

Review

Therapeutic Potential of 3D-Printed Alloys as Drug-Eluting Implants: Current Progress

Shubhangi Das ¹, Louise Carson ² and Chi-Wai Chan ^{1,*}¹ School of Mechanical and Aerospace Engineering, Queen's University Belfast, Belfast BT9 5AH, UK; sdas07@qub.ac.uk² School of Pharmacy, Queen's University Belfast, Belfast BT9 7BL, UK; l.carson@qub.ac.uk

* Correspondence: c.w.chan@qub.ac.uk

Abstract

In physiological environments, several metallic alloys, including titanium, stainless steel, cobalt–chromium, and emerging biodegradable systems such as magnesium (Mg), zinc (Zn), and iron (Fe), offer mechanical properties and biocompatibility suitable for load-bearing implants. With the rapid advancement of 3D printing technologies, these alloys can now be fabricated into patient-specific, complex geometries that enhance both structural performance and functional integration. Beyond serving as structural supports, 3D-printed alloys are increasingly engineered as localized drug-delivery platforms to release anti-inflammatory, antibacterial, anticancer, and osteogenic agents at the implant–tissue interface, addressing the dual clinical needs of site-specific therapy and mechanical stabilization. Nevertheless, this field remains underexplored because studies differ widely in alloy chemistry, surface topography, porosity, coating strategy, drug-loading methods, and release profiles, as well as in how material degradation or passivation interacts with pharmacokinetics. For the first time, this review consolidates drug-loading and elution strategies across 3D-printed alloy platforms, compares therapeutic categories in relation to alloy and coating types, and critically evaluates how the surface microstructure or alloy geometry influences release behavior.

Keywords: 3D-printed metallic implants; drug-eluting coatings; titanium alloys (Ti-6Al-4V); biodegradable magnesium alloys; local drug delivery; release kinetics

1. Introduction

Biomedical implants are essential in musculoskeletal, dental, and cardiovascular treatment, where durable mechanical support must align with demanding biocompatibility and clinical precision [1,2]. However, even fully functional implants encounter clinical difficulties such as biofilm-mediated infections, postoperative inflammation that delays healing, and the poor efficacy of systemic drug delivery, which often fails to sustain therapeutic concentrations at the implant–tissue interface without inducing unwanted toxicity. These gaps drive the development of drug-eluting implants, which are devices that provide significant local dosages when and where they are required while limiting systemic exposure [3–5].

Metallic implants made by casting, forging, or machining have been the backbone for load-bearing applications for decades, since they are durable, resistant to wear and tear, and have been shown to be effective in clinical settings. These traditional methods limit osseointegration, customization to individual patients, and the integration of functional



Academic Editor: Damien Fabrègue

Received: 19 November 2025

Revised: 16 December 2025

Accepted: 17 December 2025

Published: 24 December 2025

Copyright: © 2025 by the authors.

Licensee MDPI, Basel, Switzerland.

This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution \(CC BY\)](https://creativecommons.org/licenses/by/4.0/) license.

subsystems such as drug reservoirs [6–8]. Additive manufacturing (AM) overcomes these traditional limitations and enables new therapeutic capabilities by fabricating complex lattices with controlled porosity and patient-specific geometry that are difficult to produce via casting or machining [9–12]. AM offers more than just geometric freedom; it also allows for control over pore size, structure thickness, and surface texture. These are design variables that connect local mechanics, tissue ingrowth, and fluid transport to therapeutic function, effectively linking geometry to drug kinetics [13,14].

In various alloy groups, this design flexibility transforms “shape” into a therapeutic variable. Orthopedic and dental applications are dominated by titanium (Ti) alloys such as Ti-6Al-4V and β -Ti because they have a high specific strength and stable TiO₂ passivation [15–17]. Stainless steel 316L (SS316L) and cobalt–chromium alloys are still important for fixing trauma, making dental prosthetics, and making cardiovascular devices because they are strong, resistant to corrosion, and easy to fabricate [6,9,18,19]. On the other hand, degradable metals like magnesium (Mg), zinc (Zn), and iron (Fe) are becoming more popular for temporary implants, where controlled corrosion eradicates the need for secondary removal surgery, and have bioactive benefits. In this context, laser powder bed fusion (LPBF), electron beam melting (EBM), and directed-energy deposition (DED) are widely employed to fabricate lattices with customized stiffness, strength, and permeability, thereby generating internal surface areas and pore networks that can function as drug deliverers [17,20–24].

AM processing can add intrinsic features that lower fatigue and corrosion performance and make it easier for bacteria to thrive. These features include a lack of fusion and keyhole porosity from unstable melt pools or energy input, trapped gas porosity, partially melted particles, high roughness, micro-segregation, and residual stress [25,26]. Surface processing is what connects AM structure to drug delivery. Post-built surface modification reduces manufacturing flaws and creates drug-delivery interfaces that can be controlled. By adjusting the surface energy, chemistry, and micro/nano-texture, surface treatments control protein adsorption, host–cell responses, and release kinetics [27–35].

Surface-modification techniques such as micro/nano-texturing, anodic oxide nanotubes, plasma electrolytic oxidation (PEO/MAO), conversion coatings, and organic/inorganic thin films play several functions in this system: they create reservoirs and barriers that control drug/ion elution, and they also enhance corrosion/fatigue resistance and specify biological signaling [28,36–41]. On degradable metals, these layers control local corrosion, pH, and ion release. The thickness, cross-linking, and adhesion of the layers are approaches to changing the release routes [42].

AM structures are organized by mechanism instead of material name, and they support three different reservoir techniques. (i) Nano-topographic reservoirs, such as anodic TiO₂ nanotubes, have high-capacity nanochannels for small-molecule antibiotics. Without a barrier, they prefer a quick burst, but thin polymer caps (PLGA, chitosan) slow down early discharge to improve coverage. (ii) Ceramic/conversion layers made of MAO/PEO on Ti or Mg make micro- and nano-porous networks that protect the substrate and hold drugs and ions for diffusion-limited release over the course of a week. (iii) Polymer/hydrogel overlayers (PLGA, chitosan, gelatin, layer-by-layer films) tightly create complex lattices, enable single/multi-cargo loading (often via immersion, vacuum infiltration, electrostatic assembly, or encapsulated microspheres), and produce tunable “burst to tail” profiles via thickness and controlled cross-linking [43–47].

Now that we know how AM designs and surface treatments provide programmable reservoirs, the next step is to figure out which drug should be loaded and when. Antibiotics (vancomycin, gentamicin, minocycline, ciprofloxacin) inhibit early bacterial proliferation when local concentrations exceed the minimum inhibitory concentration (MIC), sealing nan-

otubes or incorporating chitosan/PLGA barriers reduces excessive bursts and extends coverage, with prolonged killing demonstrated in vitro and in vivo [48–52]. Anti-inflammatory drugs (e.g., corticosteroids) administered over days to weeks inhibit macrophage and pro-inflammatory signaling, potentially promoting osteogenic differentiation [53,54]. Pro-angiogenic and osteoinductive factors (VEGF, BMP-2, or VEGF + BMP-2) derived from coated porous titanium are associated with enhanced bone–implant contact and attachment [44,55,56]. Certain ions (Ag^+ , Cu^{2+} , Zn^{2+}) provide contact-killing or prolonged antibacterial effects, precise dosage maintains cytocompatibility, and certain ions (particularly Cu^{2+}) may promote osteogenesis [57–59].

Local delivery can achieve therapeutic concentrations at the implant–tissue interface while reducing systemic exposure, addressing the early postoperative infection window, and facilitating bone regeneration or tumor control in anatomically restricted locations [3–5]. But progress is not the same for all alloy chemistries, lattice geometries, and coating systems, and different studies report different elution kinetics, making the comparison of results difficult [60]. Because the dosage, burst, and sustainment windows must correspond with MICs, inflammatory cycles, and osteogenic timeframes, careful investigation of release behaviors across alloys and reservoir techniques is important [61–63]. The complete system is illustrated in Figure 1.

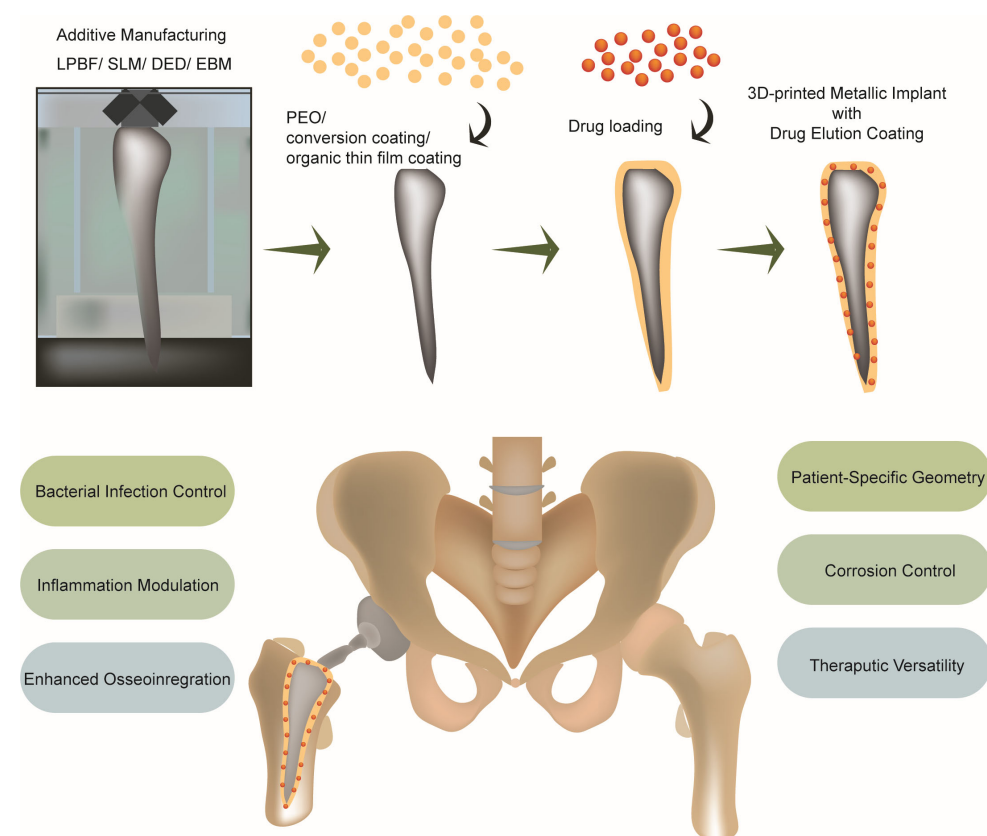


Figure 1. An overview of the design-to-outcome route for this evaluation.

These trends support a cross-alloy, design-led synthesis that connects AM architecture, such as porosity, tortuosity, and internal channels, and reservoir design, such as geometry-driven depots, nano-architectures, and coating-based systems, to drug-elution behavior across passive platforms, including Ti, 316L, and Co-Cr, and degradable platforms, including Mg, Zn, and Fe. The goals of this review are to first summarize additive-manufacturing routes and the key architectural design handles that control reservoir volume and mass transport. Second, it aims to classify and compare drug-loading strategies, including nano-

topographic reservoirs, ceramic and conversion layers, and polymer and hydrogel coatings, used on 3D-printed alloys. Third, it seeks to extract and compare reported release-kinetics metrics, including burst fraction, sustained duration, and model fits, and relate them to clinically relevant therapeutic windows for infection control, inflammation modulation, and osteogenesis or angiogenesis. Fourth, it synthesizes the in vitro and in vivo biological outcomes reported alongside these release profiles. Finally, it identifies translational gaps, particularly reproducible coating adhesion, standardized in situ release quantification, and maintenance of mechanical integrity, and proposes reporting and design recommendations for next-generation therapeutic implants.

2. Review Methodology

2.1. Bibliometric Search Strategy and Mapping Settings

A scoping bibliometric study in the Web of Science Core Collection was conducted to place this review in context. The focus was placed on drug-eluting devices made from 3D-printed metallic alloys. A total of 187 publications were identified by using a structured topic query that included AM techniques, alloy families, implant settings, and therapeutic keywords (Figure 2a).

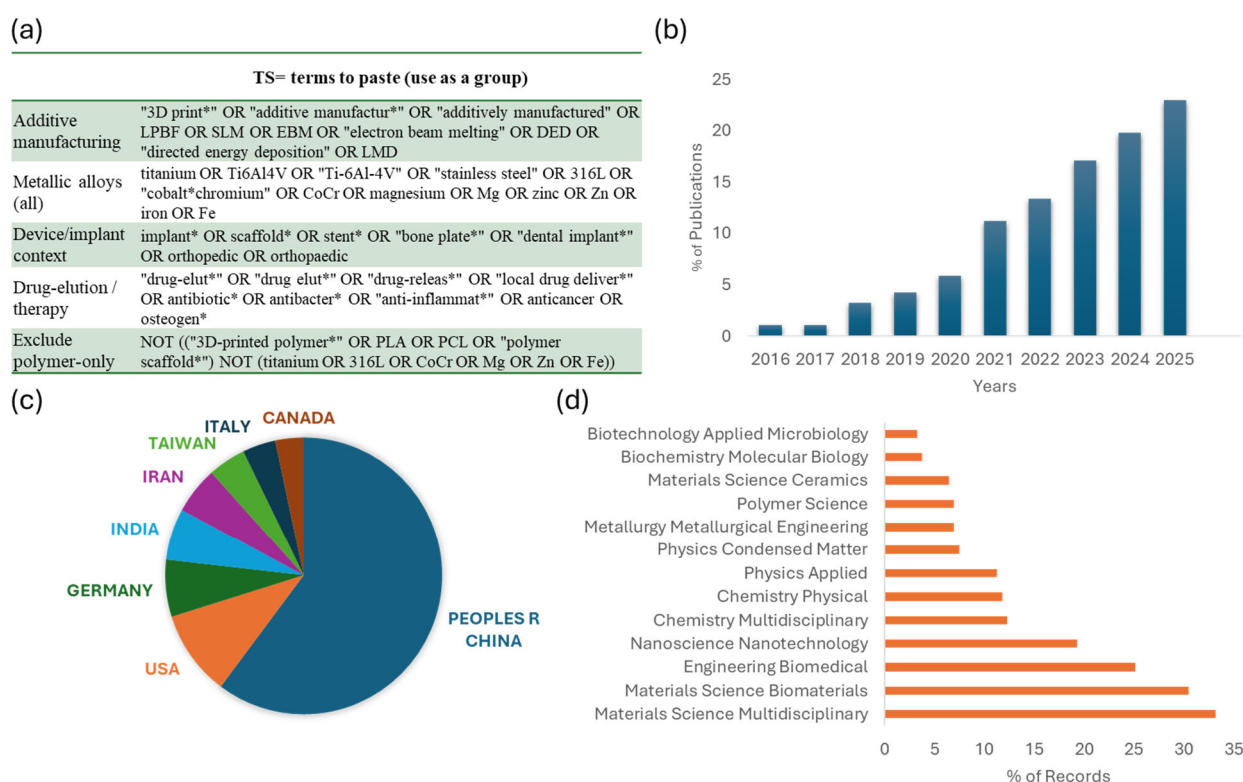


Figure 2. Current trend in drug-eluting 3D-printed metallic implants. (a) Concept blocks used in the topic (TS) search. (b) Annual publications (2016–2025). (c) Country/region contribution for the top producers (share of records). (d) Distribution by Web of Science categories (percentage of records). * denotes wildcard character in WoS searches.

Records were exported as tab-delimited Full Records and Cited References for further analysis. Using VOSviewer (version 1.6.20) for keyword co-occurrence mapping (complete counting, minimum occurrence = 2), 74 keywords were identified and grouped into nine clusters. Temporal shifts in phrasing were shown by an overlay visualization. The most salient keywords in the field were 3D printing/AM, Mg/Mg alloy, SS, Ti/Ti-6Al-4V, hydrox-yapatite, calcium phosphate/bioceramics, polycaprolactone (PCL)/polylactic acid (PLA), hydrogel, chitosan, vancomycin/antibacterial/anti-infection, graphene oxide, and copper.

The network was found to include 323 linkages, indicating extensive relationships between AM process terminology, alloy classes, coating materials, and therapeutic topics (Figure 3). A clear increase from 2020 was observed, coinciding with the wider adoption of 3D printing in biomedical research (Figure 2b). Outlet patterns were further summarized by listing the top ten contributing countries (Figure 2c) and the most common WoS categories (Materials Science—Biomaterials, Biomedical Engineering, Metallurgy/Metallurgical Engineering) (Figure 2d), indicating that the topic is positioned at the intersection of materials design and translational bioengineering.

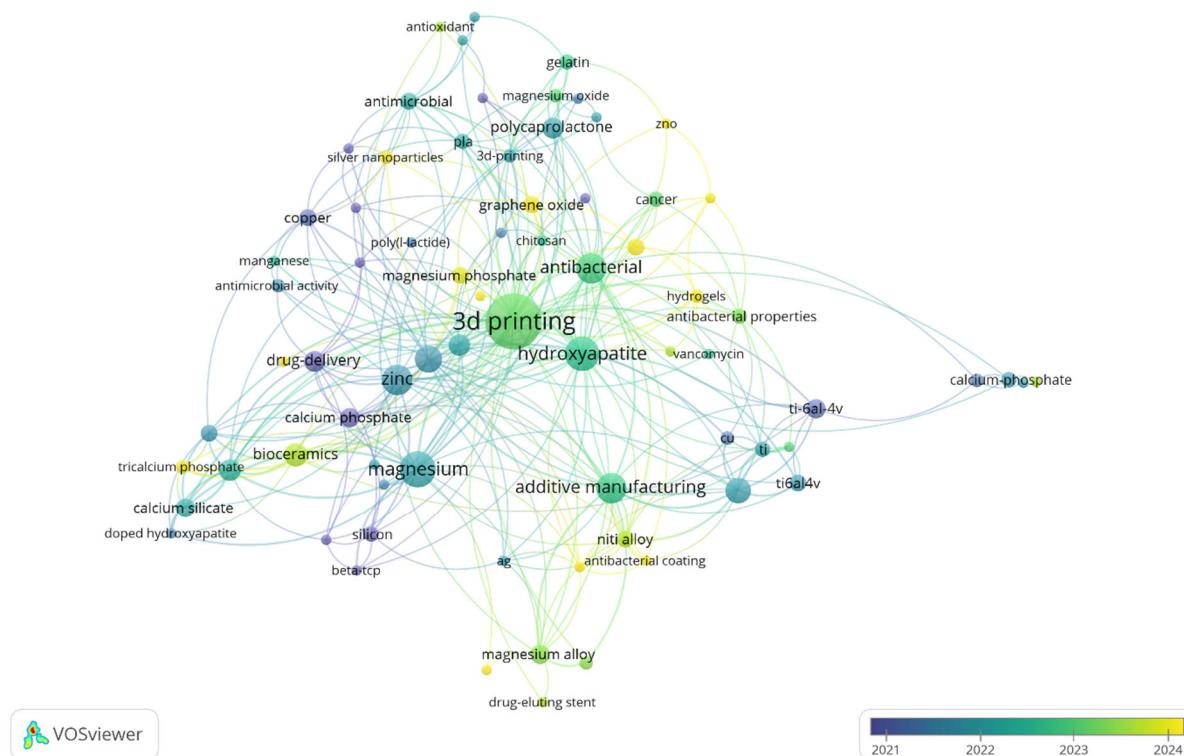


Figure 3. Keyword co-occurrence network for drug-eluting 3D-printed metallic implants (overlay visualization) using VosViewer 1.6.20.

2.2. Data Extraction Approach for Drug-Eluting Implants

The publications that were included were chosen because they provided quantitative release data and showed the variety of delivery problems that clinically relevant implant systems must solve. Specifically, each chosen study met one or more of the following requirements: (i) the platform utilized additively manufactured implants and/or AM-relevant coatings, ensuring that the reported release behavior accurately represented clinically significant porosity and geometry; (ii) the study provided extractable timepoint release data, including values at 1 h and/or 24 h, day-scale plateaus, and/or total release duration, alongside essential fabrication parameters such as anodization voltage and time, pore size, and coating or membrane thickness, facilitating cross-study comparison of kinetic behavior; and (iii) the final dataset was deliberately balanced across therapeutic categories, encompassing antibiotics, anti-inflammatory steroids, pro-angiogenic and osteogenic growth factors (VEGF, BMP-2, BMP-9), and osteogenic small molecules, to mitigate drug-specific bias and promote design-driven interpretation of release trends.

3. Additive-Manufacturing Routes and Design Handles

It is crucial to begin by understanding the bigger picture of manufacturing routes for biomedical alloys before narrowing down to AM. Historically, conventional methods,

including casting, forging, hot isostatic pressing, and powder metallurgy, have been used to make metal implants. In these techniques, metal that is either melted/compacted is molded into ingots or billets, which are then machined into the final shape of the implant. Casting remains widely used for producing cobalt–chromium and stainless-steel components because it is cost-effective and capable of forming complex geometries. However, it often leads to rough microstructures, porosity, and segregation, which make parts less mechanically uniform and less resistant to fatigue [64]. Forging and hot rolling make grains finer and stronger, but they do not let us modify the design extensively [65]. While hot pressing and powder metallurgy provide improved microstructural control, they remain dependent on molds or dies, which limits modification [6]. As the need for patient-specific and functionally graded implants has increased, these traditional methods have had challenges in providing the level of precision, surface quality, and internal structure needed for biological integration.

AM has changed the way biomedical products are made by allowing complicated structures to be built up layer by layer, straight from computer-aided designs. AM reduces waste, speeds up production cycles, and enables the direct insertion of porosity gradients and internal channels for tissue ingrowth or drug reservoirs. The ability of this innovative method to create anatomically precise implants from digital scans has already transformed dental and cranio-maxillofacial reconstruction [66]. AM-fabricated alloys have better mechanical properties and finer microstructures than cast or forged components because they cool down rapidly and have strong thermal gradients during processing [6].

AM is quickly overtaking traditional casting for metal implants because it offers more design flexibility, the ability to be customized for each patient, adjustable porosity, and built-in functionality. Metal AM allows for the development of functionally graded porous scaffolds that may concurrently meet competing design objectives, including permeability for nutrition transport, strength, and stiffness matching with bone [12]. One of the main drawbacks of conventional solid implants is that AM-derived Ti lattice implants may decrease stress shielding by up to 75% when compared to their solid counterparts [67]. The pore sizes ranging from 600 to 900 μm , produced through selective laser melting (SLM), improved in vivo bone ingrowth and fixation strength, thereby establishing that the precise architectural control attainable exclusively through AM can enhance osseointegration kinetics [68,69]. Several different methods are used for metallic biomaterials in AM:

- Selective laser melting (SLM) or laser powder bed fusion (LPBF) utilizes a powerful laser to melt metallic powders one layer at a time. This makes components that are very thick and have exceptionally good resolution. The dimensional accuracy and elastic modulus of lattice structures are directly impacted by process factors such as laser power and scan speed, highlighting the need for parameter optimization for biomedical alloys [70].
- Electron beam melting (EBM) works in a vacuum and speeds up the building of materials like Ti-6Al-4V while reducing oxidation. The cooling-rate changes in EBM-built Ti-6Al-4V cause graded microstructures, which make it possible to tune the mechanical properties of the material based on where it is located [17].
- Directed-energy deposition (DED) and Wire-Arc Additive Manufacturing (WAAM) utilize directed energy to melt wire or powder material together. This is great for big or repairable implants. WAAM can successfully deposit NiTiTa shape-memory alloys, which makes them more resistant to corrosion and easier to see with X-rays for use in medicine [24].
- For ceramics and hybrid systems, Binder Jetting and Digital Light Processing (DLP) are becoming more popular. Piezoelectric BT/HA scaffolds were made using DLP

printing. This opens new possibilities for hip devices that can have more than one use [71].

AM provides a direct approach to functionally graded, drug-eluting, and patient-specific implants. Casting and forging, on the other hand, need post-machining or coating to make implants compatible with the body. The next part expands on this manufacturing framework to look at how AM-fabricated alloys are further developed as drug-delivery platforms, connecting their micro-architectural design with release kinetics and in vivo performance.

4. Drug-Loading Reservoirs on AM-Based Alloy System

4.1. Titanium Alloy Based

Titanium and its alloys, especially Ti-6Al-4V, are the main materials used in current load-bearing implants for orthopedics, maxillofacial/dental uses, and cardiovascular devices. Their effectiveness is due to a unique combination of high specific strength, corrosion resistance via a stable TiO_2 passive coating, and established biocompatibility. In fact, Ti alloys make up most of the metallic implants that are used in long-term clinical settings [72]. In addition to the fundamental metallurgy, decades of in vivo and retrieval data link the surface chemistry of Ti to positive tissue responses. This is why Ti-6Al-4V is still the most used material for orthopedic systems today [73].

The fabrication of Ti implants has evolved considerably over the past decade. Engineers may go from solid sheets to architected lattices that change stiffness, permeability, and surface area in ways that casting, forging, and machining cannot. This is possible using AM, notably LPBF/SLM and EBM. These open-cell structures lower stress shielding, help osseointegration, and make interior surfaces that can be used as drug-reservoir spaces [74,75].

Three drug-loading strategies are the most common on this AM Ti framework:

Reservoirs based on nano-topography, such as TiO_2 nanotubes (TNTs): Controlled anodization of Ti/Ti-6Al-4V creates nanotubes that are lined up vertically. These nanotubes function as high-capacity nano-channels for tiny molecules (like antibiotics) and may be cross-linked with thin polymer overlayers to prevent bursts and prolong their release [76]. The shape of TNTs can also be optimized to confer natural antibacterial and cell-guiding properties, which makes them a perfect first option for printed Ti frameworks.

PEO/MAO (micro-arc oxidation) is used to make conversion and ceramic layers. PEO makes thick, micro- and nano-porous oxides that can be used as bioactive, corrosion-resistant scaffolds or as host matrices for drugs, ions ($\text{Ag}^+/\text{Cu}^{2+}/\text{Sr}^{2+}$), or biomolecules. By controlling the process, the pore architecture and roughness can be changed to allow for both osseointegration and elution control. Preclinical data shows promise even in osteoporotic bone [28].

Reservoirs made of polymers, such as thin-film coatings, electrospun coatings, or electrophoretic coatings: Electrospun nanofibers (e.g., PLGA/PCL) and electrophoretic biopolymers (e.g., chitosan, silk fibroin) conformally line AM lattices, allowing for single- or dual-drug release profiles and even elution. Coatings can be stacked or combined with TNTs/PEO to separate the early and late release phases and make the coating adhere better to complicated alloy shapes [16]. Thorough evaluations of antibacterial coatings on Ti explain how this polymer system maintains cytocompatibility while keeping local concentrations and antibiofilm activity high.

Table 1 (antibiotics) outlines options for early infection control on Ti/Ti-6Al-4V. Examples include titania nanotubes (TNTs) sealed with PLGA that keep vancomycin above $1.5 \mu\text{g mL}^{-1}$ for ~11 days; electrospun bilayers co-loading vancomycin and rifampicin with activity for ~6 weeks; and infection-responsive depots using a PCL membrane with

a thermogel to release drugs when needed [77]. This enables comparison of release behaviors across different alloys, reservoir architectures, and therapeutic classes. Table 2 (anti-inflammatory/immunomodulatory) includes designs such as dexamethasone LbL microcapsules (~80% in 24 h) and aspirin/PLGA films that enhance osteogenesis, clarifying which systems are designed for the day-to-weeks inflammatory phase [78]. Table 3 (pro-angiogenic/osteogenic factors) shows how the choice of factors and when they are given might affect osseointegration. For example, VEGF from collagen hydrogel (~54% day 1; ~90% day 15) and sequential VEGF/BMP-2 microspheres make it simpler to choose staged cues for vascularization and bone formation [44,79]. Table 4 (ion/element-based) lists Ag/Cu/Zn/Sr methods with dosing windows (for example, Ag release to around 3.5 ppm over 28 days) and emphasizes when ions have both antibacterial and osteogenic effects [80].

Table 1. Drug-eluting 3D-printed Ti alloy: Antibiotics.

AM Substrate	Coating/Reservoir	Loaded Drug(s)	Release Window	Key In Vitro Outcomes	Ref.
Porous Ti (lattice)	Silk fibroin (EPD) + TCP particles	Vancomycin	Controlled release (kinetics profiled)	Up to a 4-log reduction against <i>S. aureus</i> (6 h to 1 day) and increased osteogenic differentiation (ALP activity).	[81]
3D-printed TC4 Ti scaffolds (TPMS)	TiO ₂ nanotubes (TNTs) + PLGA cap	Vancomycin	Maintained > 1.5 µg/mL for 11 days, best fit Korsmeyer–Peppas	Increased MC3T3-E1 proliferation and infection control via sustained release.	[82]
3D-printed porous Ti rods	mPEG-b-PCL thermogel loaded with vancomycin, sealed by PCL membrane (lipase-degradable, infection-responsive)	Vancomycin	Stable retention in PBS, but rapid membrane degradation with lipase (0.2 mg/mL), thereby triggering release, the inner gel provides sustained delivery	In vitro—biofilm inhibition; In vivo—prevents <i>S. aureus</i> implant infection with good safety	[83]
Highly porous Ti (lattice)	Chitosan–gelatin (EPD) hydrogel	Vancomycin and/or Ag ⁺	Both agents released ≥21 days, combination improved each other's profiles	Full eradication of planktonic and adherent <i>S. aureus</i> up to 21 d with dual loading	[84]
Ti lattices (2 designs)	Electrospun nanofiber bilayer—inner PCL/Van, outer PLGA/Rif	Vancomycin + rifampicin	Tunable dual-drug release, bactericidal activity maintained 6 weeks, synergistic killing after week 6	Marked killing of planktonic and adherent <i>S. aureus</i> , durable coating	[85]
Customized 3D-printed Ti scaffold	TNTs ± PLGA cap	Minocycline	PLGA suppressed burst, ~1 week sustained release	Anti-infection activity retained while keeping micro/nano-hierarchy	[86]
β-Ti lattice (SLM, Nb-containing)	Direct in-pore dosing of Ag-alginate hydrogel	Silver (as Ag solution)	Spatially programmable filling (≤95% pore volume)	Controlled positioning/volume, wetting optimized for capillary infiltration	[87]
Ti-6Al-4V (dual-scale-SLM micro-roughness + anodised TNTs)	TNTs loaded with penicillin–streptomycin, spin-coated polymer caps (chitosan, PCL, PHB, 10–2 layers)	Penicillin–streptomycin	Polymer caps reduced burst and extended release (~+17% with one layer, ~+33% with two layers), data fitted with a power-law model	Demonstrated feasibility of drug loading on AM + TNTs while preserving micro/nano-hierarchy	[88]
Anodised TNTs on Ti (platform applicable to AM TNTs)	Electrosprayed PLGA nanoparticles bearing tetracycline onto TNTs	Tetracycline	Controlled by spray parameters (particle size, coating time), bactericidal surface while maintaining TNT osteogenic features	Antibacterial vs. <i>S. aureus</i> , biocompatible with MC3T3-E1, osteogenic gene expression (OCN/OPN), and mineralization preserved	[89]
SLM Ti-6Al-7Nb customized lattice scaffold	Bacterial cellulose (BC) grown in situ by <i>Komagataeibacter xylinus</i> (~7-day coating)	Gentamicin	Antibiotic-saturated BC depot, in vitro inhibition of <i>S. aureus</i> (no quantitative release curve reported)	Lower cytotoxicity vs. non-coated Ti for osteoblasts/fibroblasts, confocal shows viable cell layer on BC microstructure, SEM confirms conformal BC coverage, coating/cleansing did not alter scaffold integrity	[90]

Table 2. Drug-eluting 3D-printed Ti alloy: Anti-inflammatory/immunomodulatory drugs.

AM Substrate	Coating/Reservoir	Loaded Drug(s)	Release Window	Key In Vitro Outcomes	Ref.
EBM Ti-6Al-4V porous scaffold	PAH/PSS layer-by-layer polyelectrolyte microcapsules on CaCO ₃ cores	Dexamethasone	~40% loading feasible, ~80% released in 24 h (3-bilayer capsules), super-hydrophilic ($\theta < 5^\circ$)	No cytotoxicity, cells attach/spread, platform for acute post-op inflammation control	[78]
3D-printed Ti-6Al-4V (uniform micro-topography)	Aspirin/PLGA thin film on printed surface	Aspirin	Sustained ASP release (surface becomes more hydrophilic)	Enhanced osteoblast proliferation/mineralization, osseointegration improved in rat femur	[91]

Table 3. Drug-eluting 3D-printed Ti alloy: Pro-angiogenic/osteogenic factors.

AM Substrate	Coating/Reservoir	Loaded Factors	Release Window	Key In Vitro Outcomes	Ref.
EBM porous Ti alloy	Thermosensitive collagen hydrogel on Ti, loaded with VEGF	VEGF	$53.5 \pm 2.2\%$ released Day 1, $89.8 \pm 3.4\%$ by Day 15 (sampling-1 h, 3 h, 8 h, 1, 3, 7, 10, 15 d)	Increased HUVEC proliferation, migration, tube formation, and in rabbits, greater angiogenesis and osseointegration compared with hydrogel-only or bare Ti.	[79]
3D-printed porous Ti scaffold	nSiHA/TiO ₂ hierarchical coating with immobilized VEGF	VEGF	Cumulative release ~57.9% at 60 days, ~28% within 10 days (ELISA)	Improved osteogenic/angiogenic milieu reported for VEGF-functionalized composite vs. control coatings	[92]
3D-printed porous Ti alloy	Gelatin coating carrying shell–core microspheres for sequential delivery	VEGF + BMP-2 (dual)	Sequential, sampled at Days 1, 2, 4, 6, 8, 11, 14, 18, 22, 27 (27-day window, ELISA)	Dual-factor system designed for staged angiogenic/osteogenic cues, in vitro biocompatibility on MC3T3-E1	[44]
EBM porous Ti alloy	Thermosensitive collagen delivering rhBMP-9	rhBMP-9	~51.0 $\pm$ 2.3% released by 1–24 h, sustained slow release to Day 15 (same time grid as above)	Increased BMSC osteogenic markers (ALP, Runx2, OPN, BMP-2) with good biocompatibility	[93]
EBM Ti-6Al-4V-ELI scaffold	Si-substituted hydroxyapatite (SiHA) coat + VEGF adsorption	BMP-2 + VEGF	Minimal desorption measured at 0, 0.5, 24 h (ELISA, “minimal” loss) leads to effective immobilization within first 24 h	Enhanced endothelial (EC2) and MC3T3-E1 responses on VEGF-functionalized Si-HA vs. controls	[94]
SLM porous Ti (multilayered/MAO-modified)	Si-doped CaP coating surface-loaded with BMP-2	BMP-2	Quantified at Days 1, 2, 3, 5, 7, 14 (ELISA, 14-day window reported)	Increased MC3T3-E1 and HUVEC viability/proliferation, Si-ion release also characterized (1–21 d ICP)	[95]
3D-printed porous Ti (radial-gradient lattice best)	Chitosan microspheres loaded with BMP-2 and/or PDGF-BB on Ti lattice	BMP-2, PDGF-BB (alone or together)	Burst of BMP-2 in vivo noted, exact in vitro release numbers not reported	In vitro—Increased rBMSC proliferation/ALP; in vivo—BV/TV increased at 4–12 w, B + P (dual) $\geq$ single factor, synergy suggested	[96]

By taking a look at all four tables together, the design choices can be examined (uncapped nanotubes vs. polymer-sealed, ceramic vs. hydrogel reservoirs), how the

kinetics relates to biological readouts can be predicted, and the choice of antibiotic, anti-inflammatory, osteogenic, or ionic support can be justified based on the clinical needs of the implant.

Table 4. Drug-eluting 3D-printed Ti alloy: Ion/element-based compounds.

AM Substrate	Coating/Reservoir	Loaded Elements	Release Window	Key In Vitro Outcomes	Ref.
AM porous Ti (EBM/LPBF)	Silver coating (sputter/thin films)	Ag ⁺	Cumulative ~3.5 ppm up to 28 d (example), dose-response studied across 7–18 at% Ag	Decreased adhesion and biofilm (esp. <i>S. epidermidis</i>), preserved osteoblast functions, dosing needs balancing vs. <i>S. aureus</i>	[80]
AM Ti-6Al-4V (SLM)	PEO oxide, then Cu by ion implantation/grafted AgNPs into TNTs	Cu ⁺ /2 ⁺ , Ag ⁺	Slowed Ag ⁺ release via covalent tethering to TNTs, Cu as CuO/Cu ₂ O	Antibacterial behavior with maintained cytocompatibility (Cu), 100% kill with covalently anchored AgNPs on TNTs	[40]
3D-printed Ti scaffold	Mesoporous bioactive glass (MBG) doped with Zn or Ag (dip-pull)	Zn ²⁺ , Ag ⁺	Specific surface 378 leads to 175 m ² /g as dopant increased, small Ag (~0.5%) achieved 100% antibacterial rate	Improved hydrophilicity/mineralization (low dopant), strong antibacterial at low Ag	[97]
SLM Ti-6Al-4V	Sr-doped CaP coating (MAO + air-plasma treatment)	Sr ²⁺ , CaP ions	Air-plasma boosts surface energy, Sr-CaP improves wettability and BMSC response	Biocompatibility and osteogenic differentiation increased (drug-free ionic cue)	[98]

4.2. Stainless-Steel-Based Alloys

Austenitic 316L stainless steel has been a standard in orthopedics and dentistry due to its high strength, ease of manufacturing, and clinically acceptable corrosion resistance, which is a result of its passive film properties that are closely related to biocompatibility in vivo. Conventional manufacturing approaches work well for the majority of the components, but they do not allow the internal structure to change. Laser powder bed fusion (LPBF/SLM) of 316L, on the other hand, makes lattices and controls porosity that regulates rigidity to reduce stress shielding, which are hard to achieve with machining [21]. Recent evaluations also indicate that process parameters enhance surface quality and improve the permeable surface for osseointegration on AM 316L [9].

Even with adequate osseointegration, infection linked to implants takes advantage of biofilm growth at the metal–tissue interface, where systemic antibiotics fail to work effectively. Research shows the main benefit of local therapy via SS was elevating near-surface concentrations over MIC for days to weeks (for example, amikacin on 3D-printed 316L, silver–zeolite ion release) while limiting systemic exposure [99,100]. Concurrent research using dexamethasone addresses the acute inflammatory phase, demonstrating that early immunomodulation may be simultaneously administered from the same metallic framework [101]. When combined and made possible by AM’s architected porosity, 3D-printed SS becomes more than simply a structural system, as addressed in Table 5.

Table 5. Drug-eluting 3D-printed stainless-steel alloy.

AM Substrate	Coating/Reservoir	Loaded Elements	Release Window	Key In Vitro Outcomes	Ref.
3D-printed SS316L implants (roughened surface)	Gelatin–chondroitin sulfate film (airbrush deposited), glutaraldehyde cross-linked	Dexamethasone	Biphasic—initial burst then sustained up to 3 days, coating thickness $\sim 410 \pm 5.2 \mu\text{m}$	In vitro drug content uniformity ($\sim 100 \pm 5\%$), study proposes to use to dampen post-surgical inflammation, suggests large-animal testing	[101]
SLM porous SS scaffold	Silver-incorporated zeolite coating via in situ hydrothermal crystallization	Ag^+ (silver)	Antibacterial activity assessed after 24 h incubation	Inhibits <i>E. coli</i> and <i>S. aureus</i> , BMSC spreading improved with scaffold extracts (days 1–5), indicating biocompatibility/osteointegration potential	[99]
3D-printed 316L devices	Chitosan and PLGA polymer coatings loaded with aminoglycoside	Amikacin (AMK)	Controlled release up to ~ 1 month, antimicrobial effectiveness ~ 1 week noted in tests	Concentration-dependent antibacterial effect, coated substrates significantly inhibit bacterial growth vs. uncoated controls	[100]

4.3. Magnesium-Based Alloys

Mg and Mg-alloys have become popular for temporary implants due to their biodegradability, bioactivity, and stiffness that is more akin to bone than Ti/CoCr, which reduces stress shielding while generating Mg^{2+} that may facilitate osteogenesis [102–106]. Clinical experience using Mg-based cardiovascular scaffolds, such as sirolimus-eluting Magmaris, demonstrates promising safety and effectiveness indicators, highlighting their translational potential [107–109]. Early mechanical integrity can be compromised by rapid corrosion, hydrogen evolution, and local alkalization, which are still significant challenges [110]. AM has certain problems that are special to Mg, such as powder reactivity, oxidation, evaporation/spatter, hot-cracking, and porosity/fatigue. However, process controls and alloy design are improving gradually [111,112]. Drug loading on Mg and Mg-alloy implants typically involves applying a coating or porous layer that mitigates early corrosion while enabling controlled local release. Common ways to do this include ceramic conversion or micro-arc oxidation layers, which are commonly enclosed or functionalized, biodegradable polymers that are applied by dip, spray, or electro-methods, and multilayer (LbL) structures for antibiotics and anti-inflammatories [113–115]. These systems may prevent early infections and inflammation while Mg^{2+} and osteoactive drugs work together to accelerate bone growth (as shown in Table 6), turning AM Mg from a passive scaffold into a therapeutic system.

Table 6. Drug-eluting 3D-printed Mg alloy.

AM Substrate	Coating/Reservoir	Loaded Elements	Release Window	Key In Vitro Outcomes	Ref.
3D-printed Mg–Nd–Zn–Zr alloy scaffolds (porous)	Ceramic composite coating (drug-loaded)	Zoledronic acid (bisphosphonate)	Sustained, slow release, coating also reduced degradation rate of AM Mg scaffold	Degradation products + drug promoted BMSC osteogenesis, inhibited osteoclast formation/resorption, greater bone ingrowth, and better healing of osteoporotic defects vs. uncoated	[116]
3D gel-printed pure Mg scaffold (porous)	DCPD ($\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$) conversion coating	No external drug	Slow degradation, $\sim 52\%$ scaffold volume remained at 12 weeks, resorption by 24 weeks	Corrosion resistance increased, cytocompatibility, and new bone formation in 6 weeks, no systemic Mg toxicity observed	[117]

Table 6. Cont.

AM Substrate	Coating/Reservoir	Loaded Elements	Release Window	Key In Vitro Outcomes	Ref.
Pure Mg with 3D-printed grid scaffold ($\sim 10 \times 10 \times 1$ mm on PEO-treated Mg)	PEO interlayer + 3D-printed PCL/amine-PEG scaffold (PG-NH)	Dexamethasone	Burst 6.06% by 96 h, max 9.1% at 168 h, early phase fits first-order ($R^2 = 0.962$), later phase zero-order ($R^2 = 1$)	Strong adhesion (ASTM D3359 5B [118]), higher hydrophilicity, and faster degradation with PEG, i_{corr} decreased from 3.732 leads to $0.105 \mu\text{A cm}^{-2}$, osteogenic markers increased (MC3T3-E1)	[119]
L-PBF Zn-1Mg porous scaffold (pore size 600 μm , porosity $\sim 63.6\%$)	PDA (drug anchor) + HA composite, Van anchored to PDA, BMP2 in HA	BMP2 + Vancomycin	BMP2 = $\sim 60\%$ on Day 1, cumulative measured to Day 21 (burst leads to slow uptick Day 14–21). Van = 0.5 h–24 d, 40–50% by 16 h, 56–70% by Day 6, rapid release Days 6–12, slow thereafter	Coating improved corrosion resistance ($R_p = 0.245$ leads to 7.6 leads to 37 $\text{k}\Omega \cdot \text{cm}^2$), enhanced cytocompatibility and osteogenesis (BMP2 + low Zn^{2+} synergy), strong antibacterial activity from sustained Van, improved osseointegration in rats	[120]

5. Release-Rate Kinetics of Drug-Eluting AM Implants

In the preceding section, drug-eluting implants constructed from various metallic systems, encompassing Ti and Ti-6Al-4V lattices, stainless-steel alloys, and Mg-based platforms, were evaluated regarding surface architecture, coating methodologies, and their respective antibacterial, anti-inflammatory, and osteogenic efficacy. This part builds on what we have spoken about thus far and concentrates on the release-rate dynamics of drug-eluting additively made implants. It also talks about how the design of the reservoir and the coating architecture affect early burst release and sustained delivery. Table 7 summarizes representative implant–drug systems and their reported kinetic characteristics. This makes it easy to compare the release behavior of different alloys, reservoir types, and therapeutic classes across studies.

Table 7. Summary of drugs loaded onto 3D-printed metallic implants showing early-burst and sustained release behavior.

Drug/Category	Platform	Early Burst (1 h/24 h%)	Total Release/Duration	Structural/Coating Details	Ref.
Penicillin–Streptomycin (antibiotic)	SLM Ti-6Al-4V with TiO_2 nanotubes, optional chitosan/PCL/PHB top coat	$\sim 60\%$ (1 h), 90% (2 h), 100% (4 h), burst decreased 28% at 60 min with caps	~ 4 –5 h total, +17% (1 layer)/+33% (2 layers) duration vs. uncoated	Anodization 60 V at 30 min, dual-scale surface retained after coating	[88]
Minocycline (antibiotic)	3D Ti 6Al 4V scaffold with TiO_2 nanotubes sealed by PLGA	$<10\%$ (1 h), $\sim 25\%$ (5 h), $\sim 48\%$ (24 h) of uncoated at same timepoint	Sustained ~ 7 days, PLGA reduces 24 h release by $>2\times$ vs. uncoated	Anodization 60 V 1 h, MH 1 mg mL^{-1} load (2 h soak), PBS refresh q5 h	[86]
Gentamicin (antibiotic)	Halloysite nanotubes (MgO-coated) embedded in Si_3N_4 matrix	15% (1 h), 40% (6 h), 65% (24 h)	~ 4 days to $\sim 95\%$	HNT diameter ~ 50 nm, MgO shell thickness of few nm	[121]
Amikacin (antibiotic)	3D-printed 316L steel lattice coated with chitosan $\pm$ PLGA	LMW: ≤ 12 h burst leads to 74–90% (96 h), with PLGA: $\sim 50\%$ burst	Extended ~ 1 month with PLGA overcoat, $>97\%$ total	PLGA 10% w/w , MMW chitosan extends to ~ 10 days	[100]
Dexamethasone (anti-inflammatory)	PSS/PAH LbL capsules (3 bilayers) on Ti surface	20% (1 h), 50% (4 h), 80% (24 h)	~ 48 h to complete elution	Capsule diameter $2.3 \pm 0.2 \mu\text{m}$, 3 bilayers optimized	[78]
Dexamethasone (anti-inflammatory)	3D-printed stainless steel with gelatin CS film	35% (1 h), 80% (12 h)	~ 3 days total	Film thickness $\sim 410 \mu\text{m}$, cross-linked gel	[101]
VEGF (growth factor)	EBM Ti 6Al 4V pores (500 μm) filled with thermosensitive collagen	$53.5 \pm 2.2\%$ (Day 1)	$89.8 \pm 3.4\%$ (Day 15)	Scaffold porosity 70%, hydrogel porosity 40%, swelling 110% at 10 h	[79]
VEGF and BMP 2 (growth factors)	Ti rods with gelatin microspheres	VEGF = 20% (4 h) leads to 75% (72 h), BMP 2 = 5% (4 h) leads to 55% (72 h)	Sequential: VEGF 1st week, BMP 2nd week	Shell/core thickness $\sim 20 \mu\text{m}/80 \mu\text{m}$	[44]

Table 7. Cont.

Drug/Category	Platform	Early Burst (1 h/24 h%)	Total Release/Duration	Structural/Coating Details	Ref.
BMP 9 (growth factor)	Same EBM Ti framework with thermosensitive collagen carrying rhBMP 9	-	Tracked 1 h leads to 15 days (ELISA), profile gradual	rhBMP9 100 ng mL ⁻¹ (in vitro), 10 mg mL ⁻¹ (in vivo)	[93]
Rosuvastatin (statin + ion donor)	3D-printed composite scaffold with gelatin coating and MgO	-	30-day sustained release of Mg ²⁺ and RSV	Composite porosity ~ 60%, gelatin layer modulates wettability	[122]
Vancomycin (antibiotic)	EPD silk–fibroin + TCP coating on AM porous Ti	Burst on day 1, higher burst with higher vancomycin load	Continued release to Day 14	Silk/TCP/vancomycin composite, coatings uniformly cover inner pore surfaces	[81]
Vancomycin (antibiotic)	Porous 3D Ti rods filled with mPEG PCL hydrogel + outer PCL membrane	<10% (4 h), 25% (no lipase) vs. 55% (+ lipase) at 24 h	~10 days, enzyme rate increased by ~2.2-fold	PCL membrane 40–80 µm thick, hydrogel viscosity tuned by ratio	[83]
Vancomycin + Ag (antibacterial)	AM highly porous Ti lattice, chitosan–gelatin EPD hydrogel coating	Burst of each agent lowered when combined (e.g., Ag decreased ~5× at 6 h vs. Ag alone)	Both agents released ≥21 days, maintained ≥5-log kill to Day 21	EPD of chitosan/gelatin, simultaneous loading of Ag ⁺ and vancomycin, synergistic killing	[84]
Vancomycin + BMP-2 (antibiotic + growth factor)	L-PBF Zn-1Mg porous scaffold with PDA/HA bilayer, BMP-2 adsorbed, vancomycin embedded	Vancomycin ~40–50% first 16 h, BMP-2 ~60% day 1	Vancomycin to ~24 days, BMP-2 to ~21 days	PDA adhesive layer + HA, dual-factor release with antibacterial + osteogenic effects	[120]

A unique tendency is seen in all 3D-printed drug-eluting systems. The shape of the carrier and the coating method have a more significant influence on release dynamics than the drug class itself. Tubular structures like TiO₂ or halloysite nanotubes accelerated elution via diffusion, usually releasing 60–90% of the payload in the first few. Adding a thin polymer barrier (PCL, PHB, or chitosan) reduces this burst by around 25–30% and makes the release last up to one-third longer [88]. When these nanotube structures are sealed with PLGA that degrades gradually, the release window extends from hours to a week. This shows that the permeability and breakdown rates of the polymer are more important than the composition of the base alloy [86].

On the other hand, systems that use films and membranes allow for more customization in both burst strength and overall time. PLGA or chitosan coatings on 3D-printed 316L lattices extend antibiotic elution for up to a month [100], while enzyme-responsive PCL membranes enhance release about 2.2-fold in the presence of lipase [83]. Layer-by-layer (LbL) or gelatin–chondroitin coatings that are anti-inflammatory create targeted pulses that last for 24 to 72 h, which mirrors the initial inflammatory period after implantation. Collagen-based growth-factor systems maintain therapeutic levels for 1–2 weeks via mesh-limited diffusion. Overall, these findings show that aligning the chemistry of the polymer to the desired therapeutic timing is typically more beneficial than just optimizing the microstructure of the alloy.

The comparison results show an important hierarchy that thin polymer caps work best for a few hours, degradable films work best for weekly treatment, and hybrid or hydrogel matrices work best for monthly regeneration. Sequential structures, shown by VEGF-BMP-2 shell–core microspheres, exhibit deliberate programming of release order, enabling the coordination of early angiogenic and delayed osteogenic signals inside a singular construct [44]. In summary, these results confirm that in 3D-printed metallic implants, microstructural and interfacial design serve as instruments for temporal pharmacology, enabling the adjustment of surface morphology and coating degradation in correspondence with biological healing processes ranging from infection control to tissue remodeling [122].

Interval-Averaged Release Rate ($\Delta\%/\Delta t$)

The early-release behavior was initially standardized by turning the 0–1 h period into an interval-averaged rate ($\Delta\%/\Delta t$, $\% \text{ h}^{-1}$) as stated in Equation (1), where F_1 and F_2 are the cumulative fraction released at timepoints t_1 and t_2 so that the five separate investigations could be compared on various drug–implant systems. This equalizes the datasets, regardless of drug dosage or total time, and isolates the burst release component. This is the quick desorption/partition-driven flux from exposed surfaces and shallow reservoirs, before diffusion into deeper domains becomes rate-limiting.

$$\text{rate}_{t_1 \rightarrow t_2} = \frac{F_2 - F_1}{t_2 - t_1} \quad (1)$$

The first-hour release rate for each system is shown in the bar chart in Figure 4. The largest burst is seen for penicillin–streptomycin ($\sim 60\% \text{ h}^{-1}$), which is consistent with readily accessible TiO_2 nanotube openings and low early barriers [88]. Dexamethasone coated on stainless steel comes next (about $35\% \text{ h}^{-1}$), which means that the interfacial barrier is more open or thinner compared to dexamethasone coated on Ti (about $20\% \text{ h}^{-1}$) [78,101]. Gentamicin ($\sim 15\% \text{ h}^{-1}$) shows a mild burst that is characteristic of reservoir geometries that allow a greater release at first, but then start to limit transport [121]. Minocycline ($\sim 10\% \text{ h}^{-1}$) is the lowest, which is in accordance with a PLGA seal that slows down early flux and moves control toward diffusion [86]. The 1 h normalization shows that surface accessibility and barrier design are the most important factors in the initial release hierarchy. This has clear effects on whether to choose rapid-onset antibacterial coverage or a gentler start to reduce cytotoxicity or resistance pressure.

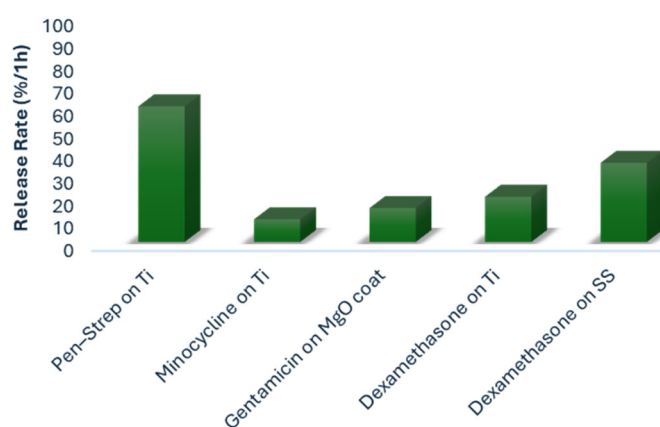


Figure 4. Normalized first-hour release rates (%/h) for representative implant–drug systems across Ti, MgO-coated Mg, and SS platforms (Adapted from Refs. [78,86,88,101,121]).

After the first hour, all systems show the classic “burst-to-tail” pattern, although the size and length of the early flux depend on the design. Penicillin and streptomycin were released most quickly from TiO_2 nanotube (NT) surfaces, with rates close to $60\% \text{ h}^{-1}$ before decreasing to $\sim 5\% \text{ h}^{-1}$ by 4 h. This quick double-log reduction over just a few hours fits with quick desorption from exposed NT openings and then transport from areas that are harder to reach. This means that the antibacterial dose is delivered early, but the coverage fails to be long-lasting [88].

Minocycline, released from PLGA-sealed nanotubes, exhibits a controlled damped burst and a more gradual decrease, about $10\% \text{ h}^{-1}$ at first hour, decreasing to around $3.75\% \text{ h}^{-1}$ and $1.39\% \text{ h}^{-1}$ after 24 h. The gradual drop shows that diffusion through or inside PLGA is becoming more important for mass transfer. Thus, the delivery on the first day is steady, which is an acceptable compromise when cytocompatibility or

antimicrobial management inhibits significant initial spikes [86]. Gentamicin released from halloysite/MgO reservoirs exhibits a three-stage decline, approximately $15\% \text{ h}^{-1}$ at first hour, $5\% \text{ h}^{-1}$, $1.39\% \text{ h}^{-1}$, and $0.42\% \text{ h}^{-1}$ by 96 h, demonstrating a diffusion-then-depletion pattern from tubular stores and providing a clinically significant extended tail for the peri-implant infection period [121].

The two dexamethasone designs incorporate adjustable early-phase control. In system 1, which is loaded on Ti, the rate is rapid but then slows down ($20\% \text{ h}^{-1}$), then goes down to around $1.5\% \text{ h}^{-1}$ and $0.83\% \text{ h}^{-1}$ after 48 h, and finally reaches completion around 72 h. This causes a quick start to the anti-inflammatory effects, which last for around two days [78]. System 2, which is loaded on stainless steel, starts with a higher flow rate ($35\% \text{ h}^{-1}$ initially) but ends up with behavior that is similar in the late phase ($1.96\% \text{ h}^{-1}$, $0.42\% \text{ h}^{-1}$ from 24 to 72 h) [101]. This suggests that the differences are mostly due to early interfacial partitioning or barrier thickness/porosity. These comparisons reveal that open, easily accessible surfaces speed up early delivery, whereas polymer sealing and reservoir shapes slow down the burst and provide a diffusion-limited tail.

6. In Vivo Performance of 3D-Printed Metallic Drug-Eluting Implants

In the previous section, the in vitro release kinetics of several therapeutic agents, including antibiotics, anti-inflammatory drugs, and growth factors, incorporated into 3D-printed metallic substrates such as Ti-6Al-4V, SS, and Mg alloys were examined. The findings demonstrated that micro/nano-architectural design, coating chemistry, and polymer degradation rates influence the rate of drug elution and the duration of therapeutic effect. Based on this mechanistic insight, the next obvious step is to test how these engineered surfaces function in biological settings. Consequently, this section reviews in vivo research (summarized in Table 8) that illustrates the antibacterial effectiveness, osseointegration, and bone regeneration results of additively made metallic implants [44,123,124]. These results correlate controlled in vitro release profiles with functional healing responses in animal models, providing insight into how alloy composition, surface modification, and ion or drug release collectively influence tissue regeneration and therapeutic outcomes [125].

Table 8. Summary of in vivo studies on 3D-printed or additively manufactured metallic implants showing antibacterial and osteogenic outcomes.

Implant and Loaded Agent	In Vivo Model and Duration	Key In Vivo Outcomes	Drug/Ion Kinetics Reported	Ref.
AM porous Ti rods, chitosan EPD coatings loaded with silver NPs (1–100 mM AgNO ₃) or vancomycin	Rat tibia (intramedullary), 28 days	Vancomycin coating decreased infection rate (~80%) vs. chitosan, Ag-NP coating failed to reduce infection and increased osteoclast activity on μ CT and histology.	No release curves, antibacterial efficacy only qualitative.	[11]
3D-printed porous Ti6Al4V with micro-arc oxidation (MAO) bioactive layer	Rabbit femoral condyle, 4 and 8 weeks	μ CT and Masson-Goldner staining: BV/TV increased ~60%, higher ALP and cell proliferation vs. untreated Ti.	No drug release	[126]
Ti6Al4V-HA functionally graded composite (FGM) made by SLM	Rabbit tibia, 4 and 8 weeks	BV/TV increased ~2.1 $\times$ and BIC% increased vs. Ti64 control, mechanical strength increased ~20%.	No drug release	[127]
3D-printed porous Ti with choline-phosphate (PMCP) surface capturing BMSC exosomes	Rabbit femoral defects, 4 and 12 weeks	μ CT and histology: bone volume increased 2.3 $\times$ (4 w), trabecular thickness increased 25% (12 w) vs. bare Ti.	Exosome release qualitative only (no μ g or t $\frac{1}{2}$ values).	[128]
cpTi + 1 wt% SiO ₂ + 3 wt% Cu (AM alloy, no separate drug)	Rat distal femur, 8 weeks	4.5 $\times$ higher bone formation at the bone-implant interface vs. cpTi, ~85% antibacterial efficacy against <i>S. aureus</i> reported (in vitro).	Cu/Si release not quantified	[129]
Si-doped MAO Ti + BMP-2 loading	Rabbit femoral defect, 8 weeks	Faster bone bridging and osseointegration, bone-fill increased ~80% vs. control.	BMP-2 release t $\frac{1}{2}$ ~10 days, sustained over 4 weeks (ELISA).	[95]
3D-printed porous Ti with Cu ²⁺ /TA/HAP composite coating (EPD)	Rabbit femoral condyle, 4 and 12 weeks	μ CT/histology: BV/TV increased ~60%, ALP increased 1.7 $\times$, bacteria decreased ~85% vs. control.	Cu ²⁺ release (qualitative, ppm not stated).	[130]
EBM Ti6Al4V + polydopamine-assisted HA coating	Rabbit femoral condyle, 4 and 12 weeks	BIC increased ~2 $\times$, mineralized bone increased ~1.6 $\times$ vs. bare Ti, excellent osteointegration.	No drug release	[131]
3D-printed porous Ti6Al4V + pH-neutral bioactive glass (PSC) coating	Rabbit femoral defect, 12 weeks	Push-out strength increased ~38%, BIC increased ~45% vs. bare Ti, enhanced osseointegration.	No drug, HA induction confirmed within 3 days in SBF.	[132]
TiCu/TiCuN coating (arc-ion plating, Cu-ion-eluting)	Rat femur osteoporotic fracture model, 8 weeks	Callus volume increased ~2 $\times$, bone quality improved vs. Ti control, Wnt/ β -catenin genes up-regulated.	Cu ²⁺ release ~0.25 ppm day ⁻¹ for 28 days.	[133]

Table 8. Cont.

Implant and Loaded Agent	In Vivo Model and Duration	Key In Vivo Outcomes	Drug/Ion Kinetics Reported	Ref.
3D-printed PCL/ β -TCP/nHA/MgO scaffold, gelatin coat + rosuvastatin (RSV)	Rat calvarial critical-size defect, 12 weeks	More bone fill and maturation vs. control in μ CT/histology, RSV + MgO combo gave the best osteogenesis	RSV release sustained ~30 days (duration stated, no μ g/day), MgO acted as pro-angiogenic cue	[122]
Loofah-inspired scaffold with HAP coating + Mg-MOF/PVA hydrogel (Mg supplies ions, GA co-ligand provides antioxidant effect)	Rabbit femoral-condyle critical-size defect, 4 and 12 weeks	Cortical coverage and cortical-cancellous reconstruction by 12 weeks, highest new bone volume among groups on μ CT/histology	pH maintained 7.1–7.4 in extracts, Mg-MOFs sustained Mg^{2+} /GA release (profile reported, values not tabulated)	[134]
PDA-Mg ion-loaded 3D-printed porous Ta (Ta-PDA-Mg2 best dose)	Rat femoral condyle, 12 weeks	Greater vascularized bone formation and stronger pull-out than Ta/Ta-PDA	Mg^{2+} release ranked ($Mg2 >$ others), but no absolute concentrations in paper text	[135]
SLM Ta scaffold with Mg-doped CaP coating (Mg-CaP)	Rabbit femoral-condyle defects, 4 and 12 weeks	Denser new bone (VG/TB), shorter fluorochrome label distances vs. CaP or bare Ta	In vitro ion release reached steady state: Ca^{2+} ~80–130 ppm, Mg^{2+} ~35–55 ppm (stable from day 2)	[136]
Mg-silicate ($MgSiO_3$)-coated 3D-printed Ti scaffold	Rabbit femoral condyle, 6 and 12 weeks	Increased bone ingrowth and volume vs. pore-shape controls (μ CT, histology)	No ion-release curve (coating chemistry described)	[137]
Mg-coating on porous Ti (micro-arc oxide Mg layer)	Rabbit distal femur, 2 months	Suppressed osteoclastogenesis and peri-implant osteolysis, improved bone-implant interface	Mg-related alkalization noted, no quantitative release reported	[138]

In vivo research on 3D-printed Ti and similar alloy substrates points to two main design levers: controlled release of bioactive ions/drugs, and customized surface microstructure that affects osseointegration. Croes et al. revealed in rat and rabbit models that chitosan–vancomycin coatings eliminated *Staphylococcus aureus* infections, but silver nanoparticle layers caused osteolysis, indicating that immunological compatibility and release kinetics are more significant than antibacterial effectiveness alone [11]. Ni et al. and Wang et al. also observed that bioactive oxide or glass-modified Ti surfaces increased bone–implant contact and release strength by 40–60% in 8–12 weeks, even without any medicines added [126,132]. Functionally graded Ti-HA scaffolds [127] further validated that a mineral gradient may autonomously facilitate osteogenesis while preserving mechanical stability. Controlled ion-releasing designs were particularly successful. Cu-ion coatings that released approximately 0.25 ppm per day for 28 days, resulting in a twofold increase in callus formation and the activation of Wnt/ β -catenin signaling [133]. Meanwhile, Mg-CaP scaffolds maintained Ca^{2+} (80–130 ppm) and Mg^{2+} (35–55 ppm) levels, which correlated with thicker bone fronts at 4–12 weeks [136]. In summary, these Ti-based substrates show that sustained ion or growth-factor release over 2–4 weeks consistently leads to 50–80% higher bone regeneration metrics than burst-type releases (like Ag). This shows that chemically tuned, slow-release coatings are the best way to combine antibacterial protection with stable osseointegration.

In contrast, Mg-based substrates and Mg-integrated systems exhibited a more self-regulating and physiologically dynamic interface, facilitated by gradual ion/drug release and degradation-mediated modification. The Mg-CaP and Mg-silicate systems [136,137] produced denser, vascularized bone within 4–12 weeks, whereas the MgO-rosuvastatin and Mg-MOF scaffolds [122,134] achieved nearly complete defect closure within three months through the integration of drug elution and angiogenic Mg^{2+} signaling. In general, Ti substrates provide architectural accuracy and mechanical strength, whereas Mg substrates offer biochemical reactivity and degradation that is in accordance with time.

7. Discussion

7.1. Design Principles Linking AM Architecture to Release Behavior

AM continuously transforms implant architecture from a merely mechanical decision to a drug-delivery design variable throughout the analyzed research [12–14]. The amount of payload that can be hosted and how fluids can reach internal surfaces are controlled by porosity, interconnection, and internal surface area [68,69]. This, in turn, affects diffusion routes and local concentration–time profiles at the implant–tissue interface [61,62]. Because geometric parameters affect accessible surface area, penetration depth, and transport resistance, systems with similar drug chemistries may still have varied burst percentages and sustained durations [88,100]. This is also why architectural characteristics (such as pore size, porosity, lattice type, and permeability proxies) are so important for understanding kinetics and comparing research [66,67,70].

7.2. Translational Interpretation by Material Platform

In translation, the evaluated alloy systems provide different but complementary therapeutic needs [12,17,28]. Titanium and Ti-6Al-4V are still the best materials for making drug-eluting orthopedic implants because they are strong and stable when they are passivated [15,16,73]. AM lattices, on the other hand, let you choose how permeable the implants are and have a vast interior surface area for therapeutic interactions [67,68]. Stainless steel (especially 316L) is still useful in medicine for fixing trauma and making temporary load-bearing parts [9,99]. Local drug release is most useful for slowing down the formation of biofilm at the metal–tissue interface [4,5,100], and the durability of the coating under cyclic loading and contact conditions must also be considered [25,26]. On the other hand, biodegradable magnesium-based implants are designed to provide temporary support before being absorbed [102–105]. However, translation is limited by rapid corrosion, hydrogen evolution, and local alkalization [110,111]. Thus, Mg drug-eluting designs should be seen as corrosion-coupled systems where coatings serve as both drug reservoirs and barriers to degradation [116,119,120]. In all three alloy groups, clinical relevance is inherently time-structured early infection prevention, short-term inflammation modulation, and longer-term osseointegration/regeneration, and release performance becomes most meaningful when concentration–time profiles, coating adhesion/uniformity within porous networks, and local safety outcomes are reported together rather than as isolated kinetics [44,95,134].

7.3. Translational Interpretation by Therapeutic Application

Most drug-eluting AM alloys are developed for orthopedic applications, where therapeutic needs are inherently time-structured [3–5]. Infection management is most critical in the immediate postoperative window, inflammation modulation is most relevant during early healing [78,101], and angiogenic or osteogenic support is typically required over longer regenerative timelines [79,95,122,136]. This highlights that “successful” release is not simply prolonged release, but delivery that aligns with biological windows while preserving osseointegration [44,79]. Drug-eluting stents provide a clinically proven model for localized therapy [107–109], combining a metallic scaffold with a drug-containing coating or matrix to control early burst release and sustain elution while maintaining mechanical function under continuous flow and cyclic loading. Their clinical success reinforces a key lesson relevant to AM lattices: drug selection must be matched by coating integrity and reproducible elution [40,80]. In this context, resorbable magnesium-based cardiovascular scaffolds, including sirolimus-eluting platforms, are a useful reference because they integrate controlled drug delivery with a degradable metal framework [107–109], while also illustrating durability challenges associated with corrosion, hydrogen evolution, and

local alkalisation [110–112]. Consequently, coating adhesion and long-term stability on complex, porous architectures should be treated as core translational metrics alongside release kinetics [25,42,88], particularly for high-internal-surface-area lattices where coating defects or delamination can significantly distort local dosing [120,122].

7.4. Local Safety and Toxicity as a Design Constraint

Local safety is a key design limitation since burst release and ion elution may go beyond levels that are safe for cells, even when antibacterial effectiveness is reached [11,80,133]. This is particularly important for techniques that use antibacterial ions, because the therapeutic window is small and the body's reactions might cancel out the benefits of the antibacterial effects [130,133]. In degradable Mg-based systems, drug release is also linked to changes in pH, hydrogen evolution, and Mg^{2+} flux caused by corrosion [106,110,111,119]. Therefore, the coating simultaneously acts as both a drug reservoir and a barrier that controls corrosion [113–115,117], indicating that release curves are easiest to understand when they are shown alongside degradation indicators and local biological effects, rather than as separate kinetics [116,119,134]. In general, dosage management should be seen as achieving enough local efficacy while minimizing peak-related toxicity and maintaining tissue integration [11,133].

Local toxicity must be regarded as a primary design limitation, particularly for antibacterial ions with a limited therapeutic window [11,80]. In vivo evidence from the reviewed studies indicates that ion-based strategies can be ineffective even with a clear antibacterial objective: in a rat tibia model, a silver nanoparticle coating on AM porous titanium did not diminish infection rates and was linked to increased osteoclast activity, while a vancomycin coating did lower infection rates [11]. This underscores that peak exposure and host response can undermine antimicrobial efficacy when release control is inadequate [80,133]. This encourages the reporting of the coupling of release kinetics with local biological readouts (cell viability, osteogenesis/osteoclast markers, and peri-implant histology) and endorses strategies that inhibit burst (barrier layers, sealed reservoirs, staged delivery) to preserve efficacy without undermining integration [40,84,88,100].

7.5. Limitations of Current Evidence and of This Review

Direct comparisons between studies are still limited by differences in AM architectures (like porosity, pore size distributions, lattice topology, and internal surface area), coating thickness and uniformity in complex pore networks, and release-testing conditions like medium selection, refresh strategy, sampling frequency, and reporting units. In vivo data is likewise inconsistent within alloy families and therapeutic categories, with several studies documenting biological consequences without measuring local exposure at specified distances from the implant surface. This analysis identifies constraints that hinder quantitative ranking across platforms. Hence, the focus is on cross-study trends and design principles that connect structure, reservoir strategy, release behavior, and reported biological consequences.

8. Conclusions

The evaluated literature indicates that additive manufacturing allows metallic implants to serve as drug-eluting therapeutic platforms, in addition to functioning as structural devices. By enabling control over porosity, interconnectivity, internal surface area, and diffusion pathways, additive manufacturing makes implant architecture a critical determinant of local concentration–time profiles at the implant–tissue interface, thereby facilitating clinically important goals such as infection prevention, inflammation control, and enhanced osseointegration.

Across alloy systems, surface modification and coating techniques consistently serve as the essential interface that transforms printed metals into controllable drug reservoirs. Nanostructured features, conversion layers, and polymer or hydrogel coatings can be designed to control burst release and sustained delivery, while concurrently affecting corrosion behavior and biological response through modifications in surface chemistry, micro- or nano-topography, and thin-film architecture.

Overall, the evidence suggests that the most effective drug-eluting implants result from an integrated design of both lattice architecture and surface reservoir chemistry, facilitating adjustable therapeutic delivery while maintaining implant functionality.

Author Contributions: Conceptualization, C.-W.C. and S.D.; Methodology, C.-W.C. and S.D.; Writing—original draft, S.D.; Writing—review and editing, C.-W.C., L.C. and S.D.; Visualization, S.D.; Supervision, C.-W.C. and L.C.; Project administration, C.-W.C. and L.C.; Funding acquisition, C.-W.C. and L.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Queen’s University, Belfast (grant number R8448MEE).

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Acknowledgments: Support from the infrastructure of Queen’s University, Belfast, is acknowledged.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

AM	Additive manufacturing
Ti	Titanium
Mg	Magnesium
Zn	Zinc
Fe	Iron
LPBF	Laser powder bed fusion
EBM	Electron beam melting
DED	Directed-energy deposition
PEO	Plasma electrolytic oxidation
MAO	Micro-arc oxidation
PLGA	Poly (lactic-co-glycolic acid)
MIC	Minimum inhibitory concentration
VEGF	Vascular endothelial growth factor
BMP-2	Bone morphogenetic protein-2
Ag	Silver
Cu	Copper
SS	Stainless steel
PC	Polycaprolactone
PLA	Poly(lactic acid)
SLM	Selective laser melting
DLP	Digital Light Processing
BT/HA	Barium titanate/Hydroxyapatite (composite)
TNTs	TiO ₂ nanotubes
LbL	Layer-by-layer
PEG	Poly (ethylene glycol)
MC3T3-E1	Mouse calvaria-derived pre-osteoblast cell line
ALP	Alkaline phosphatase
PBS	Phosphate-buffered saline
PHB	Poly(3-hydroxybutyrate)

OCN/OPN	Osteocalcin/Osteopontin
BC	Bacterial cellulose
SEM	Scanning electron microscopy
PSS/PAH	Poly (styrene sulfonate)/Poly (allylamine hydrochloride)
MH	Magnesium hydroxide
MgO	Magnesium oxide
HNT	Halloysite nanotubes
RSV	Rosuvastatin
ASP	Aspirin (acetylsalicylic acid)
EPD	Electrophoretic deposition
HUVEC	Human umbilical vein endothelial cell
nSiHA	nano-sized silicon-substituted hydroxyapatite
ELISA	Enzyme-linked immunosorbent assay
rhBMP	recombinant human BMP-2
OPN	Osteopontin
ELI	Extra-Low Interstitial (grade of Ti-6Al-4V)
CaP	Calcium phosphate
ICP	Inductively coupled plasma
PDGF-BB	Platelet-derived growth factor-BB
BV/TV	Bone volume/tissue volume
BMMSC	Bone marrow-derived mesenchymal stem cells
AgNPs	Silver nanoparticles
MBG	Mesoporous bioactive glass
Sr	Strontium
AMK	Amikacin
Zr	Zirconium
TCP	Tricalcium phosphate
mPEG	Methoxy-poly (ethylene glycol)
PDA	Polydopamine
PMCP	poly[2-(methacryloyloxy)ethyl choline phosphate]
MOF/PVA	Metal-organic framework/Poly (vinyl alcohol)
PSC	pH-neutral bioactive glass coating
μCT	Micro-computed tomography
GA	Glutaraldehyde
BIC	Bone-implant contact
Wnt	Wingless/integrated signaling pathway
VG/TB	Van Gieson/Toluidine Blue staining

References

1. Abraham, A.M.; Venkatesan, S. A Review on Application of Biomaterials for Medical and Dental Implants. *Proc. Inst. Mech. Eng. Part J. Mater. Des. Appl.* **2023**, *237*, 249–273. [\[CrossRef\]](#)
2. Amirtharaj Mosas, K.K.; Chandrasekar, A.R.; Dasan, A.; Pakseresht, A.; Galusek, D. Recent Advancements in Materials and Coatings for Biomedical Implants. *Gels* **2022**, *8*, 323. [\[CrossRef\]](#) [\[PubMed\]](#)
3. Phull, S.S.; Yazdi, A.R.; Ghert, M.; Towler, M.R. Bone Cement as a Local Chemotherapeutic Drug Delivery Carrier in Orthopedic Oncology: A Review. *J. Bone Oncol.* **2020**, *26*, 100345. [\[CrossRef\]](#)
4. Steadman, W.; Chapman, P.R.; Schuetz, M.; Schmutz, B.; Trampuz, A.; Tetsworth, K. Local Antibiotic Delivery Options in Prosthetic Joint Infection. *Antibiotics* **2023**, *12*, 752. [\[CrossRef\]](#) [\[PubMed\]](#)
5. Zhang, H.; Qiao, W.; Liu, Y.; Yao, X.; Zhai, Y.; Du, L. Addressing the Challenges of Infectious Bone Defects: A Review of Recent Advances in Bifunctional Biomaterials. *J. Nanobiotechnol.* **2025**, *23*, 257. [\[CrossRef\]](#)
6. Bartolomeu, F.; Buciumeanu, M.; Pinto, E.; Alves, N.; Carvalho, O.; Silva, F.; Miranda, G. 316L Stainless Steel Mechanical and Tribological Behavior-A Comparison between Selective Laser Melting, Hot Pressing and Conventional Casting. *Addit. Manuf.* **2017**, *16*, 81–89. [\[CrossRef\]](#)
7. Luo, A.A. Magnesium Casting Technology for Structural Applications. *J. Magnes. Alloy.* **2013**, *1*, 2–22. [\[CrossRef\]](#)

8. Xu, Y.; Jiang, W.; Li, Q.; Niu, Y.; Yu, L.; Li, G.; Fan, Z. Significantly Improved Bonding Strength of Al/Mg Bimetallic Interface by Compound Casting via FeCoNiCrCu High Entropy Alloy Coating. *J. Mater. Res. Technol.* **2024**, *30*, 6870–6876. [\[CrossRef\]](#)
9. Alam, M.S.; Campbell, S.R.; Spivey, S.R.; Dutta, G.; Pal, N.; Karan, A.; Xie, J.; DeCoster, M.A.; Murray, E.P. Additively Manufactured 316L Stainless Steel as a Potential Alternative Implant Material. *J. Mater. Res. Technol.* **2025**, *34*, 2358–2373.
10. Bai, L.; Gong, C.; Chen, X.; Sun, Y.; Zhang, J.; Cai, L.; Zhu, S.; Xie, S.Q. Additive Manufacturing of Customized Metallic Orthopedic Implants: Materials, Structures, and Surface Modifications. *Metals* **2019**, *9*, 1004. [\[CrossRef\]](#)
11. Croes, M.; Bakhshandeh, S.; van Hengel, L.; Lietaert, K.; van Kessel, K.; Pouran, B.; van der Wal, B.; Vogely, H.; Van Hecke, W.; Fluit, A.; et al. Antibacterial and Immunogenic Behavior of Silver Coatings on Additively Manufactured Porous Titanium. *ACTA Biomater.* **2018**, *81*, 315–327. [\[CrossRef\]](#)
12. Davoodi, E.; Montazerian, H.; Mirhakimi, A.; Zhianmanesh, M.; Ibhaddode, O.; Shahabad, S.; Esmaeilizadeh, R.; Sarikhani, E.; Toorandaz, S.; Sarabi, S.; et al. Additively Manufactured Metallic Biomaterials. *Bioact. Mater.* **2022**, *15*, 214–249. [\[CrossRef\]](#)
13. Booth, M.A.; Pope, L.; Sherrell, P.C.; Stacey, A.; Tran, P.A.; Fox, K.E. Polycrystalline Diamond Coating on 3D Printed Titanium Scaffolds: Surface Characterisation and Foreign Body Response. *Mater. Sci. Eng. C* **2021**, *130*, 112467. [\[CrossRef\]](#) [\[PubMed\]](#)
14. Chen, Z.; Wang, B.; Yang, C.; Lv, Z.; Wei, Y.; Pan, T.; Xuan, F.; Zhou, X.; Shen, H.; Wang, L.; et al. 3D Printed Pedicle Screws with Microarc Oxidation Ceramic Interfaces Enhance Osteointegration and Orthopedic Fixation Feasibility. *ACS Appl. Mater. Interfaces* **2024**, *16*, 31983–31996. [\[CrossRef\]](#)
15. Aufa, A.N.; Hassan, M.Z.; Ismail, Z. Recent Advances in Ti-6Al-4V Additively Manufactured by Selective Laser Melting for Biomedical Implants: Prospect Development. *J. Alloys Compd.* **2022**, *896*, 163072. [\[CrossRef\]](#)
16. Kumar, A.; Singh, G. Surface Modification of Ti6Al4V Alloy via Advanced Coatings: Mechanical, Tribological, Corrosion, Wetting, and Biocompatibility Studies. *J. Alloys Compd.* **2024**, *989*, 174418. [\[CrossRef\]](#)
17. Tan, X.; Kok, Y.; Tan, Y.; Descoins, M.; Mangelinck, D.; Tor, S.; Leong, K.; Chua, C. Graded Microstructure and Mechanical Properties of Additive Manufactured Ti-6Al-4V via Electron Beam Melting. *ACTA Mater.* **2015**, *97*, 1–16. [\[CrossRef\]](#)
18. Aguilar, L.; Lee, J.; Park, C.; Kim, C. Biomedical Grade Stainless Steel Coating of Polycaffeic Acid via Combined Oxidative and Ultraviolet Light-Assisted Polymerization Process for Bioactive Implant Application. *Polymers* **2019**, *11*, 584. [\[CrossRef\]](#)
19. Bayram, C.; Mizrak, A.; Aktürk, S.; Kursaklioglu, H.; Iyisoy, A.; Ifran, A.; Denkbaz, E. In Vitro Biocompatibility of Plasma-Aided Surface-Modified 316L Stainless Steel for Intracoronary Stents. *Biomed. Mater.* **2010**, *5*, 055007. [\[CrossRef\]](#)
20. Chen, S.; Kuo, C.; Su, Y.; Huang, J.; Wu, Y.; Lin, Y.; Chung, Y.; Ng, C. Microstructure and Fracture Properties of Open-Cell Porous Ti-6Al-4V with High Porosity Fabricated by Electron Beam Melting. *Mater. Charact.* **2018**, *138*, 255–262. [\[CrossRef\]](#)
21. Daniel, S.A.; Suya Prem Anand, P. A Review on the Utilization of SS 316L Lattice Structures for Orthopaedics Developed by the Laser Powder Bed Fusion Process. *Proc. Inst. Mech. Eng. Part E J. Process Mech. Eng.* **2025**, 09544089251317120. [\[CrossRef\]](#)
22. Grüger, L.; Jensch, F.; Dittrich, F.; Härtel, S. On the Creation of a Material Bond between L-PBF-Manufactured AZ91 and Ti-6Al-4V Components in the Context of Medical Applications. *Materials* **2024**, *17*, 4667. [\[CrossRef\]](#) [\[PubMed\]](#)
23. Zhai, C.; Wang, W.; Ma, A.; Liu, H.; Zhu, T.; Zhang, Y.; Yu, T.; Yang, Z.; Lan, J.; Wang, Z. Laser Powder Bed Fusion (LPBF) WE43 Magnesium Scaffold with EGCG/PDA-Functionalized Silk Fibroin Membrane for Antibacterial Osteoinductive Guided Bone Regeneration. *ACS Appl. Mater. Interfaces* **2025**, *17*, 51691–51706.
24. Zuo, X.; Zhang, W.; Chen, Y.; Oliveira, J.; Zeng, Z.; Li, Y.; Luo, Z.; Ao, S. Wire-Based Directed Energy Deposition of NiTiTa Shape Memory Alloys: Microstructure, Phase Transformation, Electrochemistry, X-Ray Visibility and Mechanical Properties. *Addit. Manuf.* **2022**, *59*, 103115.
25. Snow, Z.; Nassar, A.R.; Reutzel, E.W. Invited Review Article: Review of the Formation and Impact of Flaws in Powder Bed Fusion Additive Manufacturing. *Addit. Manuf.* **2020**, *36*, 101457. [\[CrossRef\]](#)
26. Wang, L.; Zhang, Y.; Chia, H.Y.; Yan, W. Mechanism of Keyhole Pore Formation in Metal Additive Manufacturing. *Npj Comput. Mater.* **2022**, *8*, 22.
27. Barberi, J.; Spriano, S. Titanium and Protein Adsorption: An Overview of Mechanisms and Effects of Surface Features. *Materials* **2021**, *14*, 1590. [\[CrossRef\]](#)
28. Cardoso, G.C.; Grandini, C.R.; Rau, J.V. Comprehensive Review of PEO Coatings on Titanium Alloys for Biomedical Implants. *J. Mater. Res. Technol.* **2024**, *31*, 311–328. [\[CrossRef\]](#)
29. Chatpaiboonwat, V.; Trachoo, V.; Promoppatum, P.; Chobaomsup, V.; Saengkiattiyut, K.; Srimaneepong, V.; Wattanasirmit, K. Optimizing the Surface Quality of L-PBF Ti6Al4V ELI Alloy via Electropolishing and Its Effect on Corrosion Resistance for Dental Applications. *Eur. J. Dent.* **2025**, *19*, 1146–1152.
30. Haribaskar, R.; Kumar, T.S. Defects in Metal Additive Manufacturing: Formation, Process Parameters, Postprocessing, Challenges, Economic Aspects, and Future Research Directions. *3D Print. Addit. Manuf.* **2024**, *11*, e1629–e1655. [\[CrossRef\]](#) [\[PubMed\]](#)
31. Jamshidi, P.; Aristizabal, M.; Kong, W.; Villapun, V.; Cox, S.C.; Grover, L.M.; Attallah, M.M. Selective Laser Melting of Ti-6Al-4V: The Impact of Post-Processing on the Tensile, Fatigue and Biological Properties for Medical Implant Applications. *Materials* **2020**, *13*, 2813. [\[CrossRef\]](#)

32. Jemat, A.; Ghazali, M.J.; Razali, M.; Otsuka, Y. Surface Modifications and Their Effects on Titanium Dental Implants. *BioMed Res. Int.* **2015**, *2015*, 791725. [[CrossRef](#)]
33. Pegues, J.W.; Shao, S.; Shamsaei, N.; Sanaei, N.; Fatemi, A.; Warner, D.H.; Li, P.; Phan, N. Fatigue of Additive Manufactured Ti-6Al-4V, Part I: The Effects of Powder Feedstock, Manufacturing, and Post-Process Conditions on the Resulting Microstructure and Defects. *Int. J. Fatigue* **2020**, *132*, 105358. [[CrossRef](#)]
34. Tjandra, J.; Alabort, E.; Barba, D.; Pedrazzini, S. Corrosion, Fatigue and Wear of Additively Manufactured Ti Alloys for Orthopaedic Implants. *Mater. Sci. Technol.* **2023**, *39*, 2951–2965. [[CrossRef](#)]
35. Wang, W.; Liu, H.; Guo, Z.; Hu, Z.; Wang, K.; Leng, Y.; Yuan, C.; Li, Z.; Ge, X. Various Antibacterial Strategies Utilizing Titanium Dioxide Nanotubes Prepared via Electrochemical Anodization Biofabrication Method. *Biomimetics* **2024**, *9*, 408. [[CrossRef](#)] [[PubMed](#)]
36. Ahmad, K.; Manzur, J.; Tahir, M.; Hussain, R.; Khan, M.; Wadood, A.; Avcu, E.; Rehman, M. Electrophoretic Deposition, Microstructure and Selected Properties of Zein/Cloves Coatings on 316L Stainless Steel. *Prog. Org. Coat.* **2023**, *176*, 107407. [[CrossRef](#)]
37. Ahmed, I.; Ahmad, A.; Abdul-Rani, A.M.; Tasnim, N.; Al-Amin, M. A Comparative Review of Surface Modification Technique Between Physical Vapor Deposition (PVD) and Plasma Electrolytic Oxidation (PEO) for Biomedical Applications. In *ICPER 2020, Proceedings of the 7th International Conference on Production, Energy and Reliability, Kuchig, Malaysia, 14–16 July 2020; Lecture Notes in Mechanical Engineering; Ahmad, F., Al-Kayiem, H.H., King Soon, W.P., Eds.; Springer: Singapore, 2023; pp. 813–829.*
38. Amaravathy, P.; Sampath Kumar, T.S. Novel Strontium Doped Zinc Calcium Phosphate Conversion Coating on AZ31 Magnesium Alloy for Biomedical Applications. *J. Biomim. Biomater. Biomed. Eng.* **2017**, *34*, 57–67.
39. Arunadevi, N.; Kirubavathy, S.J. Metal Oxides: Advanced Inorganic Materials. In *Inorganic Anticorrosive Materials: Past, Present and Future Perspectives*; Elsevier: Amsterdam, The Netherlands, 2021; pp. 21–54, ISBN 978-032390410-0.
40. Baldin, E.; de Castro, V.; Santos, P.; Aguzzoli, C.; Bernardi, F.; Medeiros, T.; Maurmann, N.; Pranke, P.; Frassini, R.; Roesch, M.; et al. Copper Incorporation by Low-Energy Ion Implantation in PEO-Coated Additively Manufactured Ti6Al4V ELI: Surface Microstructure, Cytotoxicity and Antibacterial Behavior. *J. Alloys Compd.* **2023**, *940*, 168735. [[CrossRef](#)]
41. Dabalà, M.; Brunelli, K.; Napolitani, E.; Magrini, M. Cerium-Based Chemical Conversion Coating on AZ63 Magnesium Alloy. *Surf. Coat. Technol.* **2003**, *172*, 227–232. [[CrossRef](#)]
42. Ren, J.; Jiang, Z.; He, J.; Wang, X.; Jin, W.; Yu, Z. Current Status and Perspectives on Design, Fabrication, Surface Modification, and Clinical Applications of Biodegradable Magnesium Alloys. *J. Magnes. Alloy.* **2025**, *13*, 3564–3595. [[CrossRef](#)]
43. Fan, X.; Du, J.; Li, Y.; Duan, K.; Liu, G. Electrophoretic Deposition of Magnesium Oxide Coating on Micro-Arc Oxidized Titanium for Antibacterial Activity and Biocompatibility. *J. Orthop. Surg.* **2023**, *18*, 901.
44. Liu, Z.; Xu, Z.; Wang, X.; Zhang, Y.; Wu, Y.; Jiang, D.; Jia, R. Construction and Osteogenic Effects of 3D-Printed Porous Titanium Alloy Loaded with VEGF/BMP-2 Shell-Core Microspheres in a Sustained-Release System. *Front. Bioeng. Biotechnol.* **2022**, *10*, 1028278. [[CrossRef](#)]
45. Ma, W.H.; Liu, Y.J.; Wang, W.; Zhang, Y.Z. Improved Biological Performance of Magnesium by Micro-Arc Oxidation. *Braz. J. Med. Biol. Res.* **2014**, *48*, 214–225. [[CrossRef](#)] [[PubMed](#)]
46. Wang, T.; Weng, Z.; Liu, X.; Yeung, K.W.K.; Pan, H.; Wu, S. Controlled Release and Biocompatibility of Polymer/Titania Nanotube Array System on Titanium Implants. *Bioact. Mater.* **2017**, *2*, 44–50. [[CrossRef](#)]
47. Zhang, H.; Sun, Y.; Tian, A.; Xue, X.X.; Wang, L.; Alquhali, A.; Bai, X. Improved Antibacterial Activity and Biocompatibility on Vancomycin-Loaded TiO₂ Nanotubes: In Vivo and in Vitro Studies. *Int. J. Nanomed.* **2013**, *8*, 4379–4389. [[CrossRef](#)] [[PubMed](#)]
48. Xu, W.; Zhao, J.; Li, C.; Qi, M.; Li, X.; Wang, L.; Zhou, Y. Surface Functionalization of TiO₂ Nanotubes with Minocycline and Its in Vitro Biological Effects on Schwann Cells. *Biomed. Eng. OnLine* **2018**, *17*, 88.
49. Helms, S.; O'Neill, L.; Behbahani, S.; Tzeng, J.; Jeray, K.; Kennedy, M.; Cross, A.; Tanner, S.; DesJardins, J. Efficacy of a Plasma-Deposited, Vancomycin/Chitosan Antibiotic Coating for Orthopaedic Devices in a Bacterially Challenged Rabbit Model. *Materialia* **2021**, *17*, 101122. [[CrossRef](#)]
50. Swanson, T.E.; Cheng, X.; Friedrich, C. Development of Chitosan-Vancomycin Antimicrobial Coatings on Titanium Implants. *J. Biomed. Mater. Res. A* **2011**, *97*, 167–176. [[CrossRef](#)] [[PubMed](#)]
51. Wongsuwan, N.; Dwivedi, A.; Tancharoen, S.; Nasongkla, N. Development of Dental Implant Coating with Minocycline-Loaded Niosome for Antibacterial Application. *J. Drug Deliv. Sci. Technol.* **2020**, *56*, 101555. [[CrossRef](#)]
52. Xue, K.; Liang, L.-X.; Cheng, S.-C.; Liu, H.-P.; Cui, L.-Y.; Zeng, R.-C.; Li, S.-Q.; Wang, Z.-L. Corrosion Resistance, Antibacterial Activity and Drug Release of Ciprofloxacin-Loaded Micro-Arc Oxidation/Silane Coating on Magnesium Alloy AZ31. *Prog. Org. Coat.* **2021**, *158*, 106357. [[CrossRef](#)]
53. Alotaibi, H.F.; Perni, S.; Prokopovich, P. Nanoparticle-Based Model of Anti-Inflammatory Drug Releasing LbL Coatings for Uncemented Prosthesis Aseptic Loosening Prevention. *Int. J. Nanomed.* **2019**, *14*, 7309–7322. [[CrossRef](#)] [[PubMed](#)]

54. Shen, K.; Tang, Q.; Fang, X.; Zhang, C.; Zhu, Z.; Hou, Y.; Lai, M. The Sustained Release of Dexamethasone from TiO₂ Nanotubes Reinforced by Chitosan to Enhance Osteoblast Function and Anti-Inflammation Activity. *Mater. Sci. Eng. C Mater. Biol. Appl.* **2020**, *116*, 111241. [\[CrossRef\]](#)
55. Huang, B.; Yao, Q.; Huang, Y.; Zhang, L.; Yao, Y.; Gong, P.; Tang, H. Combination Use of BMP2 and VEGF165 Promotes Osseointegration and Stability of Titanium Implants in Irradiated Bone. *BioMed Res. Int.* **2018**, *2018*, 8139424. [\[CrossRef\]](#)
56. Ramazanoglu, M.; Lutz, R.; Rusche, P.; Trabzon, L.; Kose, G.T.; Prechtel, C.; Schlegel, K.A. Bone Response to Biomimetic Implants Delivering BMP-2 and VEGF: An Immunohistochemical Study. *J. Cranio-Maxillofac. Surg.* **2013**, *41*, 826–835. [\[CrossRef\]](#)
57. Haugen, H.J.; Makhtari, S.; Ahmadi, S.; Hussain, B. The Antibacterial and Cytotoxic Effects of Silver Nanoparticles Coated Titanium Implants: A Narrative Review. *Materials* **2022**, *15*, 5025. [\[CrossRef\]](#)
58. osman, H.; Wang, F.; Zou, G.; Zhang, D.; Bai, X.; Jiang, T.; Wang, Y. Antibacterial and Osteogenic Gain Strategy on Titanium Surfaces for Preventing Implant-Related Infections. *Colloids Surf. B Biointerfaces* **2025**, *249*, 114489. [\[CrossRef\]](#)
59. Soma, T.; Iwasaki, R.; Sato, Y.; Kobayashi, T.; Ito, E.; Matsumoto, T.; Kimura, A.; Homma, F.; Saiki, K.; Takahashi, Y.; et al. An Ionic Silver Coating Prevents Implant-Associated Infection by Anaerobic Bacteria in Vitro and in Vivo in Mice. *Sci. Rep.* **2022**, *12*, 18387. [\[CrossRef\]](#)
60. Li, F.; Zhang, W.; Kooi, B.J.; Pei, Y. Eutectic Aluminum Alloys Fabricated by Additive Manufacturing: A Comprehensive Review. *J. Mater. Sci. Technol.* **2026**, *250*, 123–164. [\[CrossRef\]](#)
61. Godoy-Gallardo, M.; Eckhard, U.; Delgado, L.M.; de Roo Puente, Y.J.D.; Hoyos-Nogués, M.; Gil, F.J.; Perez, R.A. Antibacterial Approaches in Tissue Engineering Using Metal Ions and Nanoparticles: From Mechanisms to Applications. *Bioact. Mater.* **2021**, *6*, 4470–4490. [\[CrossRef\]](#)
62. Sczesny, N.F.; Wiggers, H.J.; Bueno, C.Z.; Chevallier, P.; Copes, F.; Mantovani, D. From Burst to Sustained Release: The Effect of Antibiotic Structure Incorporated into Chitosan-Based Films. *Antibiotics* **2024**, *13*, 1055. [\[CrossRef\]](#) [\[PubMed\]](#)
63. Wassif, R.K.; Elkayal, M.; Shamma, R.N.; Elkheshen, S.A. Recent Advances in the Local Antibiotics Delivery Systems for Management of Osteomyelitis. *Drug Deliv.* **2021**, *28*, 2392–2414. [\[CrossRef\]](#)
64. Giacchi, J.V.; Morando, C.N.; Fornaro, O.; Palacio, H.A. Microstructural Characterization of As-Cast Biocompatible Co-Cr-Mo Alloys. *Mater. Charact.* **2011**, *62*, 53–61.
65. Kishchik, M.S.; Mikhaylovskaya, A.V.; Kotov, A.D.; Mosleh, A.O.; AbuShanab, W.S.; Portnoy, V.K. Effect of Multidirectional Forging on the Grain Structure and Mechanical Properties of the Al-Mg-Mn Alloy. *Materials* **2018**, *11*, 2166. [\[CrossRef\]](#)
66. Dawood, A.; Marti, B.; Sauret-Jackson, V.; Darwood, A. 3D Printing in Dentistry. *Br. Dent. J.* **2015**, *219*, 521–529. [\[CrossRef\]](#)
67. Arabnejad, S.; Johnston, B.; Tanzer, M.; Pasini, D. Fully Porous 3D Printed Titanium Femoral Stem to Reduce Stress-Shielding Following Total Hip Arthroplasty. *J. Orthop. Res.* **2017**, *35*, 1774–1783. [\[CrossRef\]](#) [\[PubMed\]](#)
68. Taniguchi, N.; Fujibayashi, S.; Takemoto, M.; Sasaki, K.; Otsuki, B.; Nakamura, T.; Matsushita, T.; Kokubo, T.; Matsuda, S. Effect of Pore Size on Bone Ingrowth into Porous Titanium Implants Fabricated by Additive Manufacturing: An in Vivo Experiment. *Mater. Sci. Eng. C Mater. Biol. Appl.* **2016**, *59*, 690–701. [\[CrossRef\]](#)
69. Yan, C.; Hao, L.; Hussein, A.; Young, P. Ti-6Al-4V Triply Periodic Minimal Surface Structures for Bone Implants Fabricated via Selective Laser Melting. *J. Mech. Behav. Biomed. Mater.* **2015**, *51*, 61–73. [\[PubMed\]](#)
70. Sing, S.; Wiria, F.; Yeong, W. Selective Laser Melting of Lattice Structures: A Statistical Approach to Manufacturability and Mechanical Behavior. *Robot. Comput. Integr. Manuf.* **2018**, *49*, 170–180. [\[CrossRef\]](#)
71. Xue, R.; Yuan, P.; Zhao, B.; Jing, F.; Kou, X.; Yue, W.; Wang, Y.; Wang, D.; Sewvandi, G.; Hu, D. DLP Printing of BT/HA Nanocomposite Ceramic Scaffolds Using Low Refractive Index BT Crystals. *J. Mater.* **2024**, *10*, 1036–1048.
72. Bocchetta, P.; Chen, L.-Y.; Tardelli, J.D.C.; dos Reis, A.C.; Almeraya-Calderón, F.; Leo, P. Passive Layers and Corrosion Resistance of Biomedical Ti-6Al-4V and β -Ti Alloys. *Coatings* **2021**, *11*, 487. [\[CrossRef\]](#)
73. Quinn, J.; McFadden, R.; Chan, C.-W.; Carson, L. Titanium for Orthopedic Applications: An Overview of Surface Modification to Improve Biocompatibility and Prevent Bacterial Biofilm Formation. *iScience* **2020**, *23*, 101745. [\[CrossRef\]](#)
74. Calazans Neto, J.V.; dos Reis, A.C.; da Costa Valente, M.L. Osseointegration in Additive-Manufactured Titanium Implants: A Systematic Review of Animal Studies on the Need for Surface Treatment. *Heliyon* **2023**, *9*, e17105. [\[CrossRef\]](#)
75. Distefano, F.; Pasta, S.; Epasto, G. Titanium Lattice Structures Produced via Additive Manufacturing for a Bone Scaffold: A Review. *J. Funct. Biomater.* **2023**, *14*, 125. [\[CrossRef\]](#)
76. Kunrath, M.F.; Farina, G.; Sturmer, L.B.S.; Teixeira, E.R. TiO₂ Nanotubes as an Antibacterial Nanotextured Surface for Dental Implants: Systematic Review and Meta-Analysis. *Dent. Mater.* **2024**, *40*, 907–920. [\[CrossRef\]](#)
77. Jahanmard, F.; Dijkmans, F.; Majed, A.; Vogely, H.; van der Wal, B.; Stapels, D.; Ahmadi, S.; Vermonden, T.; Yavari, S. Toward Antibacterial Coatings for Personalized Implants. *ACS Biomater. Sci. Eng.* **2020**, *6*, 5486–5492. [\[CrossRef\]](#) [\[PubMed\]](#)
78. Chudinova, E.; Koptuyug, A.; Mukhortova, Y.; Pryadko, A.; Volkova, A.; Ivanov, A.; Plotnikov, E.; Khan, Y.; Eppe, M.; Sokolova, V.; et al. Functionalization of Additive-Manufactured Ti6Al4V Scaffolds with Poly (Allylamine Hydrochloride)/Poly (Styrene Sulfonate) Bilayer Microcapsule System Containing Dexamethasone. *Mater. Chem. Phys.* **2021**, *27*, 125099. [\[CrossRef\]](#)

79. Li, Y.; Liu, Y.; Bai, H.; Li, R.; Shang, J.; Zhu, Z.; Zhu, L.; Zhu, C.; Che, Z.; Wang, J.; et al. Sustained Release of VEGF to Promote Angiogenesis and Osteointegration of Three-Dimensional Printed Biomimetic Titanium Alloy Implants. *Front. Bioeng. Biotechnol.* **2021**, *9*, 757767. [\[CrossRef\]](#)
80. Diez-Escudero, A.; Carlsson, E.; Andersson, B.; Järhult, J.; Hailer, N. Trabecular Titanium for Orthopedic Applications: Balancing Antimicrobial with Osteoconductive Properties by Varying Silver Contents. *ACS Appl. Mater. Interfaces* **2022**, *37*, 41751–41763. [\[CrossRef\]](#)
81. Karaji, Z.; Jahanmard, F.; Mirzaei, A.; van der Wal, B.; Yavari, S. A Multifunctional Silk Coating on Additively Manufactured Porous Titanium to Prevent Implant-Associated Infection and Stimulate Bone Regeneration. *Biomed. Mater.* **2020**, *15*, 065016. [\[CrossRef\]](#) [\[PubMed\]](#)
82. Hai, J.; Zhang, X.; Lei, Y.; Shan, C.; Ma, X.; Jing, L.; Shi, W.; Yang, Q.; Li, Y.; Xu, Q.; et al. 3D Printed TC4 Titanium Alloy Bone Scaffolds with TNTs-VA-PLGA Composite Coating on the Surface: Improved Infection Resistance and Biocompatibility. *J. Drug Deliv. Sci. Technol.* **2024**, *102*, 106386.
83. Ma, Z.; Zhao, Y.; Xu, Z.; Zhang, Y.; Han, Y.; Jiang, H.; Sun, P.; Feng, W. 3D-Printed Porous Titanium Rods Equipped with Vancomycin-Loaded Hydrogels and Polycaprolactone Membranes for Intelligent Antibacterial Drug Release. *Sci. Rep.* **2024**, *14*, 21749. [\[CrossRef\]](#)
84. Bakhshandeh, S.; Karaji, Z.; Lietaert, K.; Fluit, A.; Boel, C.; Vogely, H.; Vermonden, T.; Hennink, W.; Weinans, H.; Zadpoor, A.; et al. Simultaneous Delivery of Multiple Antibacterial Agents from Additively Manufactured Porous Biomaterials to Fully Eradicate Planktonic and Adherent Staphylococcus Aureus. *ACS Appl. Mater. Interfaces* **2017**, *9*, 25691–25699. [\[CrossRef\]](#)
85. Jahanmard, F.; Croes, M.; Castilho, M.; Majed, A.; Steenbergen, M.; Lietaert, K.; Vogely, H.; van der Wal, B.; Stapels, D.; Malda, J.; et al. Bactericidal Coating to Prevent Early and Delayed Implant-Related Infections. *J. Control. Release* **2020**, *326*, 38–52. [\[CrossRef\]](#) [\[PubMed\]](#)
86. Fan, S.; Tan, Z.; Peng, Z.; Li, S.; Lei, H.; Qin, Y.; Fan, H.; Lin, Y.; Zhou, C. Customized 3D Printed Porous Titanium Scaffolds with Nanotubes Loading Antibacterial Drugs for Bone Tissue Engineering. *Rev. Adv. Mater. Sci.* **2024**, *63*, 20240030. [\[CrossRef\]](#)
87. Burger, L.; Conzelmann, A.; Ulrich, S.; Mozaffari-Jovein, H. Process Development of a Generative Method for Partial and Controlled Integration of Active Substances into Open-Porous Matrix Structures. *Materials* **2023**, *16*, 6985. [\[CrossRef\]](#) [\[PubMed\]](#)
88. Micheletti, C.; Suriano, R.; Grandfield, K.; Turri, S. Drug Release from Polymer-Coated TiO₂ Nanotubes on Additively Manufactured Ti-6Al-4V Bone Implants: A Feasibility Study. *Nano Express* **2021**, *2*, 010018. [\[CrossRef\]](#)
89. Im, S.; Kim, K.; Kwon, J. Antibacterial and Osteogenic Activity of Titania Nanotubes Modified with Electrospray-Deposited Tetracycline Nanoparticles. *Nanomaterials* **2020**, *10*, 1093. [\[CrossRef\]](#)
90. Dydak, K.; Junka, A.; Szymczyk, P.; Chodaczek, G.; Toporkiewicz, M.; Fijałkowski, K.; Dudek, B.; Bartoszewicz, M. Development and Biological Evaluation of Ti6Al7Nb Scaffold Implants Coated with Gentamycin-Saturated Bacterial Cellulose Biomaterial. *PLoS ONE* **2018**, *13*, e0205205. [\[CrossRef\]](#)
91. You, Y.; Wang, W.; Li, Y.; Song, Y.; Jiao, J.; Wang, Y.; Chen, B.; Liu, J.; Qi, H.; Liang, Y. Aspirin/PLGA Coated 3D-Printed Ti-6Al-4V Alloy Modulate Macrophage Polarization to Enhance Osteoblast Differentiation and Osseointegration. *J. Mater. Sci.-Mater. Med.* **2022**, *33*, 73. [\[CrossRef\]](#)
92. Yuan, B.; Liu, P.; Zhao, R.; Yang, X.; Xiao, Z.; Zhang, K.; Zhu, X.; Zhang, X. Functionalize d 3D-Printe d Porous Titanium Scaffold Induces in Situ Vascularized Bone Regeneration by Orchestrating Bone Microenvironment. *J. Mater. Sci. Technol.* **2023**, *153*, 92–105. [\[CrossRef\]](#)
93. Zhu, Z.; Li, X.; Li, Y.; Zhu, L.; Zhu, C.; Che, Z.; Huang, L. Three-Dimensionally Printed Porous Biomimetic Composite for Sustained Release of Recombinant Human Bone Morphogenetic Protein 9 to Promote Osteointegration. *Mater. Des.* **2021**, *208*, 109882. [\[CrossRef\]](#)
94. Izquierdo-Barba, I.; Santos-Ruiz, L.; Becerra, J.; Feito, M.; Fernández-Villa, D.; Serrano, M.; Díaz-Güemes, I.; Fernández-Tomé, B.; Enciso, S.; Sánchez-Margallo, F.; et al. Synergistic Effect of Si-Hydroxyapatite Coating and VEGF Adsorption on Ti6Al4V-ELI Scaffolds for Bone Regeneration in an Osteoporotic Bone Environment. *Acta Biomater.* **2019**, *83*, 456–466. [\[CrossRef\]](#) [\[PubMed\]](#)
95. Zhang, X.; Zhang, X.; Zhou, W.; Tang, M.; Wang, T.; Le, K.; Xi, W. Modified Multilayered Porous Titanium Scaffolds with Silicon-Doped Coating Surface-Loaded BMP-2 Prepared by Microarc Oxidation for Bone Defect Repair. *Surf. Coat. Technol.* **2025**, *495*, 131570. [\[CrossRef\]](#)
96. Jiang, C.; Gong, G.; Xiao, S.; Zhang, S.; Chen, D.; Song, S.; Dai, H.; Wu, C.; Zou, Q.; Li, J.; et al. Mechanical and Biological Properties of 3D-Printed Porous Titanium Scaffolds Coated with Composite Growth Factors. *BMC Oral Health* **2025**, *25*, 808. [\[CrossRef\]](#)
97. Zhang, J.; Bai, H.; Liu, H.; Wang, X.; Xu, M.; Zhang, G.; Di, Z.; Zhao, X.; Wang, J.; Ren, L. Augmenting Osteoporotic Osseointegration through a Temporal Release Nanocoating-Based Reversing Dysregulated Osteogenic Microenvironment. *J. Orthop. Transl.* **2025**, *51*, 360–378. [\[CrossRef\]](#)
98. Xing, H.; Li, R.; Wei, Y.; Ying, B.; Li, D.; Qin, Y. Improved Osteogenesis of Selective-Laser-Melted Titanium Alloy by Coating Strontium-Doped Phosphate with High-Efficiency Air-Plasma Treatment. *Front. Bioeng. Biotechnol.* **2020**, *8*, 367. [\[CrossRef\]](#)

99. Qing, Y.; Li, K.; Li, D.; Qin, Y. Antibacterial Effects of Silver Incorporated Zeolite Coatings on 3D Printed Porous Stainless Steels. *Mater. Sci. Eng. C Mater. Biol. Appl.* **2020**, *108*, 110430. [[CrossRef](#)]
100. Zhang, C.; Poudel, I.; Mita, N.; Kang, X.; Annaji, M.; Lee, S.; Panizzi, P.; Shamsaei, N.; Fasina, O.; Babu, R.; et al. Amikacin Coated 3D-Printed Metal Devices for Prevention of Postsurgical Infections (PSIs). *Pharmaceutics* **2025**, *17*, 911. [[CrossRef](#)] [[PubMed](#)]
101. Poudel, I.; Annaji, M.; Arnold, R.; Kaddoumi, A.; Shamsaei, N.; Lee, S.; Pegues, J.; Ahmadi, Z.; Samani, M.; Corriveau, K.; et al. Dexamethasone Eluting 3D Printed Metal Devices for Bone Injuries. *Ther. Deliv.* **2020**, *11*, 373–386. [[CrossRef](#)] [[PubMed](#)]
102. Amukarimi, S.; Mozafari, M. Biodegradable Magnesium-Based Biomaterials: An Overview of Challenges and Opportunities. *MedComm* **2021**, *2*, 123–144. [[CrossRef](#)]
103. Díaz-Tocados, J.M.; Herencia, C.; Martínez-Moreno, J.M.; Montes de Oca, A.; Rodríguez-Ortiz, M.E.; Vergara, N.; Blanco, A.; Steppan, S.; Almadén, Y.; Rodríguez, M.; et al. Magnesium Chloride Promotes Osteogenesis through Notch Signaling Activation and Expansion of Mesenchymal Stem Cells. *Sci. Rep.* **2017**, *7*, 7839. [[CrossRef](#)] [[PubMed](#)]
104. Lin, S.; Yin, S.; Shi, J.; Yang, G.; Wen, X.; Zhang, W.; Zhou, M.; Jiang, X. Orchestration of Energy Metabolism and Osteogenesis by Mg²⁺ Facilitates Low-Dose BMP-2-Driven Regeneration. *Bioact. Mater.* **2022**, *18*, 116–127.
105. Tsakiris, V.; Tardei, C.; Clicinschi, F.M. Biodegradable Mg Alloys for Orthopedic Implants—A Review. *J. Magnes. Alloy.* **2021**, *9*, 1884–1905.
106. Wang, Z.; Liu, B.; Yin, B.; Zheng, Y.; Tian, Y.; Wen, P. Comprehensive Review of Additively Manufactured Biodegradable Magnesium Implants for Repairing Bone Defects from Biomechanical and Biodegradable Perspectives. *Front. Chem.* **2022**, *10*, 1066103. [[CrossRef](#)]
107. Bennett, J.; Wlodarczak, A.; Montorsi, P.; Torzewski, J.; Starmer, G.; Buck, T.; Haude, M.; Moccetti, M.; Kang-Yin Lee, M.; Verheye, S. TCT-61 Safety and Efficacy of the Resorbable Magnesium Scaffold Magmaris in a Real-World Setting—24-Month Follow-up of the Full Cohort (2,066 Subjects) of the BIOSOLVE-IV Registry. *J. Am. Coll. Cardiol.* **2022**, *80*, B25. [[CrossRef](#)]
108. Bossard, M.; Madanchi, M.; Avdijaj, D.; Attinger-Toller, A.; Cioffi, G.M.; Seiler, T.; Tersalvi, G.; Kobza, R.; Schüpfer, G.; Cuculi, F. Long-Term Outcomes After Implantation of Magnesium-Based Bioresorbable Scaffolds—Insights from an All-Coroner Registry. *Front. Cardiovasc. Med.* **2022**, *9*, 856930. [[CrossRef](#)]
109. Wlodarczak, A.; Montorsi, P.; Torzewski, J.; Bennett, J.; Starmer, G.; Buck, T.; Haude, M.; Moccetti, M.; Wiemer, M.; Lee, M.-K.-Y.; et al. One- and Two-Year Clinical Outcomes of Treatment with Resorbable Magnesium Scaffolds for Coronary Artery Disease: The Prospective, International, Multicentre BIOSOLVE-IV Registry. *EuroIntervention* **2023**, *19*, 232–239.
110. Liu, C.; Ren, Z.; Xu, Y.; Pang, S.; Zhao, X.; Zhao, Y. Biodegradable Magnesium Alloys Developed as Bone Repair Materials: A Review. *Scanning* **2018**, *2018*, 9216314. [[CrossRef](#)]
111. Çam, G.; Günen, A. Challenges and Opportunities in the Production of Magnesium Parts by Directed Energy Deposition Processes. *J. Magnes. Alloy.* **2024**, *12*, 1663–1686. [[CrossRef](#)]
112. Chen, J.; Chen, B. Progress in Additive Manufacturing of Magnesium Alloys: A Review. *Materials* **2024**, *17*, 3851. [[CrossRef](#)] [[PubMed](#)]
113. Lin, Z.; Wang, T.; Yu, X.; Sun, X.; Yang, H. Functionalization Treatment of Micro-Arc Oxidation Coatings on Magnesium Alloys: A Review. *J. Alloys Compd.* **2021**, *879*, 160453. [[CrossRef](#)]
114. Yue, X.; Xu, K.; Wang, S.; Liu, H.; Guo, S.; Zhao, R.; Xu, G.; Wang, H.; Yue, X. SLM Magnesium Alloy Micro-Arc Oxidation Coating. *Materials* **2024**, *17*, 4988. [[CrossRef](#)] [[PubMed](#)]
115. Zhao, Y.; Bai, J.; Xue, F.; Zeng, R.; Wang, G.; Chu, P.K.; Chu, C. Smart Self-Healing Coatings on Biomedical Magnesium Alloys: A Review. *Smart Mater. Manuf.* **2023**, *1*, 100022. [[CrossRef](#)]
116. Ran, Z.; Wang, Y.; Li, J.; Xu, W.; Tan, J.; Cao, B.; Luo, D.; Ding, Y.; Wu, J.; Wang, L.; et al. 3D-Printed Biodegradable Magnesium Alloy Scaffolds with Zoledronic Acid-Loaded Ceramic Composite Coating Promote Osteoporotic Bone Defect Repair. *Int. J. Bioprint.* **2023**, *9*, 401–417. [[CrossRef](#)]
117. Zhang, Y.; Lin, T.; Meng, H.; Wang, X.; Peng, H.; Liu, G.; Wei, S.; Lu, Q.; Wang, Y.; Wang, A.; et al. 3D Gel-Printed Porous Magnesium Scaffold Coated with Dibasic Calcium Phosphate Dihydrate for Bone Repair in Vivo. *J. Orthop. Transl.* **2022**, *33*, 13–23. [[CrossRef](#)]
118. ASTM D3359-23; Standard Test Methods for Rating Adhesion by Tape Test. ASTM International: West Conshohocken, PA, USA, 2023.
119. Khoshnood, N.; Yarmand, B.; Badri, A.; Jahanpanah, M.; Zamanian, A. Improvement of Biological and Corrosion Behavior of Plasma Electrolytic Oxidized Mg Implant by 3D Printed Scaffold of Amine-Terminated PEG/PCL Loaded with Dexamethasone. *Prog. Org. Coat.* **2024**, *196*, 108705. [[CrossRef](#)]
120. Zhang, Z.; Liu, A.; Fan, J.; Wang, M.; Dai, J.; Jin, X.; Deng, H.; Wang, X.; Liang, Y.; Li, H.; et al. A Drug-Loaded Composite Coating to Improve Osteogenic and Antibacterial Properties of Zn-1Mg Porous Scaffolds as Biodegradable Bone Implants. *Bioact. Mater.* **2023**, *27*, 488–504. [[CrossRef](#)]
121. Alakija, F.; Mills, D. Fabrication of Biodegradable Silicon Nitride 3D Printed Nanocomposite with Enhanced Mechanical and Antimicrobial Properties for Bone Tissue Repair. *J. Sci. Adv. Mater. Devices* **2025**, *10*, 100890. [[CrossRef](#)]

122. Gharibshahian, M.; Salehi, M.; Kamalabadi-Farahani, M.; Alizadeh, M. Magnesium-Oxide-Enhanced Bone Regeneration: 3D-Printing of Gelatin-Coated Composite Scaffolds with Sustained Rosuvastatin Release. *Int. J. Biol. Macromol.* **2024**, *266*, 130995. [[CrossRef](#)]
123. Li, G.; Wang, L.; Pan, W.; Yang, F.; Jiang, W.; Wu, X.; Kong, X.; Dai, K.; Hao, Y. In Vitro and in Vivo Study of Additive Manufactured Porous Ti6Al4V Scaffolds for Repairing Bone Defects. *Sci. Rep.* **2016**, *6*, 34072. [[CrossRef](#)] [[PubMed](#)]
124. van Hengel, I.A.J.; van Dijk, B.; Modaresifar, K.; Hooning van Duyvenbode, J.F.F.; Nurmohamed, F.R.H.A.; Leeftang, M.A.; Fluit, A.C.; Fratila-Apachitei, L.E.; Apachitei, I.; Weinans, H.; et al. In Vivo Prevention of Implant-Associated Infections Caused by Antibiotic-Resistant Bacteria through Biofunctionalization of Additively Manufactured Porous Titanium. *J. Funct. Biomater.* **2023**, *14*, 520.
125. Li, X.; Hu, J.; Yu, Z.; Liu, M.; Xiao, X.; Qin, G.; Yang, L.; Zhang, E. A Study on the in Vitro and in Vivo Degradation Behaviour and Biocompatibility of a Mg-Mn-Zn Alloy with PLLA and Micro Arc Oxidation Composite Coating. *Surf. Coat. Technol.* **2023**, *471*, 129894.
126. Ni, R.; Jing, Z.; Xiong, C.; Meng, D.; Wei, C.; Cai, H. Effect of Micro-Arc Oxidation Surface Modification of 3D-Printed Porous Titanium Alloys on Biological Properties. *Ann. Transl. Med.* **2022**, *10*, 710. [[CrossRef](#)] [[PubMed](#)]
127. Lin, Y.; Balbaa, M.; Zeng, W.; Yang, Y.; Mahmoud, D.; Elbestawi, M.; Deng, F.; Chen, J. Osteogenic Properties of Titanium Alloy Ti6Al4V-Hydroxyapatite Composites Fabricated by Selective Laser Melting. *J. Mater. Eng. Perform.* **2024**, *33*, 9664–9675. [[CrossRef](#)]
128. Cui, X.; Li, J.; Wang, Y.; Sun, T.; Weng, J.; Li, Z.; Li, J.; Chen, X. Choline Phosphate Surface-Activated 3D-Printed Porous Titanium Scaffold Combined with Stem Cell Exosomes for Enhancing Bone Defects Repair. *ACS Appl. Mater. Interfaces* **2025**, *17*, 27788–27805. [[CrossRef](#)]
129. Ciliveri, S.; Bandyopadhyay, A. Additively Manufactured SiO₂ and Cu-Added Ti Implants for Synergistic Enhancement of Bone Formation and Antibacterial Efficacy. *ACS Appl. Mater. Interfaces* **2024**, *16*, 3106–3115. [[CrossRef](#)]
130. Xu, H.; Li, S.; Guo, S.; Guo, Y.; Xu, P.; Wang, L.; Ding, Y.; Feng, D. Preparation of Cu²⁺/TA/HAP Composite Coating with Anti-Bacterial and Osteogenic Potential on 3D-Printed Porous Ti Alloy Scaffolds for Orthopedic Applications. *Open Life Sci.* **2024**, *19*, 590–600.
131. Li, Y.; Yang, W.; Li, X.; Zhang, X.; Wang, C.; Meng, X.; Pei, Y.; Fan, X.; Lan, P.; Wang, C.; et al. Improving Osteointegration and Osteogenesis of Three-Dimensional Porous Ti6Al4V Scaffolds by Polydopamine-Assisted Biomimetic Hydroxyapatite Coating. *ACS Appl. Mater. Interfaces* **2015**, *7*, 5715–5724. [[CrossRef](#)]
132. Wang, X.; Guo, Q.; He, Y.; Geng, X.; Wang, C.; Li, Y.; Li, Z.; Wang, C.; Qiu, D.; Tian, H. A pH-Neutral Bioactive Glass Coated 3D-Printed Porous Ti6Al4V Scaffold with Enhanced Osseointegration. *J. Mater. Chem. B* **2023**, *11*, 1203–1212. [[CrossRef](#)]
133. Tan, J.; Ren, L.; Xie, K.; Wang, L.; Jiang, W.; Guo, Y.; Hao, Y. Functionalized TiCu/TiCuN Coating Promotes Osteoporotic Fracture Healing by Upregulating the Wnt/ β -Catenin Pathway. *Regen. Biomater.* **2023**, *10*, rbac092. [[CrossRef](#)]
134. Fan, S.; Zhong, J.; Xiong, J.; Ai, F.; Yu, H.; Liu, Z.; Tan, W.; Wu, Q.; Zhou, Z.; Yang, J.; et al. Loofah-Inspired Biomimetic Scaffold with Triaxial Anisotropy for Spatiotemporally Guided Cortical-Cancellous Bone Reconstruction. *Chem. Eng. J.* **2025**, *523*, 168180. [[CrossRef](#)]
135. Ma, L.; Cheng, S.; Ji, X.; Zhou, Y.; Zhang, Y.; Li, Q.; Tan, C.; Peng, F.; Zhang, Y.; Huang, W. Immobilizing Magnesium Ions on 3D Printed Porous Tantalum Scaffolds with Polydopamine for Improved Vascularization and Osteogenesis. *Mater. Sci. Eng. C Mater. Biol. Appl.* **2020**, *117*, 111303. [[CrossRef](#)] [[PubMed](#)]
136. Xu, J.; Wu, D.; Ge, B.; Li, M.; Yu, H.; Cao, F.; Wang, W.; Zhang, Q.; Yi, P.; Wang, H.; et al. Selective Laser Melting of the Porous Ta Scaffold with Mg-Doped Calcium Phosphate Coating for Orthopedic Applications. *ACS Biomater. Sci. Eng.* **2024**, *10*, 1435–1447. [[CrossRef](#)] [[PubMed](#)]
137. Luo, X.; Xiong, Z.; Wang, D.; Zhao, R.; Deng, X.; Duan, A.; Zhang, C.; Liu, W.; Ge, Z.; Zhang, Z.; et al. Highly Biologically Functional Magnesium Silicate-Coated 3D Printed Round Pore-Shaped Titanium Scaffold Alters Exosomal miRNA Expression to Promote Osteogenic Differentiation for Bone Defect Repair. *Chem. Eng. J.* **2024**, *489*, 151372. [[CrossRef](#)]
138. Du, Z.; Yu, X.; Nie, B.; Zhu, Z.; Ibrahim, M.; Yang, K.; Tan, L.; Wang, Y. Effects of Magnesium Coating on Bone-Implant Interfaces with and without Polyether-Ether-Ketone Particle Interference: A Rabbit Model Based on Porous Ti6Al4V Implants. *J. Biomed. Mater. Res. Part B Appl. Biomater.* **2019**, *107*, 2388–2396. [[CrossRef](#)] [[PubMed](#)]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.