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The Role of Dermatologic Biomaterials in Enhancing Osseointegration of Orthopedic Implants

Sriya Kakarla[1], Janae Rasmussen[2], Rachael Larkin[3], Yashi Agarwal[4], Kenny Thai[5], Guang Orestes[6], Keziah Crossley[7], Oliver Cesar[8], Kelly Frasier[9]*

[1]UT Health Houston McGovern Medical Houston, Houston, TX, USA

[2]Valley Consortium for Medical Education, Modesto, CA, USA

[3]Edward Via College of Osteopathic Medicine, Blacksburg, VA, USA

[4]SUNY Upstate Medical University, Syracuse, NY, USA

[5]UNTHSC Texas College of Osteopathic Medicine, Fort Worth, TX, USA

[6]Kirk Kerkorian School of Medicine at UNLV, Las Vegas, NV, USA

[7,8]SUNY Upstate Medical University, Syracuse, NY, USA

[9]Department of Dermatology, Northwell Health, New Hyde Park, NY, USA

[*]Corresponding author:

Kelly Frasier, DO, MS
Department of Dermatology, Northwell Health, New Hyde Park, NY, USA, Phone: 3105956882, Email: kellymariefrasier@gmail.com

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ABSTRACT

The success of orthopedic implants hinges on achieving robust osseointegration while minimizing complications at the skin-implant interface, a critical yet often overlooked aspect of implant performance. Dermatologically tested biomaterials, including medical-grade silicone, hydrophilic polymers, and antimicrobial coatings, are emerging as key innovations to address these dual challenges. Silicone coatings provide a soft, biocompatible barrier that reduces mechanical friction and irritation, particularly at percutaneous entry points, lowering the risk of skin breakdown and chronic inflammation. Hydrophilic polymers enhance adhesion to soft tissues by maintaining a hydrated interface, which improves seal integrity and reduces microbial penetration. Advanced antimicrobial coatings, such as those incorporating silver nanoparticles, bioactive glass, or antibiotic-eluting compounds, actively inhibit biofilm formation while promoting osteoblast activity at the bone-implant surface. Surface modifications, including micro- and nanopatterning, further optimize implant performance by increasing surface area and enhancing the adhesion, proliferation, and differentiation of osteogenic cells, thereby accelerating osseointegration. Additionally, dermatologically friendly biomaterials reduce the risk of adverse skin reactions, such as contact dermatitis or hypersensitivity, ensuring greater patient comfort and compliance during recovery. By addressing the interaction between skin, soft tissue, and bone, biomaterials provide a

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multifaceted approach to implant design, fostering an aseptic and mechanically stable environment that supports both tissue health and implant longevity. Incorporating dermatologically compatible innovations into orthopedic implants offers a transformative strategy to minimize complications, enhance biological integration, and ultimately improve surgical outcomes and quality of life for patients.

Keywords: Osteointegration, Dermatologically-Tested Biomaterial, Antimicrobial Coating, Surface Modification, Implant-Tissue Interface.

ABBREVIATIONS

GSM: Genitourinary Syndrome of Menopause.

INTRODUCTION

Orthopedic implants have revolutionized modern medicine by offering effective solutions for skeletal repair, joint replacement, and fracture stabilization. These implants are critical in restoring mobility and improving the quality of life for millions of patients worldwide. Despite their widespread success, challenges persist, particularly regarding osseointegration, which is the process by which bone tissue biologically integrates with the implant surface. Achieving robust osseointegration is essential to the longevity and stability of implants, ensuring they can withstand mechanical loads over time [1]. An often overlooked factor in the success of orthopedic implants is the interaction between the implant and surrounding soft tissues. The skin-implant interface plays a pivotal role in surgical outcomes by forming the first line of defense against external microbial invasion. Complications, such as mechanical irritation, local infection, and impaired wound healing are common at this interface, directly influencing the success of osseointegration and the overall efficacy of the implant [2]. Effective integration of dermatologically compatible materials at the implant's interface could potentially mitigate these risks and enhance patient outcomes. One of the primary challenges in orthopedic implants is maintaining a stable, infection-free skin-implant interface. Mechanical irritation caused by rigid implant edges can disrupt the natural healing process, while microbial infection poses significant risks of systemic complications. Delayed osseointegration, often exacerbated by these issues, reduces the lifespan of implants and necessitates revision surgeries, burdening both patients and healthcare systems [1]. Currently, the materials used in implants are often optimized for structural integrity and osseointegration but do not adequately address the dermatologic challenges of prolonged skin contact. This gap underscores the urgent need for biomaterials that not only support osseointegration but are also dermatologically compatible, reducing the risk of infection and mechanical irritation.

This literature review aims to investigate the role of dermatologic biomaterials in enhancing the performance of orthopedic implants. This review highlights innovations in material science and strategies for improving both osseointegration and skin compatibility. Emphasis is placed on developing comprehensive solutions that optimize mechanical stability while minimizing complications at the skin-implant interface. The scope of this investigation encompasses the evaluation of advanced biomaterials, including medical-grade silicone, hydrophilic polymers, and antimicrobial coatings, which are increasingly employed to address the dual challenges of osseointegration and biocompatibility. This review considers emerging surface modification techniques designed to create favorable microenvironments for cell adhesion and microbial resistance [3]. By focusing on these materials and technologies, the review seeks to provide a framework for improving orthopedic implant outcomes through interdisciplinary approaches in biomaterial science and clinical application. This holistic approach not only underscores the importance of material innovation but also bridges the gap between engineering and dermatology, paving the way for next-generation orthopedic implants.

OSSEOINTEGRATION AND SKIN-IMPLANT INTERFACE

Osseointegration demonstrates the biological process by which living bone cells attach to and integrate with the surface of a biocompatible implant to create stable and functional connections. This formation and growth of bone is a complex process involving molecular, cellular, and biochemical metabolic changes. Complete osseointegration involves three major stages: woven bone formation, lamellar bone deposition, and load-dependent bone remodeling via coupling [4]. During the initial interactions of the implant with blood cells, platelets cause the release of cytokines that induce the deposition of a fibrin network, via the coagulation cascade, to act as a scaffold for other osteoblasts and mesenchymal cells to eventually deposit bone-related proteins [4]. This non-collagenous matrix eventually undergoes remodeling into lamellar bone in direct contact with the implant.

Proper osseointegration occurs after establishing primary and secondary layers of stability around an implant. Primary stability refers to the mechanical stability established immediately after the implant is placed, and is successfully determined by the amount and quality of direct physical engagement with the surrounding bone. Successful establishment of primary stability occurs when there is minimal micromotion below 50-100 micrometers, maximal implant-bone contact, and stress is not added to surrounding tissue when load-bearing [5]. While primary stability occurs during the initial phase of woven bone formation, secondary stability refers to the long-term anchorage achieved through lamellar bone deposition and structural adaptation to mechanical load. It is characterized by proper bone remodeling and maturation, continued high bone-to-implant contact ratio, and successful containment of load. Both of these stages of stability are regulated, so are affected by biomaterial properties, biomechanical conditions, and biological responses [6]. These factors are essential to consider when establishing primary stability, as high-quality early bone deposition sets the foundation for successful secondary stability, and long-term osseous stability [5]. Both forms of stability can be optimized by selecting implants with specific morphologies and utilizing appropriate surgical techniques.

From a biomaterial standpoint, factors like the implant's composition, size, shape, and surface characteristics must be evaluated to minimize trauma and adverse reactions. Currently, materials such as titanium, cobalt-chromium, and bioinert ceramics are among the most commonly used across various types of osseointegration procedures [7]. These materials have high biocompatibility and corrosion resistance, which prevents metal ion leakage, and mechanical properties that make them durable while unstimulating to inflammation and the immune system. Parameters like thread depth, shape, pitch, implant diameter, and implant length are also tailored to specific patient-dependent variables to maximize the chances of integration [8]. Surface roughness is another critical factor, as it can enhance bone-implant adhesion, increase hydrophilicity, and reduce surface tension. Techniques like machining, sandblasting, and acid etching are used to create macro-, micro-, and nano-scale surface textures, which increase contact areas between the implant and bone, thereby directly adding to the mechanical stability [9]. These modifications also create more space for osteoblast attachment, which promotes osseous proliferation, and can even minimize bacterial biofilm formation. Nano-scale roughness has been shown to influence alkaline phosphatase (ALP) activity, further supporting osteogenic cell migration and differentiation, which are processes critical for the deposition of high-quality initial non-collagenous matrices [9].

These physical properties of implants are often considered directly in relation to the clinical context of the host bone quality and underlying comorbidities, as implant bed health can affect the innate healing potential, and can necessitate different surgical interventions. Higher-quality bone is associated with high-density bone, which has been shown to yield fewer complications and provide buffers against the response differences due to implant designs and other external factors. There are several conditions that can compromise bone quantity and quality, including rheumatoid arthritis, osteoporosis, renal insufficiency, and cancer. Patients with these pathologies may benefit from specialized implants to account for their diminished healing capacity. In a study with dog models of poor bone quality, acid-etched implants facilitated higher bone-implant contact during osseointegration when compared to machined surface implants [10]. While this study was in oral implants, it demonstrated that acid-etched surfaces may be a considerable topographical character for patients with lower-density bone in orthopedic implants. Dual sandblasted and acid-etched surface implants were also noted to yield faster primary stability and reduced recovery times [7]. These modifications help decrease inflammation, infection, and other pathological processes, which can benefit osseous healing and increase patient recovery. Another factor that affects successful osseointegration is the surgical procedure itself. Sales et al. discuss that the implant is "placed in the correct position and orientation, with adequate primary stability and avoidance of any damage to the surrounding structures," with preservation of vasculature being critical [6]. This can be achieved by optimizing drilling techniques, including the selection of appropriate tools, adjustments to drilling speed and duration, and careful management of heat generation, depending on the needs of the specific case [11].

During osseous remodeling, the implant should be left undisturbed both in regards to movement and infection, and patients should avoid poor eating habits and smoking to further minimize risks of complications [6]. Mechanical friction or micromotions at certain implant interfaces can encourage fibrous tissue development, which acts as a barrier between the bone and implant, which can reduce proper adhesion and proliferation of osteoblasts. Fibrous tissue is weaker than osseous tissue with increased shear loading, micromotion, and

implant loosening occurring more easily [12]. The cycle of chronic inflammation that results from this furthers injury. This process is largely driven by the prolonged release of pro-inflammatory cytokines such as TNF-a, IL-1B, and IL-6 via Nf-KB signaling pathways or WNT pathways [13]. Any vascular disruption through these complications can also cause tissue necrosis around the implant site, and further chronic inflammation. Prolonged microscopic tissue damage due to mechanical friction can even cause pressure ulcers in some patients [14]. These can continuously disrupt the healing skin barrier around the implant interface and risk additional complications like infection. These are regarded as the most common complications following osseointegration procedures [15].

Staphylococcus aureus (S. aureus) and Staphylococcus epidermidis (S. epidermidis) are two of the most common pathogens associated with these risks of microbial invasion and biofilm formation postoperatively [16]. These bacteria produce surface adhesins that enable attachment to host proteins like fibrinogen and fibronectin on the implant surface [17]. They can secrete polysaccharides, proteins, and DNA to create an extracellular matrix to form a biofilm [17]. A biofilm acts as a protective shield from antibiotics and the immune responses, by limiting drug penetration and preventing phagocytosis by the immune system. Additionally, *S. aureus* produces toxins, such as hemolysins and leukocidins, which damage host cells and exacerbate inflammation [18]. *S. epidermidis* also produces polysaccharide intercellular adhesin (PIA), which further strengthens biofilm cohesion and enhances resistance. In this way, infections can similarly cause chronic inflammation as a secondary consequence. These mechanisms collectively not only impair osseointegration, but also sustain bacterial persistence, leading to chronic infection.

Current dermatologic traditional implant materials work to target these issues, but they have adversely encompassed a range of adverse skin responses, including hypersensitivity, contact dermatitis, and autoimmune reactions. Metal hypersensitivities are common in North America with almost 15% and 6% of the population having a sensitivity to nickel and cobalt, respectively [19]. When metal ions are released from implants due to inevitable corrosion or due to pathological processes, these ions bind to endogenous proteins, forming metal-protein complexes that are recognized as antigens by T-lymphocytes and trigger immune responses. Hypersensitivity to nickel, cobalt, or chromium was found in 60% of patients with failed or poorly functioning hip implants [20]. Currently, some skin-friendly biomaterial coatings, such as hydroxyapatite, antimicrobial coatings, and polyethylene glycol (PEG)-based coatings, are being developed.

DERMATOLOGICALLY TESTED BIOMATERIALS IN ORTHOPEDIC IMPLANTS

Among the various materials explored for these applications, dermatologically tested biomaterials have emerged as a promising solution. See Table 1 for a summary of different dermatologically tested biomaterials. One such material that has garnered attention is medical-grade silicone. Silicone-based implants have demonstrated excellent biocompatibility, allowing for seamless integration with surrounding tissues and minimizing the risk of adverse reactions [21]. Silicone is a widely used biomaterial in various biomedical applications due to its biocompatibility, durability, and ability to mimic the mechanical properties of human tissues. This widespread use of silicone can be attributed to its strength, flexibility, temperature and chemical resistance, and inertness [22]. In orthopedics, the firm yet flexible properties of silicone allow it to be used as a replacement for damaged connective tissue, such as the treatment of arthritis in joints of the phalanges. Related to the invasive nature of orthopedic implants, these advantageous properties call for the continued development of medical-grade silicone for orthopedic implants. However, the hydrophobicity of silicone poses a major challenge, especially for percutaneous implants. The highly hydrophobic nature of silicone results in bacterial adhesions and biofilm formation, which can lead to severe infections and implant failures [23]. Percutaneous implants have a high risk of infection, due to their exposure to the external environment, and the presence of a skin-implant interface.

While research on the use of silicone-based biomaterials for percutaneous orthopedic implants is limited, studies on other percutaneous implants, like catheters and shunts, provide relevant insights. Campoli et al. reported that silicone percutaneous endoscopic gastrostomy tubes were significantly more durable than latex percutaneous endoscopic gastrostomy tubes, with no statistically significant differences observed between the two tube types in terms of complications, such as peristomal infection, granulation tissue formation, and leakage [24]. The promising durable properties of silicone make it a compelling option for percutaneous orthopedic applications, but the risk of infections must be addressed. Okada & Ikada demonstrated in a rabbit model that collagen

immobilization on silicone surfaces can help maintain a stable skin-implant interface and prevent complications associated with epidermal migration [25]. This implies that surface modifications of silicone can be a viable strategy to enhance biocompatibility and reduce infection risks for percutaneous orthopedic implants. Fleckman et al. used both porous/solid-core poly (2-hydroxyethyl methacrylate) [poly(HEMA)] and silicone rods to investigate the long-term cutaneous and inflammatory responses in mice to percutaneously implanted rods encased in sphere-templated porous biomaterials [26]. The study revealed a pronounced inflammatory response around the silicone implants, characterized by the presence of neutrophils, macrophages, and foreign body giant cells [26]. This inflammatory reaction was more severe compared to the poly(HEMA) implants [26]. Additionally, the silicone implants exhibited signs of cracking and degradation, which potentially contributed to the increased inflammation observed [26]. This implies the need for further research to address the inflammatory response and improve the long-term stability of silicone implants in percutaneous orthopedic applications.

Beyond silicone, hydrophilic polymers have also been explored as potential biomaterials for orthopedic implants due to their unique characteristics. Hydrophilic polymers create a water layer at the material's surface that acts as a lubricant and a barrier, reducing friction and preventing direct contact between the material and biological molecules [27]. This minimizes cell adhesion and subsequent immune responses, which are crucial for implants and other medical devices [27]. This implies that hydrophilic polymers could be advantageous in reducing inflammation and bacterial infections in orthopedic implants. Moreover, the hydrophilicity of these polymers can potentially improve the integration of the implant with the surrounding tissues. Buxadera-Palomero et al. investigated different methods of applying polyethylene glycol (PEG) coatings to titanium surfaces, aiming to improve biocompatibility for implants [28]. The study demonstrated that all pegylation methods used in the study reduced protein adsorption compared to uncoated titanium and modulated cell adhesion [28]. Protein adsorption represents a critical first step in a cascade of events that can lead to biofilm formation and inflammation, potentially hindering soft tissue integration. Applying polyethylene glycol coatings to implant surfaces has been shown to reduce protein adsorption, which is a crucial initial step in the sequence of events culminating in biofilm formation and inflammation. This reduction in protein adsorption may create a more favorable environment for soft tissue cells to interact with the implant surface, potentially enhancing the integration process in a clinical setting. Harris et al. evaluated the effectiveness of poly(l-lysine)-grafted-poly (ethylene glycol) (PLL-g-PEG) copolymers in reducing S. aureus adhesion to titanium oxide surfaces [29]. They found that PLL-g-PEG coatings, particularly those without peptide functionalization, can effectively reduce S. aureus adhesion to titanium oxide surfaces [29]. This suggests that hydrophilic polymer coatings may provide an effective strategy for reducing bacterial adhesions of orthopedic implants and the risk of implant-associated infections. However, further in vivo research is necessary to assess the actual soft tissue integration of coatings like PLL-g-PEG around implants.

Alongside the development of biomaterial coatings, the incorporation of antimicrobial agents into the implant's surface or bulk material is another approach to address the issue of implant-associated infections. Silver nanoparticles, for instance, release biologically active ions that bind to peptidoglycan cell walls, plasma membranes, and bacterial DNA and proteins, disrupting key cellular processes and leading to cell death [30]. This is the principal reason behind the development of various silver-containing coatings or composites for implants to inhibit bacterial adhesion and biofilm formation. Pauksch et al. discovered that silver nanoparticles exhibit cytotoxic effects on bone-forming cells in a dose- and time-dependent manner, with mesenchymal stem cells being more susceptible than osteoblasts [31]. This highlights the need to carefully balance the antimicrobial efficacy and biocompatibility when designing silver-based antimicrobial coatings for orthopedic implants to avoid compromising osseointegration. Contrarily, borate bioactive glasses (BBGs) have been reported to generate no cytotoxicity in vivo, and their degradation into boron favors osteogenesis [32]. This suggests that BBGs have regenerative wound-healing capabilities that are specifically advantageous for orthopedic implants. Naseri et al. discovered in vitro that silver-doped borate glasses exhibited significant anti-biofilm activity against *Pseudomonas aeruginosa*, with increasing efficacy at higher silver concentrations [33]. Collectively, the favorable biocompatibility profile of borate bioactive glasses, and their ability to inhibit biofilm formation when combined with antimicrobial agents like silver, indicate that this approach may represent a promising strategy to develop orthopedic implants that are resistant to infections while maintaining desirable bone-implant integration.

Another antimicrobial coating method is the use of antibiotic-eluting compounds. These compounds can be used as antibiotic-loaded implant coatings that actively release antibiotics to the surrounding tissue, as opposed to passive coating techniques that attempt to reduce biofilm formation through disruption of bacterial adhesions [34]. The active release of antibiotics from these coatings has the potential to locally eliminate bacteria and prevent implant-related infections. This could reduce the necessity for extensive systemic antibiotic administration with the associated risks of antibiotic resistance development. Lee et al. investigated a 3D-printed scaffold loaded with rifampicin for treating osteomyelitis [35]. They demonstrated effective antibiotic release over time, effective inhibition of both *Escherichia coli* and *S. aureus,* and in vitro tests using human osteoblast cells showed that the scaffold material did not significantly hinder cell proliferation [35]. This indicates a promising strategy for effectively treating infections while maintaining good biocompatibility, but further in vivo studies are still required to fully evaluate the long-term efficacy and safety of this approach. Sheehy et al. described the development of a collagen-hydroxyapatite (CHA) scaffold that employs a dual-release mechanism of antibiotics to manage osteomyelitis [36]. The scaffold features an initial rapid release of antibiotics to swiftly eliminate bacteria, followed by a slower, controlled release triggered by microbial activity [36]. In a rabbit model, which closely mimics chronic osteomyelitis in humans, the researchers evaluated both vancomycin- and gentamicin-eluting scaffolds [36]. The vancomycin-based scaffolds demonstrated the ability to reduce S. aureus infection, while the gentamicin-eluting scaffolds successfully eradicated the infection [36]. These findings suggest that antibiotic-eluting CHA scaffolds, especially those releasing gentamicin, have the potential to be an effective treatment for osteomyelitis. The dual-release mechanism and the ability to promote bone healing make these scaffolds a promising approach for addressing this challenging condition and other types of bone infections that can arise from implants. Furthermore, Chug and Brisbois discuss recent developments in multifunctional antimicrobial surfaces, focusing on nitric oxide-releasing biomaterials focusing on key advancements in the ability of nitric oxide to kill bacteria, reduce inflammation, and promote tissue regeneration making it a promising candidate for developing next-generation antimicrobial materials [37]. This new approach to integrating nitric oxide into orthopedic implant coatings may provide a broad-spectrum antimicrobial solution with enhanced biocompatibility compared to silver or antibiotic-based coatings.

Table 1. Summary of Biomaterials and Coatings for Orthopedic Implants

Biomaterial/Coating	Key Properties	Challenges
Medical-Grade Silicone	Biocompatible, durable, flexible, temperature and chemical resistant	Hydrophobicity leads to bacterial adhesion and biofilm formation
Hydrophilic Polymers	Reduce friction, minimize cell adhesion, prevent immune responses, improve tissue integration	Requires further in vivo studies for orthopedic applications
Silver Nanoparticles	Antimicrobial, disrupt bacterial cell walls and DNA	Cytotoxicity concerns for bone-forming cells
Borate Bioactive Glasses (BBGs)	No cytotoxicity, promotes osteogenesis, antimicrobial when combined with silver	Requires further research on clinical applications
Antibiotic-Eluting Coatings	Active antibiotic release, prevents implant-related infections, and reduces need for systemic antibiotics	Risk of antibiotic resistance, requires controlled release
Nitric Oxide-Releasing Biomaterials	Broad-spectrum antimicrobial, reduces inflammation, promotes tissue regeneration	Emerging technology, requires further validation

SURFACE MODIFICATIONS AND THEIR ROLE IN OSSEOINTEGRATION

Recent advancements in surface modifications have significantly enhanced osseointegration of orthopedic implants. Micro- and nanopatterning techniques, including grit blasting, acid etching, 3D-laser texturing, and biomimetic modification, increase the surface area of titanium implants used in orthopedic surgeries, promoting osseointegration by inducing osteogenic cell migration to enhance mineral matrix formation [38]. These techniques create microscale and nanoscale topographies favorable to the biological interactions necessary for healing. Modifications of the implant surface roughness, wettability, charge, and chemistry improve the physical attachment and the downstream signaling pathways, such as enhancing integrin-FAK signaling or modulating osteogenic transcription factor Runx2, to encourage early osseointegration [39]. This is a shift from purely physical optimization to targeting molecular signaling networks for bettering cell attachment, focusing on harnessing biomaterials to influence cellular behavior. Micro- and nanopatterning surfaces with TiO2 nanotubes and hydroxyapatite coatings have also been shown to improve osteoblast adhesion and proliferation, critical for early osseointegration [40]. These techniques support osteoblast function and create a microenvironment conducive to osseointegration and bone growth at the surgical sites. In addition, micro- and nanopatterning can also induce osteogenic differentiation of mesenchymal stem cells even in the absence of osteogenic supplements [41]. This suggests a strong influence of surface modification on cellular differentiation pathways, which are essential to accelerate the integration of orthopedic implants with surrounding bone tissue, reducing the risk of implant loosening early on.

Bioactive surface modifications, including the incorporation of growth factors, peptides, and other bioactive compounds, have shown improved integration of implants with surrounding bone tissue [42]. Biomolecules, for example, bone morphogenetic proteins, peptides, and extracellular matrix components enhance osseointegration. These biomolecules induce bone formation by increasing bone-to-implant contact [43]. This is important in the early stages of osseointegration when maximal contact of surface area is essential. Chimeric peptides and biomimetics active peptides like PR1P and W9 have been shown to promote angiogenesis [44]. Angiogenesis is particularly vital in the early stages of osseointegration, where the bone-to-implant interface requires essential nutrients to support cellular activity and bone formation. These bioactive surface modifications increase peri-implant bone density, facilitating rapid and efficient osseointegration with the surrounding bone tissue.

To promote long-term stability, surface modifications, and materials must be capable of withstanding continuous mechanical wear and physiological stress over time. Ensuring the durability of the surface coatings and modifications is quintessential for implant design. Research studies highlight the importance of surface modifications that balance durability with biocompatibility. One study demonstrated that gelatin methacrylate/polyacrylamide hydrogels exhibit long-term drug-release capabilities that promote long-term integration and biocompatibility [45]. This property could be advantageous for load-bearing implants, where sustained mechanical forces demand materials that maintain their structural integrity over time. In addition, integrating bioactive elements such as dexamethasone and minocycline into the coatings of the implant has also been shown to improve biomechanical strength and biocompatibility [46]. The anti-inflammatory characteristic of such surface modifications can potentially mitigate the risk of implant failure resulting from chronic inflammation or inadequate osseointegration.

CLINICAL IMPLICATIONS AND OUTCOMES

Dermatologically tested biomaterials show promise in enhancing orthopedic implant outcomes by reducing skin complications and promoting osseointegration. These coatings can significantly decrease the risk of contact dermatitis and hypersensitivity reactions, which are common issues with metal implants [47]. By creating a barrier between the metal and the patient's soft tissues, these coatings can reduce metal ion release and associated allergic reactions. This reduction in metal-related complications may lead to improved patient outcomes [48]. Clinical implications of using such coatings extend beyond skin irritation prevention. These biocompatible materials can enhance osseointegration by promoting osteoblast adhesion and proliferation, leading to better bone-implant bonding [49]. Yang and Hong discuss that these materials promote osteoblast adhesion by providing a favorable surface topography and chemical composition that mimics natural bone structure [49]. The micro-nano-scale hierarchical structures of biomimetic implant surfaces provide an optimal environment for osteoblast attachment and spreading. Some coatings have shown antimicrobial properties, which could

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reduce the risk of prosthetic infections, which is a significant cause of implant failure [50]. While long-term studies are still needed, current evidence suggests that patients with coated implants experience fewer soft tissue-related complications, potentially reducing the need for revision surgeries and improving overall surgical outcomes.

Antimicrobial coatings on orthopedic implants have shown significant efficacy in preventing periprosthetic infections in clinical settings. Savvidou et al. demonstrated that patients treated with antimicrobial-coated implants had lower infection rates compared to controls [51]. Examples of implant coating advances are gentamicin coating for tibia intramedullary implants and arthroplasty components, silver technology and povidone-iodine coating for tumor endoprostheses, and titanium implants [51]. These coatings have been shown to be effective in reducing the risk of prosthetic infections [51]. This highlights the effectiveness of gentamicin, silver, and povidone-iodine coatings. Kabata et al. discovered iodine-coated titanium hip implants used in 28 patients with high infection risk had no signs of infection after a 3-year follow-up [52]. This could help improve the current success of single-stage revision in periprosthetic joint infections, which offers a shorter hospital stay and avoids the sequelae from the current United States' gold standard of two-stage revisions. Similarly, Sambri et al. studied silver-coated megaprostheses in patients with tumor prostheses infections and found a lower reinfection rate in the coated group compared to the uncoated group (10.3% vs. 17.5%) [53]. This suggests the positive outcome and efficacy in adding silver coating to the two-stage revision strategy. The promising results from both case studies demonstrate significant potential for improving infection rate and wound healing. They suggest that antimicrobial coatings could revolutionize treatment strategies and lead to better patient outcomes. As research in this field progresses, the integration of such coatings into standard orthopedic practice could improve wound healing and reduce the burden of periprosthetic infections.

Improved osseointegration techniques have significantly enhanced implant longevity and patient outcomes in orthopedic surgeries. The direct anchorage of metal implants into bone allows for better connection and stability, leading to faster recovery times and improved functional outcomes [54]. Overmann et al. discuss the success of osseointegration depending on optimizing three synergistic systems: the host bone, the metal implant, and the skin-implant interface [54]. These are further influenced by factors, such as implant design, patient age, and fixation method. Rand et al. investigated significant risk factors for failure of total knee arthroplasty, with significant correlation to the type of implant, patient age and gender, preoperative diagnosis, type of fixation, and design of the patellar component [55]. The multifaceted nature of implant success underscores the importance of personalized approaches in orthopedic surgery, where careful consideration of the addressed factors is crucial for optimizing long-term outcomes and minimizing the risk of implant failure. Advanced monitoring techniques and patient registries allow for early detection of implant-related problems, contributing to ongoing improvements in implant design and patient care [56]. These systems enable real-time data collection, facilitating analysis and rapid responses to emerging issues, as well as informing evidence-based modifications to implant technologies. While challenges to implant breakdown over time still exist, the overall long-term implications for implant performance and patient quality of life are overall positive, with many patients experiencing improved mobility and reduced pain for extended periods [57]. The continuous refinement of implant materials and designs, coupled with advances in surgical techniques, extends the longevity of implants and reduces the need for revisions.

The incorporation of dermatologically tested biomaterials represents a significant advancement in improving patient outcomes and reducing complications. Silicone coatings and related materials have shown promise in minimizing skin irritation and enhancing the overall biocompatibility of the implants [58]. These innovations address the critical skin-implant interface as well as contribute to improved osseointegration, potentially leading to faster recovery times and favorable long-term implant stability. These materials are also finding specific areas of application, such as silicone being a prevalent type of small joint implant material [59]. Bales et al. specifically found silicone implant arthroplasty at the proximal interphalangeal joint (PIP) joint to be their recommended treatment for symptomatic osteoarthritis of the PIP joint of the hand with long-term survivorship [59]. In association, the use of bioactive coatings, such as those incorporating growth factors or antimicrobial properties, further improves the implant's ability to integrate with bone while deterring bacterial adhesion [60]. Despite these promising advancements, challenges, such as ensuring long-term biocompatibility and stability, remain significant concerns. Additionally, balancing antimicrobial properties with the promotion of osseointegration, along with

cost-effectiveness and integration into current manufacturing processes, presents hurdles for widespread clinical adoption.

CHALLENGES AND LIMITATIONS

The incorporation of dermatologic biomaterials for orthopedic implants is vital, as the interface between surgical implants and tissue presents a complex dynamic [61]. When considering this transition zone between implant material and adjacent tissue, compatibility can be achieved by adopting a protocol for biocompatibility testing. Biomaterials need to meet basic biocompatibility criteria established by the International Standards Organization (ISO), and must be nontoxic, nonthrombogenic, noncarcinogenic, and nonantigenic [62]. The present study will review the use of hydrophilic polymers, Ag nanoparticles, and bioactive glass as biomaterials. Polymers illuminate a promising capacity for biocompatibility, which can be influenced by chemical structure, functional groups, and molecular weight. Specifically, hydrophilic polymers, such as polyethylene glycol, have proven a reduced adhesion rate of Staphylococcus on the surface of polymer coatings, thus demonstrating good bacterial adhesion-resistant properties [63]. A potential threat imposed by orthopedic implants is the risk of microbial infection, thus highlighting antimicrobial technologies that implement Ag nanoparticles (AgNP) to reduce the growth of biofilms on implant surfaces. Qin et al. incorporated antibiofilm of Ag nanoparticles into the titanium surfaces of implants, which inhibits bacterial adhesion and reduces implant-associated periprosthetic infection in vivo [64]. Bioactive glass (BG) is an area of interest that can elicit a beneficial reaction between host tissue and material, serving as a scaffold for osteogenic proliferation and up-regulation of genes that facilitate osteoblast metabolism. BG rapidly attracts the adhesion of calcium ions and carbonate ions to the silica gel, forming a hydroxycarbonate apatite (HCA) layer that mimics endogenous hydroxyapatite matrix, thus fostering osteoblast formation and crystallization of the new bone [65,66]. Once biomaterials have met certain criteria that suffice mechanical stability, longevity, and sterility, can these items be considered for implantation.

Orthopedic implants need to provide support to the host over a prolonged amount of time, thereby demonstrating longevity for chemical composition, tensile strength, and load-bearing capacity. One great drawback to the osseous integration of polymers is the products released secondary to degeneration, thus expediting the deterioration of mechanical function [67]. Chronic degradation of foreign materials not only fails to provide sustainable support but could initiate unfavorable immunological responses, making it difficult for future implants to be tolerated well. Polymers often lack the mechanical integrity to withstand weight and pressure, making them unbearable for load-bearing applications, and more likely to degenerate. Mbanga et al. compared the biodurability of gold, silver, and titanium dioxide nanoparticles obtaining dissolution kinetics of particles in simulated biological fluids and synthetic environmental media. AgNP's had the highest dissolution rate when placed in both alkaline and acidic media, suggesting that these NP's are likely to have short-term health and environmental effects [68]. This study provides valuable information that scrutinizes the chemical resilience of silver nanoparticles, making it a subject for further investigation, since its antimicrobial properties have great potential. In a retrospective study looking at Swanson and Sutter-type implants, the two most common silicone finger implants for MCP joint replacement in patients with RA, they found that Sutter-type implants were much more susceptible to implant fracture than Swanson-type in all four fingers [69]. This sheds light to a paradigm, in that the procedural application of an implant material can threaten longevity, rather than the biomaterial itself.

When implementing new biomaterials, the primary concern must be to improve the quality of life for a patient, demonstrated by effective integration and minimal adverse effects. While polymers demonstrate high biocompatibility and non-toxicity, they offer poor mechanical strength, which can raise subsequent health implications, and healthcare costs [70]. The emergence of 3D printing for polymers and silicone materials demonstrates a new modality that may reduce costs. 3D printing is an adaptive digital system that optimizes cost-effectiveness, as well as environmental sustainability and recycling practices [71]. 3D printing can serve as a modality that precisely designs and personalizes the implant material, thus minimizing secondary costs. Not only has the cost of 3D printing declined over the years, but it also provides manufacturers with freedom in the design process, thereby removing customization costs involved in conventional methods [72]. By directing the osseointegration of materials to 3D printing, production and manufacturer costs could be reduced, resulting in decreased healthcare costs.

To approve new biomaterials, there is extensive preclinical testing that must assess biocompatibility and tissue integration per ISO 10993. Selecting biomaterials that can inhibit biofilm formation by preventing bacterial adhesion to the implant surface is crucial. S. aureus is a virulent pathogen that contributes to antimicrobial resistance on implant surfaces by adapting to harsh environmental conditions [73]. Additionally, antimicrobial resistance and biofilm formation can be attenuated with the innovative research of nanoparticles. Panacek et al. studied the potential underlying mechanisms supporting AgNP antimicrobial resistance, reporting that the bacterial flagellum protein flagellin causes aggregation of silver NP, thereby inhibiting the antibacterial effect against Gram-negative bacteria [74]. Another area of interest, beyond nanoparticles, might be modified polymeric biomaterials with antimicrobial properties that can upregulate humoral responses. A recent study that incorporated the small peptide, Cecropin A, into surgical polypropylene, reported the highest efficiency of anti-bacterial effects against gram-negative bacteria, showing potential in the modification of pre-existing biomaterials [75]. Further studies that incorporate inorganic bioactive layers, such as those done with silver, need to be conducted. Due to the rising prevalence of degenerative joint diseases, the demand for cutting-edge osseointegration compels a collaborative approach that focuses on engineering, microbiology, and kinematics.

CONCLUSION

The integration of dermatologically tested biomaterials into orthopedic implants represents a significant advancement in medical innovation, addressing both osseointegration and skin-implant interface challenges. These biomaterials, including medical-grade silicone, hydrophilic polymers, and antimicrobial coatings, enhance patient outcomes by improving implant stability, minimizing infections, and reducing adverse skin reactions. Advances in bioactive coatings and surface modifications have further strengthened the ability of implants to promote osteoblast adhesion and tissue integration. Innovations such as 3D printing have revolutionized orthopedic implant design by allowing for patient-specific customization, enhancing precision, and optimizing material use. Additionally, interdisciplinary collaboration between orthopedic surgeons, material scientists, and dermatologists has led to improvements in implant biocompatibility, ensuring long-term success and reducing complications such as irritation, hypersensitivity, and microbial colonization. Despite these advancements, further research is necessary to refine biomaterial properties, confirm long-term safety, and develop standardized protocols for clinical applications. By continuing to integrate biomaterial science with surgical advancements, the future of orthopedic implants holds promise for enhanced durability, reduced complications, and improved quality of life for patients.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

REFERENCES

1. Campoccia D, Montanaro L, Arciola CR. (2006). The significance of infection related to orthopedic devices and issues of antibiotic resistance. Biomaterials. 27(11):2331-2339.

2. Schierholz JM, Beuth J. (2001). Implant infections: A haven for opportunistic bacteria. J Hosp Infect. 49(2):87-93.

3. Zhao L, Chu PK, Zhang Y, Wu Z. (2009). Antibacterial coatings on titanium implants. J Biomed Mater Res B Appl Biomater. 91(1):470-480.

4. Mavrogenis AF, Dimitriou R, Parvizi J, Babis GC. (2009). Biology of implant osseointegration. J Musculoskelet Neuronal Interact. 9(2):61-71.

5. Javed F, Ahmed HB, Crespi R, Romanos GE. (2013). Role of primary stability for successful osseointegration of dental implants: Factors of influence and evaluation. Interv Med Appl Sci. 5(4):162-167.

6. Sales A, Singh A, Zehra M, Naim H. (2023). Factors Affecting Osseointegration of Dental Implants: A Review. Journal of International Dental and Medical Research. 16(3), 1272-1279.

7. Vootla N, Reddy K. (2017). Osseointegration-key factors affecting its success-an overview. IOSR Journal of Dental and Medical Sciences. 16(04):62-68.

8. Shukla S, Chug A, Mahesh L, Afrashtehfar KI, Bibra A. (2016). Implant design influencing implant success: A Review. International Journal of Dental Research & Development. 6(4):39-48.

9. Abu Alfaraj T, Al-Madani S, Alqahtani NS, Almohammadi AA, Alqahtani AM, AlQabbani HS, Bajunaid MK, Alharthy BA, Aljalfan N. (2023). Optimizing Osseointegration in Dental Implantology: A Cross-Disciplinary Review of Current and Emerging Strategies. Cureus. 15(10):e47943.

10. Weng D, Hoffmeyer M, Hürzeler MB, Richter EJ. (2003). Osseotite vs. machined surface in poor bone quality. A study in dogs. Clin Oral Implants Res. 14(6):703-708.

11. Parithimarkalaignan S, Padmanabhan TV. (2013). Osseointegration: an update. J Indian Prosthodont Soc. 13(1):2-6.

12. Gibon E, Amanatullah DF, Loi F, Pajarinen J, Nabeshima A, Yao Z, et al. (2017). The biological response to orthopaedic implants for joint replacement: Part I: Metals. J Biomed Mater Res B Appl Biomater. 105(7):2162-2173.

13. Emam SM, Moussa N. (2024). Signaling pathways of dental implants' osseointegration: a narrative review on two of the most relevant; NF-κB and Wnt pathways. BDJ Open. 10(1):29.

14. Gefen A. (2024). The complex interplay between mechanical forces, tissue response and individual susceptibility to pressure ulcers. J Wound Care. 33(9):620-628.

15. Rennie C, Rodriguez M, Futch KN, Krasney LC. (2024). Complications Following Osseointegrated Transfemoral and Transtibial Implants: A Systematic Review. Cureus. 16(3):e57045.

16. Ribeiro M, Monteiro FJ, Ferraz MP. (2012). Infection of orthopedic implants with emphasis on bacterial adhesion process and techniques used in studying bacterial-material interactions. Biomatter. 2(4):176-194.

17. Villegas M, Zhang Y, Badv M, et al. (2022). Enhancing osseointegration and mitigating bacterial biofilms on medical-grade titanium with chitosan-conjugated liquid-infused coatings. Sci Rep. 12:5380.

18. Ricciardi BF, Muthukrishnan G, Masters E, Ninomiya M, Lee CC, Schwarz EM. (2018). Staphylococcus aureus Evasion of Host Immunity in the Setting of Prosthetic Joint Infection: Biofilm and Beyond. Curr Rev Musculoskelet Med. 11(3):389-400.

19. Wawrzynski J, Gil JA, Goodman AD, Waryasz GR. (2017). Hypersensitivity to Orthopedic Implants: A Review of the Literature. Rheumatol Ther. 4(1):45-56.

20. Teo Wendy ZW, Schalock PC. (2016). Hypersensitivity Reactions to Implanted Metal Devices: Facts and Fictions. J Investig Allergol Clin Immunol. 26(5):279-294.

21. Curtis J, Steichen SD. (2020). Silicones. In Biomaterials Science. Royal Society of Chemistry. pp. 109.

22. Zare M, Ghomi ER, Venkatraman PD, Ramakrishna S. (2021). Silicone-based biomaterials for biomedical applications: Antimicrobial strategies and 3D printing technologies. Journal of Applied Polymer Science. 138(38):50969.

23. Li M, Neoh KG, Xu LQ, Wang R, Kang ET, Lau T, Olszyna DP, Chiong E. (2012). Surface modification of silicone for biomedical applications requiring long-term antibacterial, antifouling, and hemocompatible properties. Langmuir. 28(47):16408-16422.

24. Campoli P, Cardoso D, Turchi M, Mota O. (2011). Clinical trial: a randomized study comparing the durability of silicone and latex percutaneous endoscopic gastrostomy tubes. Dig Endosc. 23(2):135-139.

25. Okada T, Ikada Y. (1995). Surface modification of silicone for percutaneous implantation. J Biomater Sci Polym Ed. 7(2):171-180.

26. Fleckman P, Usui M, Zhao G, Underwood R, Maginness M, Marshall A, et al. (2012). Cutaneous and inflammatory response to long-term percutaneous implants of sphere-templated porous/solid poly(HEMA) and silicone in mice. J Biomed Mater Res A. 100(5):1256-1268.

27. Chen S, Li L, Zhao C, Zheng J. (2010). Surface hydration: Principles and applications toward low-fouling/nonfouling biomaterials. Polymer. 51(23):5283.

28. Buxadera-Palomero J, Calvo C, Torrent-Camarero S, Gil FJ, Mas-Moruno C, Canal C, et al. (2017). Biofunctional polyethylene glycol coatings on titanium: An in vitro-based comparison of functionalization methods. Colloids Surf B Biointerfaces. 152:367-375.

29. Harris LG, Tosatti S, Wieland M, Textor M, Richards RG. (2004). Staphylococcus aureus adhesion to titanium oxide surfaces coated with non-functionalized and peptide-functionalized poly(L-lysine)-grafted-poly(ethylene glycol) copolymers. Biomaterials. 25(18):4135-4148.

30. Brennan SA, Ní Fhoghlú C, Devitt BM, O'Mahony FJ, Brabazon D, Walsh A. (2015). Silver nanoparticles and their orthopaedic applications. Bone Joint J. 97-B(5):582-589.

31. Pauksch L, Hartmann S, Rohnke M, Szalay G, Alt V, Schnettler R, et al. (2014). Biocompatibility of silver nanoparticles and silver ions in primary human mesenchymal stem cells and osteoblasts. Acta Biomater. 10(1):439-449.

32. Ege D, Zheng K, Boccaccini AR. (2022). Borate Bioactive Glasses (BBG): Bone Regeneration, Wound Healing Applications, and Future Directions. ACS Appl Bio Mater. 5(8):3608-3622.

33. Naseri S, Griffanti G, Lepry WC, Maisuria VB, Tufenkji N, Nazhat SN. (2022). Silver- doped sol- gel borate glasses: Dose- dependent effect on Pseudomonas aeruginosa biofilms and keratinocyte function. Journal of the American Ceramic Society. 105(3):1711-1722.

34. Zilberman M, Elsner JJ. (2008). Antibiotic-eluting medical devices for various applications. J Control Release. 130(3):202-215.

35. Lee JH, Baik JM, Yu YS, Kim JH, Ahn CB, Son KH, Kim JH, Choi ES, Lee JW. (2020). Development of a heat labile antibiotic eluting 3D printed scaffold for the treatment of osteomyelitis. Sci Rep. 10(1):7554.

36. Sheehy EJ, von Diemling C, Ryan E, Widaa A, O' Donnell P, Ryan A, et al. (2025). Antibiotic-eluting scaffolds with responsive dual-release kinetics facilitate bone healing and eliminate S. aureus infection. Biomaterials. 313:122774.

37. Chug MK, Brisbois EJ. (2022). Recent Developments in Multifunctional Antimicrobial Surfaces and Applications toward Advanced Nitric Oxide-Based Biomaterials. ACS Mater Au. 2(5):525-551.

38. Souza JCM, Sordi MB, Kanazawa M, Ravindran S, Henriques B, Silva FS, et al. (2019). Nano-scale modification of titanium implant surfaces to enhance osseointegration. Acta Biomater. 94:112-131.

39. Chen S, Guo Y, Liu R, Wu S, Fang J, Huang B, et al. (2018). Tuning surface properties of bone biomaterials to manipulate osteoblastic cell adhesion and the signaling pathways for the enhancement of early osseointegration. Colloids Surf B Biointerfaces. 164:58-69.

40. Li Y, Li B, Song Y, Ma A, Li C, Zhang X, et al. (2019). Improved osteoblast adhesion and osseointegration on TiO2 nanotubes surface with hydroxyapatite coating. Dent Mater J. 38(2):278-286.

41. Dobbenga S, Fratila-Apachitei LE, Zadpoor AA. (2016). Nanopattern-induced osteogenic differentiation of stem cells - A systematic review. Acta Biomater. 46:3-14.

42. Meng HW, Chien EY, Chien HH. (2016). Dental implant bioactive surface modifications and their effects on osseointegration: a review. Biomark Res. 4:24.

43. López-Valverde N, Aragoneses J, López-Valverde A, Rodríguez C, Aragoneses J. (2022). Role in the osseointegration of titanium dental implants, of bioactive surfaces based on biomolecules: A systematic review and meta-analysis of in vivo studies. Inplasy protocal. DOI: 10.37766/inplasy2022.6.0076.

44. Zhao Z, Ma S, Wu C, Li X, Ma X, Hu H, et al. (2021). Chimeric Peptides Quickly Modify the Surface of Personalized 3D Printing Titanium Implants to Promote Osseointegration. ACS Appl Mater Interfaces. 13(29):33981-33994.

45. Dong W, Ma W, Zhao S, Wang Y, Yao J, Liu Z, et al. (2021). The surface modification of long carbon fiber reinforced polyether ether ketone with bioactive composite hydrogel for effective osteogenicity. Mater Sci Eng C Mater Biol Appl. 130:112451.

46. Xu X, Li Y, Wang L, Li Y, Pan J, Fu X, et al. (2019). Triple-functional polyetheretherketone surface with enhanced bacteriostasis and anti-inflammatory and osseointegrative properties for implant application. Biomaterials. 212:98-114.

47. Zemelka-Wiacek M. (2022). Metal Allergy: State-of-the-Art Mechanisms, Biomarkers, Hypersensitivity to Implants. J Clin Med. 11(23):6971.

48. Kounis NG, Koniari I. (2018). Hypersensitivity to metallic implants: pathophysiologic and diagnostic considerations. Acta Biomed. 89(3):428-429.

49. Yang KR, Hong MH. (2024). Improved Biocompatibility and Osseointegration of Nanostructured Calcium-Incorporated Titanium Implant Surface Treatment (XPEED®). Materials (Basel). 17(11):2707.

50. Shevtsov M, Gavrilov D, Yudintceva N, Zemtsova E, Arbenin A, Smirnov V, et al. (2021). Protecting the skin-implant interface with transcutaneous silver-coated skin-and-bone-integrated pylon in pig and rabbit dorsum models. J Biomed Mater Res B Appl Biomater. 109(4):584-595.

51. Savvidou OD, Kaspiris A, Trikoupis I, Kakouratos G, Goumenos S, Melissaridou D, et al. (2020). Efficacy of antimicrobial coated orthopaedic implants on the prevention of periprosthetic infections: a systematic review and meta-analysis. J Bone Jt Infect. 5(4):212-222.

52. Kabata T, Maeda T, Kajino Y, Hasegawa K, Inoue D, Yamamoto T, et al. (2015). Iodine-Supported Hip Implants: Short Term Clinical Results. Biomed Res Int. 2015:368124.

53. Sambri A, Zucchini R, Giannini C, Zamparini E, Viale P, Donati DM, et al. (2020). Silver-coated (PorAg®) endoprosthesis can be protective against reinfection in the treatment of tumor prostheses infection. Eur J Orthop Surg Traumatol. 30(8):1345-1353.

54. Overmann AL, Aparicio C, Richards JT, Mutreja I, Fischer NG, Wade SM, et al. (2020). Orthopaedic osseointegration: Implantology and future directions. J Orthop Res. 38(7):1445-1454.

55. Rand JA, Trousdale RT, Ilstrup DM, Harmsen WS. (2003). Factors affecting the durability of primary total knee prostheses. J Bone Joint Surg Am. 85(2):259-265.

56. Delaunay C. (2015). Registries in orthopaedics. Orthop Traumatol Surg Res. 101(1 Suppl):S69-S75.

57. Mathijssen NMC, Verburg H, London NJ, Landsiedl M, Dominkus M. (2019). Patient reported outcomes and implant survivorship after Total knee arthroplasty with the persona knee implant system: two year follow up. BMC Musculoskelet Disord. 20(1):97.

58. Ong KL, Yun BM, White JB. (2015). New biomaterials for orthopedic implants. Orthopedic Research and Reviews. 7:107-130.

59. Bales JG, Wall LB, Stern PJ. (2014). Long-term results of Swanson silicone arthroplasty for proximal interphalangeal joint osteoarthritis. J Hand Surg Am. 39(3):455-461.

60. Zhang BG, Myers DE, Wallace GG, Brandt M, Choong PF. (2014). Bioactive coatings for orthopaedic implants-recent trends in development of implant coatings. Int J Mol Sci. 15(7):11878-11921.

61. Grzeskowiak RM, Schumacher J, Dhar MS, Harper DP, Mulon PY, Anderson DE. (2020). Bone and Cartilage Interfaces With Orthopedic Implants: A Literature Review. Front Surg. 7:601244.

62. US Food and Drug Administration. (2023). FDA's biocompatibility guidance on use of ISO 10993-1. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-international-standard-iso-10993-1-biological-evaluation-medical-devices-part-1-evaluation-and

63. Cui X, Koujima Y, Seto H, Murakami T, Hoshino Y, Miura Y. (2016). Inhibition of Bacterial Adhesion on Hydroxyapatite Model Teeth by Surface Modification with PEGMA-Phosmer Copolymers. ACS Biomater Sci Eng. 2(2):205-212.

64. Qin H, Cao H, Zhao Y, Zhu C, Cheng T, Wang Q, et al. (2014). In vitro and in vivo anti-biofilm effects of silver nanoparticles immobilized on titanium. Biomaterials. 35(33):9114-9125.

65. Mahboubizadeh S, Noroozi P, Ashkani O. (2023). Bioactive glass in medicine: A mini-review of composition, properties, bioactivity mechanisms, and clinical applications. Journal of Environmental Friendly Materials. 7(2):65-70.

66. Chakraborty PK, Adhikari J, Saha P. (2020). Variation of the properties of sol–gel synthesized bioactive glass 45S5 in organic and inorganic acid catalysts. Materials Advances. 2(1):413-425.

67. Silver FH. (1994). Scope and markets for medical implants. In Biomaterials, medical devices, and tissue engineering: An integrated approach. Springer Netherlands. pp. 1-45.

68. Mbanga O, Cukrowska E, Gulumian M. (2023). A Comparative Study of the Biodurability and Persistence of Gold, Silver and Titanium Dioxide Nanoparticles Using the Continuous Flow through System. Nanomaterials (Basel). 13(10):1653.

69. Koenuma N, Ikari K, Oh K, Iwakura N, Okazaki K. (2024). Long-Term Implant Fracture Rates Following Silicone Metacarpophalangeal Joint Arthroplasty in Rheumatoid Arthritis. J Hand Surg Am. 49(5):443-449.

70. Al-Shalawi FD, Mohamed Ariff AH, Jung DW, Mohd Ariffin MKA, Seng Kim CL, Brabazon D, et al. (2023). Biomaterials as Implants in the Orthopedic Field for Regenerative Medicine: Metal versus Synthetic Polymers. Polymers (Basel). 15(12):2601.

71. Yadav D, Garg RK. (2020). 3D printable biomaterials for orthopedic implants: Solution for sustainable and circular economy. Resources Policy. 68:101767.

72. Wu Y, Liu J, Kang L, Tian J, Zhang X, Hu J, et al. (2023). An overview of 3D printed metal implants in orthopedic applications: Present and future perspectives. Heliyon. 9(7):e17718.

73. Lowy FD. (2003). Antimicrobial resistance: the example of Staphylococcus aureus. J Clin Invest. 111(9):1265-1273.

74. Panáček A, Kvítek L, Smékalová M, Večeřová R, Kolář M, Röderová M, et al. (2018). Bacterial resistance to silver nanoparticles and how to overcome it. Nat Nanotechnol. 13(1):65-71.

75. Szałapata K, Pięt M, Kasela M, Grąz M, Kapral-Piotrowska J, Mordzińska-Rak A, et al. (2024). Modified polymeric biomaterials with antimicrobial and immunomodulating properties. Sci Rep. 14(1):8025.