

Review



# Nanocomposites for Enhanced Osseointegration of Dental and Orthopedic Implants Revisited: Surface Functionalization by Carbon Nanomaterial Coatings

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Abstract: Over the past few decades, carbon nanomaterials, including carbon nanofibers, nanocrystalline diamonds, fullerenes, carbon nanotubes, carbon nanodots, and graphene and its derivatives, have gained the attention of bioengineers and medical researchers as they possess extraordinary physicochemical, mechanical, thermal, and electrical properties. Recently, surface functionalization with carbon nanomaterials in dental and orthopedic implants has emerged as a novel strategy for reinforcement and as a bioactive cue due to their potential for osseointegration. Numerous developments in fabrication and biological studies of carbon nanostructures have provided various novel opportunities to expand their application to hard tissue regeneration and restoration. In this minireview, the recent research trends in surface functionalization of orthopedic and dental implants with coating carbon nanomaterials are summarized. In addition, some seminal methodologies for physicomechanical and electrochemical coatings are discussed. In conclusion, it is shown that further development of surface functionalization with carbon nanomaterials may provide innovative results with clinical potential for improved osseointegration after implantation.

Keywords: carbon nanomaterials; coating; surface functionalization; osseointegration; implants

# 1. Introduction

To date, metal-based dental and orthopedic implant materials, including titanium (Ti), stainless steel, and cobalt-chromium (CoCr), have been widely used because of their suitable properties, such as high mechanical strength, light-weight chemical stability, and nonimmunogenic property. For successful implantation of orthopedic and dental implants, biometric stability immediately after implant insertion is one of the most important steps. Despite the wide clinical utilization of Ti implants, there are still potential risks because of the inherent bioinert and easily oxidizable characteristics. For example, the oxide layer of the surface of Ti often leads to thrombosis between the surface and surrounding tissue, which creates an oral cavity that promotes microbial reproduction [1,2]. Moreover, during the operation, inflammation around the surgical sites may occur due to external heat or pressure. This hinders the normal growth of new bone around the surgical sites and results in weak bonding between the bone and implant [3-5]. The risk of implantation failure rises particularly rapidly in the elderly, who have decreased bone mass and a degraded microstructure of bone tissue caused by senile disorders, such as diabetes and osteoporosis, resulting in fragile bone tissue. Recent studies have focused on surface functionalization by endowing implants' biofunctionalities for the reduction of surgery failure. The above problems can be solved by improving the surface properties of implant materials. Therefore, various surface functionalization methods have been extensively employed to enhance the biofunctionality of implants (Figure 1).



Citation: Kang, M.S.; Lee, J.H.; Hong, S.W.; Lee, J.H.; Han, D.-W. Nanocomposites for Enhanced Osseointegration of Dental and Orthopedic Implants Revisited: Surface Functionalization by Carbon Nanomaterial Coatings. *J. Compos. Sci.* 2021, *5*, 23. https://doi.org/ 10.3390/jcs5010023

Received: 28 December 2020 Accepted: 10 January 2021 Published: 14 January 2021

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**Figure 1.** Surface functionalization with carbon nanomaterials (CNMs) containing carbon nanofibers (CNFs), graphene, carbon nanotubes (CNTs), nanocrystalline diamond (ND), carbon nanodots (CNDs), and fullerene.

Surface functionalization is a powerful tool for the alteration of physicochemical properties of implant surface that allows preferred bioactivity and reduced adverse effects to be achieved. Growth factors and inducers have been administered to promote osteogenesis; however, they are complicated, expensive to produce, and easily degraded in vivo [6]. Significant advances have been made in surface functionalization by adopting a vast area of materials that endow substrates with specific characteristics (e.g., polymers and inorganics) [7,8]. Nanomaterial (NM)-based coatings in particular offer several advantages: (a) tunable micron/nanometer-sized multiporous topography, (b) high specific surface area, (c) unique cell–matrix interaction, and (d) mechanical reinforcement. These regulate bone cell behaviors and improve mechanical properties. Furthermore, it is important to pursue stable and long-lasting coating layers to confer bioactive (i.e., osteoconductive and osteogenic) properties in vivo. Therefore, many novel strategies have been introduced to achieve robust and stable coatings as described herein.

Carbon nanomaterials (CNMs) are some of the most important members of the NM family. The discovery and emergence of CNMs have impacted many aspects of nanotechnology and have contributed to significant developments in physics, electronics, optics, mechanics, biology, and medicine. Many CNMs have gained increasing attention in the biomedical field due to their extraordinary characteristics. For example, fullerenes and carbon nanotubes (CNTs) have been widely studied for numerous therapeutic and pharmaceutical purposes [9–11]. Moreover, other CNMs like graphene and nanocrystalline diamond (ND) have become popular in the past decade due to the maturation of various fabrication and modification techniques [12–14]. CNMs in particular have been shown to be capable of facilitating cellular behaviors such as adhesion; migration; proliferation; and differentiation into several lineages, including myogenesis, neuritogenesis, and osteogenesis [15–20]. Therefore, various CNMs, such as graphene, CNTs, ND, carbon nanofibers (CNFs), fullerene, and carbon nanodots (CNDs), have been considered to posses excellent potential for surface functionalization materials of implants due to their osteogenesis-inducing property and mechanical reinforcement property.

Herein, we focus on CNM-based surface modification on orthopedic and dental implants. Surface modification is conducted by various types of physicochemical coating techniques, such as plasma spray, physical adsorption, dip coating, spin coating, electrophoretic deposition, electrochemical deposition, chemical vapor deposition, and various other novel techniques. Certain techniques combine multiple physical and chemical processes; therefore, this review determines the coating techniques based on the main idea of each study due to the difficulty of strict separation. Furthermore, this review concentrates on osteogenesis/osseointegration-inducing properties and antibacterial effects achieved from CNM-based coatings on orthopedic and dental implants. A comprehensive evaluation of surface coating methods and improved biofunctionalities is provided along with their pros and cons (Table 1). **Table 1.** Recent studies on CNM-based coatings for orthopedic and dental implants are classified by the coating method, kind of CNM, conjugation, coating quality, biological evaluation, and osteogenic and antibacterial activities.

Clarification	Coating Method	CNM	Conjugation	Coating Quality (Features and Process Rate)	<b>Biological Evaluation</b>	Osteogenic and Antibacterial Activities	Ref.
Physicomechanical Method	Plasma spraying	CNT	НАр	FDA-approved method and commonly used	In vivo (rat and mouse)	Newly grown bone, no periosteal reactions, and restoration of healthy osteoblast and osteocyte	[21]
		Graphene	CS		In vivo (rabbit)	Newly grown bone cover pores in interface	[22]
	Ultrasonic atomization spraying	GO	-	Retains original particle structure; thin and uniform layer	In vitro (BM-MSC) and in vivo (rat)	Increased cell adhesion, proliferation, and osteogenic markers; in vivo osseointegration	[23]
	Dip coating	ND	-	Simple, fast, and cost-effective	In vitro (NHDF and calvariae primary osteoblast)	Enhanced cell growth; inhibition of <i>Staphylococcus aureus</i> colonization	[24]
		MWCNT	Collagen		In vitro (MSC)	Increased proliferation and ALP activity	[25]
	Spin coating	GO	Chitosan	Fast process rate and simple process	In vitro (MC3T3-E1) and in vivo (rat)	Antibacterial effect on <i>Streptococcus</i> <i>mutans</i> ; enhanced cell proliferation Enhanced cell viability and adhesion; formation of collagen type I and new bone	[26]
		rGO	Dex, AA		In vitro (MC3T3-E1) and in vivo (rat)		[27]
	MDD	GO	-	Transparent coating by precise control in nanometer scale	In vitro (MC3T3-E1) and in vivo (rat)	Enhanced proliferation and ALP activity; new bone formation	[28]

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Clarification	Coating Method	CNM	Conjugation	Coating Quality (Features and Process Rate)	<b>Biological Evaluation</b>	Osteogenic and Antibacterial Activities	Ref.
Electrochemical Method	EPD	GOMA	PBA functionalization GelMA-PBA	High versatility and cost-effectiveness; uniform coating on a porous and complex-shaped substrate with easy accessibility and low cost of equipment	In vitro (osteoblast from rat calvaria)	Enhanced cell viability, proliferation, mineralization, collagen secretion, ALP activity, and osteogenic-relative gene expression; antibacterial effect on <i>Pseudomonas geruginosa</i> and <i>S. gureus</i>	[29]
		rGO	CS		In vitro (hFOB)	Increased cell viability	[30]
		CNF	HAp, PCL		In vitro (MG63) and in vivo (rat)	Antibacterial effect on <i>S. aureus</i> and <i>Escherichia coli;</i> enhanced proliferation and ALP activity Antibacterial effect <i>on S. aureus;</i> enhanced proliferation and ALP activity	[31]
		GO	Chitosan, HAp		In vitro (MG63)		[32]
		GO	Chitosan, HAp		In vitro (BM-MSC) and in vivo (rat)	Improved proliferation and differentiation; improved in vivo osseointegration	[33]
	ECD	GO	НАр	Low process temperature; coating on geometrically	In vitro (MG63)	Enhanced proliferation and ALP activity	[34]
		SWCNT	НАр	complex surface; controllable coating properties; low cost of equipment	In vitro (human osteoblast)	Enhanced proliferation and ALP activity	[35]
	MW-PACVD	ND	НАр	Dense and homogeneous coating; varying crystalline structure;	In vitro (hMSC)	Enhanced proliferation and ALP activity	[36]
		ND	-	ultrahardness with a very low friction coefficient, chemical inertness, impermeability of the carbon coating, and highly resistant corrosion and erosion processes	In vivo (pig)	Enhanced bone-to-implant contact (BIC)	[37]

Table 1. Cont.							
Clarification	Coating Method	CNM	Conjugation	Coating Quality (Features and Process Rate)	<b>Biological Evaluation</b>	Osteogenic and Antibacterial Activities	Ref.
Electrochemical Method	Spraying and in situ crosslinking	MWCNT	-	Facile, cheap, and scalable	In vitro (ADSC)	-	[38]
	Chemical spray pyrolysis	MWCNT	Silver, HAp	Uniform deposition rate at low temperature; pure and reproducible; mass productivity	In vivo (human osteoblast)	Antibacterial property on E. coli, Shigella flexeri, S. aureus, and Bacillus subtilis	[39]
	Alkali hydrothermal reaction and silane coupling; APTES conjugation	GO	Aspirin	Stable bonding; the feasibility of functionalization	In vitro (MC3T3-E1)	Enhanced proliferation and ALP activity	[40]
	Chemical assembly	GO	Dopamine	Uniform coating on any shape or structure	In vitro (BM-MSC) and in vivo (rabbit)	Improved cell viability, ALP activity, and mineralization; improved in vivo osseointegration	[41]

CNT, carbon nanotube; HAp, hydroxyapatite; CS, calcium silicate; GO, graphene oxide; MSC, mesenchymal stem cell; BM-MSC, bone marrow-derived MSC; ND, nanocrystalline diamond; MWCNT, multiwalled CNT; NHDF, normal human dermal fibroblast; ALP, alkaline phosphatase; rGO, reduced GO; Dex, dexamethasone; AA, ascorbic acid; MDD, meniscus-dragging deposition; EPD, electrophoresis deposition; GOMA, methacryloyl GO; CNF, carbon nanofiber; PBA, phenylboronic acid; GelMA, methacryloyl gelatin; PCL, polycaprolactone; ECD, electrochemical deposition; SWCNT, single-walled CNT; MW-PACVD, microwave plasma-assisted chemical vapor deposition; hMSC, human MSC; ADSC, adipose-derived SC; APTES, (3-aminopropyl)triethoxysilane; FDA, US Food and Drug Administration.

#### 2. Physicomechanical Coating

The main idea of physicomechanical modification is to induce the physical adsorption of CNMs on implant surfaces by plasma spraying, gas or vapor radiation, solution treatment, or desorption, or by using mechanical methods such as roughening and micromanipulation. Most of the physical modification methods feature advantages such as a short processing time, simple equipment, and no preference for the intrinsic properties of the implant material. However, several disadvantages exist, including inhomogeneity, weak bonding and wear resistance, and difficulty to coat the inner surface of small holes.

Hydroxyapatite (HAp) is used as a coating material for Ti implants due to its osteoinduction and biocompatible pCSroperty [42,43]. However, neat HAp is mechanically disadvantageous as it exhibits poor wear resistance and fracture toughness [44]. Therefore, it is not possible to solve post-transplant side effects such as arthroplasty prostheses loosening with HAp-coated implants [45–47]. However, CNMs' great potential for mechanical reinforcement of brittle HAp presents a way to overcome this issue. CNT has been extensively applied as reinforcement to enhance weak mechanical characteristics of ceramics such as HAp and  $Al_2O_3$  as well as to facilitate osteoinduction [48]. Plasma spraying is a physical vapor deposition technique that uses high-velocity spraying of molten powder onto an implant surface [49]. Plasma spraying is the only US Food and Drug Administration (FDA)-approved implant coating method and forms a dense and adherent coating on implant surfaces [50]. Balani et al. and Lahini et al. proved that plasma spraying of CNT-HAp on the surface of Ti improves fracture toughness and wear resistance [51,52]. Facca et al. plasma sprayed CNT-reinforced HAp on the surface of titanium and confirmed enhanced mechanical and osteoinduction properties (Figure 2) [21]. Because there is a limited number of reports exploring in vivo responses of HAp-CNT-coated implants, this study focused on the in vivo response of implants embedded in rats and mice. The results indicated that incorporated CNT did not induce adverse or cytotoxic events, and normal bone growth was observed around the HAp-CNT-coated implant. Interestingly, the addition of CNT significantly increased new bone formation when compared to bare HAp-coated implants. The elastic modulus of the newly formed bone was similar to that of the distant bone, suggesting excellent integrity of the implant and bone. Similarly, Xie et al. plasma coated graphene-reinforced calcium silicate (CS) on a Ti implant and evaluated coating quality and in vivo osseointegration [22]. The graphene and CS were evenly coated on the surface of Ti, and the incorporated graphene enhanced the wetting behavior and wear properties via the formation of interfacial bonding between the CS particles. Moreover, in vivo experiments indicated that graphene did not hinder the biocompatibility and significantly increased the bone-implant contact ratio after three months of implantation when compared to the bare CS coating. On the other hand, ultrasonic atomic spraying is a physical coating method that enables thin coating of high performance and quality with accurate control of process parameters [53]. Li et al. fabricated a graphene oxide (GO)-coated Ti implant and evaluated the feasibility of coating quality and osteogenesis-inducing ability [23]. Ultrasonic atomic spraying retained the original structure of GO and deposited a thin and uniform layer on Ti substrate. Osteogenic differentiation of seeded bone marrow-derived mesenchymal stem cells (BM-MSCs) was characterized by upregulated osteogenic markers containing alkaline phosphatase (ALP), runt-related transcription factor 2 (RUNX2), osteocalcin (OCN), and osteopontin (OPN). The paper analyzed the mechanism of osteogenesis of BM-MSCs by Western blotting of cytoskeletal proteins. GO stimulated expression of the focal adhesion kinase (FAK) and mitogen-activated protein kinase (MARK) signaling pathways related to extracellular-signal-regulated kinase (ERK)1/2, P38, and c-Jun N-terminal kinase (JNK), and several osteogenic markers were then upregulated in a cascade. This suggests that the formation of focal adhesion between stem cells and GO induces spontaneous osteogenic differentiation, which leads to increased osseointegration in vivo.

NDs are reported to have feasibility for surface functionalization, excellent biocompatibility, osseointegration-promoting capability, and antibacterial effect; hence, they have gained tremendous interest as implant coating materials [54–56]. However, ND coating on three-dimensional structures with high coverage and uniformity has been considered to be difficult because the fabrication parameters have considerable effects on adherence, morphology, and uniformity of NDs [57,58]. Dip coating is widely applied for the deposition of NDs on the implant surface due to its simplicity and effectiveness. Rufai et al. fabricated an ND-coated Ti implant with the dip coating method and evaluated osteogenic and antibacterial properties [24]. Ti implant was dipped perpendicularly into an NDcontaining solution and immersed for ND deposition, and it thereafter formed a stable and uniform NM coating layer on the surface of Ti. As the ND coverage area increased, the cell population of normal human dermal fibroblasts and osteoblasts also increased. Moreover, most ND-covered Ti implants showed significantly decreased growth and adhesion of S. *aureus*. These results suggest that ND can be efficiently coated on the surface of Ti by the dip coating method and that it a has dose-dependent osteogenesis-promoting effect and antibacterial ability. On the other hand, CNT possesses superior electrical, thermal, and mechanical properties and bioactivity [59,60]. Collagen is the most abundant extracellular matrix protein, and it is known to promote cell adhesion and growth [61,62]. Another study conducted by Park et al. introduced multiwalled CNT (MWCNT)-collagen coating on the surface of Ti with the dip coating method [25]. The coated CNT-collagen formed stable bonding with the surface of Ti and enhanced surface roughness to facilitate cell adhesion. The CNT-collagen coating enhanced surface roughness, cell adhesion, and proliferation. Moreover, the osteogenic property of CNT significantly enhanced the ALP activity of preosteoblasts after five days of culture.



**Figure 2.** HAp/CNT-coated implant showing (**A**) a spherical Ti bead, (**B**) a Ti road, and (**C**) the top surface of the plasma-sprayed HAp-CNT coating with embedded CNTs in HAp. (**D**) X-ray images of rat femoral bones after one-month implantation showing (1) an uncoated Ti implant, (2) an HAp-coated Ti implant, (3) an HA-CNT-coated implant, and (4) no implant. (**E**–**H**) Histological results ( $40 \times$ ) for mice bones that were implanted with an HA-CNT-coated implant fabricated as (**E**,**F**) spherical beads and (**G**,**H**) a rod-shaped implant. (**E**,**G**) Mallory coloration images and (**F**,**H**) hematoxylin and eosin coloration images. Copyright © 2011 American Chemical Society, Reference [21].

Spin coating is a common technique for synthesizing thin film with a thickness ranging from a few microns to nanometers by spinning a material-containing solution at high speed so that centripetal force and surface tension of the liquid produce uniformly coated materials [63–65]. The spin coating features a fast process rate and simple process, but it also has several disadvantages for NM coating, namely, low coating performance in general and waste of material [63]. Park et al. developed a GO–chitosan-coated Ti implant with the spin coating method [26]. The coated GO and chitosan enhanced hydrophilicity and surface roughness of Ti implant, which are beneficial for cell adhesion and migration. As the GO concentration increased, the proliferation of preosteoblasts and antibacterial effect on *S. mutans* significantly increased, suggesting that the GO coating can enhance the osseointegration property of Ti implant. Meanwhile, Jung et al. enhanced the spin coating to induce electrostatic bonding of reduced GO (rGO) on the surface of Ti [27]. A uniform and dense coating was built between the outer titanium oxide layer and the rGO layer. The

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outer rGO layer enhanced the loading capacity of osteogenic factors, dexamethasone, and ascorbic acid by forming  $\pi$ – $\pi$  stacking, which induced increased preosteoblast adhesion. The in vivo analysis showed that the Dex/rGO-Ti implant induced new compact bone regeneration in the entire region around the implant. Moreover, collagen type I, which is the main component of the bone matrix, was formed around the implant, indicating excellent feasibility of osseointegration.

The meniscus-dragging deposition (MDD) technique mechanically spreads the material over the substrate with the linear back-and-forth motion of the deposition plate [66]. MDD has the advantages of easy and precise control of optoelectronic properties and coating thickness by simply varying the particle concentration and deposition number [67]. Park et al. introduced an osteogenesis-inducing GO/Ti implant by coating GO nanoparticles on a Ti membrane with the MDD technique. GO coating increased surface roughness and hydrophilicity with their hydrophilic moieties. As a result, proliferation and ALP activity of preosteoblasts were improved. Moreover, an in vivo assay showed an increase in new bone formation due to GO coating of Ti implant in rat calvaria, suggesting that the GO-coated layer was stable in the body and induced osseointegration of Ti implant.

## 3. Electrochemical Coating

Electrochemical modification changes the chemical properties of the carrier surface to produce specific interactions between cell surface molecules, which not only affect the cell surface properties but also cause closely related changes in the internal structure and function of cells. Chemical modifiers are relatively complex in process and are expensive. Current research focuses on composition control, multilayer structure design, multiscale coatings, and coatings with novel surface morphologies.

Electrophoresis deposition (EPD) uses an electric field to move the stable charged particle in the colloidal suspension to an oppositely charged conductive substrate. EPD features several advantages, such as a wide range of material choices, compact coating with thickness control from nanometers to microns, and a short process rate due to the simple apparatus [68]. Therefore, many studies use EPD to coat CNMs on implant surfaces. CS is one of the bioactive ceramics that have various excellent properties, such as osteoconductivity, osteoinductivity, and bioactivity, and previous studies have shown that CS coating on Ti implants has potential for osseointegration by inducing a bone-like apatite layer on the surface [69–71]. However, Liu et al. reported that the purity of CS can be altered after applying a conventional coating method, such as plasma spraying [72]. Meanwhile, a considerable amount of research has shown the feasibility of EPD to deposit CS on the surface of Ti [73,74]. Meharali et al. introduced an EPD-based rGO/CS coating on Ti substrate to enhance the biological and mechanical properties [30]. Compared to the pure CS coating, the 1 wt % rGO-decorated CS coating improved the mechanical property of Ti implant, which showed enhanced adhesion by 70%, hardness by 150%, and elastic modulus by 240%. Furthermore, the rGO/CS-coated Ti implant showed good apatite-forming ability in simulated body fluid with suitable cytocompatibility to hFOB cells, suggesting that CS-rGO might be a promising implant coating material. In another study conducted by Shi et al., a GO/chitosan/HA composite was coated on Ti substrate via EPD [32]. The coated layer increased corrosion resistance and was thermally stable. MG63 cells exhibited suitable viability and increased ALP activity on the rGO-chitosan-HA-composite-coated Ti. Moreover, GO-chitosan-HA showed effective antibacterial adhesion by endowing negative charges and physical stress to the bacterial membrane in order to induce membrane damage. A similar study conducted by Suo et al. adopted GO/chitosan/HAp composite coating on Ti substrate [33]. The interaction between GO, chitosan, and HAp induced dense coating on the surface of Ti by reducing the surface cracks with a bonding strength of  $27.1 \pm 1.2$ MPa. Cell viability, ALP activity, and calcium deposition of BM-MSCs were significantly improved on the GO/CS/HAp coating. Moreover, fluorescence staining and polymerase chain reaction analysis (qPCR) showed upregulated expression of osteocalcin and osteopontin, which are representative osteogenic regulation factors. The in vivo study demonstrated

that the GO/chitosan/HAp-coated implant showed superior new bone formation and maintained its mechanical property after 12 weeks of implantation. These results suggest that EPD represents a powerful method for deposition of GO/chitosan/HAp composite coatings on Ti implants, and this coating may be applied in the field of dental implants.

Electrochemical deposition (ECD) is used to fabricate a tight adherent coating on the conductor substrate by electrolysis of the solution containing the coating material, including metal ion or a chemical complex. ECD has several advantages, such as uniform coating on a porous and complex-shaped substrate with easy accessibility, low cost of equipment, low process temperature, and controllable coating properties (Figure 3) [28,31]. Zeng et al. introduced GO/HAp composite coating on Ti substrate with the ECD technique [34]. The composite coating exhibited enhanced crystallinity and a bonding strength of  $25.4 \pm 1.4$  MPa after GO was incorporated. Moreover, GO and HAp facilitated proliferation and the early stage of osteogenesis of MG63 cells, revealing that utilization of the ECD-coated GO/HAp layer is a promising strategy for the production of Ti implant coatings for clinical application. In another study conducted by Elangomannan et al., CNF/PCL/HAp nanofibrous coating layer deposited by ECD on a Ti implant were prepared. [31]. CNF is a stack of nanocones of graphitic nanosheets that is known for exceptional electrical, mechanical, thermal, and structural properties. Notably, the topography of CNF can mimic the inorganic HAp crystal of bone when embedded for reinforcement of the matrix [75,76]. The nanofibrous membrane has a multiporous structure, which would be beneficial for adhesion and migration of surrounding cells due to the similar structure of natural extracellular matrices. The results indicate that incorporation of CNF into the PCL/HAp composite significantly improves the adhesion strength and elastic modulus of the Ti substrate. The incorporation of CNF particularly enhanced corrosion resistance of the implant, which was determined by a positive shift in polarization curves.



**Figure 3.** (**A**) Formation of a nanofibrous layer composed of CNF/polycaprolactone (PCL)/mineralized HAp (M-HAp) on Ti; (**B**) photographs of the zone of inhibition on 2 wt % CNF/PCL/M-HAp at different volume concentrations; (**C**,**D**) antibacterial effects on *S. aureus* and *E. coli* according to CNF concentration, respectively; (**E**) live/dead assay of MG63 cells cultured on control and 2 wt % CNF/PCL/M-HAp-coated Ti substrates; (**F**) toluidine blue-stained sections from the uncoated Ti group I (1,2), PCL/M-HAP-coated Ti group II (3,4), and 2 wt % CNF/PCL/M-HAP composite-coated Ti group III (5,6), taken after two and four weeks of implantation. Copyrights © 2017 American Chemical Society, Reference [31].

The basic principle of chemical vapor deposition (CVD) is to inject coating material to be deposited on a substrate as a gaseous state through high-temperature decomposition or high-temperature chemical reaction on the substrate in the reaction chamber. Microwave plasma CVD (MPCVD) is one of the most commonly used CVD processes that initiate a chemical reaction with microwave plasma. MPCVD enables nucleation and growth of various types of CNMs, including graphene, CND, and CNT with the bulk carbon source [77–79]. The carbon source for MPCVD is not limited to graphite; for example,

Elliot et al. reported the use of CO<sub>2</sub> with CH<sub>4</sub> in MPCVD to synthesize diamond films, and Krishnia et al. produced a diamond film from sugarcane bagasse, which is a secondary product of the sugarcane industry, and they also produced carbon sources, including glucose and CH<sub>4</sub> [80,81]. Strakowska et al. developed conductive boron-doped ND coatings on Ti5Al4V substrate with the MPCVD technique, which enabled efficient ECD of HAp to form ND/HAp bilayer coatings [33]. ND/HAp formed a homogeneous and dense layer with regular submicron topography on the Ti5Al4V implants. The in vitro cell assays showed favorable cell viability and osteoconductivity of the ND/HAp coating layer to seeded human MSCs. Metzler et al. also prepared an ND-coated TiAl6V4 implant by MPCVD for a histomorphometric study of pigs [37]. The in vivo results indicated that newly developed bone integration showed close contact within the implant grooves of the mature bone with the ND-coated surface. Interestingly, ND-coated TiAl6V4 showed enhanced bone-to-implant contact when compared to bare TiAl6V4 after two and five months of implantation. Moreover, the MPCVD-coated ND layer showed a tight interface between the implant and newly formed bone without any delamination or particle dissociation, indicating the advantages of this coating method.

Excluding the previously described coating methods, various other types of electrochemical coatings have been applied. Sivaraj et al. fabricated Ag-HAp/MWCNT nanosheets on a 316L stainless steel implant with chemical spray pyrolysis, which offers many advantages, such as a uniform deposition rate, low processing temperature, high purity, and mass productivity with reproducibility [39]. SEM microscopy demonstrated that Ag-HAp/MWCNT coatings showed desirable and crack-free morphology with a particle size of less than 100 nm. Notably, incorporated Ag showed efficient antibacterial activity against S. aureus, Providencia stuartii, E. coli, and Klebsiella pneumonia. Furthermore, the addition of MWCNT, a reinforcing material, enhanced the corrosion resistance. Another study conducted by Ren et al. employed alkali hydrothermal reaction and a silane-coupling agent to fabricate an aspirin-loaded GO coating on the surface of Ti [40]. GO was conjugated with the APTES-modified Ti surface, and aspirin was loaded onto the Ti-GO surface via  $\pi$ - $\pi$  stacking. The incorporation of aspirin, which is a nonsteroidal anti-inflammatory drug, and the cyclooxygenase-2 (COX-2) inhibitor can relieve initial aches from bone fractures and orthopedic postoperative pain due to its thrombosis prevention and anti-inflammation abilities as well its various chemotactic abilities [82–84]. The torsion test indicated that the GO–Ti interface had stable bonding strength at a torque of 9.48 Nm. The in vitro cell studies revealed that the aspirin/GO-Ti substrate promoted proliferation and osteogenic differentiation of the preosteoblast, suggesting its potential for further clinical applications in patients with postimplantation pains. On the other hand, chemical assembly features uniformly distributed GO coating on the complex-shaped surface. Taking into account the weak bonding strength of GO, Wang et al. introduced APTES and dopamine as an intermediate layer for bioactive coating on the microgrooved Ti–6Al–4V implant [41]. The GO-coated layer showed excellent adhesion on the implant surface and facilitated adhesion and proliferation of BM-MSCs. Moreover, the osteoinduction ability of GO induced spontaneous osteogenesis of BM-MSCs and enhanced osseointegration and new bone formation in vivo.

### 4. Conclusions and Future Perspectives

Vigorous research that interfaces these new carbon forms with orthopedics has laid the foundation for utilizing carbon nanostructures as coatings for dental and orthopedic implants and bone tissue engineering scaffolds [85,86]. The physicochemical property, mechanical enhancement, biocompatibility osteogenesis, and osseointegration in relation to the material characteristics and fabrication methods have been discussed. Moreover, from the results described herein, the surface functionalization methodology, mechanical stability, biocompatibility, and osteoinduction properties were significantly improved by introducing several novel strategies, including material composition and combination of several types of coating methods. In this minireview, various methodologies and recent research trends in surface functionalization of orthopedic and dental implants using carbon nanomaterial are summarized. Although the exploration of carbon nanoscience in the field is affirmative, the intrinsic toxicity and safety, large-scale manufacturing, and in vivo applications are still controversial. However, it is shown that further development of surface functionalization with carbon nanomaterials may soon provide revolutionary changes to dental and orthopedic implants.

**Author Contributions:** Conceptualization, D.-W.H. and J.H.L. (Jong Hun Lee); writing—original draft preparation M.S.K., J.H.L. (Jong Ho Lee), and S.W.H.; project administration, D.-W.H. and J.H.L. (Jong Ho Lee); funding acquisition, D.-W.H. All authors have read and agreed to the published version of the manuscript.

**Funding:** This work was supported by a National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. 2016R1D1A1B03931076 and 2019R1A4A1024116) and a Korea Evaluation Institute of Industrial Technology (KEIT) grant funded by the Ministry of Trade, Industry, and Energy (MOTIE, Korea) (No. 20002010).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data is contained within the article.

**Conflicts of Interest:** The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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