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Application of biomaterial titanium alloy as an osseointegration prosthesis: Literature review

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Abstract

Osseointegration prosthetic limbs are garnering considerable interest from both professionals and patients. Titanium alloy implant prostheses provide superior performance compared to conventional socket-based prostheses in mobility, comfort, tactile perception, and overall patient satisfaction, thereby improving a patient's independence and comfort. Osseo Sense is an important aspect that enables the patient to perceive enhanced tactile sensations with the prosthesis compared to a conventional socket. Moreover, osseointegration is challenged by limitations that require continuous investigation, including infection and periprosthetic fracture. This study offers an extensive review of the literature on osseointegrated prostheses, highlighting their advantages and limitations, the various systems utilizing this concept, the surgical techniques employed, the application of surface modifications, and the selection of suitable materials for different implant systems. Moreover, it is essential to continuously enhance titanium alloys, such as Ti-13Nb-13Zr, to resolve current implant-related issues. This study emphasizes the necessity for increased multidisciplinary research and the potential usefulness of the implant system once existing limitations are resolved. This study offers an alternative perspective on osseointegration, clarifying the latest developments in the field.

1. Introduction

The global amputation rate is high due to the aging population, civilian accidents, regional wars, and terrorist activities, despite recent developments in medical and surgical techniques for limb salvage surgeries. Prosthetic devices are designed specifically to enhance mobility, autonomy, safety, and overall quality of life for amputees [1]. Traditionally, a socket secures an artificial limb to an amputee's stump. The socket exerts pressure on the soft tissues to securely attach the prosthesis to the stump. However, a socket-stump connection often leads to complications, including pressure sores, sweating, dermal irritation, discomfort, and inadequate stump adaptation. An alternative method of attaching prostheses for limb

amputation to a patient's body involves transmitting load directly to the skeletal system, avoiding the soft tissue in the stump. The proximal end of a percutaneous implant system is surgically implanted into the bone stump. An external prosthesis can be attached to the distal end of the implant system via percutaneous skin penetration, including an extended percutaneous segment within the residual limb. Osseointegration offers significant benefits for the direct skeletal attachment of limb prostheses, including enhanced range of motion, improved ambulation, increased sitting comfort, reduced energy expenditure, and strengthened postural awareness through tactile sensation, as illustrated in Fig. 1. This approach eliminates the need for a compression socket and effectively addresses common socket-related issues [2].

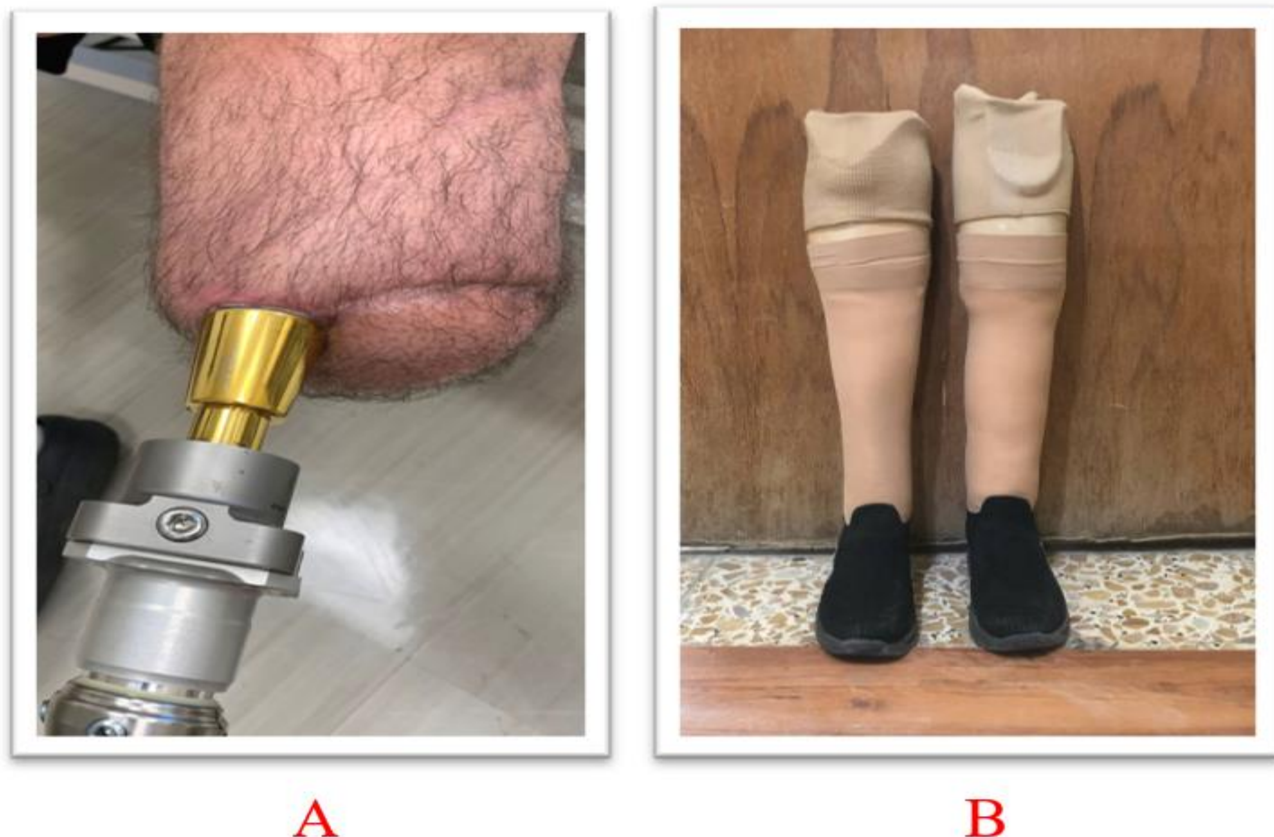

Fig. 1. (A) Osseointegration prosthetic limb (B) Traditional below-knee prosthetic socket [3].

Successful osseointegration relies on a combination of numerous confounding factors, including the biocompatibility of the implant material, the macro and microscopic topography of the implant surface, the design of the implant, the morphology and quality of the bone at the implant site, the surgical technique utilized, the stability of local and systemic health during the healing phase, and the loading conditions and protocols implemented [4,5]. A commonly cited consequence is the possibility of infection; distinguishing among a typical skin reaction, irritation, and a bacterial infection is not easy. The analysed infections encompass surface or stoma infections, deep-tissue infections such as osteomyelitis, and peri-implant infections. Fractures linked to osseointegration (OI) have the second-highest occurrence [6].

Biomedical components, made from natural or synthetic materials, are commonly used to replace lost or malfunctioning biological structures, thereby enhancing quality of life [7]. The integration of dermatologic biomaterials into orthopedic implants is essential, given the complex interactions at the interface between implants and surrounding tissues. They must

be nontoxic, non-thrombogenic, noncarcinogenic, and nonantigenic [8]. The aluminium and vanadium ions produced by the Ti-6Al-4V implant can induce both local and systemic toxicity. Moreover, its limited flexibility may lead to osteolysis around the implant [9]. Advanced surface treatments for Ti-6Al-4V, such as radio-frequency (RF) magnetron sputtering with hydroxyapatite (HAp), are effective for preventing harmful ion emission and enhancing surface properties by promoting osseointegration and bone fusion [10]. Al2O3 and TiO2 coatings deposited on Ti-6Al-4V by radio-frequency (RF) magnetron sputtering exhibited in vitro antibacterial activity against Escherichia coli, with activity increasing with increasing thin-film thickness. The effect is attributed to surface properties rather than gamma radiation exposure [11]. Ti-13Nb-13Zr alloys are a novel titanium alloy formulated specifically for medical implants. This alloy exhibits a low elastic modulus, high strength, excellent workability in both hot and cold conditions, and corrosion resistance [12].

2. Biomaterial consideration

Cappellini et al. [13] emphasized that a reliable prosthetic implant must be mechanically robust, biocompatible, and capable of achieving osseointegration. In that regard, Ti-6Al-4V has been used as an implant material. Common metallic biocompatible materials include stainless steels, cobalt-chromium alloys, and titanium alloys. Of these, the most commonly used material in biomedical settings is Ti-6Al-4V for joint and bone replacements and dental implants. Because of its biocompatibility, corrosion resistance, and mechanical properties, it has been widely used in biomedical research.

Nemcakova et al. [14] indicated that Ti-6Al-4V has excellent biocompatibility, bone compatibility, and corrosion resistance compared to CP titanium and Co-Cr. This is due to the presence of a spontaneous adhesive TiO2 layer appearing superficially, which reveals the greatest degree of spontaneous recovery following mechanical perturbation. Even though Ti-6Al-4V is a leading metallic implant material, it has been associated with elevated local pain, swelling, hypersensitivity reactions, and inflammation, which can lead to implant migration, aseptic loosening, and osteolysis in numerous patients. Such reactions lead to more expensive and more difficult revision procedures. Wear debris (mainly metallic ions from Ti-6Al-4V), poor osseointegration, or bacterial infection are some principal routes leading to implant failure. Many such problems are now being investigated using various functional coatings for metallic implants, including hydroxyapatite- and ceramic-based (carbon-based, such as diamond-like carbon or fullerene/silver nanoparticle-containing) nanocomposites that may address one or more of the above-mentioned issues.

While Ti-6Al-4V offers excellent mechanical strength and corrosion resistance, several studies have highlighted its biological and mechanical limitations. For example, Liu et al. [15] highlighted a major limitation of this alloy: its elastic modulus is much higher than that of bone, which may contribute to stress shielding and osteolysis. The main challenge lies in the intrinsic properties of Ti-6Al-4V. For instance, the elastic modulus for Ti-6Al-4V is in the order of 110 GPa, whereas the elastic moduli for cortical and cancellous bone are approximately 17-20 GPa and ~4 GPa, respectively. Moreover, Ti-6Al-4V is bioinert, lacking biological activity or osteoinductivity, which makes achieving good osseointegration with the surrounding bone tissue after implantation difficult. In addition, these alloys contain two toxic elements: vanadium and aluminum. It was found that V is more toxic than Cr and Ni, and the former can deposit in other organs during long-term implantation to induce cancer.

Aluminum may accumulate in the body and has been associated with organ toxicity, including osteomalacia, neurological disorders, and anemia. A possible relation between aluminum exposure and Alzheimer's disease has been suggested, although conclusive clinical evidence remains lacking. Similarly, Vanaclocha et al. [9] discussed local and systemic toxicity resulting from the release of aluminum and vanadium ions from the Ti-6Al-4V implant. It also has a limited range of motion, which may lead to osteolysis around the osteosynthetic device. Its low bond-to-bone and interface stability are its major shortcomings; therefore, the search for additional titanium alloys with suitable properties continues. The implants' immediate pull-out resistance is due to passive press-fit and their design. Long-term retention depends on bone ingrowth into the implant's porous interstices and chemical bonding with the surrounding bone. The strength of the initial micromechanical bond between bone and an implant is low and requires time to fully develop. A number of coatings, such as hydroxyapatite, lactoferrin, and boron-containing calcium silicate nanostructures, are enhancing titanium's potential for osseointegration. The material used in the manufacture of the dental implants exhibits insufficient resistance to fracture under chewing forces due to corrosion and low fatigue strength. Also, metal debris enters the tissue space and the bloodstream. As a result, work on new titanium implants and materials with improved mechanical and chemical properties continues. The most commonly used material for dental implants today is the Ti-6Al-4V alloy. This alloy includes aluminum (Al) and vanadium (V), which are excellent for mechanical strength. V is cytotoxic, antiproliferative, and capable of promoting oxidative stress, and these features are similar to those of Ti-6Al-4V (tit. Increased corrosion resistance was observed, and niobium (Nb) ions are also less toxic than vanadium (V) ions. Ti-6Al-7Nb exhibits good biocompatibility with osteocytes. The Ti-Al6Nb7 alloy could be a potential candidate for bulk implants.

Building on these findings, Mahdi and Hamdi [16] Discuss current research on materials suitable for osseointegrated prostheses. Optimal implants have long durations that exceed those of human patients. Titanium as an implant material has become increasingly popular over time, with a greater focus on quality of life. Among titanium alloys, the Ti-6Al-4V alloy stands out for its high mechanical strength and widespread use across various fields. But metal implants have many drawbacks, including rusting. The surface of titanium implants can be enhanced with bioactive and biocompatible materials to address this problem.

According to Assis et al. [17] The Ti-6Al-4V and the Ti-6Al-7Nb alloys are commonly used as implant materials, especially in dentistry, orthopedics, and osteosynthesis. Research has shown that vanadium, used to stabilize the phase, forms oxides that are deleterious to human health. The toxicity of vanadium has accelerated investigations into alternative materials to Ti-6Al-4V. The Ti-6Al-7Nb alloy was developed to replace vanadium-containing Ti alloys and is now commercially available. Niobium acts as a phase stabilizer. Additionally, there is unverified concern about a possible link between aluminum and Alzheimer's disease. The Ti-13Nb-13Zr alloy, a near-β alloy, was developed recently. This alloy contains three of the four elements (Ti, Nb, Zr, and Ta) recognized as non-toxic and highly biocompatible.

Ji et al. [18] reported that Ti-6Al-4V dominates the titanium alloy market for hip arthroplasty, but its high elastic modulus and release of aluminum and vanadium ions may hinder osseointegration. Additionally, the elastic modulus of Ti-6Al-4V is four times greater (110 GPa) than that of cortical bone (27 GPa). The elastic modulus of Beta Ti-Nb-Zr alloys, which ranges from 62 to 65 GPa, is lower than that of Ti-6Al-4V. Binary Ti-Zr alloys are

appealing for biomedical implants because of their biocompatibility, mechanical strength, and in vivo corrosion resistance. Moreover, in vivo tests on rabbits' tibia suggest that titanium and zirconium behave similarly towards bone. The biocompatibility of materials for medical use depends on the passivation film on the alloy's surface, which influences physicochemical and biological phenomena at both the biomaterial-implant and tissue-biomaterial interfaces. The stability of this passivation film is crucial when selecting a metallic material for biomedical applications. Despite the high corrosion resistance of Zr alloys compared to Ti alloys, the passivation film on Zr alloys can be prone to pitting in chloride-containing solutions such as body fluids. Alloying Zr with titanium can reduce pitting sensitivity.

The study conducted by Fan et al. [19] found that research on medical titanium alloys can generally be classified into three stages. In the first place, pure titanium and the Ti-6Al-4V alloy are employed as representative materials; however, when implanted, they may cause toxic effects due to the presence of aluminum and vanadium. The other is the advanced α-β dual-phase alloys, such as Ti-6Al-7Nb and Ti-5Al-2. 5Fe. However, those two alloys exhibit low hardness and wear resistance, leading to poor long-term stability of these implants in the human body. For the third stage, materials such as Ti-13Nb-13Zr, Ti-12Mo-6Zr-2Fe, and Ti-15Mo, as well as other β or near-β alloys without Al or V, exhibit excellent processability and toughness. Their microstructure can be altered by heat treatment to increase their hardness, elastic modulus, toughness, wear resistance, and corrosion resistance, making them more similar to those of human bone and soft tissue. The third-generation titanium alloys contain no harmful aluminum, have excellent biocompatibility, and are replacing second-generation medical titanium alloys. The low elastic modulus, high toughness, fatigue strength, resistance to corrosion, and biocompatibility are some of the properties that make the Ti-13Nb-13Zr alloy a prospective bone replacement material in academic studies.

Klinge et al. [20] Study of new dental implant systems manufactured from a Ti-13Nb-13Zr titanium alloy. Long semi-finished bars, which have very good strength and ductility, enable automated fabrication of small implants with a low Young's Modulus (<80 GPa) to minimize stress shielding, bone resorption, and gaps between the implant and bone. Alterations of microstructure will reduce bacterial colonization and enhance adherence to bone. Mechanically, the nanocomposite complies with ASTM F1713 standards, exhibiting an ultimate tensile strength of 990 MPa and a Young's modulus of 73 GPa. In contrast to CP–Titanium Grade 4 and Ti-6Al-4V ELI, etched surfaces retard the formation of biofilm and favor the growth of osteoblasts. The implant and abutment have different mechanical characteristics, e.g., strength, which can lead to relative movement, causing wear and abrasion, damaging the oxide layer, and releasing metal particles into the bloodstream. Ti–13Nb–13Zr (TNZ) and Ti-15Mo are second-generation titanium alloys designed to mitigate health issues associated with titanium.

Khan et al. [21] Titanium alloys have received significant attention in orthopedics for their high corrosion resistance and mechanical properties. Titanium and other metals can be leached into biological tissue through passive corrosion or abrasion. Since wear can damage the passive layer, it is crucial to study the repassivation of these materials in biological media, especially in the presence of proteins, and to understand how a repassivated surface differs from the original. We examined the repassivation of Ti-6Al-4V, Ti-6Al-7Nb, and Ti-13Nb-13Zr in phosphate-buffered saline (PBS), bovine milk solutions, and 10% FBS calf serum as a function of pH and albumin concentration. Ti-6Al-4V and Ti-6Al-7Nb were more sensitive to

pH variation in PBS than Ti-13Nb-13Zr. Proteins reduced the effect of pH on all metals. Re-passivation, along with corrosion, decreased the surface oxide hardness in all metals. The smallest decrease in PBS was observed for Ti-6Al-4V, whereas the largest was observed for Ti-13Nb-13Zr. Corrosion in the protein solution further inhibited the development of surface oxides. This effect was more noticeable for Ti-6Al-4V and Ti-6Al-7Nb than for Ti-13Nb-13Zr. In summary, environmental proteins influence both the re-passivation process and the surface characteristics of these alloys.

Ghodrati et al. [22] Titanium quickly oxidizes in oxygen, forming a corrosion-resistant TiO2 coating on implants. This thin oxide layer is crucial for the biocompatibility of titanium implants. Mechanical pressure can weaken the TiO2 layer through repeated implant-osseous tissue interactions, leading to localized degradation and corrosion. Implant corrosion can compromise stability and may release metallic particles or ions into surrounding tissues. Nanotechnology in dentistry has accelerated treatment time, improved service quality, and reduced complications. These advancements offer lasting stability, promote bone repair, and reduce limitations.

Nnamchi et al. [23]**.** Studies have shown that chemical alloying can reduce Young's modulus and improve resistance to corrosion, superelasticity, and stress-induced phase transformation from BCC-metastable beta to orthorhombic α″ martensite. This work analyzes the effect of Nb and/or Zr micro-additions on balancing elastic modulus, yield strength, microstructure characteristics, and mechanical/electrochemical properties for four new β-Ti-8Mo-xNb-xZr alloys (x = 2–5). Methods include tensile testing, X-ray diffraction, SEM analysis, ultrasound technology, and potentiodynamic polarization. The results indicate that Nb-rich alloys are more affected by microstructural changes, with higher β-stability correlating with increased strength. All alloys exhibited good corrosion resistance, with a Young's modulus of 35 GPa, which is lower than that of commercially available medical implant alloys.

Kaur et al. [24] Any material implanted in the human body provokes a response. This reaction is especially noticeable at the tissue-implant interface, where the surface is more reactive than the material's core. The interface appears as a two-dimensional defect, with atoms not bonded to the maximum possible number of neighbors. As a result, these atoms have higher energy than the core atoms of the material. Cortical bone possesses a tensile strength ranging from 70 to 150 MPa, a yield strength between 30 and 70 MPa, and an elastic modulus of 15 to 30 GPa. Titanium-based alloys exhibit a tensile strength of 690 to 1100 MPa, a yield strength of 585 to 1060 MPa, and an elastic modulus of 55 to 110 GPa.

Schneider et al. [12] Ti-13Nb-13Zr is a new titanium alloy for medical implant applications. It has a low elastic modulus, high strength, and good ductility under continued exposure to high temperatures (up to 330°C), and also exhibits very good migration resistance in the food and beverage industry. It has been found that the alloy's mechanical behavior can be tailored through hot working, heat treatment, and cold working. They report on the mechanical features and cytotoxicity of arc-furnace-heated Ti-13Nb-13Zr alloy in an argon environment. The materials comprised pure titanium, niobium, and zirconium sheets. A quantitative colony suppression assay with Chinese Hamster Ovary (CHO) cells was used to assess the alloy's cytotoxicity using diluted extracts from the biomaterial. The FA-processed Ti-13Nb-13Zr alloy did not exhibit cytotoxic effects.

Brunke and Rösler [25] report that the alloys currently used in implant applications are Ti-6Al-4V (ELI) and Ti-6Al-7Nb. Both alloys are classified as (α+β)-alloys and contain

aluminum as an alloying element. Aluminum has cytotoxic properties and may contribute to the development of breast cancer. Additionally, the rigidity of (α+β)-alloys is relatively high; it may result in stress shielding, bone degradation, and implant failure. Therefore, second-generation titanium alloys such as Ti-15Mo (a solute-lean metastable β-alloy) and Ti-13Nb-13Zr (a β-rich (α+β)-alloy) have been developed.

Tęczar et al. [26] received and laser-processed Ti-13Nb-13Zr to investigate the influence of laser treatment on surface morphology and specific mechanical parameters, such as nano-hardness, Young's modulus, and roughness. This gives a complex response over the substrate material that shows a decrease in penetration depth followed by an increase in hardness after the first laser treatment, and continues accordingly at increasing pulse power, whereas depression in hardness and rise in penetration occur after additional laser treatment with lower power, which leads to better surface finishing free from defects. Young's modulus was found to evolve in a coordinated manner with other mechanical parameters, but not with roughness. Despite this phenomenon, laser treatment consistently increased the hardness of the surface layer by a large margin.

Dąbrowski et al. [27] The microstructure and mechanical characteristics of medicinal titanium alloy Ti-13Nb-13Zr. The alloy was aged at 350°C, 450°C, and 550°C after cooling to the β range (900°C). Cooling to the β region resulted in martensitic transformation and the appearance of titanium martensite (α') in the microstructure. During aging at 350-550°C, microstructural variations were observed with the formation of new α and β phases besides titanium martensite. Increasing the aging temperature from 350 to 550°C increased hardness, tensile strength, yield strength, and fatigue strength. The changes reduced resistance to fracture and increased flexibility. Elevated-temperature samples showed fracture dispersion and changes in the intercrystalline crack ratio. These changes increased the alloy's strength but reduced its fracture toughness.

Table 1. Comparison between the most frequently used titanium alloys.

Titanium Alloy	Elastic Modulus	Biocompatibility	Toxicity Concerns	Clinical Usage
CP-Titanium	~100–105 GPa [28]	Good biocompatibility and corrosion resistance;	Minimal toxicity; considered to have a good biological effect	Common in dental implants and early osseointegration systems
Ti-6Al-4V	~110 GPa (much higher than cortical bone = 17-20 GPa)	Good corrosion resistance & mechanical properties	Release of aluminium and vanadium ions may cause local & systemic toxicity	Most widely used titanium alloy
Ti-6Al-7Nb	~105 GPa [29]	High biocompatibility as an improvement over Ti-6Al-4V	Lower toxicity than Ti-6Al-4V (replace the element V with Nb)	Used in orthopedics, dentistry, and osteosynthesis as an alternative alloy
Ti-13Nb-13Zr	Lower than Ti-6Al-4V (about <80 GPa)	Excellent biocompatibility and corrosion resistance	No significant cytotoxicity reported; designed to reduce toxic ion release from previous alloys	Emerging biomedical alloy proposed for next-generation implants

In conclusion, Ti-13Nb-13Zr has emerged as a promising titanium alloy for biomedical applications due to its reduced ion release and mechanical properties that more closely match those of bone. These characteristics may help reduce stress shielding and potentially enhance osseointegration between an implant and bone compared with Ti-6Al-4V.

3. Osseointegration implant systems

Osseointegration implant systems have been developed to provide a direct functional and structural connection between the host bone and the prosthesis. Several implant systems have been introduced and evaluated in previous studies as follows:

Hoellwarth et al. [30] An extensive review of the first person to remain successfully integrated with a prosthetic limb transcutaneously. The procedure was carried out on May 15, 1990, by Rickard Brånemark in Sweden for a young woman who lost both legs after an accident involving a streetcar. As a result of the osseointegrated implant, the patient was able to stand and walk without a conventional socket prosthesis. This treatment was the start of a new age in amputee care called here 'modernity'. Brånemark et al. [31] Before 1999, early implants were custom-designed; however, that year marked the introduction of the Swedish system known as OPRA (Osseointegrated Prostheses for the Rehabilitation of Amputees, Integrum AB, Mölndal, Sweden) is essentially composed of three parts: a fixture surgically implanted into the bone (externally threaded, and generally cylinder-shaped); an abutment in which is press fitted at the distal end of the fixture where it joins with a percutaneous portion adapted to connect with an implantable prosthesis secured by means of an abutment screw; and a distal end of the abutment that connects to the auxiliary safety device having a torsional release mechanism which further connects to the external prosthesis. An abutment serves as a mechanical fuse, protecting the fixture from mechanical overloading during bending. In the recommended kiln-day operation, the abutment can be replaced if it shows signs of deformation or cracking. Therefore, the removal of the fixture was considered the failure-severance point in the clinical portion of this trial. On the other hand, Li and Fellander-Tsai [32] used commercially pure titanium (cpTi) with a smooth, machined surface. The Ti-6Al-4V alloys were added to the recent platform because it was observed that mechanical failures at the connection between the abutment and abutment screws increased. The current-generation OPRA features proximal threads with a macro-micro-nano-textured composite surface structure in the thread pathways, produced by site-specific laser ablation and known as the 'Bio-helix' design. In vivo tests showed that the "Bio-Helix" surface achieved better biomechanical fixation and increased osseointegration, which may be beneficial in high-load situations such as early loading and compromised conditions. The end threads have a smooth, machined surface to eliminate bacterial retention at the bone-implant-skin interface. A safety device," Axor II", is placed between the distal end of the abutment and the limb prosthesis in lower extremity applications. This safety feature releases the prosthesis under high loads, protecting both the implant system and the bone.

In the OPRA system, a threaded titanium fixture is initially manufactured from commercially pure titanium (cpTi), with later incorporation of Ti-6Al-4V components to improve mechanical performance. This system represents the most clinically mature osseointegration system with long-term follow-up data, but a longer rehabilitation period (up to 6–12 months).

In contrast, Juhnke et al. [33] reported a new technique, the Integral Leg Prosthesis (ILP), that enables direct skeletal attachment of the prosthesis to the host bone. One German surgeon implanted ILPs into 69 transfemoral amputation patients between January 1999 and December 2013. Between these years, considerable progress was made in device design iterations and surgical techniques. The osseointegrated intramedullary device, combined with a soft-tissue prosthesis and a low-energy interfacial surface, enabled the formation of a physiologically stable, non-infected bilayer skin stoma that did not require long-term antibiotic treatment. The reduction in infection rates was attributed to clinically focused, experience-based changes in design and surgical techniques. Similarly, Frölke et al. [34] "Endo-Exo/ILP" system is composed of a 140 to 180 mm length chromium cobalt molybdenum or titanium stem with a macroporous or rough surface coating. This stem is intended to be impacted into the marrow space for a press-fit and then loaded within 6 to 8 weeks. Full weight-bearing is possible in 8–12 weeks for the" Endo-Exo/ILP" system and, in some cases, from 6 to 12 months for the OPRA system. Because of the time-saving osseointegration and training, the Endo-Exo/ILP concept was applied in a case series conducted in the Netherlands. The macroporous coated chromium cobalt molybdenum cast stem (Endo-Exo/ILP system) is covered with a 1.5-mm-thick layer of hydroxyapatite (HAp). This reduces the core diameter of the femoral stem by 3 mm. Webster et al. [35] report that design alterations focus predominantly on managing the soft tissue barrier by eliminating the porous-tripod structure at the skin-implant interface, which involves a bone-capping component of the device. The most recent version of the design has replaced the porous tripod with a low-surface-energy titanium-niobium-oxynitride surface. This surface is low-wettable, which promotes drainage and the elimination of tissue fluids, facilitating stomal hygiene. A cast cobalt-chrome alloy has always been the main material during all three design transformations. A hallmark of the ILP design is its unique porous coating strategy that promotes bone ingrowth into the endoprosthesis stem. Except for small areas at or near the distal resection plane and the implant's proximal end, all surfaces are implanted with a metal spongiosa in a dense, porous form.

According to Sun et al. [36] OI history has evolved continuously over the last 30 years. The development of press-fit-type Endo-Exo-Prosthesis (EEP) technology, employing a porous cobalt-chromium metal stem as an intramedullary stump replacement, represents a major step forward in orthopedic management. Dr. Al Muderis et al. subsequently developed the Osseointegration Prosthetic Limb (OPL) system and modified the implant material by replacing cobalt-chromium with titanium. The OPL implant was introduced after preclinical investigations and later evaluated in clinical studies involving human subjects. Press-fit systems may reduce the need for repeated fixation surgery and rehabilitation time and have become a popular option among patients and surgeons in recent years.

Tropf and Potter [37] Discuss the clinical introduction of this implant system in Italy in 2013. This implant system design consists of an intramedullary press-fit stem with a roughened porous coating to enhance osseointegration. Alternative designs include a distal femoral endoprosthesis or a proximal intramedullary implant manufactured from titanium alloys such as Ti-6Al-4V. The surgical procedure is typically performed in a single stage and includes reaming and sequential broaching to achieve stable press-fit fixation.

Building on these findings, the ILP and OPL systems achieve fixation through press-fit implantation and bone ingrowth, allowing earlier loading and faster rehabilitation than OPRA.

Generally performed as a single-stage surgery. Uses cobalt-chromium-molybdenum material in ILP and titanium stems in the OPL system.

In a separate study, McGough, Goodman, et al. [38] According to the Compress website, Biomet Corporation (now Zimmer Biomet) developed the device in the 1990s, and about 15 years ago, it was approved by the FDA for use with Biomet endoprostheses, such as distal femoral replacements. This implant was expanded to obviate the bone-resorptive properties of closely press-fit implants. The Compress device is based on the principle that strained bone is stronger. It consists of inserting a macro-surfaced implant at the end of a finely engineered bone diaphysis. Osseointegration takes place within 12 weeks, and the risks of loosening or bone resorption caused by stress shielding are reduced because the integration process is stable and a constant axial force is applied. Regulatory hurdles in the US have severely limited transdermal osseointegration. The Compress device has been designed as a substitute fixation method for larger resections, e.g., distal femur replacements. Securely attached to the cortical bone and undergoes heavy axial loads after a proper prosthesis shape is designed. The bone rapidly integrates with the device, achieving long-term osseointegration.

The research team led by Fitzpatrick et al. [39] developed the intra-osseous transcutaneous amputation prosthesis (ITAP) to address specific problems at the interfaces between stump socket prostheses (SSPs) and skin implants. The ITAP is derived from deer antlers; in this case, the bone pedicle undergoes continuous remodeling throughout the antler cycle. At the same time, dermal tissue adheres tightly to the osseous structure, resisting infection, marsupialization, and failure of the soft-tissue interface. ITAP boys of distal limb diseases, some dogs for which the ITAP Article. The device was fabricated to fit the dog and consisted of a Ti-6Al-4V stem for intramedullary insertion into the bone, a perforated, umbrella-like flange positioned subcutaneously to promote skin ingrowths, and a distal extracutaneous peg linking the stem, flange, and apparatus that secures exoproteins. These three parts were engineered as a single monolithic module, with each subpart having distinct biological and mechanical properties to perform a particular function. It has already been shown that implantation of an ITAP into the distal forelimb appears possible in dogs and may provide functional benefits. Similarly, Kang et al. [40] reported that the combination of ITAP offers amputees the option to attach the prosthesis externally. The placement procedure is rapid, and the bone surgery is less complex than with other bone-anchored systems, such as the Brånemark Integrum system. The principal operation consists of thinning the epidermis over the porous flange and connecting it to the ITAP implant during cutaneous integration. However, all the procedures are simple enough for any upper-limb surgeon to pick up. ITAP may facilitate comfortable and functional prosthetic reconstruction in any patient with an upper limb amputation. If it were possible to implant the ITAP at the time of initial amputation, this would also minimize the delay in achieving long-term function.

Shelton et al. [41] reported that percutaneous Osseo-integrated prostheses are being studied as an alternative method for attaching prosthetic limbs to patients. Despite promising results from clinical studies, maintaining the skin barrier around the osseointegrated implant interface remains a significant challenge for preventing both superficial and deep periprosthetic infections. Percutaneous Osseo-integrated prostheses (POPs), used as docking systems, offer an alternative to traditional sockets.

The groundbreaking implant was reviewed by Rokosz et al. [42]**.** The development of a new osseointegrated implant device, the Percutaneous Osseointegrated Prosthesis (POP), has

been ongoing over the past decade, with preclinical trials underway. The goal is to reduce infections and create a mechanically durable implant that enables a quick return to walking. The "FDA" has approved an Early Feasibility Study (EFS) for the POP device, which is presently in progress. Ten transfemoral amputees have undergone a two-stage surgical process: the first stage involved implanting an endo-prosthetic stem into the remaining bone, and the second phase involved attaching a percutaneous post to the stem after at least five weeks. Clinical results to date show low initial infection rates, preservation of distal cortical bone, improved functional outcomes, increased periprosthetic bone density, and better patient-reported outcomes with a staged surgical approach and earlier weight-bearing compared with other established osteotomy techniques.

Cano et al. [43] Conducted a clinical trial to assess the effect of a distal weight-bearing implant on function, health, and well-being in patients with above-knee amputations. The study enrolled 29 patients from five hospitals, all of whom received an osseoanchored distal weight-bearing implant following the same protocol. Patients were monitored for 14 months and evaluated both before and after surgery. The distal weight-bearing implant designed for this research consists of four components. The femoral stem was made of a titanium alloy (Ti-6Al-4V) to improve fixation into the remaining femoral canal, and a spacer made of ultra-high-molecular-weight polyethylene was attached distally to the stem with a titanium screw and a polyethylene plug. The spacer provided distal support for the residual limb within the socket, resulting in a significant and clinically meaningful improvement in the Physical Component Score and across various individual domains, indicating an overall enhancement in health-related quality of life for patients who received the distal weight-bearing implant. In conclusion, extensive research on medical implant systems was conducted to illustrate their advances and differences, enabling researchers and interested individuals to choose suitable implants for specific applications. This publication covers the latest implant technologies and notes that Ti-6Al-4V alloys are widely used in several medical applications.

There are alternative osseointegration systems, such as the compress system, which uses axial compression rather than traditional press-fit fixation, and ITAP, which incorporates a porous flange to encourage skin integration. These systems are innovative but have substantially less clinical evidence than OPRA or OPL. Table 2 presents the most widely used osseointegration systems, along with their fixation methods, materials, and other key information.

Table 2. Comparison between the major osseointegration implant systems.

Implant System	Fixation Method	Main Materials	Complications	Clinical Maturity
OPRA	Screw-type fixation with a threaded fixture into the bone.	Initially, CP-Titanium, later with Ti-6AL-4V, with a modified bio-helix surface design.	Mechanical failure at the abutment connection is reported in the early design as a general risk, including at the skin-implant interface and at	One of the earliest systems, introduced in 1999, is based on clinical procedures that began in 1990.

			the periprosthetic fracture.	
ILP	Press-fit intermedullary stem implanted into a marrow cavity.	Cobalt-chromium-molybdenum.	Design changes focused on reducing infection at the skin–implant interface and complications similar to those of other OI implants.	Clinically used since 1999 with multiple design irritation.
OPL	Press-fit intermedullary fixation.	Titanium implant (Ti-6Al-4V) that replaces the early cobalt-chromium material used in the ILP system.	Typical osseointegration complications such as infection and mechanical stress at the bone–implant interface.	Developed after the ILP system and increasingly used in recent years.
ITAP	Intermedullary insertion with external peg and subcutaneous flange to promote skin ingrowth.	Ti-6Al-4V with flange for dermal integration.	Challenges related to skin–implant interface and infection prevention.	Early clinical stages, tested initially in animal studies, and with limited clinical application.
POP	Two-stage fixation: an intermedullary stem is implanted, followed by attachment of a percutaneous part.	Ti-6Al-4V. [2]	Typically, (OI) complications of the implant and skin-implant interface.	Under clinical investigation with the FDA.
Compress Implant	Axial compression fixation to cortical bone.	Ti-6Al-5V. [2]	Typically, (OI) complications of the implant and skin-implant interface.	Approved for clinical use in certain orthopedic applications.
Distal Weight Bearing Implant	Intermedullary fixation with a distal support component.	Ti-6Al-4V femoral stem, ultra-high-molecular-weight polyethylene spacer, titanium screw.	Similar to other OI implants.	Evaluated in clinical trials involving transfemoral amputees.

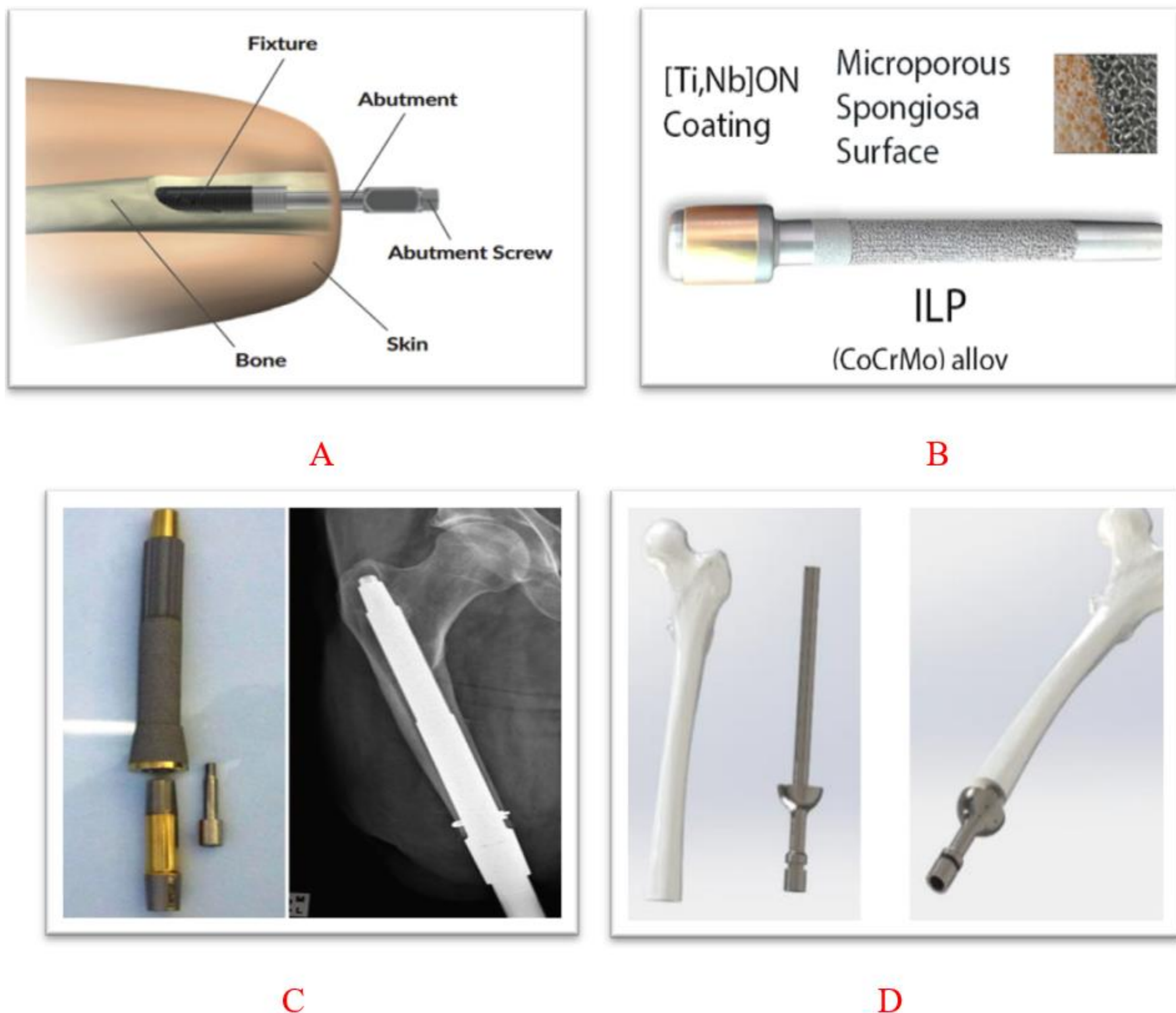

Fig. 2. A component of the implant systems of (A) OPRA, (B) ILP, (C) OPL, (D) ITAP [30], [44].

3.1 Surgical approach

Reif et al. [3] defined two basic types of implants in use: screw type and press fit. They involve different surgical techniques, rehabilitation, and time to full weight bearing, but both are based on the same molecular process designed to generate a proportionate bone-metal interface at the microscopic level. This is analogous to that of uncemented femoral stems in hip arthroplasty and appears stable for complete estimation—osseointegration prostheses for the rehabilitation of amputees (OPRA). In use in amputation surgery on long bones, Osseointegrated prosthesis screwing once back and forth through a healthy skeletal site. Conventional OPRA consists of two operations, separated by six months, to ensure optimal integration of the prosthesis with the surrounding host bone. The proximal end intramedullary bone anchor was introduced first, and only the distal soft tissue was to be sutured. The second operation forms a stoma at the skin-implant junction and connects the transcutaneous abutment to the implant body. In ILP and OPL, the intramedullary canal is prepared by repeated reaming and broaching until a press-fit is achieved between the implant and bone. Then a temporary stopper is inserted into the implant's distal end. Roughly six weeks later, a hollow coring blade is plunged into the skin above the abutment to create a stoma. The implant plugin is then withdrawn, and a dual-cone adapter is inserted directly.

In a different study by Rehani et al. [45] There have been improvements in implants and in best practices for bone-anchored prostheses over recent years. There are basically two kinds of fixations used in these applications today. Based on these two fixation techniques, six implant constructs are supported by the peer-reviewed literature. The first surgery on an individual with a transfemoral amputation took place in Sweden back in 1990, using the initial design of Osseo-integrated Prostheses for the Rehabilitation of Amputees (OPRA). It is the only implant that requires screw fixation. The development of implants in Germany. The success of osseointegrated prostheses in Sweden led to the initiation of implant research in Germany at the end of the 90ies. The present implants have transitioned from screw-based to socket-filled, intramedullary, alloy-press-fit devices, akin to joint-replacement technology.

Palmquist et al. [46] described a patient in a case report: a 60-year-old woman. She had an above-knee transfemoral amputation secondary to carcinoma in 1976. In 1993, she was fitted with a personalized bone-anchored implant. The technique was performed in two steps. 1 involved the insertion of a titanium fixture into the remaining part of the femoral bone following reaming without opening up the intramedullary canal and placing a 3D guiding centre under fluoroscopy. In stage 2, six months later, we shortened it by removing a disbudded skin flap of subcutaneous fat and then suturing it to the end of the femur. Distally, the titanium fixture broke after several years of use and had to be replaced with a custom-made one. She has had no further fractures after a successful revision of the implant. Histologically, mature cortical bone was observed on the implant, filling the threads and projecting centrally into the transverse holes.

Atallah et al. [47] Amp amp) were compared: screw versus press-fit abutment systems for bone-anchored implants. Interventions related to these issues were also investigated in the study. Results: There was a low rate of infection in implant ends for transfemoral implants: 0%–3% press fit, 2%–11% screw type. For implant loosening in the transfemoral cohort, a similar trend was observed for screw versus press-fit fixation (6% vs 0-3%). Among transfemoral implants, there were rare intramedullary device fractures: 0% and 1% for screws and press-fit devices, respectively. The authors concluded that cases with press-fit-type transfemoral implants tended to have fewer severe complications, such as infection and implant loosening, than those with screw-type implants.
Overall, both screw-type and press-fit implants have demonstrated successful clinical outcomes. However, press-fit systems generally provide faster rehabilitation and may be associated with lower rates of infection and implant loosening, whereas screw-type systems benefit from longer clinical follow-up and established long-term performance.

3.2 Advantages and limitations of osseointegration

Several clinical studies have reported that osseointegration prostheses improve mobility and quality of life in amputees compared with conventional socket prostheses. Studies have also investigated their potential limitations.

Shih Hoellwarth et al. [48] Osseointegrated prostheses provide a rehabilitation solution for people with amputations, offering improved mobility, greater satisfaction, and better usability than traditional socket prostheses. The main challenges, infection and periprosthetic fracture, do not seem to be particularly common or insurmountable. Osseo-integrated implants can connect to advanced sensory and motor prostheses. According to Atallah et al. [49]**,** Osseointegration may be a good treatment option for amputees who have difficulty

wearing a socket, are unable to use a socket prosthesis, or need a more comfortable option. Although the most common indication for limb amputation is vascular disease, this has been considered a contraindication for osseointegration surgery. They describe the outcome of osseointegrated rehabilitation in a group of five patients with peripheral vascular disease-related amputation. Clinical and functional outcomes were assessed, including pain scores, time in prosthesis use, mobility, gait function, and quality of life. Adverse incidents such as infection, fracture, implant failure, and revision surgery, together with subsequent amputation and mortality, were observed and recorded. For individuals with peripheral vascular disease, an osseointegrated implant may be considered as an alternative treatment to the socket prosthesis.

Brånemark et al. [50] A clinical study involving 51 patients with transfemoral amputations (TFAs) to evaluate the outcomes of osseointegration prostheses. The clinical application of osseointegrated percutaneous prostheses for transfemoral amputees began in 1990, based on successful experience with osseointegration of dental implants. Fifty-one patients with '55' TFAs were prospectively enrolled (1999-2007) in a single-centre, non-randomized trial and followed up at 2 years. Osseointegrated percutaneous implants have been shown to be a novel treatment option for patients with TFA. The excellent 2-year cumulative survival rate (92%) and improvements in prosthetic use, walking ability, and quality of life reflect a "real transformation" in patients with TF amputation following implantation. Mahdi and Hamdi [51] made several changes to the implant's mechanical design and analyzed them using the finite element analysis program ANSYS. The modifications included replacing the threads of the femoral stem with a groove (internal cut thread) or an external thread. The groove's depth was adjusted to optimize stability, while the thread pattern was designed to maximize mechanical fixation to the bone; four different designs were tested. Midstance mechanical loading on the implant within the femur was adapted and compared to that of a conventional implant under the same conditions. The finite element analysis indicated reduced total deformation and improved safety factors compared with the previously reported design. However, these findings are based on numerical simulation and require further experimental and clinical validation.

According to a study by Overmann et al. [52] Several studies report on osseointegration implants in individuals with amputation. These implants rely on different methods to fix and treat the implant surface, enabling osseointegration with the host bone. Both types of osseointegration (OI) implants are commonly used; screw-type and press-fit implants share the same problem: infections. Other considerations are that it is unknown whether integration occurs and that its loss might be very subtle. Future research may explore the integration of sensors into implants to monitor the interface between the bone and the implant, and potentially improve the long-term stability of osseointegration systems.

Mahdi and Hamdi [44] report that the domain of Osseointegrated prosthetics has attracted significant attention from both specialists and amputees. This advanced technology offers several significant advantages that enhance the amputee's quality of life, boost independence, increase range of motion (ROM), and reduce discomfort. Additionally, osseointegration offers a crucial function called Osseoperception, allowing the person to feel full sensation with their new prosthesis.

Several studies consistently report that osseointegrated prostheses provide significant advantages over conventional socket prostheses. These benefits include improved mobility,

enhanced range of motion, increased prosthetic wearing time, improved gait performance, greater patient satisfaction, and better overall quality of life. reported complications because the implant penetrates the skin, creating a permanent transcutaneous interface. Other complications include implant loosening, periprosthetic fractures, mechanical irritation, and the need for revision surgery. Although recent implant designs and engineering modifications have aimed to improve implant stability and reduce mechanical stress, long-term monitoring and prevention of complications remain important challenges for widespread clinical adoption.

4. The current state and the recommendations for the future

Osseointegration (OI) technology is increasingly popular among the amputee population as an alternative to prostheses. Earlier socket-based prostheses were widely used for amputees, whereas current osseointegrated systems appear to be an improvement. By anchoring the prosthesis to the skeleton, information is transmitted through the stronger skeletal system, which can better support it. New developments in osseointegration are essential for improving interfacial materials and fostering interdisciplinary efforts. Studies on new titanium alternatives, such as Ti-13Nb-13Zr, have been encouraging and offer a good compromise in addressing the toxicological problems associated with current commercial systems. In a similar vein, biocompatible and infection-resistant coatings should rank among the top research priorities. Cooperation among patients, biomedical engineers, doctors, and materials scientists is critical for developing novel devices to improve patient care. Clinical trials also need to be extended to include long-term follow-up and standardized protocols. Long-term investigations are required to assess the durability and safety of newer implant designs and materials. Standardized protocols for surgery and postoperative care result in fewer complications and better outcomes for all patients. Research should focus on the patient experience, quality of life, and functionality when designing and evaluating prosthetic systems. Such initiatives will likely promote advanced and user-friendly technology in the future. Patient education on osseointegration, including its advantages and disadvantages, can facilitate adaptation and support informed consent.

In the near future, regulations and economic conditions may influence the broader adoption of osseointegration techniques. Furthermore, cost-effectiveness analyses comparing osseointegrated with socket-based solutions may provide valuable data for health policy decisions and resource allocation.

5. Conclusions

This literature review on osseointegrated implants has emphasized recent advancements in prosthetics for persons with limb amputations. The reviewed literature consistently indicates that osseointegration offers an alternative to traditional socket-based prostheses by enabling direct skeletal attachment of the prosthetic limb to the host bone. This approach has been associated with greater freedom of movement, comfort, prosthetic stability, and satisfaction compared with a conventional socket. Despite these functional benefits, osseointegrated implants can be associated with several clinical challenges. Complications such as infection at the skin-implant interface and periprosthetic fractures remain major concerns. The literature indicates that, while these problems are severe, careful evaluation and treatment are necessary during and after the procedure. Advances in implant

design, biomaterials, and surface modification techniques have been widely investigated to improve implant stability and enhance the bone-implant interface. These advances include improved biocompatible materials, such as titanium alloys, surface modification techniques, and novel coatings that enhance osseointegration and minimize complications. New biomaterials, such as Ti-13Nb-13Zr, have been developed to address problems associated with older materials, including toxicity and mechanical limitations, while offering performance comparable to Ti-6Al-4V. These advancements can lead to better implant stability, greater durability, and improved patient outcomes.

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