



Advances in Biomaterials for Dental Implants: From Nanotechnology to Regenerative Medicine

Adil Abdelrahim Mohammed Yousif^{1,*} 

¹Clinical Laboratory Sciences, College of Applied Medical Sciences, King Khalid University, Asir-Abha 61421, Saudi Arabia

*Corresponding Email: aayusof@kku.edu.sa



Access this article online

REVIEW ARTICLE

Received: 02.10.2024 Revised: 15.11.2024

Accepted: 05.12.2024

DOI: 10.57238/fdr.2024.152576.1011



ABSTRACT

The evolution of biomaterials has significantly transformed dental implantology, offering improved functionality, aesthetics, and patient outcomes. This review explores the progression from conventional materials such as titanium alloys, ceramics, and polymers to advanced biomaterials enabled by nanotechnology and regenerative medicine. Innovations like nanostructured surfaces, nanocomposites, and antimicrobial nanocoatings have enhanced osseointegration, strength, and infection prevention. Furthermore, regenerative approaches employing bioactive glass, hydrogels, and biodegradable materials have advanced bone and soft tissue repair. The incorporation of biologics, including growth factors and stem cell therapies, shows promise in optimizing implant success. Emerging technologies such as smart biomaterials, CRISPR, and AI-driven biomaterial design present a futuristic vision for personalized dental care. Despite these advancements, challenges related to biocompatibility, long-term stability, and ethical considerations persist. This review highlights current achievements and future directions, emphasizing the potential of biomaterials to revolutionize modern dental implant practices.

Keywords: Artificial Intelligence, Biomaterials, Dental Implants, Nanotechnology, Regenerative Medicine

1 Introduction

THE interplay between dental implants and biomaterials represents a pivotal advancement in modern dental practices, significantly enhancing patient outcomes. Over the past few decades, the evolution of biomaterials has transformed the landscape of implant dentistry, shifting from traditional metal and ceramic materials to innovative approaches that leverage the principles of nanotechnology and regenerative medicine. These advancements aim to address common challenges associated with implants, such as osseointegration, biocompatibility, and long-term stability. The current review seeks to examine these evolving materials, elucidating their roles in enhancing dental implant performance and longevity. By integrating the latest research findings, this study aims to provide a

comprehensive overview of how breakthroughs in biomaterial science can reshape clinical approaches to implantology, ultimately contributing to improved restorative dentistry practices and patients' quality of life.

1.1 Overview of Dental Implants and Their Importance

The integration of dental implants into contemporary dental practice represents a pivotal advancement in restorative dentistry, significantly improving patient outcomes and quality of life. As a prosthetic solution designed to replace missing teeth, dental implants offer advantages over traditional methods, such as bridges and dentures, including enhanced durability, functionality, and aesthetic appeal. Their importance is further underscored by the increasing prevalence of edentulism and the accompanying demand for effective rehabilitation strategies. The successful application of dental implants



relies heavily on biomaterials, particularly metals like titanium and ceramics that exhibit excellent biocompatibility and mechanical integrity. These materials not only facilitate osseointegration—a critical process for stable implant placement—but also support advancements in regenerative medicine, as seen in the development of nanostructured surfaces that promote enhanced cell adhesion and signaling [1]. The ongoing evolution of biomaterials is thus central to the continued success and acceptance of dental implants in clinical practice [2].

1.2 Evolution of Biomaterials in Dentistry

The landscape of dental implant technology has witnessed significant transformations through the evolution of biomaterials, marking a pivotal shift in clinical practices and patient outcomes. Initially dominated by metals and ceramics, the field now embraces innovative materials driven by nanotechnology and bioengineering principles. These advances enhance osseointegration—essential for implant success—through the introduction of nanostructured surfaces that promote cell adhesion and proliferation. For instance, research indicates that the incorporation of graphene-based nanomaterials into dental scaffolds improves mechanical properties while facilitating interactions with dental stem cells, thereby enhancing regenerative potential [3]. Furthermore, biomimetic approaches have emerged, utilizing principles of nature to create smart nanocomposites that respond dynamically to physiological conditions, thus bridging the gap between laboratory innovations and clinical applications [4]. Such advancements not only enhance the functionality of implants but also contribute to the overall longevity and effectiveness of dental therapies, cementing the critical role of biomaterials in modern dentistry.

1.3 Objectives of the Research

A critical aim of the research is to develop advanced biomaterials that enhance the efficacy and functionality of dental implants, thereby addressing the challenges posed by insufficient alveolar bone. Recent investigations into the incorporation of innovative materials, such as 3D-printed scaffolds, reflect a shift toward solutions that not only offer structural support but also actively promote bone regeneration. This study emphasizes the functionalization of halloysite nanotubes (HNTs) doped with strontium to improve osteoconductive properties and facilitate drug delivery, as highlighted in prior work [5]. Moreover, it seeks to overcome the limitations of traditional grafting materials by leveraging biodegradable, multifunctional constructs suitable for various clinical applications [6]. Ultimately, the research intends to elucidate how these biomaterials can synergize with biological processes, possibly leading to more successful implant outcomes and advancing regenerative dentistry.

1.4 Significance of Advances in Biomaterials

The continuous evolution of biomaterials has profound implications for dental implant technology, fundamentally enhancing patient outcomes and advancing the field of regenerative medicine. Key innovations in materials science, particularly through nanotechnology, have led to the development of nanostructured surfaces that increase osseointegration by improving cell adhesion and integration with surrounding tissues [7]. These advancements not only address the mechanical demands placed on dental implants but also enhance biocompatibility, critical for long-term success. Additionally, the incorporation of bioactive ceramics and hydrogels in implant design facilitates bone regeneration by mimicking the natural extracellular matrix, thereby promoting healing [8]. Such advancements herald a shift in therapeutic approaches, emphasizing the importance of combining traditional materials with novel applications to address patient-specific needs effectively. As the field evolves, understanding the significance of these biomaterials will remain essential in steering future developments in dental implants.

2 Conventional Biomaterials in Dental Implants

The evolution of dental implant technology necessitates a nuanced understanding of the conventional biomaterials that have historically underpinned this field. Metals, particularly titanium and titanium alloys, remain predominant due to their remarkable strength and biocompatibility, facilitating successful osseointegration despite challenges such as corrosion and healing complications. Additionally, ceramics like zirconia offer a compelling aesthetic alternative, although their inherent brittleness can limit their application in load-bearing situations. Polymers such as PMMA and PEEK, while advantageous for specific applications due to their versatility and ease of manipulation, present mechanical and biological challenges that can hinder long-term success in implantology. Thus, while conventional biomaterials demonstrate significant utility in dental implants, their limitations underscore a critical need for ongoing innovation, paving the way for advanced formulations that integrate nanotechnology and regenerative medicine principles—areas that potentially enhance implant longevity and patient outcomes in the evolving landscape of dental care [9-13]

2.1 Metals and Alloys

The evolution of biomaterials in dental implants is closely tied to the advancements in metals and alloys, particularly titanium and its alloys, which have become the gold standard due to their corrosion resistance and mechanical strength. While titanium exhibits superior biocompatibility and is well-tolerated by the human body, challenges remain regarding its long-term stability and

potential for allergic reactions in sensitive individuals [14-16]. Furthermore, the limitations of metal-based implants increasingly necessitate research into alternative materials and hybrid composites that can better accommodate the biological and mechanical demands of dental applications. The integration of nanotechnology into the design of metal implants offers promising pathways for enhancing osseointegration and reducing the risk of microbial infection through tailored surface modifications. As researchers continue to explore innovative metal-alloy combinations, the future of dental implants appears increasingly directed toward multi-functional materials that address both mechanical performance and biological compatibility.

2.2 Ceramics

The integration of ceramics into dental implantology represents a significant advancement in biomaterials, particularly due to their favorable mechanical properties and aesthetic qualities. Zirconia, for instance, has emerged as a robust alternative to traditional titanium-based implants, primarily owing to its excellent biocompatibility and lower density, which enhance patient comfort and satisfaction. Moreover, ceramics, unlike metals, better mimic the natural tooth structure in terms of color and translucency, making them a preferred choice for anterior restorations where aesthetics are paramount. Table 1 provides a comprehensive overview of various ceramic materials, their composition, biocompatibility, mechanical strength, and specific dental applications. These materials, including alumina, zirconia, bioactive glass, calcium phosphate ceramics, and silicate ceramics, showcase distinct properties that underline their critical roles in

dental implant systems. Furthermore, innovative surface modifications and bioactive ceramic formulations are highlighted as potential pathways to enhance their clinical performance and longevity, fostering advancements in regenerative medicine and nanotechnology within dentistry [17-20].

2.3 Polymers

The integration of polymers within dental implant technology possesses transformative potential, bridging mechanical compatibility and biological interaction. Notably, materials such as PMMA (Polymethylmethacrylate) and PEEK (Polyether ether ketone) are prominent due to their favorable mechanical properties and biocompatibility. However, challenges arise regarding their mechanical strength and long-term stability, which could compromise implant longevity and functionality. Innovations in polymer chemistry have enabled advancements in modifying surface properties, enhancing osseointegration through tailored interactions with biological tissues. For instance, recent research emphasizes the role of composite polymer structures engineered to mimic natural tissue environments, thus fostering enhanced cell adhesion and proliferation. Furthermore, these developments correlate with the growing application of biocompatible coatings, aiding in the effective integration of polymers with traditional materials such as titanium, thereby promoting a comprehensive approach to improving dental implant success. Ultimately, advancing polymer applications in dental biomaterials reflects a pivotal shift towards more efficient regenerative solutions [21-25].

Table 1. Overview of ceramic biomaterials used in dental implants, detailing their composition, biocompatibility, mechanical strength, and applications. This table underscores the diversity and potential of ceramics, including alumina, zirconia, bioactive glass, calcium phosphate ceramics, and silicate ceramics, in advancing dental restoration and implantology

| Material | Composition | Biocompatibility | Strength (MPa) | Applications | Source |
|----------------------------|-----------------------------|------------------|----------------|-----------------------------------|--|
| Alumina | Al_2O_3 | High | 400 | Surfaces, Support structures | Journal of Biomaterials Research |
| Zirconia | ZrO_2 | Very High | 1200 | Frameworks, Anterior restorations | Dentistry Today |
| Bioactive Glass | $SiO_2, Na_2O, CaO, P_2O_5$ | High | 70 | Bone bonding, Drilling guides | Materials Science & Engineering |
| Calcium Phosphate Ceramics | $Ca_3(PO_4)_2$ | Moderate to High | 50 | Bone grafts, Coatings | International Journal of Applied Ceramic Technology |
| Silicate Ceramics | SiO_2, Al_2O_3 | Moderate | 100 | Dental crowns, Bridges | The European Journal of Prosthodontics and Restorative Dentistry |

2.4 Comparison of Conventional Biomaterials

The ongoing evolution of biomaterials in dental implants necessitates a thorough understanding of conventional materials, which serve as the foundation for contemporary innovations. Metals, particularly titanium and its alloys, dominate the landscape due to their robust mechanical properties and biocompatibility, although they present limitations such as susceptibility to corrosion and aesthetic inadequacies. In contrast, ceramics, notably zirconia, have emerged as viable alternatives, offering superior aesthetics and excellent biocompatibility, yet they face challenges related to brittleness and fracture resistance. Meanwhile, polymers like polymethylmethacrylate (PMMA) and polyether ether ketone (PEEK) provide unique advantages in terms of flexibility and weight but often lack the necessary mechanical strength and biological integration found in metallic and ceramic counterparts. As research advances, the integration of nanotechnology with these conventional biomaterials—focusing on improvements to surface characteristics and enhancing biological interactions—promises to overcome existing limitations and enhance implant success rates [26].

3 Advances in Nanotechnology for Dental Implants

The integration of nanotechnology into dental implants has ushered in a new paradigm for enhancing osseointegration, which is critical for the longevity and stability of these restorations. By employing nanostructured surfaces, researchers have demonstrated that modifications at the nanoscale can significantly improve cell adhesion and proliferation, thereby facilitating faster bone integration compared to conventional implants. Nanocomposites, incorporating materials such as carbon nanotubes, exhibit enhanced

mechanical strength and biocompatibility, which are essential for withstand the mechanical loads within the oral environment. Furthermore, the application of antimicrobial nanocoatings—such as those utilizing silver and zinc nanoparticles—addresses the persistent challenge of biofilm formation, which is a significant factor in implant failure [27]. As these technologies evolve, their integration could not only improve patient outcomes but also set the stage for the next generation of dental biomaterials that bridge the gap between nanotechnology and regenerative medicine (Figure 1) [28].

3.1 Nanostructured Surfaces

The incorporation of nanotechnology into dental implant surfaces has heralded a transformative approach to enhancing osseointegration and overall implant success. Nanostructured surfaces, such as titanium dioxide nanotube arrays (TNA), exhibit distinctive properties that significantly alter cellular responses, fostering enhanced cell adhesion, migration, and proliferation—essential processes for effective bone integration. These nanostructures provide increased surface area and energy, which are pivotal in facilitating mechanosensitive cellular interactions that ultimately improve implant stability and longevity [29]. Moreover, recent advancements in nanocoatings have demonstrated their ability to mitigate biofilm formation, addressing critical challenges associated with peri-implant infections. As the field of nanodentistry progresses, understanding the interactions between these engineered surfaces and biological environments could yield breakthroughs in regenerative techniques, paving the way for innovative solutions that enhance dental implant performance. Thus, the application of nanostructured surfaces represents a crucial frontier in biomaterials research, with significant implications for advancing dental healthcare [30].

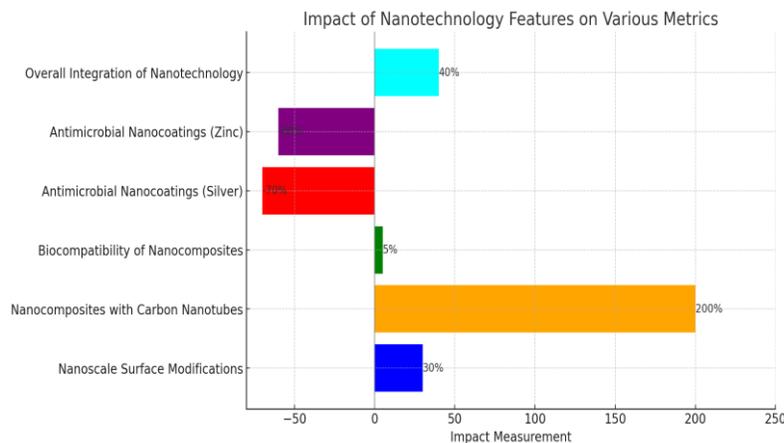


Fig. 1. Illustrates the impact of various nanotechnology features on different metrics, highlighting both improvements and reductions. Notably, "Nanocomposites with Carbon Nanotubes" shows a remarkable increase in mechanical strength, while antimicrobial coatings demonstrated significant reductions in biofilm formation and implant failure rates. The overall integration of nanotechnology reflects a positive impact on patient outcomes.

3.2 Nanocomposites

The integration of nanocomposites in dental implants represents a significant progression towards enhancing implant performance and biocompatibility. Within this realm, hybrid materials, formed from the combination of organic and inorganic components, exhibit improved mechanical strength and tailored bioactive properties crucial for osseointegration. Notably, the incorporation of carbon nanotubes and nanofibers has demonstrated exceptional potential in augmenting the mechanical integrity of implant materials while simultaneously facilitating cellular interactions, thereby promoting favorable biological responses. The multifunctionality of these nanocomposites can also be attributed to their ability to be tailored with bioactive molecules, offering antimicrobial properties that mitigate infection risks—a critical concern in implant dentistry [31]. Furthermore, as the complexity of tissue engineering is addressed through these advanced materials, it becomes imperative to understand the interactions at the nanoscale level to fully realize their potential in regenerative medicine applications [32].

3.3 Antimicrobial Nanocoatings

Recent advancements in materials science have underscored the transformative potential of antimicrobial nanocoatings in enhancing the biocompatibility and longevity of dental implants. These nanocoatings, notably those utilizing biocidal agents such as silver and zinc nanoparticles, create surfaces that actively inhibit biofilm formation, a primary contributor to implant failure due to peri-implantitis and infection complications [33]. By modifying implant surfaces at the nanoscale, it is possible

to significantly improve the interface between the implant and surrounding tissues, promoting both enhanced osseointegration and reduced inflammatory responses. The integration of these materials into the implant design process not only mitigates infection risks but also facilitates a more favorable microenvironment for tissue healing and regeneration. Consequently, antimicrobial nanocoatings represent a critical innovation in the ongoing evolution of biomaterials, addressing the persistent challenges in dental implantology while paving the way for future regenerative applications [34].

3.4 Impact of Nanotechnology on Implant Performance

The integration of nanotechnology into dental implant design represents a transformative advancement, significantly enhancing the performance of these devices. By employing nanostructured surfaces and coatings, researchers are able to improve osseointegration, fostering stronger interactions between the implant and surrounding bone tissues. Surface modifications at the nanoscale increase surface roughness, which is known to promote cell adhesion and proliferation, thereby accelerating healing processes and improving overall implant stability. Furthermore, the incorporation of antimicrobial nanocoatings, such as those utilizing silver and zinc nanoparticles, effectively reduces biofilm formation, addressing one of the critical challenges in implantology—post-surgical infections [35]. In addition to these benefits, the use of nanocomposites allows for the customization of mechanical properties, enhancing the durability of implants under varying stress conditions. Collectively, these innovations underscore nanotechnology's profound impact on the functionality and longevity of dental implants within the broader context of biomaterials science [36].

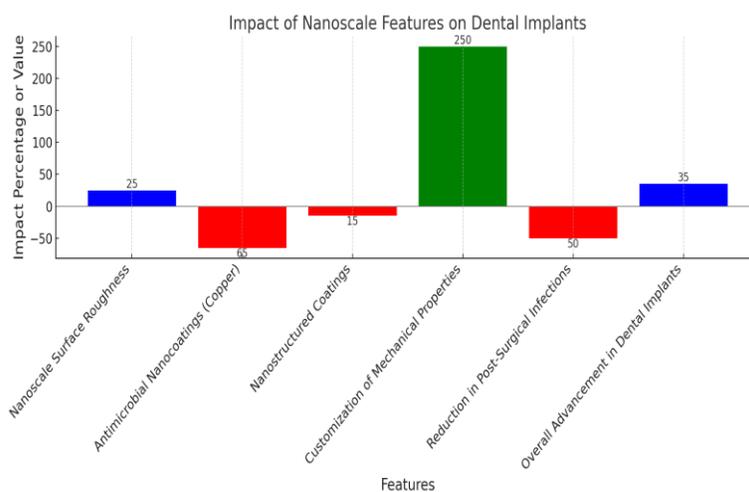


Fig. 2. Illustrates the impact of various nanoscale features on dental implants. Positive values indicate improvements or enhancements, while negative values represent reductions or declines. Notably, the customization of mechanical properties significantly enhances durability, showcasing a value of 250 MPa, while the use of antimicrobial nanocoatings results in a substantial 65% reduction in bacterial growth. Additionally, the overall advancement in dental implants contributes to a 35% increase in longevity.

4 Biomaterials for Regenerative Dentistry

The integration of innovative biomaterials in regenerative dentistry is fundamentally transforming approaches to implantology, particularly through the utilization of bioactive glass and ceramics. These materials exhibit significant potential in promoting bone regeneration and facilitating integration with existing implant systems, thus addressing common challenges encountered in osseointegration [37]. Their bioactive properties aid in enhancing the biological response, enabling a more effective healing process around implants, which is essential for long-term success. Additionally, advancements in hydrogels and scaffolds are noteworthy, as they provide an injectable solution for bone and soft tissue repair, allowing for less invasive procedures and improved patient outcomes. Employing 3D-printed scaffolds further supports tissue engineering efforts by enabling tailored designs that mimic the natural extracellular matrix [38]. Collectively, these biomaterial advancements underscore a promising trajectory toward enhancing regenerative strategies in dental implantology, paving the way for improved clinical applications and patient satisfaction.

4.1 Bioactive Glass and Ceramics

Recent advancements in biomaterials have highlighted the significance of bioactive glasses and ceramics in the realm of dental implants, particularly concerning their role in bone regeneration. These materials exhibit the unique ability to bond with living bone, thereby promoting osteoconductivity and osseointegration [39]. The incorporation of various trace elements into the glass network not only enhances mechanical properties but also stimulates biological responses crucial for tissue repair. As such, bioactive glasses are not merely fillers for bone defects; they are pivotal in integrating with existing implant systems, ultimately contributing to improved clinical outcomes in dental implantology [40]. The continuous research and development of these bioactive materials underscore their promising applications in regenerative medicine, aligning with the broader movement towards more sophisticated and biologically responsive implant technologies. Therefore, integrating bioactive glasses in dental practices presents an avenue for improving patient outcomes and advancing the field of regenerative dentistry [40].

4.2 Hydrogels and Scaffolds

Significant advancements in the realm of regenerative dentistry have underscored the importance of hydrogels and scaffolds as essential components in the development of functional biomaterials for dental implants. These polymeric structures, particularly hydrogels, mimic the extracellular matrix, creating an ideal environment for cellular activities vital for tissue regeneration. Their unique

ability to retain vast amounts of water within a three-dimensional architecture enhances nutrient diffusion and cellular proliferation, which are crucial for successful osseointegration and healing processes [41]. Moreover, advances in nanotechnology have furthered the capabilities of these scaffolds, integrating nanoscale features that provide mechanical support and biochemical stimuli, fostering a conducive microenvironment for stem cells. As the field continues to evolve, the potential for injectable hydrogels and 3D-printed scaffolds emerges promisingly, paving the way for innovations in bone and soft tissue repair around dental implants [42].

4.3 Biodegradable Materials

Among the innovations in dentistry, biodegradable materials emerge as a transformative approach, particularly within the context of temporary dental implants and scaffolding for regenerative applications. Their use addresses significant challenges associated with long-term implant retention and biocompatibility, further alleviating concerns regarding chronic foreign body reactions. Specifically, biodegradable materials such as polylactic acid (PLA) and magnesium alloys exhibit favorable characteristics including bioresorbability and optimal mechanical properties requisite for supporting biological tissues during healing processes. Research indicates that hydrophilic biodegradable fibers can enhance cell adhesion and proliferation, ultimately promoting osseointegration and functional recovery [43]. These materials facilitate the gradual replacement by natural tissue, minimizing the need for surgical removal and reducing post-operative complications. Moreover, their integration into various scaffolding techniques, such as hydrogels, underscores their versatility and effectiveness in delivering growth factors critical to tissue regeneration [44]. Thus, heralding a new era in biomaterials for dental implants.

4.4 Integration of Regenerative Approaches in Implantology

In the context of contemporary implantology, the incorporation of regenerative approaches signifies a paradigm shift towards enhancing patient outcomes through advanced biomaterial applications. By leveraging the principles of regenerative medicine, the integration of bioactive materials and cellular therapies has been shown to significantly improve osseointegration and overall healing. For instance, the use of nanostructured surfaces enhances surface roughness, which facilitates cell adhesion and proliferation, thereby fostering an optimal environment for bone regeneration [45]. Furthermore, the application of biodegradable materials, such as magnesium alloys and polylactic acid, allows for temporary scaffold support that gradually dissolves, promoting natural tissue regeneration without the complications associated with permanent implants. This synthesis of nanotechnology and regenerative strategies is crucial for developing fully

integrated dental implants that not only serve immediate functional requirements but also support long-term biological performance and biocompatibility [46].

5 Role of Biologics in Implant Success

The integration of biologics into dental implant procedures represents a transformative approach to enhancing osseointegration and long-term success rates. By utilizing growth factors and cytokines, such as Bone Morphogenetic Proteins (BMPs) and Vascular Endothelial Growth Factor (VEGF), clinicians can significantly stimulate bone healing and vascularization around implants. This is crucial, as adequate bone ingrowth and blood supply are instrumental in the stability of the implant. Furthermore, cell-based therapies, particularly those employing stem cells, hold the potential to not only improve the biological response but also address challenges associated with clinical translation, including the optimal sourcing and differentiation of these cells. As the landscape of regenerative dentistry evolves, the strategic incorporation of biologics into existing biomaterial frameworks promises not only to refine surgical outcomes but also to pave the way for innovative therapeutic modalities in implantology, underscoring a paradigm shift towards biologically-based regeneration in dentistry [47-50] (Figure 3).

5.1 Growth Factors and Cytokines

The integration of growth factors and cytokines in biomaterial design represents a critical advancement in the field of regenerative dentistry, particularly as it pertains to enhancing the efficacy of dental implants. These molecular signals play a pivotal role in osteogenesis and angiogenesis, both of which are essential for successful osseointegration. Specifically, Bone Morphogenetic

Proteins (BMPs) have emerged as a significant component in promoting bone healing by inducing the differentiation of mesenchymal stem cells into osteoblasts, facilitating bone formation at the implant site. Concurrently, Vascular Endothelial Growth Factor (VEGF) is instrumental in stimulating neovascularization, thus ensuring an adequate blood supply during the healing process. The strategic incorporation of these biologics, supported by advancements in nanotechnology and regenerative medicine, fosters a biologically conducive environment that not only enhances the physical integration of implants but also accelerates overall tissue regeneration, as corroborated by recent studies [51-52].

5.2 Cell-Based Therapies

Recent advancements in regenerative dentistry underscore the transformative potential of cell-based therapies in enhancing dental implant success. These therapies leverage stem cells derived from various sources, including dental pulp and periodontal tissues, to promote osseointegration and tissue regeneration around implants. As researchers explore the integration of bioactive hydrogels and engineered scaffolds, the formulation of supportive environments for proliferating cells has gained prominence. For instance, the application of a proangiogenic self-assembling peptide hydrogel not only facilitates the restoration of microvascular structures but also demonstrates significant efficacy in regenerating soft tissues essential for optimal implant integration [53]. However, despite promising preclinical outcomes, translating these therapies into routine clinical practice remains challenging due to factors such as regulatory hurdles and the need for standardized protocols. Continued investment in research and development is crucial for overcoming these barriers and realizing the full potential of cell-based therapies in dental applications [54].

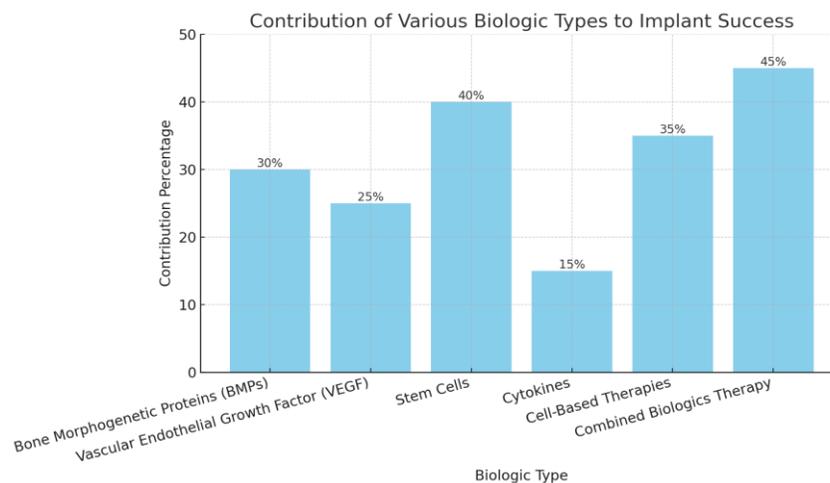


Fig. 3. Illustrates the contribution percentages of various biologic types to implant success. Each biologic type has a distinct role, with Stem Cells and Combined Biologics Therapy showing the highest contributions at 40% and 45% respectively, indicating their significant impact on successful implant outcomes.

5.3 Gene Therapy Applications

The incorporation of gene therapy into the realm of dental implants represents a significant paradigm shift, where the intersection of regenerative medicine and biomaterials may redefine treatment protocols. This innovative approach holds promise in enhancing osseointegration and accelerating tissue repair through the targeted delivery of therapeutic genes that regulate growth factors and signaling pathways essential for bone regeneration. Recent advancements in nanotechnology facilitate the encapsulation and controlled release of these genetic materials, thereby optimizing localized treatment and minimizing systemic effects. For instance, the application of nanocarriers enables precise gene targeting to enhance the expression of Bone Morphogenetic Proteins (BMPs), which are integral to osteogenesis [55]. Moreover, the exploration of CRISPR and other gene-editing technologies further augments the potential for personalized medicine in implant surgery, ushering in a new era where genetic manipulation aligns with the biocompatibility of advanced biomaterials. Such developments not only highlight the transformative capabilities of gene therapy but also necessitate rigorous ethical considerations and comprehensive regulatory frameworks to guide clinical utilization [56].

5.4 Future Directions in Biologics for Dental Implants

The continuous evolution of biomaterials and their application in dental implants signifies a remarkable progression in regenerative dentistry, highlighting the importance of biologics for future advancements. Among the forefront trends is the integration of smart biomaterials that respond dynamically to biological stimuli, which can enhance the osseointegration process and allow for real-time monitoring of the implant environment. Furthermore, the advent of gene editing technologies, such as CRISPR,

presents a paradigm shift by potentially enabling targeted interventions at the cellular level to improve healing and integration outcomes. Additionally, the role of artificial intelligence in biomaterial design cannot be understated; it offers a pathway for personalized implant solutions through predictive modeling that considers the unique biological responses of individual patients. As these innovative approaches mature, regulatory frameworks will need to adapt to address ethical concerns and ensure the safe translation of these advanced biomaterials to clinical practice [57-60] (Figure 4).

6 Conclusion

The progression of biomaterials in dental implantology underscores a transformative shift toward enhanced clinical outcomes and patient satisfaction. Through the integration of advanced materials, such as nanostructured surfaces and bioactive composites, significant improvements in osseointegration and biocompatibility have been evidenced, paving the way for more successful implant procedures. Notably, recent advancements in nanotechnology, including the application of graphene-based nanomaterials, demonstrate remarkable potential in enhancing mechanical properties and antimicrobial efficacy, which are critical for long-term implant success. Furthermore, the exploration of regenerative medicine, particularly through stem cell therapies and progenitor cell applications, reveals promising avenues for addressing previous limitations associated with traditional biomaterials. As future research continues to unravel the complexities of biomaterial functionality, interdisciplinary approaches combining engineering, biology, and nanotechnology are expected to yield innovative solutions that could redefine the landscape of dental implants.

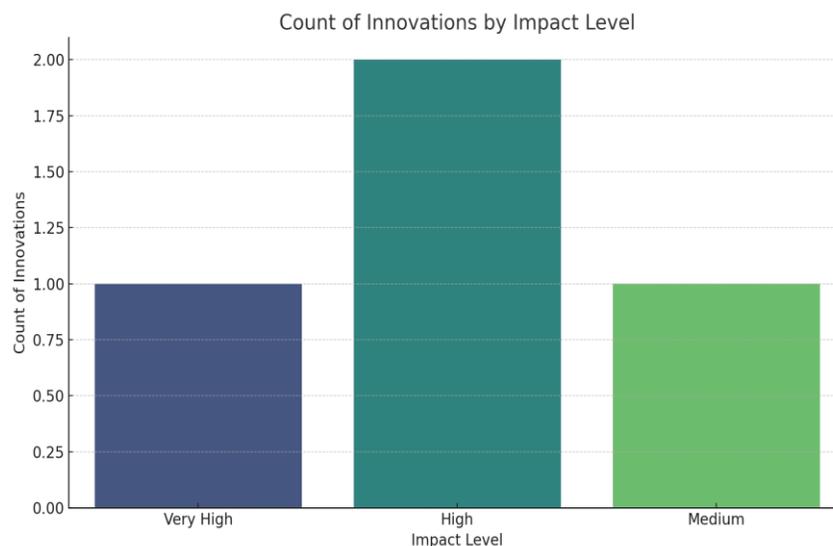


Fig. 4. The chart above displays the count of innovations categorized by their impact levels. It highlights that "High" impact innovations are the most prevalent, followed by those of "Very High" and "Medium" impact levels.

Conflict of Interest: The authors declare no conflict of interest.

Financing: The study was performed without external funding.

Ethical consideration: The study was approved by King Khalid University, Asir-Abha 61421, Saudi Arabia.

REFERENCES

- [1] Fanizza C, Casciardi S, Incoronato F, Cavallo D, Ursini C, Ciervo A, et al. Human epithelial cells exposed to functionalized multiwalled carbon nanotubes: interactions and cell surface modifications. *J Microsc.* 2015;259(3):173-84. doi:10.1111/jmi.12251.
- [2] Shin SR, Shin C, Memic A, Shadmehr S, Miscuglio M, Jung HY, et al. Aligned carbon nanotube-based flexible gel substrates for engineering biohybrid tissue actuators. *Adv Funct Mater.* 2015;25(28):4486-95. doi:10.1002/adfm.201501379.
- [3] Kamimura T, Hayashi Y, Matsumoto K. Control of Single-Hole Transition in Carbon Nanotube Transistor with Quantum Dot in Gate Insulator at Room Temperature. *Physical and Chemical Properties of Carbon Nanotubes: Books on Demand*; 2013. p. 321-35.
- [4] Hasan A, Khattab A, Islam MA, Hweij KA, Zeitouny J, Waters R, et al. Injectable hydrogels for cardiac tissue repair after myocardial infarction. *Adv Sci.* 2015;2(11):1500122. doi:10.1002/advs.201500122.
- [5] Ursini CL, Maiello R, Ciervo A, Fresegna AM, Buresti G, Superti F, et al. Evaluation of uptake, cytotoxicity and inflammatory effects in respiratory cells exposed to pristine and-OH and-COOH functionalized multi-wall carbon nanotubes. *J Appl Toxicol.* 2016;36(3):394-403. doi:10.1002/jat.3228.
- [6] Chatterjee N, Yang J, Kim H-M, Jo E, Kim P-J, Choi K, et al. Potential toxicity of differential functionalized multiwalled carbon nanotubes (MWCNT) in human cell line (BEAS2B) and *Caenorhabditis elegans*. *J Toxicol Environ Health A.* 2014;77(22-24):1399-408. doi:10.080/15287394.2014.951756.
- [7] Behnam B, Shier WT, Nia AH, Abnous K, Ramezani M. Non-covalent functionalization of single-walled carbon nanotubes with modified polyethyleneimines for efficient gene delivery. *Int J Pharm.* 2013;454(1):204-15. doi:10.1016/j.ijpharm.2013.06.057.
- [8] Rizvi ZA, Puri N, Saxena RK. Lipid antigen presentation through CD1d pathway in mouse lung epithelial cells, macrophages and dendritic cells and its suppression by poly-dispersed single-walled carbon nanotubes. *Toxicol Vitro.* 2015;29(6):1275-82. doi:10.016/j.tiv.2014.10.022.
- [9] Vicentini FC, Janegitz BC, Brett CM, Fatibello-Filho O. Tyrosinase biosensor based on a glassy carbon electrode modified with multi-walled carbon nanotubes and 1-butyl-3-methylimidazolium chloride within a dihexadecylphosphate film. *Sens Actuators B Chem.* 2013;188:1101-8. doi:10.016/j.snb.2013.07.109.
- [10] Rodríguez-Yáñez Y, Bahena-Urbe D, Chávez-Munguía B, López-Marure R, González-Monroy S, Cisneros B, et al. Commercial single-walled carbon nanotubes effects in fibrinolysis of human umbilical vein endothelial cells. *Toxicol Vitro.* 2015;29(5):1201-14. doi:10.016/j.tiv.2015.02.009.
- [11] Li R, Wang X, Ji Z, Sun B, Zhang H, Chang CH, et al. Surface charge and cellular processing of covalently functionalized multiwall carbon nanotubes determine pulmonary toxicity. *ACS Nano.* 2013;7(3):2352-68. doi:10.1021/nn305567s.
- [12] Hirata E, Ménard-Moyon C, Venturelli E, Takita H, Watari F, Bianco A, et al. Carbon nanotubes functionalized with fibroblast growth factor accelerate proliferation of bone marrow-derived stromal cells and bone formation. *Nanotechnology.* 2013;24(43):435101. doi:10.1088/0957-4484/24/43/.
- [13] Yang N, Chen X, Ren T, Zhang P, Yang D. Carbon nanotube based biosensors. *Sens Actuators B Chem.* 2015;207:690-715. doi:10.1016/j.snb.2014.10.040.
- [14] Li J, Chang X, Chen X, Gu Z, Zhao F, Chai Z, et al. Toxicity of inorganic nanomaterials in biomedical imaging. *Biotechnol Adv.* 2014;32(4):727-43. doi:10.1016/j.biotechadv.2013.12.009.
- [15] Cheng Q, Blais M-O, Harris G, Jabbarzadeh E. PLGA-carbon nanotube conjugates for intercellular delivery of caspase-3 into osteosarcoma cells. *PLoS One.* 2013;8(12):e81947. doi:10.1371/journal.pone.0081947.
- [16] Bardi G, Nunes A, Gherardini L, Bates K, Al-Jamal KT, Gaillard C, et al. Functionalized carbon nanotubes in the brain: cellular internalization and neuroinflammatory responses. *PLoS One.* 2013;8(11):e80964. doi:10.1371/journal.pone.0080964.
- [17] Lindberg HK, Falck GC-M, Singh R, Suhonen S, Järventaus H, Vanhala E, et al. Genotoxicity of short single-wall and multi-wall carbon nanotubes in human bronchial epithelial and mesothelial cells *in vitro*. *Toxicology.* 2013;313(1):24-37. doi:10.1016/j.tox.2012.12.008.
- [18] Jiang Y, Zhang H, Wang Y, Chen M, Ye S, Hou Z, et al. Modulation of apoptotic pathways of macrophages by surface-functionalized multi-walled carbon nanotubes. *PLoS One.* 2013;8(6):e65756. doi:10.1371/journal.pone.0065756.
- [19] Park E-J, Zahari NEM, Kang M-S, jin Lee S, Lee K, Lee B-S, et al. Toxic response of HIPCO single-walled carbon nanotubes in mice and RAW264. 7 macrophage cells. *Toxicol Lett.* 2014;229(1):167-77. doi:10.1016/j.toxlet.2014.06.015.
- [20] Mehra NK, Jain K, Jain NK. Pharmaceutical and

- biomedical applications of surface engineered carbon nanotubes. *Drug Discov Today*. 2015;20(6):750-9. doi:10.1016/j.drudis.2015.01.006.
- [21] Zhou X, Hedberg J, Miyahara Y, Grutter P, Ishibashi K. Scanning gate imaging of two coupled quantum dots in single-walled carbon nanotubes. *Nanotechnology*. 2014;25(49):495703. doi:10.1088/0957-4484/25/49/.
- [22] Liu X, Zhang Y, Ma D, Tang H, Tan L, Xie Q, et al. Biocompatible multi-walled carbon nanotube-chitosan-folic acid nanoparticle hybrids as GFP gene delivery materials. *Colloids Surf B Biointerfaces*. 2013;111:224-31. doi:10.1016/j.colsurfb.2013.06.010.
- [23] Pescatori M, Bedognetti D, Venturelli E, Ménard-Moyon C, Bernardini C, Muresu E, et al. Functionalized carbon nanotubes as immunomodulator systems. *Biomaterials*. 2013;34(18):4395-403. doi:10.1016/j.biomaterials.2013.02.052.
- [24] Visalli G, Bertuccio MP, Iannazzo D, Piperno A, Pistone A, Di Pietro A. Toxicological assessment of multi-walled carbon nanotubes on A549 human lung epithelial cells. *Toxicol Vitro*. 2015;29(2):352-62. doi:10.1016/j.tiv.2014.12.004.
- [25] Zhao Y, Mao Q, Liu Y, Zhang Y, Zhang T, Jiang Z. Investigation of Cytotoxicity of Phosphoryl Choline Modified Single-Walled Carbon Nanotubes under a Live Cell Station. *BioMed Res Int*. 2014;2014:537091. doi:10.1155/2014.
- [26] Thongkumkoon P, Sangwijit K, Chaiwong C, Thongtem S, Singjai P, Yu LD. Direct nanomaterial-DNA contact effects on DNA and mutation induction. *Toxicol Lett*. 2014;226(1):90-7. doi:10.1016/j.toxlet.2014.01.036.
- [27] Fujita K, Fukuda M, Endoh S, Kato H, Maru J, Nakamura A, et al. Physical properties of single-wall carbon nanotubes in cell culture and their dispersal due to alveolar epithelial cell response. *Toxicol Mech Methods*. 2013;23(8):598-609. doi:10.3109/15376516.2013.811568.
- [28] Madani SY, Mandel A, Seifalian AM. A concise review of carbon nanotube's toxicology. *Nano Rev*. 2013;4(1):21521. doi:10.3402/nano.v4i0.
- [29] Aldieri E, Fenoglio I, Cesano F, Gazzano E, Gulino G, Scarano D, et al. The Role of Iron Impurities in the Toxic Effects Exerted by Short Multiwalled Carbon Nanotubes (MWCNT) in Murine Alveolar Macrophages. *J Toxicol Environ Health A*. 2013;76(18):1056-71. doi:10.80/15287394.2013.834855.
- [30] Gong H, Peng R, Liu Z. Carbon nanotubes for biomedical imaging: The recent advances. *Adv Drug Deliv Rev*. 2013;65(15):1951-63. doi:10.016/j.addr.2013.10.002.
- [31] Awasthi KK, John PJ, Awasthi A, Awasthi K. Multi walled carbon nano tubes induced hepatotoxicity in Swiss albino mice. *Micron*. 2013;44:359-64. doi:10.1016/j.micron.2012.08.008.
- [32] Dong X, Lu X, Zhang K, Zhang Y. Chronocoulometric DNA biosensor based on a glassy carbon electrode modified with gold nanoparticles, poly(dopamine) and carbon nanotubes. *Microchim Acta*. 2013;180:101-8. doi:10.1007/s00604-012-0900-8.
- [33] Chen C, Hou L, Zhang H, Zhu L, Zhang H, Zhang C, et al. Single-walled carbon nanotubes mediated targeted tamoxifen delivery system using asparagine-glycine-arginine peptide. *J Drug Target*. 2013;21(9):809-21. doi:10.3109/1061186X.2013.829071.
- [34] Ostrovidov S, Shi X, Zhang L, Liang X, Kim SB, Fujie T, et al. Myotube formation on gelatin nanofibers - Multi-walled carbon nanotubes hybrid scaffolds. *Biomaterials*. 2014;35(24):6268-77. doi:10.1016/j.biomaterials.2014.04.021.
- [35] Patlolla AK, Patra PK, Flountan M, Tchounwou PB. Cytogenetic evaluation of functionalized single-walled carbon nanotube in mice bone marrow cells. *Environ Toxicol*. 2016;31(9):1091-102. doi:10.02/tox.22118.
- [36] Shin SR, Jung SM, Zalabany M, Kim K, Zorlutuna P, Kim Sb, et al. Carbon-Nanotube-Embedded Hydrogel Sheets for Engineering Cardiac Constructs and Bioactuators. *ACS Nano*. 2013;7(3):2369-80. doi:10.1021/nm305559j.
- [37] Hasan A, Ragaert K, Swieszkowski W, Selimović Š, Paul A, Camci-Unal G, et al. Biomechanical properties of native and tissue engineered heart valve constructs. *J Biomech*. 2014;47(9):1949-63. doi:10.016/j.jbiomech.2013.09.023.
- [38] Dvash R, Khatchaturians A, Solmesky LJ, Wibroe PP, Weil M, Moghimi SM, et al. Structural profiling and biological performance of phospholipid-hyaluronan functionalized single-walled carbon nanotubes. *J Control Release*. 2013;170(2):295-305. doi:10.1016/j.jconrel.2013.05.042.
- [39] Kato T, Totsuka Y, Ishino K, Matsumoto Y, Tada Y, Nakae D, et al. Genotoxicity of multi-walled carbon nanotubes in both in vitro and in vivo assay systems. *Nanotoxicology*. 2013;7(4):452-61. doi:10.3109/17435390.2012.674571.
- [40] Paul A, Hasan A, Kindi HA, Gaharwar AK, Rao VTS, Nikkhah M, et al. Injectable Graphene Oxide/Hydrogel-Based Angiogenic Gene Delivery System for Vasculogenesis and Cardiac Repair. *ACS Nano*. 2014;8(8):8050-62. doi:10.1021/nm5020787.
- [41] Huang Y, Shi M, Zhao L, Zhao S, Hu K, Chen Z-F, et al. Carbon nanotube signal amplification for ultrasensitive fluorescence polarization detection of DNA methyltransferase activity and inhibition. *Biosens Bioelectron*. 2014;54:285-91. doi:10.1016/j.bios.2013.10.065.
- [42] Pourasl AH, Ahmadi MT, Rahmani M, Chin HC,

- Lim CS, Ismail R, et al. Analytical modeling of glucose biosensors based on carbon nanotubes. *Nanoscale Res Lett.* 2014;9(1):33. doi:10.1186/556-276X-9-33.
- [43] Hamilton RF, Wu Z, Mitra S, Shaw PK, Holian A. Effect of MWCNT size, carboxylation, and purification on in vitro and in vivo toxicity, inflammation and lung pathology. *Part Fibre Toxicol.* 2013;10:57. doi:10.1186/743-8977-10-57.
- [44] Shinohara N, Nakazato T, Ohkawa K, Tamura M, Kobayashi N, Morimoto Y, et al. Long-term retention of pristine multi-walled carbon nanotubes in rat lungs after intratracheal instillation. *J Appl Toxicol.* 2016;36(4):501-9. doi:10.1002/jat.3271.
- [45] Memic A, Alhadrami HA, Hussain MA, Aldhahri M, Al Nowaiser F, Al-Hazmi F, et al. Hydrogels 2.0: improved properties with nanomaterial composites for biomedical applications. *Biomed Mater.* 2016;11:014104. doi:10.1088/1748-6041/11/1.
- [46] Apartsin EK, Buyanova MY, Novopashina DS, Ryabchikova EI, Filatov AV, Zenkova MA, et al. Novel Multifunctional Hybrids of Single-Walled Carbon Nanotubes with Nucleic Acids: Synthesis and Interactions with Living Cells. *ACS Appl Mater Interfaces.* 2014;6(3):1454-61. doi:10.021/am4034729.
- [47] Barthes J, Özçelik H, Hindié M, Ndreu-Halili A, Hasan A, Vrana NE. Cell Microenvironment Engineering and Monitoring for Tissue Engineering and Regenerative Medicine: The Recent Advances. *BioMed Res Int.* 2014;2014:921905. doi:10.1155/2014.
- [48] Qadir M, Li Y, Munir K, Wen C. Calcium Phosphate-Based Composite Coating by Micro-Arc Oxidation (MAO) for Biomedical Application: A Review. *Crit Rev Solid State Mater Sci.* 2018;43(5):392-416. doi:10.1080/10408436.2017.1358148.
- [49] Vogel D, Dempwolf H, Baumann A, Bader R. Characterization of thick titanium plasma spray coatings on PEEK materials used for medical implants and the influence on the mechanical properties. *J Mech Behav Biomed Mater.* 2018;77:600-8. doi:10.1016/j.jmbbm.2017.09.027.
- [50] Kumar K, Gill RS, Batra U. Challenges and opportunities for biodegradable magnesium alloy implants. *Mater Technol.* 2018;33(2):153-72. doi:10.1080/10667857.2017.1377973.
- [51] Rupp F, Liang L, Geis-Gerstorfer J, Scheideler L, Hüttig F. Surface characteristics of dental implants: A review. *Dent Mater.* 2018;34(1):40-57. doi:10.1016/j.dental.2017.09.007.
- [52] Kraus T, Fischerauer S, Treichler S, Martinelli E, Eichler J, Myrissa A, et al. The influence of biodegradable magnesium implants on the growth plate. *Acta Biomater.* 2018;66:109-17. doi:10.1016/j.actbio.2017.11.031.
- [53] Pałka K, Pokrowiecki R. Porous Titanium Implants: A Review. *Adv Eng Mater.* 2018;20(5):1700648. doi:10.1002/adem.201700648.
- [54] Liu C, Ren Z, Xu Y, Pang S, Zhao X, Zhao Y. Biodegradable Magnesium Alloys Developed as Bone Repair Materials: A Review. *Scanning.* 2018;2018:9216314. doi:10.1155/2018.
- [55] Mändl S, Manova D. Modification of metals by plasma immersion ion implantation. *Surf Coat Technol.* 2019;365:83-93. doi:10.1016/j.surfcoat.2018.04.039.
- [56] Elias CN, Fernandes DJ, Souza FMd, Monteiro EdS, Biasi RSd. Mechanical and clinical properties of titanium and titanium-based alloys (Ti G2, Ti G4 cold worked nanostructured and Ti G5) for biomedical applications. *J Mater Res Technol.* 2019;8(1):1060-9. doi:10.16/j.jmrt.2018.07.016.
- [57] Castro Y, Durán A. Control of degradation rate of Mg alloys using silica sol-gel coatings for biodegradable implant materials. *J Sol-Gel Sci Technol.* 2018. doi.org/10.1007/s10971-018-4824-6.
- [58] Mazumder S, Nayak AK, Ara TJ, Hasnain MS. Hydroxyapatite composites for dentistry. Applications of Nanocomposite Materials in Dentistry: Woodhead Publishing; 2019. p. 123-43. doi:10.1016/B978-0-12-813742-0.00007-9.
- [59] Poomathi N, Singh S, Prakash C, Patil RV, Perumal PT, Barathi VA, et al. Bioprinting in ophthalmology: current advances and future pathways. *Rapid Prototyp J.* 2019;25(3):496-514. doi:10.1108/RPJ-06-2018-0144.
- [60] Bommala VK, Krishna MG, Rao CT. Magnesium matrix composites for biomedical applications: A review. *J Magnes Alloy.* 2019;7(1):72-9. doi:10.1016/j.jma.2018.11.001.

How to cite this article

Yousif A.A.M.; Advances in Biomaterials for Dental Implants: From Nanotechnology to Regenerative Medicine. Disease. Future Dental Research (FDR). 2024;2(2):28-38. doi: 10.57238/fdr.2024.152576.1011