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Original Article

Effect of micro-arc oxidation coatings with graphene oxide and graphite on osseointegration of titanium implants-an in vivo study

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ABSTRACT

Background: This in vivo study evaluated the effect of graphene oxide and graphite coatings, coupled with the micro-arc oxidation (MAO) surface roughening technique, known for their mechanical strength, chemical stability, and antibacterial properties. The main objective was to assess the degree of improvement in osseointegration of titanium implants resulting from these interventions.
Materials and methods: In this study, 32 female rats were utilized and randomly allocated into four groups ($n = 8$ each): machined surface titanium implants (control), those roughened by the MAO method, those coated with graphene oxide-doped MAO, and those with a graphite-doped MAO coating. Titanium implants were surgically placed in the right tibia of the rats. Rats undergoing no additional procedures during the 4-week experimental period were sacrificed at the end. Then, the implants and surrounding bone tissues were separated and embedded in acrylic blocks for reverse torque analysis. Using a digital torque device, the rotational force was applied to all samples using a hex driver and racquet until implant separation from the bone occurred, with the corresponding values recorded on the digital display. Then, statistical analysis was performed to analyze the data.
Results: No statistically significant difference between the groups was observed in the biomechanical bone–implant connection levels (N/cm) ($P = 0.268$). Post-hoc tests were not required because no discernible differences were identified between the groups.
Conclusion: Within the scope of this study, implants treated with the MAO method, along with those coated with graphene oxide- and graphite-doped MAO method, did not exhibit significant superiority in terms of osseointegration compared to machined surface titanium implants.

1. Introduction

Titanium alloys are favored for orthopedic and dental implants owing to their remarkable mechanical strength, fracture resistance, and corrosion resistance (Chen and Thouas, 2015; Clavell et al., 2016; Gopi et al., 2015; Najeeb et al., 2019). The success of dental implant applications is intricately linked to the interplay of surface properties, geometric design, implant procedural efficacy, and the inherent characteristics of the host bone tissue. Achieving success in dental implant treatments hinges on harmonizing the implant's mechanical and biological attributes (Bozoglan et al., 2019; Khurshid et al., 2020). In addition to these properties, the stability and long-term osseointegration of the implant and bone interface are crucial to implant success. Titanium implant surfaces undergo oxidation, forming a dense and robust titanium dioxide (TiO_2) layer that imparts resistance to corrosion. Owing to these properties, titanium has gained widespread use in dental implants. Implants undergo various processes to preserve or modify their surface properties, including several addition and subtraction processes that increase the implant's surface area (Lacefield, 1999; Özcan and Hämmerle, 2012).

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Graphene, an extraordinary material with a two-dimensional atomic crystal structure, is created through the sp^2 hybridization of carbon atoms, forming an intricately layered, single-atom-thick lattice (Allen et al., 2010; Du et al., 2010). The fascination with graphene arises from its exceptional mechanical, chemical, and electrical properties, distinguishing it as a promising material compared to traditional counterparts (Allen et al., 2010; Du et al., 2010; Mao et al., 2013). This appeal has ignited a surge of intense scrutiny and dedicated exploration, spanning a broad spectrum of scientific domains, including electronics, chemistry, and the burgeoning field of biomedicine (Lü et al., 2012; Zhou et al., 2012).

The versatile nature of graphene has spurred pioneering applications across numerous disciplines. In the pharmaceutical field, graphene's capabilities have been harnessed as a drug carrier, revolutionizing drug delivery and enhancing therapeutic efficacy (Georgakilas et al., 2012). Its proficiency in facilitating biological imaging and functioning as a sensor has revolutionized diagnostics, enabling sensitive and accurate detection at unprecedented scales (Sun et al., 2013). In the dynamic field of bioengineering, graphene serves as a bioactive scaffold, seamlessly interfacing with living tissue to drive regeneration and repair (Yang et al., 2013). Meanwhile, the profound impact of graphene resonates even within the field of medicine, where it is explored as a potent tool in cancer therapy, providing targeted approaches for treatment and diagnosis (Park et al., 2011; Tian et al., 2011).

Beyond these captivating applications, recent advances have highlighted graphene's potential to influence cellular behavior. Pioneering research underscores the asymmetric nonpolar structure of graphene, coupled with its unique properties such as layer stiffness and surface roughness, as inducers of an osteogenic response in human mesenchymal cells (Liu et al., 2016; Xie et al., 2019). These insights reveal an intriguing prospect: the ability to leverage graphene's inherent attributes to actively promote osseointegration—a pivotal element in successful dental implantation.

Modifying titanium dental implants with biocompatible materials has been a focus of research to enhance osteogenic activity and assess antibacterial effects. However, coating the dental implant surface with certain materials may result in bone loss around the implant neck. While producing biocompatible graphene coatings poses challenges, these coatings have been shown to increase bone fusion with dental implants and facilitate tissue regeneration in dentistry (Mansoor et al., 2022).

The micro-arc oxidation (MAO) coating method is a transformative technique employed to enhance the surface bioactivity of materials crucial for diverse biological applications (Cerchier et al., 2017; Gnedenkov et al., 2016; Mohedano et al., 2017). In biomaterials, this method emerges as an outstanding contender, endowing surfaces with many advantages that transcend mere aesthetics. Through the interplay of controlled electrical discharges and precise manipulation of electrochemical reactions, MAO endows materials with corrosion resistance, microporosity, and intricately engineered surface roughness (Cerchier et al., 2017; Gnedenkov et al., 2016; Mohedano et al., 2017).

The appeal of MAO extends beyond surface enhancements, encompassing its potential for materials designed to interface with living systems. The microporosity on the material's surface generates suitable locations for cellular adhesion, proliferation, and differentiation of biological molecules and cellular components. This surface modification facilitates seamless interactions between the host material and the biological components. However, MAO faces criticism owing to concerns regarding the bioactivity and potential toxicity of MAO-treated inorganic coatings. This scientific discourse is essential, allowing us to elucidate interactions occurring at the nanoscale interface of materials and biological materials. Among the various viewpoints, the use of MAO in mitigating implant-associated infections seems promising (Cerchier et al., 2017; Durdu, 2018; He et al., 2017; Pezzato et al., 2019). This study investigated the effects of combining graphene (possessing antibacterial properties) and MAO (a surface roughening method) on the osseointegration of titanium implants placed in the rat tibia.

The scarcity of studies on reverse torque values, representing an objective biomechanical analysis of osseointegration when utilizing graphene oxide and graphite coatings on titanium for dental implants, underscores the significance of our study for the clinical application of these coating materials. We hypothesized that the MAO roughening method and the application of graphene oxide and graphite coatings would not enhance the osseointegration of dental titanium implants.

2. Materials and methods

2.1. Animals and experimental design

This study was approved by the Fırat University Animal Experiments Local Ethics Committee in Elazig, Turkey, and the surgical procedures were conducted at the Fırat University Experimental Research Center (2020/11). Adhering to the guidelines of the World Medical Association Declaration of Helsinki for the protection of experimental animals, the research involved 32 Sprague–Dawley rats (weight: 280–320 g; age: 0.5–1 year; female) housed in temperature-controlled plastic cages with free access to food and water throughout the four-week experimental period. A full-time veterinarian at Fırat University Experimental Research Center monitored the rats during all experimental stages, and the care of included rats was provided by relevant technical personnel.

The total number of animals in the study was determined through power analysis, incorporating an 8 % deviation, a type 1 error rate (α) of 0.05, and a type 2 error rate (β) to achieve a power of 0.80. The rats were grouped, and a minimum of seven animals were determined for each group. However, eight rats were included in each group to account for potential losses during surgical and experimental periods. The rats were divided into four groups ($n = 8$): control, MAO, MAO with graphene oxide, and MAO with graphite.

1. Control: machined surface titanium implants (2.5-mm diameter, 4-mm length). These were implanted in the metaphyseal parts of the rats' right tibia bones. No additional treatment was administered to the subjects throughout the four-week duration of the experiment (Albrektsson and Wennerberg, 2004; Le Guéhennec et al., 2007).
2. MAO: titanium implants roughened using the MAO method.
3. MAO-GO: titanium implants coated with graphene oxide using the MAO method.
4. MAO-G: titanium implants coated with graphite using the MAO method.

Surface coating techniques for implants involved oxidizing graphite powder (Nanography Nano Technology, Turkey, ~5–10 µm) using the procedure (Tour method) developed by Marcano et al. (2010) as an alternative to the Hummers' method, resulting in the synthesis of graphene oxide powder. The obtained graphene oxide powder was introduced into an aqueous electrolyte solution comprising potassium hydroxide (KOH), sodium metasilicate (Na_2SiO_3), and sodium hydrogen phosphate (Na_2HPO_4) to obtain doped TiO_2 composite coatings on the titanium base material (Marcano et al., 2010).

The samples subjected to the coating process were divided into groups, as outlined in Table 1. The additives were mixed using a magnetic stirrer until uniformly dispersed in the standard electrolyte solution. Subsequently, the samples divided into the respective groups were affixed to the sample holder, with the stainless steel bath serving as the cathode. Then, they underwent MAO treatment in bipolar mode using an

Table 1
The composition of the electrolyte employed for coating the samples.

Sample encoding	Electrolyte composition
MAO	KOH, Na_2SiO_3, Na_2HPO_4
MAO-G	KOH, Na_2SiO_3, Na_2HPO_4, graphite
MAO-GO	KOH, Na_2SiO_3, Na_2HPO_4, graphene oxide

AC power supply. The coating parameters are detailed in Table 2. The system was cooled with water to prevent the deterioration of the electrolyte solution during the coating process. After the coating process, all samples were heated in an oven at 100 °C for 1 h (Marcano et al., 2010).

2.2. Surgical procedures

The surgical intervention was conducted under deep anesthesia, with the administration of ketamine (50 mg/kg) and xylazine (10 mg/kg) to anesthetize the rats. Researchers ensured a sterile environment during surgical procedures. Following anesthesia, the targeted area was cleaned with povidone–iodine, and the skin over the right tibia was shaved. Subsequently, a 20-mm-long horizontal incision was made in the soft tissue around the right tibia bone. After the skin incision, muscle dissection in the area was completed. Utilizing a periosteal elevator, the metaphyseal region of the tibia connected to the femur bone was reached. Implant sockets were created using suitable drills perfused with saline. Implants were placed with appropriate primary stability in all surgeries. After implantation, subcutaneous tissues were sutured using 5–0 polyglactin sutures, and the skin tissue was sutured with 6–0 prolene. Following surgical procedures, 0.1 mg/kg tramadol hydrochloride was administered intramuscularly as an analgesic and 50 mg/kg penicillin was given as an antibiotic for three days to prevent potential infection. The same researcher performed all surgical and subsequent medical procedures (Bozoglan et al., 2019) (Fig. 1). No fatal or non-fatal complications, such as wound infection, were encountered during the experimental protocol. All surgical procedures were performed at Firat University Experimental Research Center (FUERC).

2.3. Mechanical analysis

Mechanical analysis was performed four weeks postoperatively. Before the analysis, all rats were sacrificed using the carbon dioxide ventilation method under the supervision of the same researcher, and no complications arose during the sacrifices. After dissecting the soft tissues, the implants, along with the surrounding bone tissues, were extracted. The samples were then fixed in a 10 % formaldehyde solution and promptly assessed to avoid dehydration. Subsequently, the implant blocks were embedded in polymethylmethacrylate. A hex driver and ratchet were affixed to the implants, and each sample was secured to a digital torque tool (Mark-10 Corporation, 11 Dixon Avenue, Copiague, NY 11726 USA). The force was manually, slowly, and gradually applied counterclockwise. The procedure was terminated when the implant began to rotate within the socket. The highest torque value (N/cm) achieved with the digital torque device at the first breaking turn of the socket was automatically recorded (Tekin et al., 2021) (Fig. 2). The biomechanical analysis was conducted in a blinded manner by a single investigator experienced in experimental animal studies.

2.4. Statistical analysis

Statistical analysis was performed with SPSS 23.0 for Windows software (SPSS Inc., Chicago, IL, USA). Mechanical bone implant connection parameters (N/cm) are nonparametric. The normal data distribution was assessed with the Shapiro–Wilks and Kolmogorov–Smirnov tests, indicating a non-normal distribution. Differences between groups were assessed using the Kruskall–Wallis test, and significance was considered at $P < 0.05$.

Table 2
Coating parameters.

Frequency	Voltage	Coating time	Duty cycle
250 Hz	450/−100 V	20 min	10 %

Fig. 1. Insertion of the titanium implants into bone sockets.

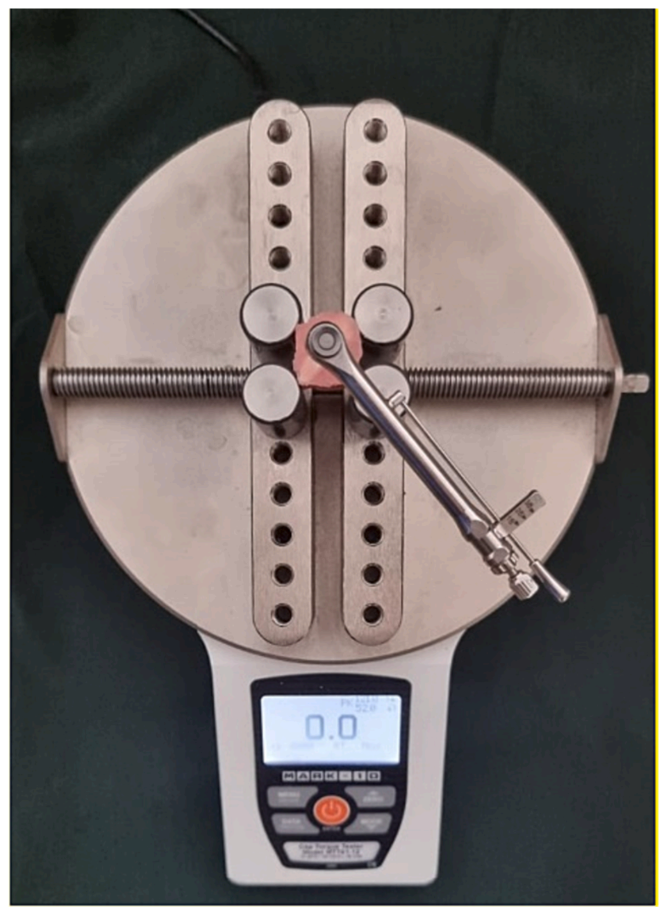

Fig. 2. Reverse torque analysis of the titanium implants (Mark-10 Corporation, 11 Dixon Avenue, Copiague, NY 11726 USA).

3. Results

No signs of wound tissue separation or infection were observed following the surgical procedure. The statistical data obtained from the analysis performed on the control, MAO, graphene oxide MAO, and graphite MAO groups are presented in Table 3. No statistically significant differences were identified between the groups ($P > 0.05$). Post-hoc tests were unnecessary because no discernible differences were found between the groups.

Table 3
Biomechanical bone–implant connection levels of the groups (N/cm). V: Volt, *Kruskal–Wallis testm ($P = 0.268$). The result indicated no statistically significant difference between the groups ($P > 0.05$).

Groups	*n*	Mean	Std. Dev.	Min.	Max.	*P**
Control	8	1.23	0.62	0.50	2.50	
MAO	8	1.15	0.50	0.60	2.20	
MAO with graphene oxide	8	1.55	0.46	0.50	2.00	0.268
MAO with graphite	8	1.40	0.50	0.80	2.10	

4. Discussion

Recent studies have shown that modifying Ti surfaces with various coatings can enhance the osteogenic aspect of the implant–bone attachment mechanism (Li et al., 2010; Zeng et al., 2016). For example, Shi et al. (2016) incorporated graphene oxide into coatings on titanium substrates to enhance the mechanical properties of titanium. While investigating its impact on mechanical properties, it was discovered that graphene oxide also enhanced biocompatibility. Therefore, graphene oxide can be applied to oral implants to enhance osseointegration. Further exploration is required to understand the osteogenic properties of graphene and its derivatives with different surface treatments. In our study, we applied a graphene oxide coating to the surface of titanium implants and explored its potential contribution to osseointegration.

Based on the findings of an animal study conducted by Li et al. (2018) investigating the relationship between graphene and osseointegration, graphene is a potential new nanocoating material that enhances the surface biological activity of Ti-based alloy materials. It may also promote in vivo osseointegration and osteogenesis. In our study, we coated titanium implants with graphite to examine its potential contribution to osseointegration.

MAO applied to titanium implants before surface coatings has enhanced chemical reactions at the implant surface, promoting improved osteoblast adhesion, proliferation, and osteogenic differentiation. This enhancement improves osseointegration between the implant and bone (Zhou et al., 2022).

Ding et al. (2022) conducted a histomorphometric study to examine the early osseointegration of titanium implants coated using the MAO method and containing Ag. The MAO treatment involved subjecting titanium implants to voltages up to 465 V to create a thick oxide layer. Study observers noted a positive impact on osseointegration owing to this treatment.

Du et al. (2018) studied the structure of the MAO coating formed on the titanium surface with voltages of 300, 350, 400, 450, and 500 V. The results revealed that numerous 1–3-μm micropores were observed after the MAO treatment at 350 V. However, as the applied voltage increased, it was observed that the average size of the micropores on the MAO coating surface increased, accompanied by a decrease in pore density. Therefore, in our study, we applied MAO at a voltage of 450/−100 V to titanium implant surfaces, aligning with the procedures in previous MAO studies. Additionally, we investigated whether this application contributed to osseointegration.

Our study employed the reverse torque test to assess osseointegration, comprehensively evaluating the entire bone surrounding the implant. While histological analysis can evaluate only a specific section, reverse torque analysis allows to assess the entire bone–implant interface (Gunes et al., 2021; Tekin et al., 2021). Although not utilized clinically, reverse torque analysis is an objective criterion in animal and laboratory studies, providing an indirect measure of the force required to break the bone–implant connection (Di Stefano et al., 2018; Gunes et al., 2021). In our study, reverse torque analysis revealed no significant differences between the groups.

It is essential to acknowledge several limitations in our study. First, the molecular mechanisms underlying the association between implant surfaces and bone tissue were not elucidated owing to the methodology employed. Second, while experimental animal research is valuable for understanding pathways involved in bone–implant interactions, the extrapolation of these results to humans is limited. Third, the study did not examine titanium implants' survival rate or assess osseointegration's long-term success. Fourth, long bones such as the tibia and femur have different osteogenic properties (endochondral–intramembranous ossifications) than the jaw bones (mandible–maxilla) and may respond differently to different implants.

5. Conclusion

This study revealed no significant difference in the contribution of graphene oxide or graphite to the surface of titanium-coated implants regarding osseointegration compared to the control group. Regardless of whether MAO was applied to the implant surface at 450/−100 V, there was no difference from the control group in terms of osseointegration. Further investigations are warranted to provide deeper insights.

CRediT authorship contribution statement

Bahar Tekin: Conceptualization, Writing – original draft, Validation. **Serkan Dundar:** Conceptualization, Validation, Investigation, Visualization. **Samet Tekin:** Methodology, Project administration, Funding acquisition. **Ebru Emine Sukuroglu:** Methodology, Software, Formal analysis, Resources, Data curation, Investigation. **Zohaib Khurshid:** Project administration, Supervision. **Yusuf Ezgi:** Writing – original draft, Funding acquisition. **Fatih Demirci:** Formal analysis, Resources, Data curation. **Muhammad Faheemuddin:** Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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This study was approved by the Firat University Animal Experiments Local Ethics Committee, Elazig, Turkey, and the surgical procedures were performed at the Firat University Experimental Research Center (2020/11).

References

Albrektsson, T., Wennerberg, A., 2004. Oral implant surfaces: Part 2–review focusing on clinical knowledge of different surfaces. Int. J. Prosthodont. 17 (5), 544–564.
Allen, M.J., Tung, V.C., Kaner, R.B., 2010. Honeycomb carbon: a review of graphene. Chem. Rev. 110 (1), 132–145.
Bozoglan, A., Dundar, S., Yildirim, T.T., Bulmus, O., Ertugrul, A.S., Bozoglan, M.Y., Tekin, S., Toy, V.E., 2019. Effects of Different Levels of Restraint Stress on Bone-Implant Contact. J. Craniofac. Surg. 30 (4), 1294–1297.
Cerchier, P., Pezzato, L., Brunelli, K., Dolcet, P., Bartolozzi, A., Bertani, R., Dabalà, M., 2017. Antibacterial effect of PEO coating with silver on AA7075. Mater. Sci. Eng. c. Mater. Biol. Appl. 75, 554–564.
Chen, Q., Thouas, G.A., 2015. Metallic implant biomaterials. Mater. Sci. Engineer: r: Reports. 87, 1–57.
Clavell, R.S., de Llano, J.M., Carda, C., Ribelles, J.G., Vallés-Lluch, A., 2016. In vitro assessment of the biological response of Ti6Al4V implants coated with hydroxyapatite microdomains. J. Biomed. Mater. Res. a. 104 (11), 2723–2729.
Di Stefano, D.A., Arosio, P., Gastaldi, G., Gherlone, E., 2018. The insertion torque-depth curve integral as a measure of implant primary stability: An in vitro study on polyurethane foam blocks. J. Prosthet. Dent. 120 (5), 706–714.
Ding, M., Shi, J., Wang, W., Li, D., Tian, L., 2022. Early osseointegration of MAO coated titanium alloy implants containing Ag: a histomorphometric study. BMC. Oral. Health. 22 (1), 628.
Du, Q., Zheng, M., Zhang, L., Wang, Y., Chen, J., Xue, L., Dai, W., Ji, G., Cao, J., 2010. Preparation of functionalized graphene sheets by a low-temperature thermal exfoliation approach and their electrochemical supercapacitive behaviors. Electrochimica. Acta. 55 (12), 3897–3903.

Du, Q., Wei, D., Wang, Y., Cheng, S., Liu, S., Zhou, Y., Jia, D., 2018. The effect of applied voltages on the structure, apatite-inducing ability and antibacterial ability of micro arc oxidation coating formed on titanium surface. Bioact. Mater. 3 (4), 426–433.
Durdu, S., 2018. Characterization, bioactivity and antibacterial properties of copper-based TiO2 bioceramic coatings fabricated on titanium. Coatings. 9 (1), 1.
Georgakilas, V., Otyepka, M., Bourlinos, A.B., Chandra, V., Kim, N., Kemp, K.C., Hobza, P., Zboril, R., Kim, K.S., 2012. Functionalization of graphene: covalent and non-covalent approaches, derivatives and applications. Chem. Rev. 112 (11), 6156–6214.
Gnedenkov, S.V., Sharkeev, Y.P., Sinebryukhov, S.L., Khrisanfova, O.A., Legostaeva, E. V., Zavidnaya, A.G., Puz, A.V., Khulusov, I.A., Opra, D.P., 2016. Functional coatings formed on the titanium and magnesium alloys as implant materials by plasma electrolytic oxidation technology: fundamental principles and synthesis conditions. Corrosion. Reviews. 34 (1–2), 65–83.
Gopi, D., Shinyjoy, E., Kavitha, L., 2015. Influence of ionic substitution in improving the biological property of carbon nanotubes reinforced hydroxyapatite composite coating on titanium for orthopedic applications. Ceramics. International. 41 (4), 5454–5463.
Gunes, N., Gul, M., Dundar, S., Tekin, S., Bozoglan, A., Ozcan, E.C., Karasu, N., Toy, V.E., Bingül, M.B., 2021. Biomechanical evaluation of implant osseointegration after guided bone regeneration with different bone grafts. J. Craniofac. Surg. 32 (4), 1545–1548.
He, X., Zhang, X., Wang, X., Qin, L., 2017. Review of antibacterial activity of titanium-based implants' surfaces fabricated by MAO. Coatings. 7 (3), 45.
Khurshid, Z., Hafeji, S., Tekin, S., Habib, S.R., Ullah, R., Sefat, F., Zafar, M.S., 2020. Dental Implants. In: Zafar, M.S., Khurshid, Z., Khan, A.S., Najeeb, S., Sefat, F. (Eds.), Titanium, Zirconia, and Polyetheretherketone (PEEK) as a Dental Implant Material. Woodhead Publishing, Cambridge, pp. 5–35.
Lacefield, W.R., 1999. Materials characteristics of uncoated/ceramic-coated implant materials. Adv. Dent. Res. 13 (1), 21–26.
Le Guéhennec, L., Soueidan, A., Layrolle, P., Amouriq, Y., 2007. Surface treatments of titanium dental implants for rapid osseointegration. Dent. Mater. 23 (7), 844–854.
Li, Y., Li, Q., Zhu, S., Luo, E., Li, J., Feng, G., Liao, Y., Hu, J., 2010. The effect of strontium-substituted hydroxyapatite coating on implant fixation in ovariectomized rats. Biomaterials. 31 (34), 9006–9014.
Li, K., Wang, C., Yan, J., Zhang, Q., Dang, B., Wang, Z., Yao, Y., Lin, K., Guo, Z., Bi, L., Han, Y., 2018. Evaluation of the osteogenesis and osseointegration of titanium alloys coated with graphene: an in vivo study. Sci. Rep. 8 (1), 1843.
Liu, Y., Chen, T., Du, F., Gu, M., Zhang, P., Zhang, X., Liu, J., Lv, L., Xiong, C., Zhou, Y., 2016. Single-layer graphene enhances the osteogenic differentiation of human mesenchymal stem cells in vitro and in vivo. J. Biomed. Nanotechnol. 12 (6), 1270–1284.
Lü, K., Zhao, G., Wang, X., 2012. A brief review of graphene-based material synthesis and its application in environmental pollution management. Chin. Sci. Bull. 57, 1223–1234.
Mansoor, A., Khurshid, Z., Khan, M.T., Mansoor, E., Butt, F.A., Jamal, A., Palma, P.J., 2022. Medical and dental applications of titania nanoparticles: an overview. Nanomaterials 12 (20), 3670.
Mao, H.Y., Laurent, S., Chen, W., Akhavan, O., Imani, M., Ashkarran, A.A., Mahmoudi, M., 2013. Graphene: promises, facts, opportunities, and challenges in nanomedicine. Chem. Rev. 113 (5), 3407–3424.
Marcano, D.C., Kosynkin, D.V., Berlin, J.M., Sinitskii, A., Sun, Z., Slesarev, A., Alemany, L.B., Lu, W., Tour, J.M., 2010. Improved synthesis of graphene oxide. ACS. Nano. 4 (8), 4806–4814.
Mohedano, M., Luthringer, B.J.C., Mingo, B., Feyerabend, F., Arrabal, R., Sanchez-Egido, P.J., Blawert, C., Willumeit-Roemer, R., Matykina, E., 2017. Bioactive plasma electrolytic oxidation coatings on Mg-Ca alloy to control degradation behaviour. Surf. Coat. Technol. 315, 454–467.
Najeeb, S., Mali, M., Syed, A.U.Y., Zafar, M.S., Khurshid, Z., Alwadaani, A., Matinlinna, J. P., 2019. In Advanced dental biomaterials. In: Khurshid, Z., Najeeb, S., Zafar, M.S., Sefat, F. (Eds.), Dental Implants Materials and Surface Treatments. Woodhead Publishing, Amsterdam, pp. 581–598.
Özcan, M., Hämmerle, C., 2012. Titanium as a reconstruction and implant material in dentistry: advantages and pitfalls. Materials. 5 (9), 1528–1545.
Park, J.K., Jung, J., Subramaniam, P., Shah, B.P., Kim, C., Lee, J.K., Cho, J.H., Lee, C., Lee, K.B., 2011. Graphite-coated magnetic nanoparticles as multimodal imaging probes and cooperative therapeutic agents for tumor cells. Small. 7 (12), 1647.
Pezzato, L., Cerchier, P., Brunelli, K., Bartolozzi, A., Bertani, R., Dabalà, M., 2019. Plasma electrolytic oxidation coatings with fungicidal properties. Surf. Eng. 35 (4), 325–333.
Shi, Y.Y., Li, M., Liu, Q., Jia, Z.J., Xu, X.C., Cheng, Y., Zheng, Y.F., 2016. Electrophoretic deposition of graphene oxide reinforced chitosan–hydroxyapatite nanocomposite coatings on Ti substrate. J. Mater. Sci. Mater. Med. 27, 1–13.
Sun, H., Wu, L., Gao, N., Ren, J., Qu, X., 2013. Improvement of photoluminescence of graphene quantum dots with a biocompatible photochemical reduction pathway and its bioimaging application. ACS. Appl. Mater. Interfaces. 5 (3), 1174–1179.
Tekin, S., Dundar, S., Demirci, F., Bozoglan, A., Yildirim, T.T., Gunes, N., Acikan, I., Ozcan, E.C., 2021. Biomechanical and biochemical evaluation of the effect of systemic application of omeprazole on the osseointegration of titanium implants. Int. J. Implant. Dent. 7, 1–7.
Tian, B., Wang, C., Zhang, S., Feng, L., Liu, Z., 2011. Photothermally enhanced photodynamic therapy delivered by nano-graphene oxide. ACS. Nano. 5 (9), 7000–7009.
Xie, H., Cao, T., Franco-Obregón, A., Rosa, V., 2019. Graphene-induced osteogenic differentiation is mediated by the integrin/FAK axis. Int. J. Mol. Sci. 20 (3), 574.
Yang, K., Feng, L., Shi, X., Liu, Z., 2013. Nano-graphene in biomedicine: theranostic applications. Chem. Soc. Rev. 42 (2), 530–547.
Zeng, Y., Pei, X., Yang, S., Qin, H., Cai, H., Hu, S., Sui, L.e., Wan, Q., Wang, J., 2016. Graphene oxide/hydroxyapatite composite coatings fabricated by electrochemical deposition. Surf. Coat. Technol. 286, 72–79.
Zhou, D., Cui, Y., Han, B., 2012. Graphene-based hybrid materials and their applications in energy storage and conversion. Chin. Sci. Bull. 57, 2983–2994.
Zhou, Y., Wang, G., Wang, T., Wang, J., Wen, X., Sun, H., Yu, L., Liu, X., Zhang, J., Zhou, Q., Sun, Y., 2022. Multidynamic osteogenic differentiation by effective polydopamine micro-arc oxide manipulations. Int. J. Nanomed. 4773–4790.