

Research Progress on the Effects of Different Implant Materials on Osseointegration

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Abstract: Successful dental implantation fundamentally relies on effective osseointegration, wherein the choice of implant material plays a critical role. Currently, a wide range of implant materials are used in clinical practice, including metals, ceramics, polymers, and composites. The intrinsic properties of these materials—such as elastic modulus, surface characteristics, and biocompatibility—profoundly influence the stress distribution at the implant-bone interface, cellular responses, and the progression of osseointegration. This study aims to systematically analyze and summarize the performance and osseointegration capacity of various implant materials, thereby identifying their respective advantages and limitations in promoting bone integration. A review of domestic and international literature indicates that titanium alloys demonstrate superior osseointegration efficiency compared to commercially pure titanium. Ceramic implants, such as those made from zirconia, exhibit comparable osseointegration performance to titanium alloys, while offering additional benefits in terms of mechanical strength and aesthetic properties. Although polyetheretherketone (PEEK) shows relatively limited innate osseointegration capacity, surface modification techniques and the development of bioactive composites have been shown to enhance its bioactivity to varying degrees. Further investigation is warranted to optimize PEEK-based materials for clinical applications.

Keywords: Osseointegration; Titanium; Titanium Alloy; Zirconia; PEEK; Implant Materials.

1. Principles and Process of Osseointegration

In 1952, Professor Per-Ingvar Brånemark of the University of Gothenburg in Switzerland unintentionally discovered the phenomenon of osseointegration while studying the microcirculation of the rabbit fibula. During his experiment, titanium optical chambers were implanted into rabbit fibulae and, upon conclusion, were found to be firmly integrated with the surrounding bone tissue, making removal impossible. Brånemark subsequently coined this phenomenon as “osseointegration” [1]. Further studies revealed that after titanium implants were placed into the maxillary and mandibular bones of rabbits and dogs and allowed to heal, a layer of dense cortical bone formed around the implants, and attempts to remove them resulted in jaw fractures [2]. These findings laid the groundwork for the exploration of titanium implants in humans, leading to the first successful dental implant surgery in 1965. The theory of osseointegration has since become foundational not only to implant dentistry but also to orthopedic surgery, rehabilitation medicine, and plastic surgery [3]. Initially, osseointegration was defined as a structural and functional connection between living bone and the surface of an implant [4]. The contemporary understanding describes it as a state in which there is no relative movement between the implant and the directly contacting bone tissue [2]. Primary stability of an implant, achieved immediately after placement into the alveolar bone, is largely dependent on mechanical interlocking and frictional forces at the bone-implant interface. Secondary stability is derived from the biological strength of osseointegration and typically develops over a period of 3 to 6 months, marking the transition from mechanical to biological fixation [5]. Implantation creates a bleeding wound within the jawbone, and osseointegration represents a well-orchestrated biological

healing and tissue regeneration process. Osteoblasts, osteoclasts, immune cells, and signaling molecules in the blood coordinate this healing. Initially, implantation causes disruption of local vasculature, allowing blood to come into direct contact with the implant surface. Proteins from blood and interstitial fluid rapidly adsorb onto the implant [6]. Studies have shown that fibronectin (Fn) and vitronectin (Vn) play crucial roles in mediating the adhesion and spreading of osteogenic cells on implant surfaces [7]. These proteins contain Arg-Gly-Asp (RGD) sequences that interact with integrin receptors on cell membranes, influencing cellular adhesion and migration [8]. Platelets adhere to the implant surface, forming microparticles (MPs), expressing P-selectin, and releasing various regulatory factors—such as platelet-derived growth factor (PDGF) and transforming growth factor-beta (TGF- β)—to promote bone healing. These cytokines, along with erythrocytes, are essential during the bone conduction phase [9, 10]. In the first 1–2 weeks post-implantation, the body mounts an immune-inflammatory response. Neutrophils and macrophages remove necrotic tissue and bacteria. M1 macrophages release pro-inflammatory cytokines (e.g., IL-1, TNF- α), while M2 macrophages exhibit anti-inflammatory effects by secreting PDGF and TGF- β 1, thereby promoting fibroblast growth and tissue regeneration [11]. Under hypoxic conditions, macrophages also release vascular endothelial growth factor (VEGF), stimulating angiogenesis [12]. As the initial blood clot is gradually replaced by newly proliferating fibrin tissue and capillaries, granulation tissue begins to form. Angiogenesis is crucial for new bone formation, as blood supply delivers essential nutrients. New bone then forms concentrically around the neovasculature [13]. Osteoprogenitor cells adhere to the implant surface via integrins and differentiate into osteoblasts, which express osteocalcin and alkaline phosphatase, initiating bone matrix

deposition [12]. Osteoclasts, also integrin-dependent, degrade bone matrix by secreting enzymes upon contact, creating space for new bone formation by osteoblasts [14]. New bone initially forms as woven bone trabeculae, which subsequently mature into parallel-fibered bone and eventually transform into lamellar bone with increased density, constituting primary bone tissue [15]. The dynamic interplay and balance between osteoblasts and osteoclasts is essential for continuous bone remodeling and homeostasis. In summary, osseointegration is a biological process analogous to soft tissue healing and can be divided into four overlapping but distinct stages: the hemostatic phase, inflammatory phase, proliferative phase, and remodeling phase [12]. The ideal outcome of this process—robust osseointegration—is fundamental to the long-term success of implant surgery. Currently, the osseointegration efficacy of implant materials is commonly assessed using parameters such as bone–implant contact (BIC), bone volume (BV), bone density (BD), removal torque (RT), and the implant stability quotient (ISQ).

2. Common Implant Materials in Clinical Use and Their Effects on Osseointegration

2.1. Titanium and its Alloys

2.1.1. Commercially Pure Titanium

In recent years, significant advancements have been made in the study of dental implant materials by researchers both domestically and internationally. Titanium has garnered widespread clinical use due to its high strength, low density, lack of cytotoxicity, and absence of immune rejection, which collectively endow it with excellent biocompatibility and a superior strength-to-weight ratio [16]. Titanium and its alloys readily undergo surface oxidation in ambient air, forming a thin layer of titanium dioxide (TiO_2). This passive oxide film isolates the metal from environmental exposure, providing chemical stability and inertness, and endowing titanium with outstanding corrosion resistance [17]. Furthermore, high-purity titanium exhibits considerable ductility and fatigue resistance, which are critical for the long-term mechanical stability of dental implants [18]. The superior clinical performance of titanium implants is underpinned by these physicochemical properties. According to Saini R.S. et al., titanium possesses an almost fully closed drum-shaped Fermi surface, indicative of a stable electronic structure and orderly atomic arrangement within its crystal lattice—factors that contribute to its mechanical robustness. The strong interatomic bonding in titanium enhances its integration with bone tissue, promoting stable and durable osseointegration [19]. However, despite the high stability of the titanium dioxide surface layer, titanium implants may still undergo corrosion and ion release within the oral cavity due to factors such as exposure to saliva, occlusal loading, and friction with prosthetic crowns [20]. Released metal ions can trigger localized inflammatory responses by promoting immune cell infiltration and osteoclast activation, potentially leading to tissue discoloration and peri-implant inflammation [21]. Rodrigues et al. reported that the TiO_2 surface layer may be compromised in acidic environments associated with inflammatory conditions, thus impairing the implant's osseointegration capacity. Additionally, meta-analyses have identified hypersensitivity reactions to titanium in a small subset of patients, which may also contribute to implant failure [22]. These limitations have driven the development

and clinical adoption of titanium alloys with enhanced properties. Currently, the most widely used titanium alloy implant materials in clinical practice include Ti-6Al-4V (titanium–aluminum–vanadium), TiZr (titanium–zirconium) alloys, and TiUnite-treated surfaces.

2.1.2. Ti6Al4V Alloy

Ti6Al4V is the most commonly used titanium alloy in clinical practice. Compared with commercially pure titanium, Ti6Al4V exhibits higher strength and toughness, enabling it to better withstand masticatory forces [23]. Its favorable elastic modulus facilitates the adhesion and retention of a thicker oxide layer, enhancing its corrosion resistance [24]. Ti6Al4V also demonstrates superior fatigue resistance compared to pure titanium [25]. Numerous studies have shown that Ti6Al4V implants promote the proliferation and osteogenic differentiation of bone marrow-derived mesenchymal stem cells (BMSCs), thereby enhancing new bone formation [26, 27]. Dehurtevent et al. reported that Ti6Al4V implants with porous surface structures not only increase the contact area between the implant and surrounding bone tissue but also reduce the alloy's elastic modulus, bringing it closer to that of natural bone. This improves bone regeneration and repair, strengthens the adhesion of newly formed bone to the implant surface, and consequently enhances biological stability and osseointegration efficiency [28]. In an animal study using rats, Yang et al. further demonstrated that smaller pore sizes on the surface of Ti6Al4V implants favor osteogenic differentiation of BMSCs, while larger pores enhance their proliferation [26]. With the development of advanced fabrication techniques, such as three-dimensional fiber deposition and selective electron beam melting (SEBM), it is now possible to produce Ti6Al4V implants with precisely controlled pore size and porosity [29, 30]. Despite these advantages, Ti6Al4V alloys also present certain limitations. Purely porous Ti6Al4V structures exhibit limited biocompatibility and only modest capacity to stimulate BMSC proliferation and differentiation, which may compromise the outcomes of osseointegration and bone repair [31]. Recent orthopedic research has explored the use of tantalum (Ta) coatings on Ti6Al4V scaffolds. Tantalum coatings not only enhance osteoblast adhesion and proliferation, thereby promoting osteogenesis, but also help suppress inflammatory responses and facilitate wound healing [27, 32]. In the dental field, porous tantalum-coated implants—most notably developed by Zimmer—are among the best-known applications [33]. Multiple studies have shown that tantalum-coated implants can achieve more rapid osseointegration, improved secondary stability, and lower cytotoxicity compared to conventional titanium implants, suggesting strong clinical potential for broader application [33–35]. Nevertheless, the presence of multiple alloying elements in Ti6Al4V compromises its corrosion resistance. During wear and corrosion, aluminum and vanadium ions may be released, which are potentially cytotoxic and could negatively affect osseointegration. However, definitive evidence on this matter remains lacking, and further experimental research is required [20, 36]. Recent studies have proposed the use of graphene-based nanocoatings to inhibit corrosion and ion release from Ti6Al4V implants [37]. Additionally, because the elastic modulus of Ti6Al4V is significantly higher than that of human cortical bone, the resulting stress-shielding effect may lead to bone resorption post-implantation [38]. Therefore, the development of titanium alloys with more appropriate elastic moduli and

enhanced biocompatibility—such as β -phase titanium alloys—remains a key objective in ongoing implant material research.

2.1.3. Titanium-Zirconium (TiZr) Alloy

Titanium has long been established as a standard material for dental implants. However, when the available bone volume is limited—such as in narrow or thin alveolar ridges—narrow-diameter implants (NDIs) are required. In such cases, the relatively high elastic modulus of commercially pure titanium may increase the risk of implant fracture or mechanical failure. To address this issue, titanium-zirconium (TiZr) alloys have been developed in recent years as a novel class of implant materials. TiZr alloys combine two highly biocompatible elements—titanium and zirconium—resulting in superior tensile strength, hardness, and a reduced elastic modulus. These mechanical advantages enhance the alloy's ability to withstand higher occlusal forces, making it well-suited for load-bearing implant applications [39, 40]. TiZr alloys are commonly used to manufacture narrow-diameter implants (3.0–3.5 mm) for clinical indications such as narrow anterior alveolar ridges, edentulous jaws with apical bone resorption or atrophy, and cases where bone augmentation may be contraindicated or has failed [41]. The use of TiZr alloys helps prevent implant fractures and stress-induced bone damage, thereby reducing the risk of implant failure. It is well recognized that the biocompatibility of the implant surface with osteogenic cells is a critical determinant of cell adhesion and subsequent osseointegration. TiZr alloy surfaces typically feature abundant spherical nanostructures, which contribute to their excellent cellular activity and biocompatibility [42]. Studies have demonstrated that TiZr surfaces promote greater cell adhesion than pure titanium, and osteoblast differentiation occurs more rapidly on TiZr surfaces [43]. In an animal model using mini pigs, Gottlow et al. found that titanium-zirconium alloys containing 13–17% zirconium (TiZr1317) exhibited significantly higher removal torque (RT) values and greater bone-to-implant contact (BIC) compared to pure titanium, indicating a stronger bone tissue response [44]. However, some studies have reported a delayed vertical bone conduction response with TiZr implants [45], and long-term clinical data remain insufficient. As such, the long-term clinical performance and prognosis of TiZr alloy implants require further investigation and longitudinal studies.

2.1.4. TiUnite

TiUnite is a novel type of dental implant developed using an anodic oxidation technique. Its surface features a porous structure coated with a layer of crystalline titanium dioxide (TiO_2), which facilitates the deposition of hydroxyapatite, thereby enhancing bioactivity [46]. In a study by Huang et al., TiUnite implants were placed in the edentulous posterior maxillae of crab-eating macaques. Bone mineral density and bone-to-implant contact (BIC) were measured at multiple time points following implantation and before euthanasia. The results indicated that TiUnite implants were capable of establishing reliable bone-implant contact and exhibited considerable osteoconductive potential, effectively promoting osseointegration in the posterior maxillary region [47]. Xiropaidis et al. also demonstrated, through animal experiments in Labrador dogs, that the porous TiUnite surface resulted in significantly higher levels of BIC compared to conventional implant surfaces [46]. In addition, recent studies have explored surface modification strategies such as magnesium ion coatings, which have been shown to enhance

osseointegration by promoting bone regeneration at the implant interface [48].

2.2. Zirconia (ZrO_2)

With the continuous advancement of dental aesthetic technologies and increasing patient demand for superior esthetic outcomes, the limitations of traditional titanium implants have become more apparent. Titanium dioxide particles and nanoparticles released from the surface of titanium implants can accumulate in the gingival tissue, potentially leading to issues such as peri-implant soft tissue discoloration (e.g., grayish gingival appearance) [49]. In contrast, zirconia ceramics, which possess a tooth-like color, offer improved aesthetic outcomes along with favorable biocompatibility and mechanical properties. These features help reduce the risk of peri-implant inflammation and gingival staining, making zirconia a promising alternative to conventional titanium implants [50]. Zirconia is a bioinert material characterized by minimal soft tissue reactions, excellent cellular adhesion, high biocompatibility, and superior esthetics. It exhibits no cytotoxicity toward osteoblasts or fibroblasts and may even support extracellular matrix repair [51, 52]. Compared with traditional titanium implants, zirconia surfaces exhibit lower wettability and surface energy, making them less conducive to bacterial adhesion and biofilm accumulation [53, 54]. These advantages position zirconia as a next-generation dental implant material. Numerous studies have reported that zirconia implants achieve bone-to-implant contact (BIC) and removal torque (RT) values comparable to those of conventional titanium implants [15, 55, 56]. In a 1998 animal study by Akagawa et al., zirconia implants were placed in the mandibles of monkeys. Follow-up at 12 and 24 months revealed successful osseointegration and long-term stability [57]. Some domestic researchers have suggested that zirconia elicits no adverse tissue reactions and may even outperform titanium in terms of osseointegration rate [58]. Overall, the results of animal studies on zirconia implants have been encouraging, and clinical applications have already commenced in some countries. However, there remains a lack of large-scale, long-term clinical data and randomized controlled trials to fully validate their long-term efficacy and safety.

2.3. Polyetheretherketone (PEEK)

Polyetheretherketone (PEEK) is an emerging high-performance polymer that has gained increasing attention in the field of oral implantation. It exhibits excellent thermal stability, corrosion resistance, and hydrolytic resistance, along with favorable mechanical properties and biocompatibility [59]. PEEK has been successfully applied in various biomedical fields, including craniofacial reconstruction, joint orthopedics, spinal repair, and oral and orthodontic rehabilitation [60–62]. Compared with traditional titanium and titanium alloy implants (with elastic moduli of approximately 102–110 GPa), PEEK has a much lower elastic modulus (~ 3.6 GPa), which is closer to that of human cortical bone (~ 14 GPa) [62, 63]. Large differences in elastic modulus between implant and bone can lead to stress shielding effects, negatively impacting osseointegration and implant stability. Therefore, modified PEEK and its composites have been proposed as alternatives to titanium implants, offering reduced risk of marginal bone resorption and improved secondary stability [64]. For example, carbon fiber-reinforced

PEEK composites used in hip joint replacements exhibit an elastic modulus up to 18 GPa, closely approximating that of cortical bone [65]. Additionally, compared to titanium, PEEK surfaces are less prone to bacterial colonization, less likely to cause allergic reactions, and free from metallic coloration—resulting in improved esthetic outcomes [66]. These advantages contribute to PEEK's growing potential in oral implantology. However, as a bioinert material, unmodified PEEK suffers from poor surface properties and limited interaction with surrounding bone tissue, making it difficult to achieve strong osseointegration [67]. In a canine mandibular model, Koch et al. compared implants made of titanium, zirconia, and PEEK. After four months, the bone-to-implant contact (BIC) for PEEK was 26.8%, significantly lower than that of zirconia (59.2%) and titanium (41.2%) [68]. Similarly, Cook et al. demonstrated that titanium-coated implants outperformed PEEK implants in terms of BIC [69]. These findings underscore the need for surface modification strategies to enhance the osteoinductivity of PEEK. Unmodified PEEK surfaces have low osteoconductivity and surface activity, which not only hinder osseointegration but also promote biofilm formation, increasing the risk of peri-implantitis [66]. Currently, surface modification methods for PEEK fall into two main categories. The first involves physical techniques such as sandblasting, plasma spraying of calcium carbonate or titanium coatings. Ourahmoune et al. found that sandblasted PEEK surfaces achieved higher osseointegration rates compared to untreated surfaces [70]. Torstrick et al. implanted three types of PEEK into rat tibiae—porous PEEK, titanium-coated PEEK, and smooth PEEK—and found that the porous PEEK group exhibited greater expression of vascular endothelial growth factor (VEGF) and osteocalcin, indicating improved osseointegration potential [71]. The second approach involves coating the PEEK surface with bioactive materials to promote bone conduction, such as hydroxyapatite (HA), zinc, titanium dioxide, or magnesium. Durham et al. applied ion beam-assisted deposition to fabricate HA and yttria-stabilized zirconia (YSZ) composite coatings on PEEK implants, which were then implanted into the lateral femoral condyles of 18 rabbits. Compared with uncoated implants, the heat-treated HA/YSZ-coated implants demonstrated superior surface stability, greater bone regeneration, and higher BIC at 8 and 16 weeks post-implantation [72]. Zheng et al. developed a chitosan coating containing zinc-doped bioactive glass nanoparticles for PEEK implants. This coating not only enhanced BMSC osteogenic differentiation and osseointegration but also promoted M2 macrophage polarization, reduced inflammation, and improved the immunomodulatory capacity of the implant [73]. Wei et al. engineered a porous PEEK implant coated with a polydopamine (PDA) layer chelated with magnesium ions (Mg^{2+}). This coating exhibited high hydrophilicity and sustained Mg^{2+} release, which accelerated angiogenesis and early-stage bone growth, demonstrating considerable clinical potential.

3. Conclusion and Future Perspectives

The choice of implant material is critical to the success rate and long-term clinical outcomes of dental implantation. Selection must take into account factors such as mechanical strength requirements and biocompatibility. In anterior regions, esthetic considerations are paramount, and bioceramic implants should be prioritized. For patients with metal allergies, high-performance polymeric materials such

as PEEK offer viable alternatives. Rational development and clinical application of diverse implant materials can enhance therapeutic outcomes, reduce treatment duration, and improve patient comfort. With ongoing advances in materials science and bioengineering, a variety of novel implant materials have emerged. However, their long-term clinical efficacy and safety remain to be fully validated through large-scale, longitudinal studies. The development of next-generation implant materials has become a key driving force in the evolution of implantology. Future efforts should focus on the integration of advanced materials and technologies to optimize both functional performance and biocompatibility. The ultimate goal is to achieve personalized, efficient, and durable implant-based oral rehabilitation.

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