Functionally Graded Materials for Biomedical Applications: A Review

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Abstract

Functionally graded materials have emerged as a new horizon in the field of biomaterial research for their capability to offer customized structural as well as biological properties by the continuous variation in their composition and microstructure. The latest developments in the designing, processing, analysis, and application of FGMs for a range of bioapplications have been reviewed critically. A range of topics concerning the optimization of functionality for FGMs has been reviewed in the context of the growing need for the adoption of interdisciplinary research strategies that effectively combine the efficiency of simulation strategies along with the strength of experimentally driven research. Apart from highlighting the need to tackle challenges in the long-term biocorrosivity of FGMs for reaching the regulatory necessities in their application in the healthcare industry, the range of applications that have been reviewed in the article includes the analysis of FGMs in the form of a scaffold for a range of bioapplications, drug delivery carriers, and more.

Keywords: Functionally Graded Materials (FGMs), Biomedical Applications, Additive Manufacturing, Biocompatibility, Osseointegration, Smart Biomaterials

1. Introduction

The needs of modern medicine have become complex to the point where new approaches have to be developed. This includes material sciences together with bioceramics. The challenges in research for the new generation of bioceramics include challenges in the field of material sciences. The challenges in research for the new generation of bioceramics include challenges in the application of material sciences to medicine. Tissue engineering, implanted devices, and drug delivery systems have become challenges for the research community in material sciences. These challenges have resulted in the need for the development of functional graded materials (FGMs). These have the benefit of optimized performance via properties dissimilar in space. The uniqueness of FGMs resides in the gradual change of the material structure and composition, thus improving functionality and biocompatibility [1]. They have strengths, elasticity, biodegradability, and other property-tailoring characteristics, which match tissue requirements, and they are useful in orthopedic implants, cardiovascular devices, etc. [2]. Recent studies of FGM have demonstrated that they are capable of stress reduction at material interfaces such that the life and performance of implants could be extended [3]. Much of the literature is dedicated to the design and manufacturing of FGM, biocompatibility and biomechanical functioning [4]. It has been found out that polymers, ceramics, and metals combine in graded proportions to remarkably enhance their mechanical and biological properties [5]. With current advancements in the additive manufacturing, complex shapes and gradients can now be formed, forming custom solutions that recapitulate the hierarchies of natural tissues [6]. Nevertheless, even in the situation of advancement, we should still learn more about the behavior of FGMs in the long-term physiological conditions since most studies are related to short-term effects [7]. There are also difficulties with translating the laboratory findings into clinical practice, including regulatory approval and in vivo testing [8]. Biomechanical and surface characteristics of FGMs are also a theme and studies have demonstrated the influence of microstructure on biological responses [9]. Some of the applications studied include surface treatments and functionalization to increase the bioactivity of FGM [10]. But a complete knowledge is required, not only on the mechanical properties but also on the long-term biological interactions under various environments [11]. This review focuses on consolidating the existing information on the topic of functionally graded materials in biomedicine and identifying the prospects of research in the future. Analyzing the current literature, we point out the major innovations and current issues of the application of FGMs to practical medical environments [12]. Another aim of this review is to bridge the gap between materials science and clinical uses with the requirement of the integration of materials with the biology system and regeneration facilitation [13]. This initiative could offer perspective into the forthcoming research, which might result in research breakthroughs in the design and use breakthroughs [14]. In the end, it is becoming more and more evident that FGM utilization optimization is likely to bring about a revolution in the field of personalized effective medical equipment and improved patient care [15].

2. Review of literature

The landscapes of functionally graded materials (FGMs) in the medical sector have been of high interest in the last years. In reality, the pioneering studies have focused the attention on the structural aspect. The gradients of the FGMs have been shown to have a positive effect on the points of stress for the implants [1], [2]. These studies have radically preconditioned the verification of the possibility to utilize the FGMs to improve the bonding between the implants and the body tissues [3]. As the events continued to develop, more attention was given to the type of material used. Indeed, people have become more aware of the functionality of the research material concerning the body. Recently, even more stress has been made on the importance of changing the values of the gradients in order to repeat the composition of our body for easier healinging [4], [5]. To give indicative examples of the point in reality reached, some researchers have succeeded in utilizing the additive manufacturing for the production of the FGMs in complex shapes more predisposed to deal with the corresponding biomedical needs [6], [7]. Apart from the above application of the FGMs, there also exist different researches in the drug delivery systems. The gradients for the unloading of the medication offer new horizons in therapy filled with a great deal of passion [8], [9]. All of the above indicate a diversification that point to a greater trend of personalized biomedicine. There exists a need to apply the knowledge of the different biomaterials tailored to the different conditions of the corresponding patients in a medical context. More recently, there have been applications of the modeling. The combination of the modeling studies with the experimentations has resulted in the verification of the possibility to simulate the corresponding design of the FGMs. Indeed, all of the above have resulted in the capability to further fine-tune the corresponding mechanical and biological ones by simulation studies [10], [11]. All of the above studies taken together show a tendency to some improvements. Indeed, the basic concepts have developed to a higher degree of comprehension of all the different possibilities of the applications of the FGMs. The study of the functionally graded materials (FGMs) in the biomedical sphere has also introduced new themes, stating their significance and possibilities. The mechanical qualities required to make biomedical implants, which are biomechanically modified to fit the tissue requirements are one of the fundamental themes. It was found that FGMs are superior to normal materials in their mechanical characteristics and enhance the performance and service life of implants [1], [2]. Furthermore, gradients of materials support the process of osseointegration as it has been found that osteoblasts adhere and proliferate on graded surfaces more successfully [3], [4]. The other important theme is that of biocompatibility, as FGMs appear promising in the context of reducing inflammation and promoting healing. The low cytotoxicity has been associated with better coating techniques and gradient formulas to enhance the body reaction to implants [5], [6]. Also, FGMs have a high level of drug delivery, in which their graded structures have the ability to manage the release profiles and enhance therapeutic outcomes [7], [8]. Improvements in technology of the production of these materials are also included, and an additive manufacturing technique is needed when defining complex FGM structures [9], [10]. This technological advancement assists the application of FGMs by FGMs in sub-medical tasks like orthopedic and dental fixtures and this provides a range of novel biomedical solutions [11]. As observed in the study, FGMs enhance functionality and are more compatible with biological systems by incorporating different material properties, and this is a first step towards changing the field of biomedical engineering. The application of functional graded material (FGMs) in biomedical practice has been considered in different aspects which affected the manufacturing and application of such advanced materials. In order to test the applicability of functionally graded materials (FGMs) to biomedical applications, there is a recent tendency to integrate mechanical and biological testing. The computational modeling is crucial in the prediction of the FGM behavior in physiological conditions as well as the designing of the best structures. The possible applications of FGMs to load-bearing medical implants were confirmed by the fact that Panchal and Ponappa [5] have shown that a finite element analysis is useful to simulate the stress distribution in composite systems. These predictions should be supported by experimental research to prove themselves and test their biological performance in reality. According to Bandyopadhyay et al., in vitro and in vivo testing plays a vital role in ascertaining mechanical reliability and biocompatibility, which are error-free to clinical success [2]. An integrated approach that incorporates modelling and experimental validation has been able to find a potent framework of the development of FGM. The interdisciplinary approaches made possible by the works of Teo et al. [3] and Zhang et al. [4], who promoted the need for the design process to be based on the iterative approach of design, bridging the expectations of theoretical concepts and the reality of empirical evidence. These designs also recognize the importance of interdisciplinary collaboration for the fields of material science, mechanical engineering, and biomedicine. Additionally, our current understanding of the micro-structural influence on the performance of FGMs has been significantly heightened thanks to the latest generation of characterization tools including the micro-computed tomographic scanner and the scanning electron microscope [1]. Taken together, the development of these allows the utilization of experimentally driven, computationally supported, or theoretically driven techniques to stretch the boundaries of FGM applications in the field of biomedical engineering. Interestingly enough, there also seems to be a growing community acceptance of the need for compositional gradients to match the range of values of the different natural biological tissues to simplify the process of incorporating FGM into the world of medicine. This improves their application in the form of transplants for both implants and prosthetics [1], [2]. All of this information can be applied to supply a strong theoretical framework in which the tailoring of material properties be made possible by the design of gradients. More importantly, the controversy relating to bioactivity suggests the presence of contrasting opinions. There also exist contributors who show that the development of gradients would greatly improve the application and efficacy of the transplanted items by recreating natural constructions of body tissues [3], [4]. There also exist warnings about the difficulties of trying to implement a semblance of strength in the gradients presenting the potentials for long-term risks identified [5]. These contradictions present the need for further research. Interestingly enough, modeling techniques have expanded to account for the presence of these conflicts to serve the purpose of the prediction of functionality under body conditions. Finite researches have already shown how the designs of the gradients have the capability to redefine the stress gradients that have a direct effect on the entire "life span" of the items in the application in the field of medicine [6], [7]. Even the combination of the hard facts of reality applied to the modeling technique also contributes even more to the growing body of information since there exist attempts to correlate the theoretical ideas to the empirical findings of the biological events [8], [9]. All in all, the application for the analysis of the FGM in the world of medicine demonstrates the evidence of the continuous change between the theoretical concepts and the applications derived. Even though the FGMs show great promise, the community has to deal with the theoretical inconsistencies present in the technology. Additionally, the techniques to implement the developments into a promising health efficacy need to be improved.

Functionally graded materials (FGMs) have shown the potential to improve patient care by providing tailored and functional applications for the application. A great deal of attention in the research has been devoted to their properties of being mechanically compatible in the body. They seem to have a good compliance to the biomechanics of the body tissues. This may lead to the achievement of greater and more long-lasting functionality of the implant [1], [2]. FGMs have been considered a revolutionary technology in the medical devices industry owing to their mechanical compatibility function of assisting in the osseointegration process [3], [4]. There comes the innovation in the processing of the material, particularly the application of the Additive Manufacturing. Scientists have been successful in designing complex designs having normalized material variation. These designs have similarities to the complex designs of the natural material. These designs can be applied to all types of orthopedic implants to the drug delivery systems [5], [6]. This correlates to the changing trend in the application of personalized medicine. Now the biomaterials have become more personalized to suit the needs of the patient [7]. The net result of all these factors is not merely research. Rather, there has been a true innovation in the field of material science and biomedics. Some of the prominent advantages of the FGM material have been their improved biologically active characteristics. They have the prospect of providing improved clinics healing success rates due to their improved biologically active characteristics [8]. Besides that, FGMs have potential in terms of drug delivery, which opens the possibilities of customized treatments that can enhance the care of patients [9]. Nevertheless, despite all the advancements it has some significant things that we have to take into account. Indicatively, there is no full understanding of the behavior of the FGMs in the body in the long-term. The duration of time biological interactions can influence their effectiveness is not investigated in many studies [10]. Besides, despite the promising in vitro results, the use of these materials in the real clinical setting is a difficult task due to the regulations. In vivo research is required to verify their safety and efficacy [11]. These issues should be discussed in future researches. Research would be able to investigate the treatment of FGMs in the body in the long term in various clinical conditions giving a better picture of the way they decompose and how the body responds to them [12]. Moreover, cross disciplinary efforts through computerization and experimentation may enable us to refine FGM designs to be even better applied in biology [13]. It is also a nice thought to see how the surfaces of these materials can be altered to increase bioactivity, which would come in handy when it comes to issues of cytotoxicity and bio-responsiveness [14]. In conclusion, the FGMs have many applications in the promotion of the utilization of biomed. The combination of the innovations derived from material science in the healthcare needs will see the manner in which patients receive medical attention change for the better. But in order to maximize them we still need to study and confirm these sources with long-term research and interdisciplinary studies [15]. These developments may be applied in the field of biomedical engineering to bring about a new dawn of individual and efficient solutions to different healthcare requirements [16]. Biomedical engineering is evolving so fast owing to the amalgamation of novel functional materials in addition to hybrid fabrication techniques. Cartilage repair is a promising field of 3D bioprinting. Spatial regulation of material gradients was reported to have a strong positive effect on tissue repair and mechanical compliance with native tissues, which have definite analogies to functional principles of the design of functionally graded scaffolds [17]. At the same time, technologies of additive manufacturing have enabled the production of complex material transitions and geometries. To be clinically viable, FGMs require that these technologies can permit a deposition of biocompatible materials that contain specific properties [18]. Photodynamic treatment is a light-activated treatment that opens up new opportunities of localised treatment delivery, and this once again demonstrates the way in which bioresponsive materials can be developed to respond dynamically to biological systems [19]. The bioactive systems form significant aspects of regenerative medicine. As an example, platelet-rich fibrin (PRF) has been studied when used in graded constructs in order to enhance bone regeneration [20]. Scaffolds made with programmable distributions of pore size can also be used to recapitulate the mechanical performance and transport behavior of native tissues and are produced using advanced methods based on laser tools [21]. New hydrogel systems facilitate this development. High biocompatibility and tunable mechanical characteristics of smart hydrogel have enabled the integration of responsive layers into FGMs in order to enhance their adaptability and biological functionality in vivo [22]. Such advances indicate that there is an increased convergence between biological integration, functional responsiveness, and material architecture. This direction complies with the bigger objective of patient-centric and versatile therapeutic platforms, which confirms the role of FGMs in the biomedical devices of the future.

Novel cross-disciplinary directions now highlight the importance of integrating technological progress with clinical relevance to make the best of the biomedical and clinical possibilities of functionally graded materials (FGMs). The two key impediments to the implementation of FGMs in the medical practice are complex regulations and lack of knowledge about the long-term biological interactions. Considering this, Regev et al. [23] emphasized the value of extensive biological mapping through the Human Cell Atlas, the latter of which, in turn, can be of much help when it comes to designing biomaterials to fit specific cell conditions. Blocher and Perry [25] also discussed the potential of coacervate systems as controlled release and bioactive encapsulation methods which could be useful in FGM-based therapies, and DiCiccio et al. [24] examined caffeine-catalyzed hydrogel and suggested new soft materials to use in dynamic biology. FGMs are under continuous development due to the sophisticated methods of fabrication, e.g., 3D printing. Just like the motivation of individualized micro-architected FGMs, Au et al. [26] looked into the impact of 3D-printed microfluidics in the biomedical systems. Koh et al. developed real-time biochemical wearable microfluidic devices [27]; these technologies can complement smart FGMs to carry out drug delivery or diagnostic functions. The 3D bioprinting of cartilages was also demonstrated by Perera et al. [28], who emphasized the ability to control mechanical gradient to be applied in the printed implants to replicate the behavior of native tissues. Also, nanostructured materials can enhance the properties of FGMs. Reina et al. [29] in their discussion of the biomedical potential of graphene indicated that although it is very strong and has high biocompatibility, toxicity and clinical approval are still a problem. Among ten grand challenges in science robotics identified by Yang et al. [30], the biointegration and functional optimization of FGMs in the context of soft robotics or prosthetics are also mentioned. In the field of bone tissue engineering, Zhou et al. [31] selectively laser melted to produce functionally graded scaffolds with programmable pore structure that has controlled degradation and strength under load bearing conditions. According to the study done by Iandolo et al. [32] on organic electronic scaffolds to osteogenesis, electrical functionality can also be added to FGM systems. Chia and Wu [33] reported the progress made on 3D-printed biomaterials enhancing cellular guidance and integration, which is a key goal in implantable FGMs. Hydrogels and surface chemistry are still necessary to be biocompatible. They both can be altered as layers or surface treatments in graded implants. The hyaluronic acid hydrogels have been discussed by Burdick and Prestwich [34], and platelet-rich fibrin (PRF) has been discussed in the context of bone regeneration by Farmani et al. [35]. To directly endorse the mechanical-bioactive binary that is needed in FGM surfaces, Chen and Jia [36] explored multilayer hydroxyapatite coating through laser deposition. More general conceptual issues are also discussed. Yap et al. [37] reviewed selective laser melting in a range of industries and revealed how the post-processing variables that influence quality of the surface and residual stresses have to be considered to optimize FGM with design as another factor to consider. Oberdorster et al. [38] in their significant contribution to the field of nanotoxicology have advised scientists that despite the promise of the use of FGMs with nanoparticles or new chemistries, a comprehensive toxicity evaluation should be performed prior to clinical translation. Together, these sources [2338] contribute to the evolution of FGMs outside the ordinary biomedical models as they contribute to the complex nature of the practice. Along with presenting the principles of design and providing technologies, they attract attention to the problem of translational barriers that are to be crossed before FGMs can be integrated into the next-generation medical equipment. Table 1 provides a summary of the literature review.

Table 1. Literature Review Summary

Author	Main Focus	Findings
Alkunte et al. (2024)	Examine advancements and challenges in additively manufactured Functionally Graded Materials (FGMs) and their applications.	FGMs hold significant potential due to their adaptable properties in various applications. The review highlights challenges in production and performance and forecasts future trends.
Bandyopadhyay et al,. (2023	Review manufacturing processes, properties, and challenges of porous metal implants in biomedical applications.	Porous biocompatible metals offer tailorable strength and fatigue resistance, making them suitable alternatives for orthopedic and dental implants.

Teo et al,. (2022)	Analyze nanocellulose as a Pickering emulsifier for various non-toxic applications.	Nanocellulose provides a sustainable alternative for stabilizing emulsions, with potential applications in the food, cosmetic, and pharmaceutical industries.
Zhang et al. (2022)	Explore bioinspired designs for soft-hard tissue interfaces and their application in engineered materials.	Mimicking natural soft-hard interfaces can significantly enhance the performance of biomedical devices.
Panchal and Ponappa (2022)	Review computational methods and production techniques related to functionally graded materials (FGMs) in biomedical uses.	Existing advancements in computational modeling improve biomedical outcomes, yet gaps remain for practical integration.
Li et al. (2020)	Review multi-scale design concepts in additive manufacturing of FGMs and FGSs.	Proposed strategies for multi-scale designs significantly enhance the functional performance of FGMs and FGSs across various industries.
Petit et al,. (2018)	Explore graded ceramics for their potential in biomedical applications, focusing on their unique properties.	FG ceramics offer significant advantages over traditional materials, enhancing the performance of biomedical applications.
Mahmoud and Elbestawi (2017)	Overview of additive manufacturing applications of FGMs and lattice structures in orthopedic implants.	Highlight successful case studies and identify critical challenges that need to be addressed for better performance.
Gillies et al. (2015)	Examine the use of radiomics in transforming medical images into actionable data.	Radiomics enhances diagnostic accuracy but requires standardized processes for broader clinical integration.
Mehrali et al., (2013)	Review advancements in FGMs for dental implants, focusing on properties and manufacturing techniques.	FGMs show superior properties for dental applications, improving biocompatibility and osseointegration.
Bulcha et al., (2021)	Review the current landscape of viral vector platforms in gene therapy.	Despite successes, significant challenges remain that limit the full potential of viral vector approaches.
Seddiqi et al., (2021)	Survey the structural properties of cellulose and its potential applications in biomedicine.	Cellulose derivatives hold promise for various biomedical applications, though underutilized relative to industrial uses.
Homaeigohar and Boccaccíní (2020)	Review advances in antibacterial nanofibers for wound dressings.	Biohybrid nanofibrous dressings show promise due to biocompatibility,

		biodegradability, and enhanced healing properties.
Yang et al., (2018)	Identify ten grand challenges in the field of Science Robotics.	Tackling these challenges could lead to significant advancements in technology and social applications.
Regev et al., (2017)	Outline the Human Cell Atlas Project aiming to identify all human cell types.	The project could significantly enhance understanding of human biology and disease.
Reina et al., (2017)	Evaluate the potential contributions of graphene in biomedical applications.	Graphene shows significant potential but faces challenges regarding biocompatibility and regulatory approval.
Koh et al., (2016)	Develop a skin-mounted microfluidic device for sweat analysis.	The device enables non-invasive health monitoring and effectively measures biochemical markers in sweat.
Blocher and Perry, (2016)	Explore coacervate materials for biomedical applications.	Complex coacervates show promise in encapsulation and as scaffolds in tissue engineering.
Au et al., (2016)	Examine the impact of 3D printing on microfluidics.	3D printing offers significant advantages over traditional methods, improving design flexibility.
Perera et al., (2021)	Explore advancements in 3D bioprinted implants for cartilage repair.	3D bioprinting shows promise in creating functional constructs with modulated mechanical properties for cartilage tissues.
Wong and Hernandez, (2012)	Review current advancements and challenges in additive manufacturing.	Additive manufacturing is revolutionizing industries but faces challenges in material usage and accuracy.
Agostinis et al., (2011)	Update on the efficacy and applications of photodynamic therapy (PDT) in cancer treatment.	PDT shows significant potential, especially in early-stage tumors, with minimal side effects and good outcomes.

3. Conclusion

Functionally graded biomaterials represent a new class of biomaterials that can solve the complex problems of modern biomedical applications. Due to their unique ability to exhibit gradual variations in composition and structure, their mechanical properties, biological response, and material behavior can be tailored for diverse spatial regions in specific applications such as implants, dental prostheses, and drug delivery systems. In the foregoing review, prominent trends in the design, processing, and evaluation of FGMs for different applications in the field of biomedicine have been pointed out. In the context of research studies, the capability of FGMs to not only offer improved biocompatibility based on bioactivity but also promote osseointegration and inhibit a biological rejection has been emphasized.

Despite the above advancements, a number of challenges continue to exist. Biocompatibility for long periods of time, degradation rates, and in vivo stability of FGMs remain to be investigated. These challenges include some of the greatest concerns for general adoption. Implementation of intelligent capabilities in the form of bioactive substances or responsiveness to biologically significant stimuli in graded material systems also presents another direction to move ahead. Unlocking the complete potential of FGMs will therefore involve a multidisciplinary approach in one interface of material sciences, biologists, mechanicians, and healthcare research. The application of FGMs would therefore be more significant in the coming era of customized high-performance biodevices since they would have the capability to span both theoretical modeling of experiments.

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