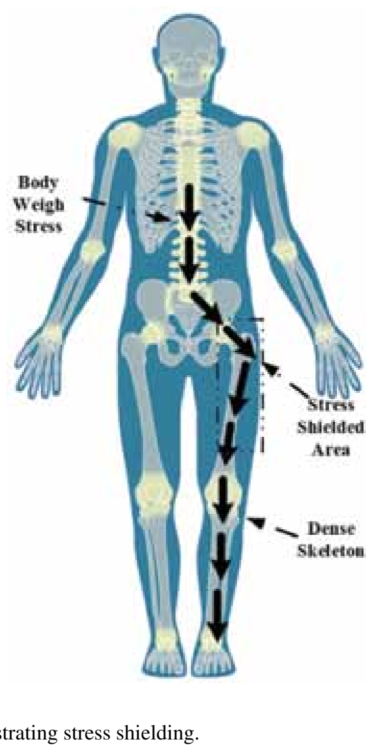

FIGURE 2
A schematic diagram illustrating stress shielding.

stress shielding through re-design. Weinans *et al.* [25], also came up with a definition of stress shielding that it works like a change in strain energy (SE) in each element of the implanted bone relative to a reference value of SE in the contacting bone and SS is for stress shielding as shown in Equation 1.

$$SS = \frac{SE(Treated) - SE(Reference)}{SE(Reference)} \tag{1}$$

1.3.2 Implant Infection Caused by Bacterial

As we may be surprised that even it was under aseptic conditions such as Intensive Care Units (ICUs), there would still be around 5000 to 50000 microparticles, broadcasted daily from each physician to patients[26]. In addition, although the wounds were clean when procedures were finished, the number of pathogenic bacteria such as staphylococci still can be recovered to around 90%[27]. Therefore, bacteria were able to find their pave into the human body despite the strict environment. Thus, minor contamination areas of pre-inserted medical devices may be regarded as infectious.

Typically, the main sources of bacteria causing implant infections are from the physician and the skin of the patients themselves near the wound during implant insertion. Thereafter, bacteria migrated through incision channels to the surface of implants inside the patients' body, spreading towards vivo environment during the haematogenesises [28].

The bacteria adhesion is the first and most important step during implants infections caused by bacteria. The bacteria become adhered and immobile to the implant which provides surfaces for biofilm formation, bacterial attachment and proliferation. In the surfaces of inserted medical devices, the adherent bacteria generate a protective polymeric, extracellular substance, protecting these bacteria from being eradicated. Without it, bacteria could float around the body.

Although a wide variety of bacteria can lead to implant infections, majority cases are infected by a small group of species. As mentioned above, Staphylococci, prominently account for nearly 70% of orthopaedic implant infections. Moreover, Pseudomonas aeruginosa accounts for another 8% of infections [29]. Thus, it warrants the development of a new type of sophisticated anti-bacterial orthopaedic implants.

1.3.3 Wear of Implant Material

Wear is also another critical challenge for medical devices such as hip, knee and medial proximal tibia. It can cause loss of mass from the implanted materials, which leads to critical degradation of the function of orthopaedic prostheses. For instance, wear debris generated from Polyethylene acetabular components could lead to osteolysis in THA. Zhu *et al.* [30] pointed out that the osteolysis caused by wear debris can result in loosening between the femoral head and proximal femur. Additionally, John *et al.*[31], conducted a 12-years of research, investigating the relationship between wear and osteolysis. They have found that there is no correlation between the amount of polyethylene wear and osteolysis volume.

In a titanium alloy such as Ti-6Al-4V, Vanadium (V) is found to be a toxic element to the human body[32]. When the stable coating TiO_2 layer on the TC4 is worn out due to wear behaviour, the V ion will be released into the vivo environment, leading to ion toxicity [33, 34].

The wear properties of biomedical materials play an important role when choosing a suitable medical device. What is more, adhesive wear, fatigue wear and abrasive wear, also have a great influence in analysing the degradation of medical prostheses. Decreasing wear of medical devices was always an important research topic to study for many researchers.

2 STATE-OF-THE-ART IN TITANIUM ALLOYS AND OTHER METALLIC AS USED FOR MEDICAL APPLICATIONS

2.1 Titanium and its alloy in orthopaedic implantation

It is in the early 1940s that Titanium alloys were introduced in the medical areas such as the Bothe *et al* [35]and Okabe *et al* [36], investigated the reaction of bone to metallic implants. Titanium has been widely used in orthopaedic implantations due to its excellent biocompatibility and mechanical properties [37]. A great variety of implants for many different designs are now made from titanium in either its pure or its alloyed forms.

2.1.1 Mechanical properties of titanium and its alloys for orthopaedic applications

Metallic materials, which under concern for fabricating medical devices were mainly considered from mechanical properties such as tensile strength, modulus, hardness and elongation. The elastic modulus mismatch between implantation devices and bones also causes "stress shield" phenomenon. Since the 1960s, such as titanium alloy, stainless steel and Co-Cr alloys have been widely employed in the medical area. However, metallic based implants possess much higher Young's Modulus than human bones which will cause stress shielding. According to Wolff's Law, the higher modulus components will bear more loads than the lower one. Thus, due to the high Young's modulus of metallic, the bone will become less dense and weaker. Because there is not enough stimulus for remodelling which is required for human bones growth. That is called stress shielding. Thus, the design and manufacturing orthopaedic materials should possess an equal modulus to the bone for bearing loads. Figure 3 shows the elastic modulus of titanium alloys compared with bones, Cr-Co alloy and 316l SS[38]. As we know that the bone modulus

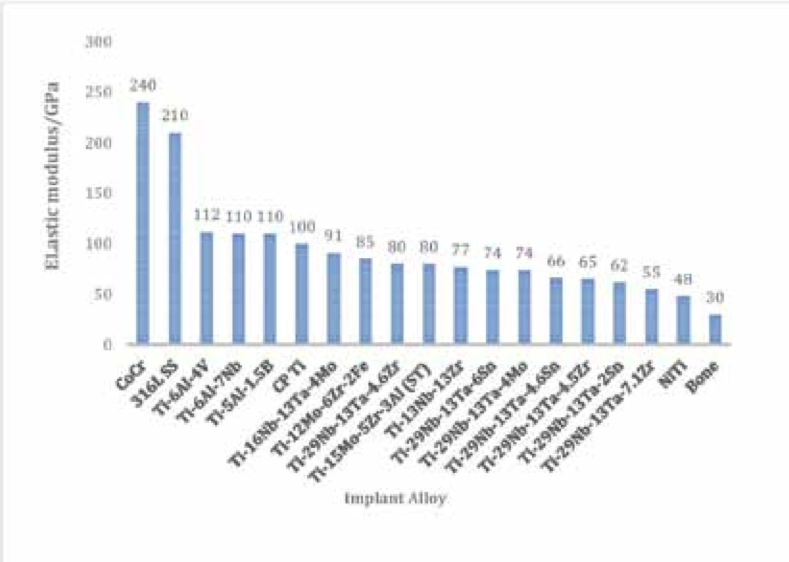

FIGURE 3
The elasticity modulus of titanium alloys are compared with bones, Cr-Co alloy and 316l SS.

varies from 4 GPa to 30 GPa differentiating from the bearing type of bone and direction of measurements [39]. However, both the modulus of Cr-Co alloy and stainless steel are greatly higher than load bones. This will lead to a stress shielding effect, thereby, causing the implant to loosen. Compared to 316L stainless steel (210 GPa) and Cr-Co alloy (240GPa), the titanium alloys possess a lower modulus varying from 55 GPa to 120 GPa. Thus, among those implant metallic materials, titanium alloys are selected for most medical applications due to its high strength and low modulus.

Although the elastic modulus Ti-6Al-4V alloy is half than that of stainless steels or Cr-Co alloy, the modulus of Ti64 is still high (100 GPa) compared to bone modulus (30 GPa). Phase α and phase α/β titanium alloys were the first generations to reduce the elastic modulus of orthopaedic implants from the 1950s to 1990s [7]. Song et. al. [40], found that adding elements Nb, Zr, Mo, and Ta into titanium alloy can decrease the elastic modulus of bcc Ti without weakening the strength. Since the 1990s to date, researchers focused on the β type titanium alloys that process closer elastic modulus to bones and excellent cold workability, high strength. Ti-13Nb-13Zr [41], Ti-12Mo-6Zr-2Fe [42], Ti-15MO-5Zr-3AL [43], Ti-29Nb-13Ta-4.6Zr [44] and Ti-35Nb-7Zr-5Ta [45] alloy are all the second generation orthopaedic titanium that modulus vary from 55 GPa to 84 GPa. Ti-35Nb-7Zr-5Ta (TNZT) elastic modulus ranks the lowest places amongst theses β titanium alloys at 55 GPa. From a mechanical point of view, the strength of β type titanium alloys can be increased with Young's modulus law by cold working. Therefore, β type titanium alloys are attracting more attention to research.

Additionally, when orthopaedic implants are undergoing repeat daily body action, they are naturally affected by cyclic loading. For the long term, this can lead to alternating plastic deformation of small zones of the stress of concentration. The response of the material to repeated cyclic loading is determined by the fatigue strength of the material. Factors such as strength, materials, shape, loading type determine the long-term success of the implant subjected to cyclic loading [46]. Amongst these factors, if the strength of metallic materials is not enough to support the repeated cyclic loads or object impacts, patients will not need to undergo another revision surgery, due to the fracture of orthopaedic implants. Although fatigue is so critical properties among biomaterials, the standard fatigue test methods have not been established as simulating actual implantation and loading condition is too expensive and difficult. 'Standard' fatigue tests including tension/compression, bending, torsion, and rotating bending/flexural fatigue testing are normally used to evaluate the mechanical properties of materials, candidates before implantations.

TABLE 3
Mechanical properties of titanium alloys [47-49].

	Titanium	YS (MPa)	TS (MPa)	E (GPa)	T_β(°C)	Hardness
a	High purity Ti (99.98% Ti)	140	235	100-145	882	100
	CP-Ti grade 1(0.2Fe-0.18O)	120	170-310	>210	-	120
	CP-Ti grade 4 (0.5Fe-0.4O)	260	480-655	>550	100-120	260
	Alloy grade 6 (Ti-5Al-2.5Sn)	827	861	109	1040	300
Near a	Ti-6-2-4-2-S (Ti-6Al-2.7Sn-4Zr-2Mo-0.1Si)	990	1010	114	995	340
	TIMETAL 1100 (Ti-6Al-5Zr-0.5Mo-0.25Si)	900-950	1010-1058	112	1010	-
	TIMETAL 685	850-910	990-1020	120	1020	-
a+b	Ti-6-4 (Ti-6Al-4V)	800-1100	900-1200	110-140	995	300-400
	Ti-6-6-2(Ti-6Al-6V-2Sn)	950-1050	1000-1100	110-117	945	300-400
	Ti-6-2-4-6(Ti-6Al-2Sn-4Zr-6Mo)	1000-1100	1100-1200	114	940	300-400
	Ti-17 (Ti-5Al-2Sn-2Zr-4Mo-4Cr)	1050	1100-1250	112	890	400
Near β	SP 700 (Ti-4.5Al-3V-2Mo-2Fe)	900	960	110	900	300-500
	Beta III(Ti-11.5Mo-6Zr-4.5Sn)	800-1200	900-1300	83-103	760	250-450
	Beta C(Ti-3Al-8V-6Cr-4Mo-4Zr)	800-1200	900-1300	86-115	795	300-450
	Ti-10-2-3(Ti-10V-2Fe-3Al)	1000-1200	1000-1400	110	800	300-470
	Ti-15-3(Ti-15V-3Cr-3Al-3Sn)	800-1000	800-1100	80-100	760	300-450

YS: Yield strength; TS: Tensile strength; E: Elastic modulus: T_β: Beta transus temperature

Nonetheless, titanium and its alloys process excellent mechanical performance, required by the aforementioned tests, which are summarized in Table 3 Mechanical and fatigue properties of titanium alloys are mainly determined by microstructures that are formed during thermal and manufacturing processes. Titanium has two allotropic forms. One of them is a hexagonal close-packed crystal structure (HCP, α phase,) at room temperature [50, 51]. This structure is stable at temperatures up to 873^{0}C, above which, α phase transferred to a body-centred cubic structure (β-phase body-centred cubic (bcc)) [52]. Intermediate amounts of alloying additions allow both alpha and beta phase stability at room temperature. Using this principle, two-phase alloys have been developed with superior mechanical properties; an example of this is Ti-6Al-4%V. This alloy contains, mostly, α+β titanium, due to its balanced strength and toughness and it is the first registered titanium alloy (ASTM standard F136). In terms of β-alloy, although, it's elastic modulus is much lower than that of α+β titanium, the smooth fatigue resistance of β-titanium is lower under the same fatigue testing condition. For instance, Under RBF (R=-1/60 Hz) 19, the fatigue limit of Ti-35Nb-7Zr-5Ta is 265 MPa, which is much lower than that of Ti-6Al-4V (610) at the same testing condition [7].

However, although β-titanium alloy has comparably poor performance in smooth fatigue resistance, the behaviour of orthopaedic implants are more closely associated with notch fatigue behaviour in vivo conditions. For example, hip stems and femoral normally coated which induced stress concentration sites. Thus, regarding notch fatigue behaviour, β titanium alloy has a comparable or higher performance than Ti-6Al-4V.

2.1.2 Biocompatibility of orthopaedic titanium alloys and osseointegration

Biocompatibility denotes the ability to be in contact with a living system without producing an adverse effect [53]. The reasons why titanium is considered as biocompatible is attributed to its resistance to corrosion from body environment, bio-inertness, capacity for osseointegration and high fatigue strength. Once titanium is inserted into the human body, a serious of reactions with proteins, cells and body fluid will happen in the biological micro-environment (Figure 4).

Osseointegration refers to the formation of an interface between implant surface and bones. More specifically, Branemark [54], stated that a direct structural and functional connection between ordered living bone and the surface of a load-carrying implant. According to its definition, it was used to describe the interaction of implants and bones. Thus we should know, what has happened after the implant is inserted in the human body. Once the implant is inserted in *vivo*, within 10^{-9}s, water molecules layer is formed around the surface of the implant, which contributes to the adsorption of proteins and cells[55]. Onwards, within 30s to hours, proteins cover the surface of water molecules layers. Those proteins are from tissue fluid and blood near the insertion site and the ones later come from cellular activity.

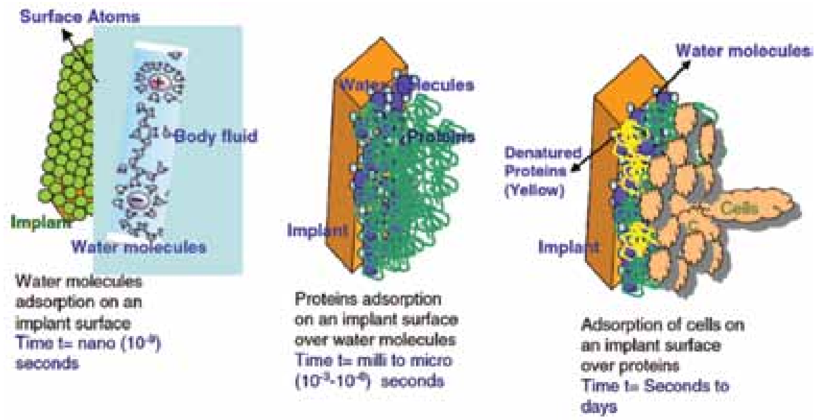

FIGURE 4
The evolution of interaction between human bone with implants at different time intervals [7].

After the proteins adsorption, from few hours to days, cells adsorption occurs on the adsorbed protein layers, thereby, starting cellular adhesion, migration and differentiation [56-59]. Degree of the interaction of the above stages is determined by the implant surface chemical composition and surface topography, which determines the healing effects of orthopaedic implants. There is no evidence shown that the implant materials have a completely no-adverse effect. Compared with stainless steel, and Co-Cr alloys, titanium has a better performance in osseointegration, and it is nearly an inert material in the human body environment. Additionally, a stable TiO_2 layer is formed on the surface of titanium alloys, which also contributes to the bio-compatibility.

2.1.3 Corrosion behaviour of orthopaedic titanium alloy

Orthopaedic implants made from titanium and its alloys all undergo corrosion when they are placed in the human body, contacting body fluid. Also, the body environment is corrosive due to the chloride ions and proteins, thereby, causing different kinds of chemical reaction on the implant surface. The metallic components of the alloy are oxidized to their ionic forms and dissolved oxygen is reduced to hydroxide ions [60].

The human body fluid is a complex environment, including amino acids, proteins, organic compounds etc [61]. Thus, corrosion would take place when the implant was inserted in the body, contacting the body fluid. This gives rise the need for surface modification techniques to avoid and pre-long the onset of corrosion. Such a technique could be in the form of plastic burnishing, shot peening, or laser-based peening technique.

Compared to stainless steel, it is well known that titanium and its alloys have immunity to both pitting corrosion and stress corrosion cracking in chloride solution[62, 63]. The reason why titanium has such excellent performance in corrosion resistance can contribute to the formation of a very chemically stable, highly adherent, and continuous protective oxide film (TiO_2 film) on the titanium surface [64-66]. The passive TiO_2 film is formed spontaneously in nature and remain stable, which separates the metal from the outside environment. Normally, the thickness of the passive film is around 10-20nm [67] would affect the oxide stability. As stated previously, in section 2.1.2, the TiO_2 can provide favourable osseo-integration. The passive films prevent further transport of metallic ions or electrons across the film. For instance, Ti-6Al-4V has been widely used in the medical area. However, element Al and V are toxic to the human body. Once the film covered the metal surface is broken, Al and V ion will be released into the body fluid as metal ions, causing Alzheimer's and neuropathy disease[68]. Thus, the films must be compact, and possess an atomic structure, thereby, limiting the transportation of ions across the films from the body fluid.

In terms of corrosion, the biggest weakness of titanium appears to be crevice corrosion in industry, while for medical applications, it is not the main concern. Liang et. al. [69], examined the crevice corrosion behaviour of CP Ti, Ti-6AL-4V and Ti-Ni Shape memory alloy (SMA) in Ringer's fluids at the potential of 400 mV. In terms of temperature, the crevice corrosion of all three titanium alloys have a positive correlation with that. Among these three alloys, Ti-6Al-4V have better performance in crevice corrosion resistance than CP Ti and SMA Ti-Ni.

Most of the medical implants are subjected to low-frequency loads that may lead to corrosion fatigue. For example, simple walking can result in cyclic loading at about 1Hz, causing fatigue corrosion of titanium hip implants. Yu et al [70], investigated the corrosion resistance of Ti-6Al-4V alloy under a cyclic loading condition at 1.25Hz. They found that surface treatment such as nitrogen ion implantation and heat-treatment can improve the fatigue corrosion resistance, through refining prior-β grains.

Fretting corrosion is also very common in all load-bearing metallic orthopaedic implants. Fretting occurs at bone-stems interface, the stem-cement interface and on the interface of modular connection between implant components. As discussed above, cyclic loading can not only lead to fatigue corrosion but also fretting corrosion due to the small motion (1-100 μm) between implants parts. What is more, surface roughness is another factor affecting fretting corrosion of titanium. For that case, Sivakumar *et al* [71]studied the effect of roughness from 43nm, 116nm,177nm and 474 nm on fretting corrosion of pure titanium in Ringer's solution for the bio-implant application. The anodic polarization and EIS results showed that the sample with Ra 43nm exhibits the best corrosion resistance performance as the formation of less defective and impermeable TiO_2 layer. In addition, Fretting corrosion phenomenon is also found in a joint between titanium and nitinol. Fretting corrosion of nitinol spinal rods with TC4 was tested in simulated body fluid by Lukina *et. al.* [66]. Their study reveals that nitinol spinal rods with TC4 screw are vulnerable to fretting corrosion.

2.1.4 Wear in titanium alloy

As we know the biomaterials shouldn't be cytotoxic which is caused by increasing ion content in the human body from the metallic implant. That disease is called metallosis which is a side effect from replacements, such as metal-on-metal hip implants, made from different metals [72, 73]. The metal particle will be released into human blood from the metal implants when the two metal parts wear against each other.

Wear is a vitally important problem in any joint substitution, and it contributes 13.6% of all implants failure reasons [14]. Wear is inevitable that it always occurs in the articulation of artificial joints as a result of the mixed lubrication regime. When the artificial joint is working, billions of microscopic particles are rubbed off cutting motions as the movement of the joint. The cutting particles are trapped inside the tissues, thereby, maybe leading to foreign body reaction such as the activations of macrophages and foreign body giant cells [74]. A revision surgeon not only means money-cost and time-consuming but also extremely pains for patients. Thus, the wear resistance of titanium plays a very important role in manufacturing orthopaedic implants.

Due to the low hardness, titanium alloys have poor fretting fatigue resistance and tribological properties, which has normally been presented with a high coefficient of friction, severe adhesive wear and low abrasion resistance [75, 76]. Titanium has a tendency that it moves or slides to gall, thereby, seizing, when titanium is rubbing between itself or other materials. The movement of these two bodies may cause to more intensity wear because adhesion couplings are created and the surface oxide layer becomes unstable, especially third bodies show up, Figure 5 [77]. Due to these drawbacks, 10%-20% of titanium-made head and polymer cup of joints need to be replaced with 15-20 years [19]. More, aseptic Loosen (50.1%, 1st) and wear (13.6%, 3rd) are the main two failure reason for implant devices according to NHS annual reports [14]. Due to the human body activity, the wear debris is released from the implant to the surrounding human body tissue, leading to bone resorption, which will finally result in aseptic loosening which is 32.54%. Amongst the aseptic loosened of femoral heads made by Co-Cr-Mo system alloy, 316l SS and Ti-6Al-4V EI, titanium alloy possess the highest average wear 74.3% against high molecular weight polyethylene acetabular component [78]. That drives us to explore another surface modification techniques, such as shot peening, surface coating, laser shock peening, blast cleaning, or laser polishing. However, to improve the wear resistance of titanium alloys, a technique that enhances the mechanical property and gives better structural integrity is more favourable in this instance. Thus, laser shock peening would be more

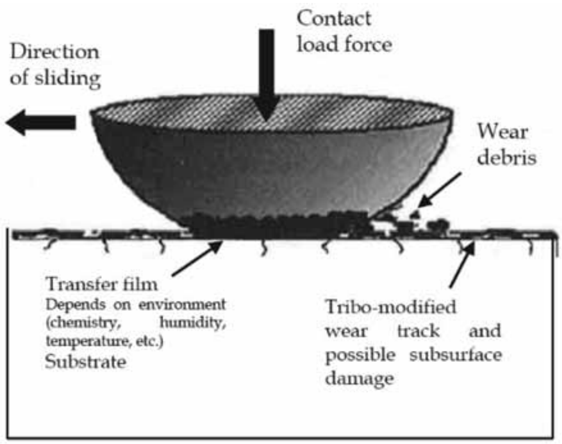

FIGURE 5
A schematic diagram showing the sliding tribology with the ball pin [77].

suitable as it induces a deep level of compressive stresses in comparison to their techniques mentioned.

2.2 Titanium alloys for medical applications

2.2.1 Dental application

Titanium alloys are widely used for manufacturing dental implants and orthopaedic prostheses. This cost around more than 1000 tones in manufacturing titanium devices over the world every year [79]. Before titanium alloys, Cobalt-Chromium and stainless steel were used as dental implant materials. However, the low success-implanting rate and poor osseointegrative performance limit their further applications in manufacturing dental prosthesis. For now, endosseous dental implant applications specifically require titanium alloys. This is because titanium alloys possess excellent corrosion resistance, high strength-to-weight ratio and outstanding osseointegration. Therefore, titanium alloys have a long history of clinical applications in both dental and orthopaedic implants dating back to 1965 [80]. Since the 1980s, with the development of the computer-aided design (CAD), dentistry devices such as dental bridges, dental implant prosthesis components (screw and abutment), crowns and over-dentures are manufactured by titanium alloys.

As shown in Figure 6, in the bottom, it is a titanium screw with a longitude of 8-16 mm which is implanted into a prepared dental alveolus in the jaw and acts as a replacement root for the missing tooth. In the top, a special attachment component called the abutment is used to fit the top of the implant, thereby, forming the external connection with a dental crown or dental bridges.

FIGURE 6
Dental implant (d) includes dental implant abutment (b), the porcelain crown (a) and the titanium prost (c) [81].

In titanium dental implanting surgeries, there is a 9 out 10 success rate and the service life of the components could last 30 years or more due to its strong and durable properties. However, some patients are allergic to titanium that exhibit in the form of urticaria, mucosa, atopic dermatitis, pain and necrosis. [82] Therefore, it is necessary to undergo a MELISA (Memory Lymphocyte Immunostimulation Assay) test to diagnose a number of different metal allergies[83].

2.2.2 Hip joint implants and other applications

Commercially pure (CP) titanium and its alloy such as Ti-6Al-4V alloy is a good choice around the world for orthopaedic joint replacements, namely, total knee replacement and total hip replacements (Figure 7 and 8).

Hip joint replacement surgery is the most common clinical surgery over the world for most patients[86]. A hip joint implant can be divided into four categories according to the connection between ball and socket. They are: metal-on-plastic; ceramic-on-plastic; ceramic-on-ceramic and metal-on-metal[87]. In a metal hip joint system, structural components such as acetabulum, the socket of the ball-and-socket joints are normally made of titanium alloys[88]. Although the metal-on-metal system presented a very low wear rate in the laboratory experiment, the bearing surface using titanium alloys is no longer suitable for long-term replacement as there is the record that patients require the revision surgeries due to metal-on-metal system. For now, the combination of ceramic and plastic with titanium is more popular than just metal hip systems. What is more, titanium alloys are also involved in manufacturing elbow and shoulder

FIGURE 7
Digital image showing a prosthetic hip implant [84].

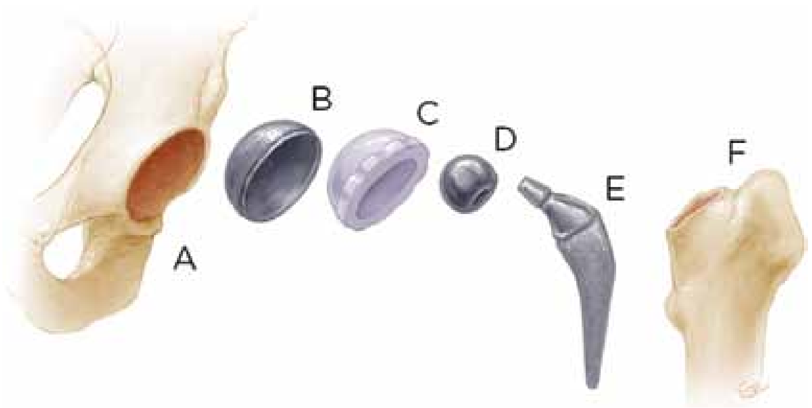

FIGURE 8
Components of hip replacement surgery: the acetabulum in (a), or socket of the ball-and-socket joint, is reamed to receive the cup in (b) and the liner in (c). The ball (d) is placed on the stem (e) which is then inserted into a hollowed-out femur in (f), or thigh bone liner ball are made of titanium alloys [85].

joint replacements. Bone screws, plates, staples, mesh and cables made of titanium support broken bones and facilitate fixation[89].

More than orthopaedic applications, titanium alloys are not only involved in surgical instruments such as forceps, dental drills and laser electrodes but also be used in neurosurgical applications include cranial plates, acrylic and mesh[90]. What is more, it has been 3-D printed manufacturing rib cages for use by children and elder people[91].

3. REVIEW ON SURFACE MODIFICATIONS FOR TITANIUM AND ITS ALLOYS

As surface properties decide the long-term performance of implant devices, a variety of surface modifications are needed prior to implants stabilization [92]. There are many reasons to carry out the surface modification of implants before implantations, which are summarized in Table 4.

Liu *et al* [93]summarized the main surface modification methods of Titanium and its alloys are in Table 5. In this section, those methods will be reviewed, together with the last research evaluating the use of surface modification of titanium and its alloys for orthopaedic application, as well as future perspectives. The goal is to improve biocompatibility, wear resistance and corrosion resistance of titanium and its alloys.

3.1 Mechanical methods for surface topography modification

Mechanical methods including grinding, machining, polishing, have been wildly used for acquiring a rough or a smooth surface through shaping, removal of the material's surface. The objective is to obtain specific surface topographies and roughness which contributes to the adhesion within a body environment. Alternatively, cleaning-off surface contamination is another option. In terms of metallic materials, machining changed deformations and the surface structure, as well as the increased surface hardness. In general, mechanical methods lead to a rough structure. Increased surface roughness is considered more beneficial to cell attachment, proliferation and differentiation of osteogenic cells which are key factors of osseointegration [96-98]. Among those mechanical methods, sand-blasting is the most used technique[99]. The usual abrasive particle of the blasting media are alumina, silicon carbide, biphasic calcium phosphates (BCP), hydroxyapatite and β-Tricalcium phosphate [100]. Sand-Blasting consists of the impact of a jet of abrasive particles against the surface by compressed air which may lead to

TABLE 4
Rationale for surface modification of Ti and its alloys.[94, 95]

Surface modification effect	Reasons
Mechanical purpose	Improve the fatigue life
	Increase the hardness for wear resistance
	Improve adhesion in bonding
Biological purpose	Increase the osseointegration
	Introduce a passive layer to prevent toxic ion release into the body
	Clean surface material and improve bacterial resistance

TABLE 5
A summary of main surface modification of titanium and its alloys [92, 93].

Surface modification methods	**Modified layers**	**Objective**
Mechanical methods: Machining, grinding Polishing blasting	The rough or smooth surface formed by the subtraction process	Produce specific surface topographies; clean and roughen surface improve adhesion in bonding
Chemical methods Alkaline treatment Acidic treatment Hydrogen peroxide treatment	<10 nm of the surface oxide layer ~1 μm of sodium titanate gel ~5nm of dense inner oxide and porous outer layer	Remove oxide scales and contamination Improve biocompatibility, bioactivity or bone conductivity
Anodic oxidation	~10 nm to 40μm of TiO_2 layer, adsorption and incorporation of electrolyte anions	Produce specific surface topographies; improved corrosion resistance; improve biocompatibility, bioactivity or bone conductivity
Sol-gel	~ 10μm of thin film, such as calcium phosphate, TiO_2 and silica	Improve biocompatibility, bioactivity or bone conductivity
Biochemical methods	Modification through silanizaed titania photochemistry, sel-assembled monolayers, protein-resistance etc	Induce specific cell and tissue response by means of surface-immobilized peptides, proteins, or growth factors
Physical methods Thermal spray Flame spray HVOF DGUN	30~200 μm of coatings, such as titanium, HA, calcium silicate, Al_2O_3, ZrO_2, TiO_2	Improve wear resistance, corrosion resistance and biological properties
PVD(Physical Vapour deposition) Evaporation Ion plating sputtering	~1 μm of TiN, TiC, TiCN, diamond and diamond-like carbon thin film	Improve wear resistance, corrosion resistance and blood compatibility
Ion implantation and deposition Beam-line ion implantation PIII	~10 nm of surface modified layer and/ or ~1 μm of thin film	Modify surface composition; improve wear, corrosion resistance, and biocompatibility
Glow discharge plasma treatment	~ 1nm to ~ 100 nm of surface modified layer	Clean sterilize, oxide, nitride surface remove the native oxide layer

surface contamination and local inflammatory reactions of surrounding tissues as a result of the dissolution of abrasive particles into the body environments [101]. Fini *et al* [102], found that rougher surface showed stronger bone response after the implantation in the vivo environment.

3.2 Acide and Alkali Treatments

Acid treatment is often used to remove the oxide and contamination for achieving desired clean and equilibrium surface finishes [103]. TiO_2 consists of the main oxide layered of titanium alloys as titanium can easily react with O_2. In order to remove the oxide layer before further coating, 10-30vol% HNO_3 and 1-3 vol% in distilled water involve the standard solution for acid-pretreatment of titanium and its alloys. Hydrofluoric acid is able to react with TiO_2 rapidly, forming soluble titanium fluorides and hydrogen. A ratio of 10 to 1 of mixed hydrofluoric acid and nitric acid can be used for decreasing the formation of free hydrogen to prevent from embrittlement surface layers caused by the inclusion of hydrogen [104]. Normally, a thin oxide layer is formed by acid etching with a depth under 10 nm. More than that, its growing speed is much slower than that of untreated, from 3-6nm within 400-day period [105].

Alkali-Heating Treatment (AHT) is a surface modification technique of immersing titanium alloy in alkali solution (NaOH or KOH), in order to form bioactive porous layers on the material surfaces, followed by heating treatment to dehydrate and transform the amorphous structure into porous crystalline [106]. Kim et al [107] started by immersing in a 5-10 ml[108] NaOH or KOH for 24 h, followed by rinsing in distilled water and ultrasonic cleaning. Then, dried in the oven and the carried on the thermal treatment that heating the material at the temperature of 600-800 C° for 1h. The heating treatment is required to be performed at a low pressure of 10^{-4} to 10^{-5} bar to avoid titanium oxidation at high temperature. After the thermal treatment, the porous sample is soaked in simulated body fluid (SBF) for 4 weeks, onwards bioactive bone-like apatite is formed on the surface of the titanium. This processing can also be described by the following chemical formulations:

$$TiO_2+NaOH \rightarrow HTiO_3^-+Na^+$$

$$Ti+3OH^- \rightarrow Ti(OH)^+{}_3+4e^-$$

$$Ti(OH)_3^++e^- \rightarrow TiO_2\ H_2O+1/2\ H_2\uparrow$$

$$Ti(OH)_3^++OH^- \leftrightarrow Ti(OH)_4$$

Hydroxyl attack on the hydrated TiO_2 generates negatively charged hydrates on the surfaces:

$$TiO_2{*}H_2O+OH^- \leftrightarrow HTiO_3^-{*}nH_2O$$

An alkalinic titanate hydrogel layer is formed as the negatively charged substances combine with the alkali ions in the solution. Onward, when it is heating, the hydrogel layer is dehydrated and become thicker, finally forming a stable amorphous or crystalline alkali titanate layer

3.3 Osseointegration enrichment by Ion implantation

Ion implantation (Figure 9) is a procedure in which ions of a material are accelerated in an electric field and impacted into the solid substrate surface to modify its physical characteristics[109-111]. There are various kinds of ions can be used to bombarded into substrate materials such as oxygen, nitrogen, carbon. Two common types of ions implantation methods are well known. One is Conventional beam line ion implantation, and the other one is Plasma immersion ion implantation (PIII). Additionally, Silver plasma immersion ion implantation (Ag-PIII) technique is used for implanted into Ti implant to enrich the osseointegration of sand blasted and acid-etched medical implants. What is more, Nitrogen (N) dual ions are also implanted with Silver (Ag). Ti-6Al-4V with an aluminium oxide-blasted surface was treated by Ag-PIII by Jorg et al, measuring the biocompatibility in vitro environment, and antibacterial effects. Ag-PIII gave a promising present for antibacterial functionalization of titanium from the results.

There are PIII-Ag-N (Ag ions prior to N implantation), PII-N-Ag (N priors to Ag ions implantation) and PII-Ag+N (Ag/N dual ions co-implantations). Li *et al.* [113] employed SEM, and XPS to compare the effect of antibacterial activity, corrosion resistance of titanium subject to PII-Ag+N, PII-Ag-N and PII-N-Ag. The results showed the PII-Ag+N is the most efficient process to achieve high antibacterial activity and corrosion resistance.

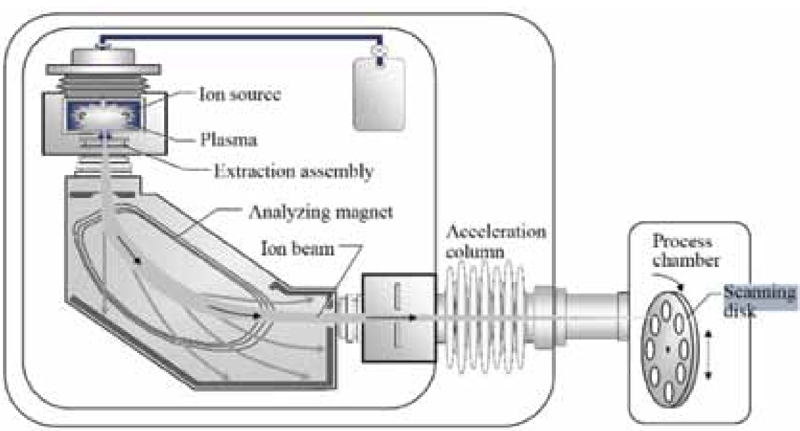

FIGURE 9
A schematic diagram of ion implantation [112].

PIII-Zn+Mg were also employed to improve the ossoeintegration. PIII-Zn+Mg modified titanium implants were implanted into rabbit femurs for 4 and 12 weeks by Yu *et al*.[114]. Micro-CT, histological analysis and push-out test indicates that PIII-Zn+Mg implant presents superior capacities for enriching bone formation, and enhancing sustained biomechanical stability.

3.4 Plasma Spray

Plasma spray is a thermal spray coating process used to produce a high-quality coating by a combination of high temperature, high energy heat source, a relatively inert spraying medium, usually argon, and high particle velocities [115-117]. The schematic diagram is shown in Figure 10.

Plasma spraying is one kind of thermal spraying techniques. It has been widely used in industrial gas turbines, automotive, aerospace, medical, biomedical and electronics[118]. Among those fields, currently, DC plasma arc devices are the most used in the commercial market[119]. The plasma gun is consist of a copper anode and tungsten cathode which are cooled by water. Plasma gas, such as Ar, He, H_2 and N_2, flow around the cathode and through the anode which is shaped as a constricting nozzle and ionized such that a plasma plume several centimeters in length develops [120]. During the spraying processing, the powder material is melted by using an electrical arc in the plasma plume, sprayed onto the substrate surface. In the plasma jet, the energy, density and velocity of plasma are very high, which are very important to the formation of coatings. Additionally, the temperature is another critical factor which is controlled by parameters of the plasma torch and the type of plasma gas. It is very impressive that the core region area temperature can reach a stable and extremely high value of 15726.9°C. Under that temperature, nearly no metal materials can "survive", being turning into plasma gas. The equation 2 to describe the relation between plasma beam intensity, gas volume and the nozzle diameter by Matejka *et al* [121], is:

$$\mathrm{v} = \mathrm{A}\frac{Q_0}{d^2}\frac{T}{M} \qquad 2$$

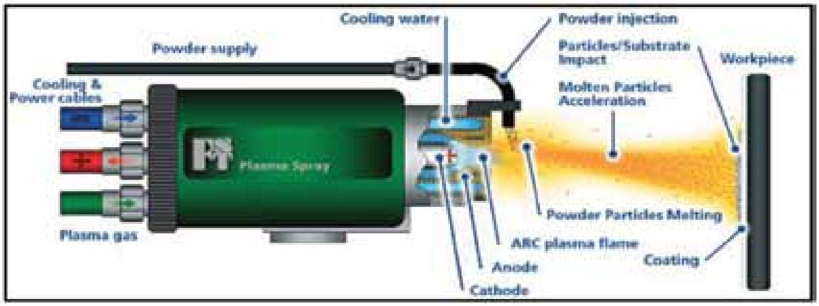

FIGURE 10
A schematic diagram of Plasma spray [116].

where V is the velocity of plasma(ms^{-1}); A is a constant value; Q is the volume of gas flow rate (m^3s^{-1}); T is gas temperature (K); d is the diameter of nozzle (m) and M is the molecular weight of gas Plasma has its advantage over other surface modification techniques. The advantage is that it can spray the materials with a very high melting point. What is more, a broader powder particle size range, typically 5-100 μm, and a wide range of coating materials for meeting different needs can be coated onto the substrate surface. The sprayed coating possess a rough surface which contributes to the adhesion of bone cells. Therefore, in terms of titanium, Al_2O_3, ZrO_2, and Ti_2O_2 are normally sprayed onto the titanium surface due to their excellent wear and corrosion resistance. Utu et al [122], deposited Al_2O_3+TiO_3 coatings on the commercial titanium using plasma spray. SEM, XRD and sliding wear test were employed and the results witness the improvement of wear resistance properties due to the increased surface coating hardness. However, such Al_2O_3 and TiO_3 can be used as the bond surface material between body and titanium. Thus, some more biocompatible materials need to be coated on the implant titanium alloy which is the focus of the next section.

3.4.1 Plasma sprayed Hydroxyapatite Coating on Titanium Alloy

In order to better promote the growth of body tissue, Hydroxyapatite (Hap) coating is coated onto the implant surface to enhance the osseointegration[123, 124]. HAp is a naturally occurring mineral form of calcium apatite with the formula $Ca_{10}(PO_4)_6(OH)_2$ [125]. It is a calcium phosphate which is very similar to human bones in composition. The Ca/P ratio is 1.67 which is identical to human bones and about 70% of the mineral fraction of bone has an HA-like structure. In addition, Hap is very stable under human body conditions such as pH, temperature, and body fluids. Previous work [126], indicated that implants with an HA surface coating form a strong connection between the implants and the bone tissue in short-time.

However, one of the disadvantages of HA is that the mechanical properties are relatively weak. Focusing on the mechanical properties of HA coating, many researchers have contributed plenty of works. Specifically, in vivo and vitro study, Thian *et al.* presented the morphology and mechanical properties of HA/Ti-6Al-4V composition immersed by Simulated Body Fluid (SBF) solution for 2 weeks. The secondary phase such as TCP, TTCP, and Cao were all found after immersion. The strength and modulus were found to decrease after immersing 4-6 weeks. What is more, Chu et al [127] conducted a vivo experiment of HA/Ti composite with New Zealand rabbits. The results demonstrated that there was excellent biocompatibility of HA/Ti after implant integration with bones. HA/TiO_2 coating on porous titanium (Ti) was investigated as well. Chen *et al* [128] found that the data of protein adsorption and cellular shows the composite lay allows more adsorption of serum protein. This enhances the biological properties of Titanium implants.

In order to improve the compressive strength, Zhang *et al* [129] studied the compressive strength of porous HA/Ti composites made by spark plasma sintering (SPS). They found that with 5 ~ 30 wt% HA content, the composite possessed high compressive strength (86 - 388 MPa) and low elastic modulus (8.2 ~ 15.8 GPa). In terms of corrosion resistance, Singh *et al* [130, 131] acquired a better corrosion performance of titanium with HA-SiO_2 coating on the AISI 304 steel and Ti-6Al-4V titanium compared with uncoated. In addition, the mechanical and corrosion properties of HA coating on Ti-13Nb-13Zr composite was also investigated by He *et. al.* [132]. Composite with 10% of HA exhibited outstanding corrosion resistance in SBF.

Another problem for HA coating is the poor bonding strength between the substrate and plasma sprayed HA coatings. Kweh et al. [133] found that, in vitro, the mechanical properties of the bonding coatings deteriorate with the increasing immersion time in SBF. The reason for this was due to the mismatch of the thermal expansion of HA ($13.3\times10^{-6}K^{-1}$) and titanium (8.4-8.8) $\times10^{-6}K^{-1}$), residual stress is formed and found to be the reason for the low bonding strength.

Resorption and degradability of HA coatings are another two important concerns in body environment. This leads to the disintegration of the coating, resulting in loss of the bonding strength and implant fixation. During the spraying, the temperature of the core plasma torch could reach extremely high. When the HA powder particles experience the high flame temperature, thermal decomposition happens. This might lead to the different crystal structure formations of substances, such as Calcium oxide (CaO), a-tricalcium phosphate(a-TCP), β-tricalcium phosphate, oxyhydroxyapatite (OHA), calcium-deficient hydroxyapatite (CDHA) and tetra-calcium phosphate (TTCP). The thermal effects on Hydroxyapatite are listed in Table 3.3.

TABLE 5
Thermal effects on Hydroxyapatite.

Temperature	**Reactions**
25-600°C	Evaporation of absorbed water
600-800°C	Decarbonation Dehydroxylation of HA forming partially
800-900°C	Dehydroxylated(OHA) or completely dehydroxylated oxyapatite (OA)
1050-1400°C	HA decomposes to form β-TCP and TTCP
<1120°C	β-TCP is stable
1120-1470°C	β-TCP is converted to a-TCP
1550°C	Melting temperature of HA
1630°C	Melting temperature of TTCP, leaving behind CaO
1730°C	Melting of TCP

It has been reported that these amorphous and metastable compounds are more soluble than crystalline HA [134]. These dissolved phases have shown good performance in proteins and cell attachments, which benefit the implant fixation, promoting bone remodelling. However, the dissolution of the amorphous and metastable compounds in HA coating is undesirable as it leads to the decreasing of the mechanical bonding strength. Therefore, from long term prospect, high pure crystallinity Hydroxyapatite is more preferred in plasma spraying industry.

4 SUMMARY

This paper is the first of the two part papers focused on the use of titanium based orthopaedic implants. The paper focuses on the physical characteristics, problems and the need for surface modification. Based on a national joint registry report in 2016 within the UK, a total of 1698395 primary surgeries were performed. The breakdown was 875585 for knee, 800686 for hips, 17300 for shoulders, 3185 for ankles and 1636 for the elbow replacements. Likewise, the primary surgery breakdown was 54287 for knees, 89023 for hips, 2045 for shoulders, 358 for ankles, and 507 for elbows that equates to a total of 146220. This indicates that; as the use of implants increase, the revision surgeries also increase. The impact of these revision surgeries on the patients are significant as they bring added costs and time. The reasons why failures take place post the primary surgeries are because of aseptic loosening, pain, wear, and infection. The important mechanical properties for implant are yield strength, tensile strength, Young's Modulus, hardness and wear based on literatures on both the biomedical and mechanical properties (including wear) as well as corrosion of titanium alloys employed in oral and orthopaedic applications. In addition, the reasons why titanium is considered as biocompatible are attributed to its resistance to corrosion from body environment, bio-inertness, capacity for osseointegration and high fatigue strength. The osseointegration of the implants can be improved by roughening surfaces using grinding technique or chemical etching methods or coating a biocompatible layer (HA) using plasma spray.

Implant surface modification methods using mechanical means such as shot blasting, shot peening, acid/alkai treatments; ion implantation and plasma spray and laser based technique, namely: laser shock peening and laser polishing were also discussed in this paper.

Furthermore, the part two paper will focus on the application of laser based techniques, in particular, laser shock based techniques that are useful for surface modification of these titanium based implants because it has the potential to improve key mechanical and potentially biological properties of the aforementioned titanium based implants for improved performance, both mechanically and biologically. Part two paper will consist of in-depth review of (selected) laser shock peening technique for surface processing these implants and the broader applications of the process.

NOMENCLATURE

α-TCP	α-Tricalcium Phosphate
β-TCP	β-Tricalcium Phosphate
A	A Constant Value
Ag	Silver
Ag-PIII	Silver Plasma Immersion Ion Implantation
AHT	Alkali-Heating Treatment
BCP	Biphasic Calcium Phosphates
CAD	Computer-aided Design
Cao	Calcium Oxide
CDHA	Calcium-Deficient Hydroxyapatite
CP Ti	Commercially Pure Titanium
D	The Diameter of Nozzle
Hap/HA	Hydroxyapatite
HCP	Hexagonal Close Packed
ICUs	Intensive Care Units
M	The Molecular Weight
MELISA	Memory Lymphocyte Immunostimulation Assay
N	Nitrogen
NHS	National Health Service
NJR	National Joint Research
OHA	Oxyhydroxyapatite
PIII	Plasma Immersion Ion Implantation
Q	The Volume of Gas Flow Rate
SBF	Simulated Body Fluid
SE	Strain Energy
SMA	Shape Memory Alloy
SS	Shield Stress
T	Gas Temperature
TC4	Ti-6Al-4V
THA	Total Hip Arthroplasty
THR	Total Hip Revision
TTCP	Tetra-Calcium Phosphate
V	The Velocity of Plasma

Greek symbols

α	Hexagonal Close Packed Crystal Structure
β	Body Centred Cubic Structure

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