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Biomimetic and personalized optimization of additively manufactured metallic bone implants: Design, simulation, and clinical outcomes

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Abstract

Additive manufacturing (AM) has transformed the field of metallic bone implants by enabling the production of patient-specific, biomimetic, and high-performance devices. This review focuses on the personalized design of bone implants using AM technologies, particularly selective laser melting and electron beam melting, which allow the fabrication of complex lattice structures that replicate the trabecular architecture of native bone. These architectures enhance load transfer, reduce stress shielding, and promote osseointegration. The review also explores current strategies and digital tools for biomimetic design, as well as numerical simulation methods—including finite element analysis, computational fluid dynamics, and multi-field coupling models—used to optimize implant geometry, porosity, and mechanical performance. Furthermore, recent clinical and preclinical data on *in vivo* functionality and biological integration are synthesized, with emphasis on the latest advancements to enhance functional outcomes. Altogether, the work provides a comprehensive roadmap for researchers and clinicians seeking to advance implant innovation and improve skeletal tissue repair.

Keywords: Additive manufacturing; Biomimetic implants; Electron beam melting; Lattice structures; Numerical simulation; Personalized bone implants; Selective laser melting

1. Introduction

Musculoskeletal disorders are among the most prevalent global health conditions, affecting more than 1.7 billion people worldwide, according to the World Health Organization.[1] Chronic conditions such as osteoarthritis, osteoporosis, and trauma-induced fractures often result in significant pain, loss of mobility, and reduced independence. As global populations age, the incidence of these disorders continues to

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rise, contributing to an increasing demand for bone repair and replacement procedures. According to *The Lancet*, over 2.86 million knee and 1.32 million hip replacements are performed each year,[2] a number expected to increase with longer life expectancy and the rising burden of degenerative joint diseases. This growing clinical need has led to major innovations in implant technology, particularly the development of metallic implants capable of enduring high mechanical loads while promoting biological integration. However, conventional manufacturing processes are often limited in their ability to produce geometrically complex, anatomically tailored, and functionally graded structures. These constraints have accelerated the adoption of additive manufacturing (AM). The biomedical AM market is experiencing unprecedented growth, projected to reach USD 4.7 billion by 2027, with metallic implants comprising more than 45% of this market.[3] Unlike subtractive techniques, AM offers unprecedented design freedom, paving the way for the development of patient-specific implants with precise control over geometry, porosity, and internal architecture. This capability is particularly valuable for creating lightweight structures with mechanical properties that closely mimic natural bone.[4] Since its inception in the 1980s with stereolithography (SLA), AM has evolved from a rapid prototyping tool to a robust platform for fabricating end-use medical devices. Notable milestones include the first fully 3D-printed prosthetic leg in 2008 and the first mandibular implant in 2012.[5] According to classifications by the International Organization for Standardization and the American Society for Testing and Materials, AM comprises a wide range of processes, including powder bed fusion (PBF), SLA, directed energy deposition (DED), material extrusion fused deposition modeling/fused filament fabrication, and vat photopolymerization digital light processing.[6] Among these, PBF technologies have emerged as the leading methods for metallic implant fabrication due to their precision, microstructural control, and ability to produce highly complex designs. Concurrently, polymer-based AM techniques remain widely used for anatomical models, surgical guides, and bioresorbable scaffolds, particularly in regenerative medicine.[7,8]

Importantly, AM is no longer regarded merely as a fabrication technique, but rather as a central component of an integrated digital workflow. This ecosystem encompasses medical imaging for anatomical data acquisition, image segmentation, biomimetic lattice design, computer-aided design (CAD) modeling, and advanced numerical simulations. Within this context, biomimetic design strategies are increasingly adopted to replicate the hierarchical structure and mechanical behavior of native bone, thereby improving implant functionality and integration.

This review focuses on the personalized design of bone implants using AM technologies, the implementation and outcomes of numerical simulation models, and the clinical performance of additively manufactured metallic implants. As illustrated in **Figure 1**, the paper begins with an overview of AM technologies, comparing selective laser melting and electron beam melting (EBM) in terms of process parameters and suitability for biomedical applications. It then critically analyzes mechanical properties and material selection, emphasizing the clinical relevance of Ti–6Al–4V and cobalt–chromium (Co–Cr) alloys for their strength, biocompatibility, and long-term reliability. A dedicated section discusses *in vivo* performance and clinical validation of AM implants. Subsequently, the review presents key digital tools and strategies for biomimetic implant design, including porous and lattice architectures and the latest advancements in personalized bone implant optimization. Finally, an in-depth analysis is provided on numerical simulation techniques—including finite element analysis (FEA), computational fluid dynamics (CFD), and multi-field coupling models—employed to predict mechanical behavior, assess stress distribution, and optimize implant geometry and functionality.

2. Applications for additive manufacturing in metallic bone implants

AM has rapidly gained prominence in the biomedical field, especially in the development of bone implants. As shown in **Figure 2**, the exponential rise in AM-related publications between 2007 and 2024 highlights its growing integration into disciplines such as materials science and orthopedic surgery. AM constructs components layer by layer from CAD models, offering exceptional geometric flexibility and personalization. The general digital workflow is illustrated in **Figure 3**, enabling the fabrication of implants directly adapted to patient anatomy using medical imaging data.

In orthopedic surgery, AM is increasingly used to produce load-bearing implants such as femoral stems, femoral heads, acetabular cups, and tibial trays. These components benefit from precise anatomical fit, reduced intraoperative adjustments, and design freedom that supports functional optimization.[9,10] Similarly, in spinal applications, AM enables the creation of intervertebral fusion cages and vertebral body replacements with tailored mechanical behavior and surface structures to support spinal stability and biological integration.[11,12] In maxillofacial and craniofacial reconstruction, AM is widely used to fabricate custom implants for the mandible, zygomatic arch, and orbital floor, particularly in trauma or

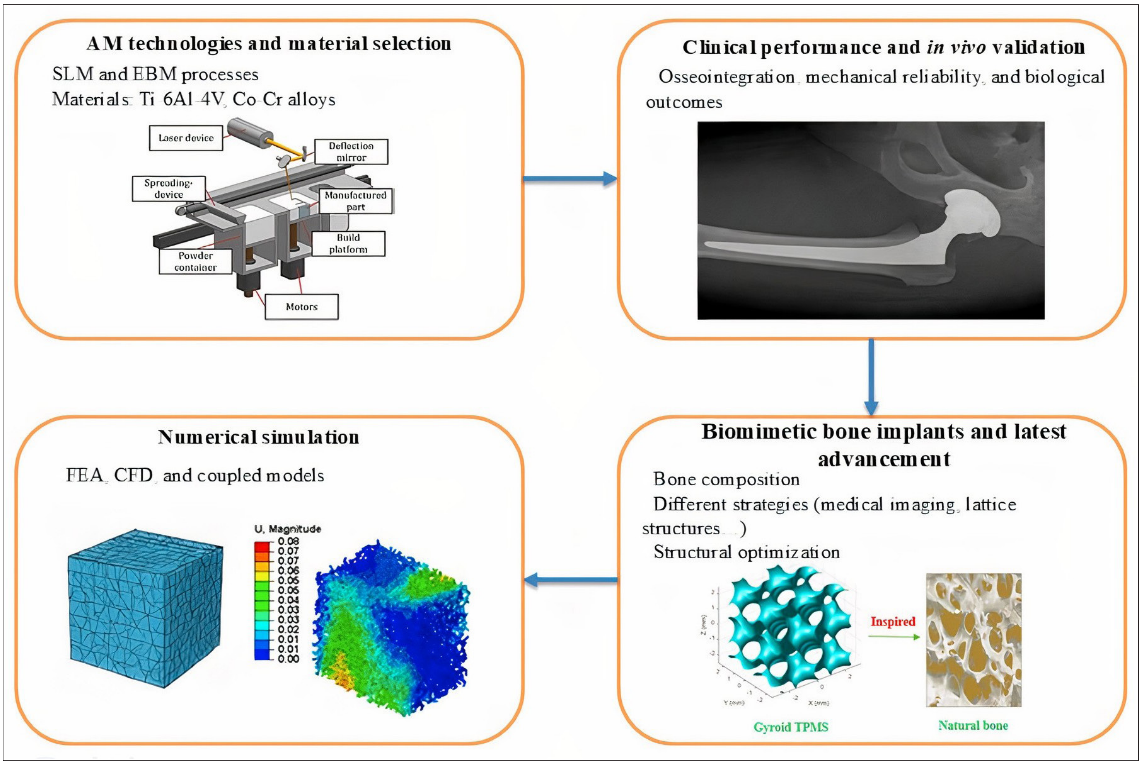

Figure 1. Graphical summary of the review paper. Abbreviations: AM:, additive manufacturing; EBM, electron beam melting; CFD, computational fluid dynamics; FEA, finite element analysis; SLM, selective laser melting; Ti–6Al–4V, titanium alloy with 6% aluminum and 4% vanadium.

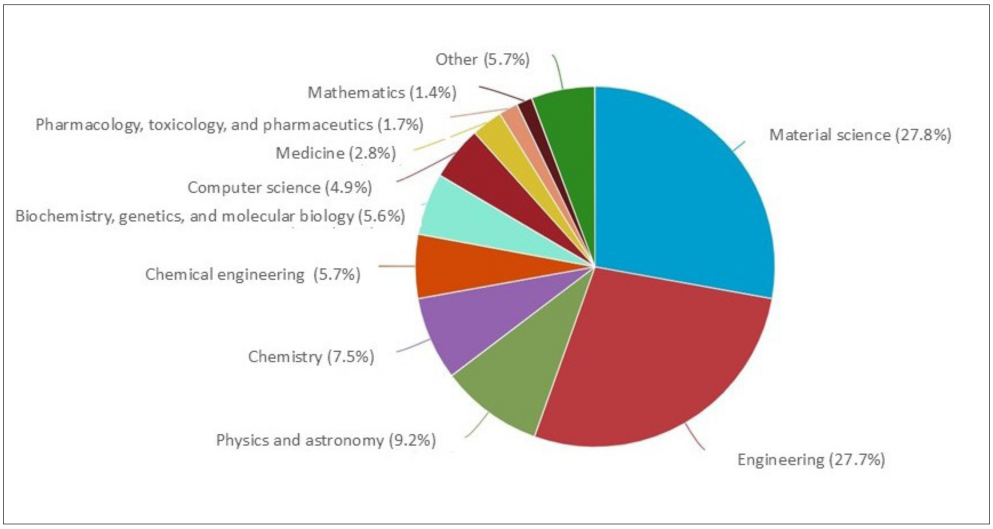

Figure 2. Distribution of publications on AM in biomedicine. Source: SCOPUS. Abbreviation: AM, additive manufacturing.

tumor resection cases. The ability to reproduce complex bone contours and integrate functional elements, such as fixation holes, contributes to improved surgical outcomes.[13] Another critical application is in revision surgeries and the management of large bone defects, particularly in the pelvis or proximal femur, where standard implants are insufficient due to irregular or deficient bone structures. AM allows for the rapid production of customized implants with integrated design features, thereby improving fixation and long-term clinical stability.[14] An overview of these metallic AM applications across various anatomical regions is presented in **Figure 4**.

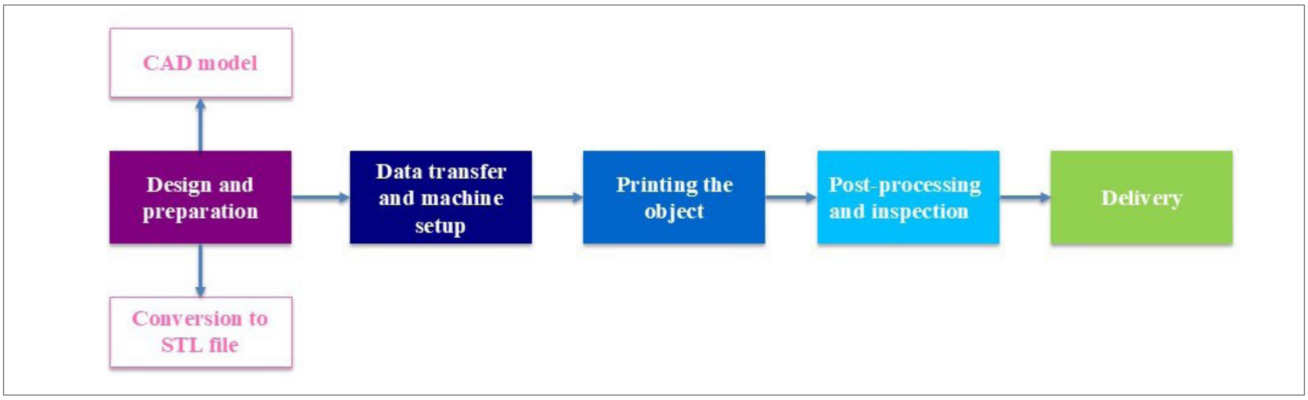

Figure 3. General steps of AM. Abbreviations: AM, additive manufacturing; CAD, computer-aided design; STL, standard tessellation language.

Figure 4. Examples of metallic implants using AM. (A) Knee implant. (B) Craniofacial implant. (C) Spinal implant. (D) Hip implant. Adapted from ref. [13] Abbreviation: AM, additive manufacturing.

Building on these diverse anatomical applications, recent advancements have introduced new paradigms in AM—such as 4D, 5D, and 6D printing—considered evolutionary extensions of conventional 3D printing aimed at further enhancing implant functionality, adaptability, and patient-specific integration. For example, 4D printing incorporates smart materials, such as shape-memory alloys or stimuli-responsive polymers, allowing implants to adapt dynamically to physiological changes. This opens the door to self-adjusting orthopedic devices capable of improving fit or functionality post-implantation.[15,16] Similarly, 5D printing utilizes multi-axis deposition of curved layers,

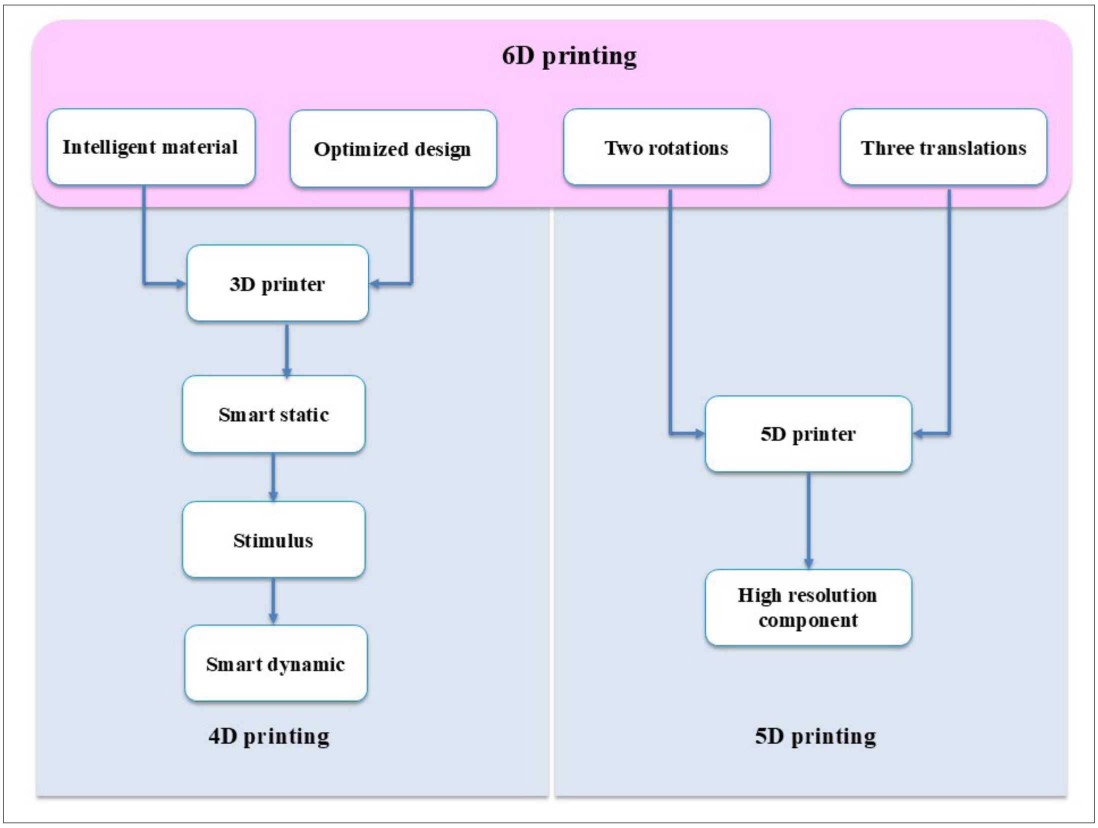

Figure 5. The 6D printing method as a combination of 4D and 5D printing.

resulting in enhanced mechanical performance, improved fatigue resistance, and optimized load distribution in anatomically complex implants like acetabular cups or spinal cages.[17,18] As illustrated in **Figure 5**, 6D printing combines both structural adaptability and responsive behavior, potentially enabling real-time adaptation of implants to patient-specific biomechanical environments. Although still in early development, these advances hold great promise for the future of smart, personalized bone repair solutions.[19,20]

3. Additive manufacturing of metallic bone implants: properties, processes, and clinical performance

3.1. Additive manufacturing processes for metallic implants

3.1.1. Selective laser melting

SLM has established itself as a leading technology in the manufacture of metallic implants due to its unique ability to create complex, optimized, and biocompatible structures with unmatched precision. Direct fabrication of biocompatible alloys like Ti–6Al–4V has been reported using SLM, allowing customization of architecture and mechanical properties to match patients' physiological conditions.[11] As shown in **Figure 6**, the principle of SLM involves the use of a high-power laser beam to selectively fuse fine layers of metal powder inside an inert atmosphere chamber, ensuring full and homogeneous melting of material.[21]

The robustness and quality of SLM-fabricated implants highly depend on processing parameters, including laser power (P), scanning speed (v), layer thickness (t), and hatch spacing (h), all of which directly influence the final density, residual porosity, and internal stresses of the implant.[22] A key parameter used to optimize these settings is the volumetric energy density (E_v), defined by **Equation I**.

$$Ev = \frac{P}{h \times v \times t} \tag{1}$$

Precise calibration of E_v helps prevent typical defects associated with SLM, such as thermal cracking, gas porosity, and residual deformation, which may compromise implant reliability.[23] Optimized implant designs fabricated by SLM have demonstrated relative densities greater than 99.5%, providing excellent mechanical properties and durability.[12]

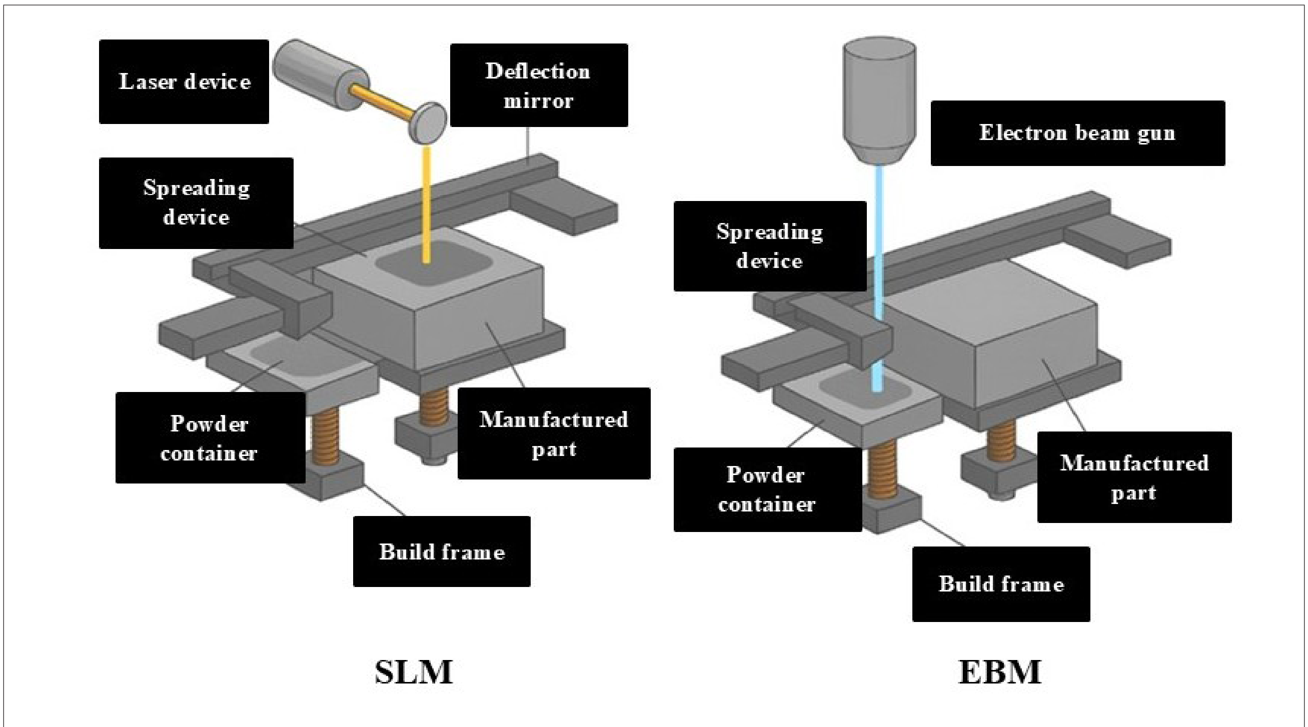

Figure 6. SLM and EBM processes. Abbreviations: EBM, electron beam melting; SLM, selective laser melting.

Additional advantages of SLM include post-processing treatments, such as heat treatment for residual stress relief and improved corrosion resistance.[22]

From a technical standpoint, the success of SLM fabrication relies on an optimized scanning strategy. Different scanning strategies—including hatch, stripes, chess, and spiral patterns—have been analyzed to minimize thermal distortion and maintain homogeneous fusion of material.[21] For example, offset contour scanning reduces residual stress by adjusting the laser direction and angle for each layer, while the partition scanning divides the build area into several subregions to homogenize temperature distribution and limit deformation.[24]

Despite its numerous advantages, challenges remain. The high cost of metal powders and laser equipment restricts wider adoption in clinical settings. Manufacturing precision can also be affected layer accumulation, leading to deviations between the CAD model and the final implant. However, advancement in artificial intelligence and numerical simulations are expected to enable real-time optimization of manufacturing parameters, potentially reducing defects and improving the consistency of implant fabrication.[6,25]

3.1.2. Electron beam melting

EBM is another advanced AM technology that has gained significant traction in the production of biomedical devices, particularly metallic bone implants.[26] Similar to selective laser sintering (SLS) and SLM, EBM uses a high-energy electron beam to selectively melt layers of metal powder in a vacuum environment (**Figure 6**). The controlled atmosphere prevents oxidation of the materials and improves the mechanical properties of the produced components. The process starts with the deposition of a thin metal powder layer onto the building platform. A precisely controlled electron beam then scans the layer according to a 3D CAD model, selectively melting the material. Upon solidification of the layer, the platform is lowered, and a new layer of powder is added. This cycle repeats until the final part is completed.[27,28]

EBM offers several advantages for implant fabrication, including the ability to produce dense, homogeneous structures with reduced deformation and higher energy efficiency compared to laser-based technologies. The controlled scanning system based on the magnetic coil of the electron beam allows for faster and more accurate beam positioning. However, EBM is limited by lower resolution compared to SLM, as the larger electron beam diameter

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reduces the ability to reproduce fine details and results in higher surface roughness. Additionally, processing parameters such as beam current, scanning speed, acceleration voltage, and powder layer thickness directly influence density, porosity, and mechanical strength.[29]

Current research on EBM optimization focuses on surface modification and defect minimization, with special emphasis on post-processing treatments like hot isostatic pressing (HIP). HIP effectively reduces residual porosity and strengthens the fatigue resistance of implants. Despite the high costs of metal powders and equipment, increasing interest in metallic AM for biomedical applications has driven investments and research efforts toward improving efficiency and lowering costs. This progress is expected to accelerate the clinical adoption of EBM for next-generation metallic implants.[30] A comparative analysis of SLM and EBM technologies is provided in **Table 1**.

3.2. Mechanical properties and material selection for additive manufacturing metallic bone implants

3.2.1. Material selection and classification

In the manufacturing and development of metallic bone implants, choosing the ideal metal is important because the material choice greatly impacts the characteristics of the manufactured implants.[31] The ideal material for metallic bone implants must satisfy four fundamental criteria: biomechanical compatibility, biocompatibility, corrosion and wear resistance, and osseointegration. Biomechanical compatibility ensures that the material's elastic modulus is as close as possible to cortical bone (10–30 GPa), thereby reducing stress shielding. Biocompatibility is crucial to minimize inflammatory responses, hypersensitivity reactions, and toxicity risks, ensuring a stable and long-lasting implant. Corrosion and wear resistance are essential for implant durability, preventing material degradation in physiological environments and the release of metallic ions that could induce osteolysis and implant failure. Finally, osseointegration is vital for direct bone-implant bonding, reducing the risk of fibrous encapsulation and enhancing long-term fixation.[32]

In addition to biological and mechanical requirements, materials should be compatible with AM processes. For instance, titanium alloys are highly compatible with SLM.[33] Cost-effectiveness is also an important consideration, as balancing material expense with performance determines the economic viability and accessibility of implants.[34] In this review, we classified the metallic biomaterials into two categories: the commonly used and less commonly used materials (**Tables 2** and **3**).

Among metallic biomaterials, titanium alloys—particularly Ti–6Al–4V—are the most widely used owing to their high strength-to-weight ratio, excellent corrosion resistance, and superior biocompatibility. These characteristics contribute to their long-term clinical success. Clinical studies have reported survival rates of up to 99% over 10 years for titanium-based implants, with consistent osseointegration and minimal biological complications, making them a reliable option for both dental and orthopedic applications.[41] Furthermore, surface modifications of titanium alloys have been shown to enhance bone bonding and cellular responses, thereby improving clinical outcomes.[42] However, the relatively high elastic modulus of Ti–6Al–4V compared to cortical bone can lead to stress shielding, and concerns over the cytotoxicity of vanadium have prompted the development of β-type titanium alloys. These newer alloys, incorporating elements such as niobium, zirconium, or tantalum, demonstrate improved biomechanical compatibility and enhanced bioactivity.[43,44]

Beyond titanium, Co–Cr alloys are widely used for orthopedic applications due to their exceptional wear resistance, mechanical strength, and corrosion stability. They are especially suitable for load-bearing prostheses such as hip and knee joints. Clinically, Co–Cr alloys have

Table 1. Comparative analysis of SLM and EBM for metallic implants

Criteria	SLM	EBM
Energy source	Laser beam melting	Electron beam melting
Processing environment	Inert gas (argon, nitrogen)	Vacuum (no oxidation)
Material suitability	Ti–6Al–4V, Co–Cr, stainless steel	Ti–6Al–4V, Co–Cr–Mo
Surface quality and resolution	High resolution, smoother surfaces	Lower resolution, rougher surfaces
Microstructure and mechanical properties	Fine-grained, strong	Coarser grains, lower residual stress
Build speed and energy efficiency	Slower, less energy-efficient	Faster, more energy-efficient
Post-processing requirements	Heat treatment to relieve stress	HIP required to reduce porosity

Abbreviations: Co–Cr, cobalt–chromium; Co–Cr–Mo, cobalt–chromium–molybdenum; EBM, electron beam melting; HIP, hot isostatic pressing; SLM, selective laser melting; Ti–6Al–4V, titanium alloy with 6% aluminum and 4% vanadium.

Table 2. The most used metals in bone metallic implants

Materials	Young's modulus (GPa)	Yield strength (MPa)	Tensile strength (MPa)	Properties	Applications	References
Titanium	105	695	785	Lightweight, corrosion-resistant, biocompatible	Hip and knee implants; spinal implants; bone plates	35
Ti–6Al–4V	110	850–900	960–970	Versatile alloy, high mechanical strength, biocompatible	Hip and knee implants; spinal implants; bone plates	35
Tantalum	186	140–350	200–520	Highly biocompatible, excellent osseointegration	Acetabular cups; bone augmentations	36
Stainless steel (316L)	190	290	580	Corrosion-resistant; mainly used for temporary implants	Bone plates; bone screws; joint implants	37,38
Co–Cr–Mo	230	200–800	430–1000	High wear resistance, high strength	Hip and knee implants; dental implants	38
Magnesium	45	160	250	Biocompatible, biodegradable, low density	Orthopedic implants	38,39
Zirconium alloys	100	200–500	400–800	Biocompatibility, corrosion resistance	Spinal applications	32
Cortical bone	10–30	30–70	70–150	Natural reference material	–	38

Abbreviations: Co–Cr–Mo, cobalt–chromium–molybdenum; Ti–6Al–4V, titanium alloy with 6% aluminum and 4% vanadium.

Table 3. Less commonly used metals in bone metallic implants

Materials	Young's modulus (GPa)	Yield strength (MPa)	Tensile strength (MPa)	Properties	References
Iron	200	50	540	High mechanical strength, potentially biodegradable	38
Zinc	83–108	30	37	Biocompatible, biodegradable	38
Silver	80	30	150	Antibacterial, biocompatible	40
Palladium	110–120	50	150–200	Corrosion-resistant; alloyed	40
Platinum	150	150	240	Corrosion-resistant, biocompatible	40
Gold	79	25	130	Biocompatible, highly corrosion-resistant	40

demonstrated excellent durability and low revision rates, particularly in young and active patients.[45] Their use in femoral heads and articulating components has shown reliable long-term performance. Studies report that even after 18 years of implantation, systemic metal ion levels remain below clinically accepted thresholds, with no evidence of adverse immune responses.[46] Nevertheless, their high stiffness can contribute to stress shielding and bone resorption, while the release of metal wear debris remains a concern in some cases.[47]

Several other metallic biomaterials have also been investigated. For example, stainless steel (316L) is widely used for temporary metallic implants such as bone plates and screws due to its good mechanical strength and cost-effectiveness. However, its relatively low corrosion resistance in physiological environments and limited biocompatibility restrict its long-term use.[44,48] Tantalum, by contrast, is highly biocompatible and exhibits excellent osteoconductivity, making it particularly suitable for bone augmentation and porous implants; yet, its high cost remains a significant barrier to widespread clinical adoption.[49,50] Magnesium alloys have emerged as promising biodegradable materials capable of providing temporary mechanical support before gradually resorbing *in vivo*. Despite their bioresorbable nature and potential for reducing secondary surgery, their rapid degradation and poor mechanical stability under physiological conditions remain major limitations for long-term structural applications.[51,52]

3.2.2. Microstructure and mechanical properties

Compared to traditionally manufactured implants, metallic AM implants often exhibit distinct microstructural characteristics. The rapid cooling and solidification inherent to AM processes can result in finer grain structures, potentially enhancing mechanical properties such as fatigue resistance.[31] However, microstructural defects—including incomplete melting, unmelted particles, and non-equilibrium phases—may compromise mechanical performance.[31] Therefore, the study of morphology in AM biomaterials is crucial, as both surface characteristics and microstructure directly influence mechanical and biological performance. Key morphological factors such as surface roughness, porosity, pore interconnectivity, and overall structural integrity play a vital role in implant–tissue integration and the ability to endure physiological loads. In orthopedic and dental applications, surface morphology significantly impacts osseointegration, the process by which bone cells adhere to and grow on an implant surface. Rough, micro-textured surfaces have been shown to promote better cell attachment and accelerate tissue integration.[53] Additionally, strategic design of porosity and pore architecture enhances vascularization, nutrient diffusion, and tissue ingrowth, all of which are essential for long-term implant stability.

The mechanical strength of metallic AM implants—including their tensile, yield, and ultimate strengths—may differ from that of traditionally manufactured implants. Some studies report that AM implants, particularly those made from Ti–6Al–4V, exhibit comparable or superior mechanical strength.[31] However, variations in porosity and density, often process-dependent, can negatively influence mechanical behavior.

Fatigue resistance (Figure 7) is a critical consideration, as implants are subject to cyclic loading *in vivo*. To ensure long-term functionality, implants must withstand high durability demands and resist fatigue failure. However, the fatigue behavior of AM implants remains inconsistent across studies.[54] While some studies indicate improved fatigue performance compared to conventional manufacturing, others point to process-induced defects as causes of failure. These defects include lack of fusion, gas porosity, and incomplete melting, which act as stress concentrators, initiating cracks under physiological loads and reducing fatigue life.[55]

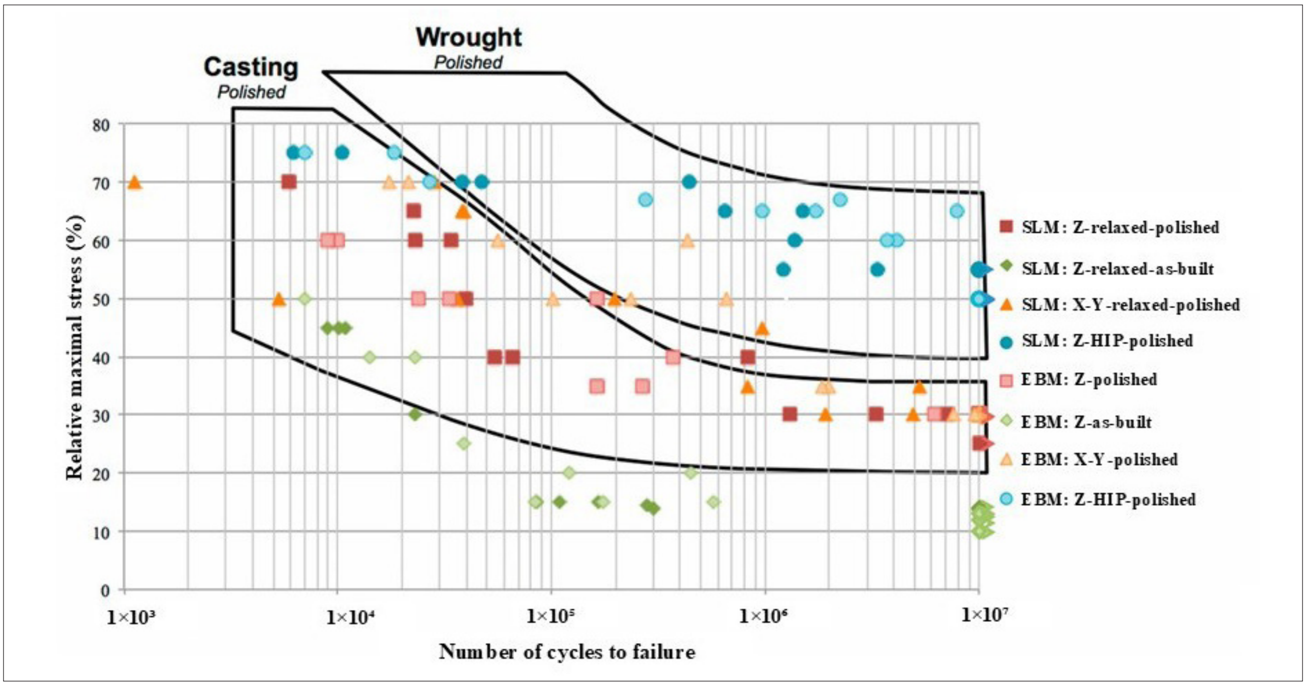

Figure 7. Comparison of fatigue resistance of metallic materials produced by SLM, EBM, casting, and wrought processing. Adapted from ref.[56]. Abbreviations: EBM, electron beam melting; HIP, hot isostatic pressing; SLM, selective laser melting.

Moreover, the thermal cycles and directional solidification intrinsic to AM create heterogeneous grain structures and residual stresses, leading to mechanical anisotropy and variability across orientations. These inconsistencies raise concerns about structural reliability, patient safety, and regulatory approval. Several studies confirm that AM parts may have lower fatigue performance without post-processing treatments, such as HIP, precision surface machining, or laser shock peening.[57] These treatments significantly improve outcomes by minimizing internal porosity, homogenizing microstructure, and enhancing fatigue resistance.[58] Without these measures, the risk of premature failure or poor osseointegration remains high, especially in load-bearing orthopedic implants. Thus, ensuring clinical reliability requires a comprehensive defect-control strategy throughout the AM process chain.

3.3. Long-term *in vivo* performance and clinical reliability of additive manufacturing implants

While mechanical properties, material selection, and manufacturing parameters are fundamental to the development of high-performance metallic implants, these factors must ultimately translate into reliable and durable clinical outcomes. AM has enabled the production of metallic implants—including titanium and its alloys—with complex geometries and tunable surface features that promote osseointegration and long-term biological integration. Clinical data remain limited, but available evidence is encouraging. In a 3-year multicenter study, Tunchel *et al.*[59] reported a survival rate of 94.5% and a crown success rate of 94.3% for 3D-printed titanium dental implants, with minimal marginal bone loss, suggesting high potential for sustained clinical performance. Similarly, Shu *et al.*[60] demonstrated that SLM-fabricated titanium implants exhibited significantly higher removal torque and early bone interlocking, confirming improved biomechanical anchorage compared to conventionally manufactured implants.

Preclinical investigations support these findings. Gu *et al.*[61] reviewed 46 animal studies and reported that Ti–6Al–4V porous scaffolds with 500–600 μm pore sizes and 60–70% porosity achieved bone area fractions up to 59.3% within 8–10 weeks, highlighting the importance of microarchitectural optimization for bone ingrowth. From a broader perspective, Gao *et al.*[33] emphasized that metallic AM scaffolds can reduce stress shielding, improve bone–implant mechanical compatibility, and allow bone ingrowth without the need for additional coating—provided that pore architecture and surface roughness are well controlled. Park *et al.*[62] further advanced this approach by embedding Ti–6Al–4V implants with biogenic hydroxyapatite (HAp), resulting in enhanced osseointegration and reduced inflammatory response *in vitro* and *in vivo*. Collectively, these findings illustrate how AM can enable not only geometric precision but also surface-level functionalization, producing implants that are both structurally robust and biologically responsive.

Nonetheless, as noted by Matsko and França,[63] the current clinical reports are constrained by small patient cohorts and short follow-up durations—often less than 3 years—thereby limiting our ability to assess the long-term safety and functional durability. Extending beyond conventional intraosseous applications, Onică *et al.*[64] reported the longest follow-up to date for 3D-printed subperiosteal titanium implants, with 6 years of monitoring. Despite complications in over half the cases—such as metal frame exposure and late-stage mobility—some implants maintained stable integration and satisfactory outcomes. These findings highlight the potential of customized AM implants, particularly for patients with severe anatomical deficits where careful design and precise surgical planning are critical. **Figure 8** shows the intraoral clinical appearance of AM implants at different time points. The images reveal peri-implant mucosal changes ranging from stable conditions to inflammation and late complications, underlining the need for long-term monitoring. **Table 4** summarizes the clinical studies reviewed, with the findings collectively emphasizing that long-term clinical reliability depends not only on material performance but also on patient-specific anatomical factors, surgical technique, and post-operative care.

Altogether, the current body of evidence supports the clinical viability of metallic AM implants, particularly regarding biological integration, stress transfer optimization, and short- to mid-term reliability. Yet, the durability of these implants under long-term mechanical and biological loads—especially in weight-bearing skeletal regions—remains insufficiently documented. To transition from promising prototypes to clinically validated solutions, future studies should prioritize large-scale, multicenter longitudinal trials with standardized outcome measures and detailed failure mode analyses. Such efforts are essential to securing regulatory approval, ensuring patient safety, and establishing AM as a reliable option for the long-term treatment of musculoskeletal disorders.

4. Biomimetic bone implants

The purpose of this paper is to highlight the importance of AM, supported advanced design and tools, in the manufacturing of biomimetic implants that address the limitations of conventional counterparts. Biomimicry is key to this approach, drawing inspiration from the structural and functional features of natural bone. The

Figure 8. Intraoral views at different follow-up intervals. (A) 24 months. (B) 42 months. (C) 72 months. Adapted from ref.[64].

Table 4. Key preclinical and clinical studies on AM metallic implants

Study	Implant type	Key outcome	Remarks	References
Tunchel *et al.*	3D-printed titanium dental implants	94.5% survival in 3 years; minimal bone loss	Multicenter; limited to dental applications	59
Shu *et al.*	SLM titanium implants	Higher removal torque and improved early bone interlocking	Superior to conventional implants	60
Gu *et al.*	Porous Ti–6Al–4V scaffolds (animal model)	59.3% bone area at 8–10 weeks (500–600 µm pores; 60–70% porosity)	Emphasizes the importance of pore design	61
Gao *et al.*	Metallic AM scaffolds	Effective osseointegration without coating if porosity and surface roughness are optimized	General review; supports design strategies	33
Park *et al.*	Ti–6Al–4V with biogenic HAp	Enhanced osseointegration and reduced inflammation (*in vitro* & *in vivo*)	Promising material–biology synergy	62
Matsko and França	Clinical review	Limited data (<3 years follow-up; small cohorts)	Stresses the need for large-scale longitudinal trials	63
Onică *et al.*	3D-printed subperiosteal implants	6-year follow-up; >50% complications, though some stable outcomes observed	Custom designs are useful in severe bone loss cases	64

Abbreviations: AM, additive manufacturing; Hap, hydroxyapatite; SLM, selective laser melting; Ti–6Al–4V, titanium alloy with 6% aluminum and 4% vanadium.

ultimate objective is to reconstruct artificial bones rather than to simply replace damaged or fractured natural bones with conventional implants. To achieve this, a deep understanding and mastery of the bone's composition is essential.

4.1. Bone composition

Bone is a hierarchically organized composite, consisting of a mixture of organic and inorganic phases. The organic phase represents 30–40% of the bone's dry weight and is dominated by collagen type I, which contributes about 90% of the organic fraction. This fibrillar protein forms the extracellular matrix (ECM), imparting phase flexibility and resilience against deformations.[65] The remaining 10% is composed of non-collagenous proteins such as osteocalcin, which regulates calcium ion binding during mineralization; osteopontin (OSP), associated with *osteopontin (OSP),* which is associated with cell adhesion; and osteonectin, which is involved in the regulation of mineralization; and osteonectin, which is involved in cell adhesion and regulation of mineralization.[66]

The inorganic phase, on the other hand, accounts for 60–70% of the bone's dry weight and is dominated by nanometric HAp crystals [$Ca_{10}(PO_4)_6(OH)_2$]. These crystals are integrated within collagen fibrils, forming a fiber–mineral composite. The bone mineral is not a pure stoichiometry HAp but incorporates ionic substitutions including carbonate (CO_3^{2-}), magnesium (Mg^{2+}), sodium (Na^+), potassium (K^+), and silicon (Si). These ionic variations critically influence bioactivity, crystallinity, and chemical resistance of the bone matrix systems.[67] These ions can partially substitute OH^{-} or PO_4^{3-} groups in the crystals, enabling bone to adapt its composition according to physiological requirements and anatomical location.[68]

In addition, water content accounts for approximately 15–25% of the total bone matrix, distributed within the matrix intercrystalline spaces. This water is fundamental in nutrient diffusion, mechanical force transmission, and hydration of organic proteins, thus contributing to the viscoelastic properties of the bone.[66]

Structurally, bone exists in two primary forms: cortical (compact) bone and trabecular (spongy) bone, as illustrated in **Figure 9**. Cortical bone is dense and rigid, composed of osteons—cylindrical units of concentric lamellae surrounding Haversian canals that house blood vessels and nerves. In contrast, trabecular bone has a porous, interconnected architecture of thin trabeculae, providing sites for vascularization, bone marrow storage, and rapid remodeling.[67,68] The relative proportion of cortical and trabecular bone varies across skeletal sites, reflecting the specific functional and mechanical demands of each bone type.

4.2. Types and properties of bone implants

Bone implants, including prostheses, screws, and plates, are essential in the treatment of different orthopedic diseases and traumatic injuries. These implants enhance the patient's quality of life, provide structural support, and improve damaged bones, thereby improving and ameliorating mobility. The main advantage of these devices lies in their ability to treat fractures and degenerative bone diseases while accelerating recovery and reducing pain.[70] This section explores the different types of bone implants (**Figure 10**), their classifications, properties, and specific applications in orthopedic surgery.

4.2.1. Craniofacial and dental implants

Craniofacial and dental implants are specialized medical devices designed to reconstruct lost or damaged bone structures in the craniofacial region and oral cavity caused by trauma, congenital anomalies, or surgical resections such as tumor removal.[13] These implants serve both functional and aesthetic purposes, significantly enhancing patients' quality of life.[71] Craniofacial implants play a crucial role in multiple procedures: orbital reconstructions to restore the integrity of the eye socket; maxillofacial surgeries to realign the jaws and support dental prostheses; and mandibular reconstructions to stabilize bone structure following tumor removal or trauma.[72,73] The anatomical integration of these implants is essential, requiring advanced customization to ensure a perfect fit with the patient's unique cranial and facial structure.[72] Dental implants replace missing teeth by integrating a metallic anchor directly into the jawbone, providing stability and functionality comparable to natural teeth.

These implants come in various types to meet different clinical needs. Endosteal implants, in the form of screws, cylinders, or blades, are the most common and are inserted directly into the bone.[74] Subperiosteal implants are placed beneath the gum but above the bone and are used when bone height is insufficient. Transosteal implants are fixed at the base of the mandible using metal plates, while

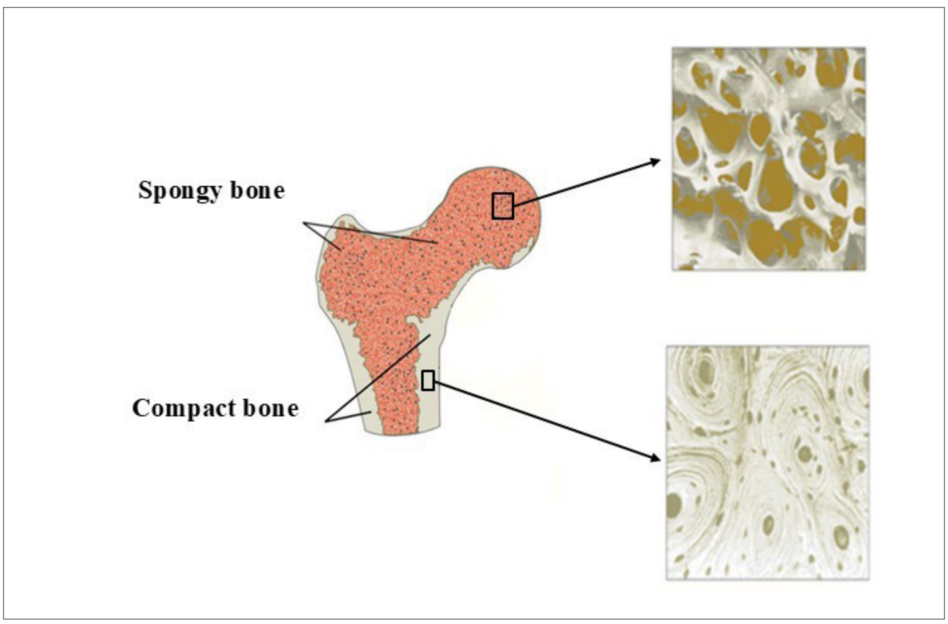

Figure 9. Structural organization of bone, illustrating the microarchitecture of trabecular and cortical bone

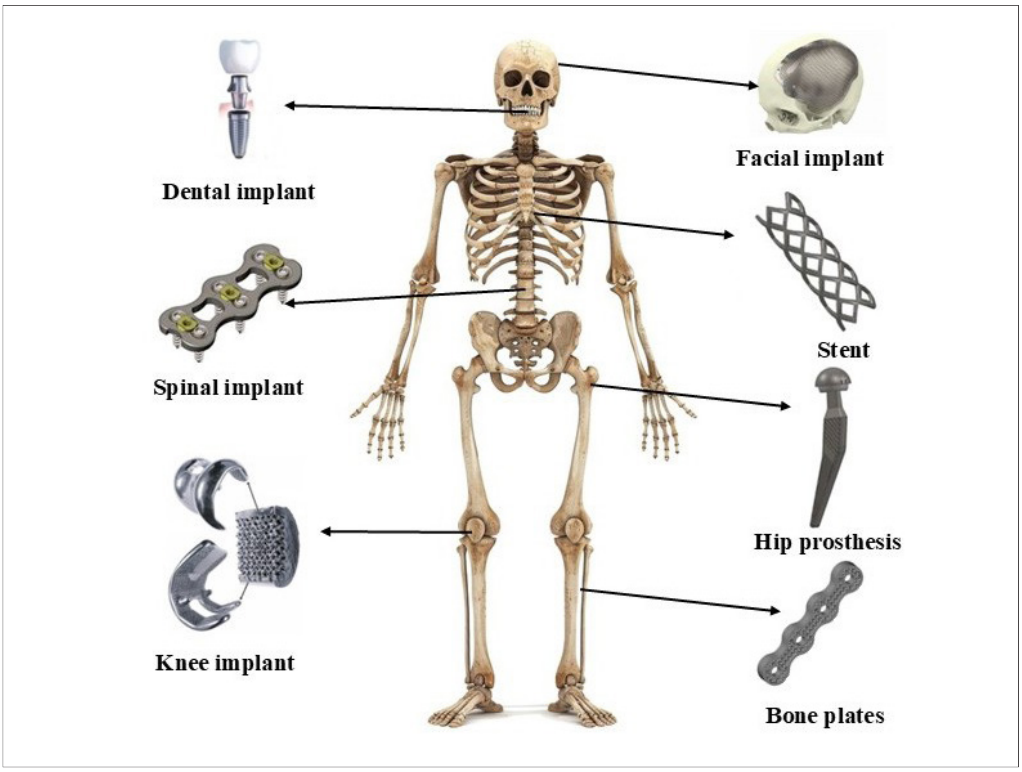

Figure 10. Types of bone implants

zygomatic implants—anchored in the zygomatic bone—provide an alternative to bone grafts for patients with severe bone loss.[75] The commonly used materials for these implants include titanium and its alloys.

4.2.2. Spinal implants

Spinal implants are essential orthopedic devices used to treat disorders affecting the vertebral column and spinal cord, playing a fundamental role in stabilizing and protecting the spine. They are commonly employed to address vertebral fractures, scoliosis, and spinal instability. The implantation of the first titanium intervertebral fusion cage by C.D. Ray and J.W. Brantigan in 1989 marked a significant milestone in spinal surgery.[13] Since then, spinal implants have evolved into multiple categories based on specific clinical needs. Pedicle screws—often made of titanium or stainless steel—enhance stability and facilitate bone fusion, particularly in cases of spinal deformities or fractures. Stabilizing rods are attached to these screws to align the spine and restrict unnecessary movements. Intervertebral cages—inserted between two vertebrae—promote bone growth and reinforce spinal stability. Artificial discs represent a major advancement, preserving spinal mobility and preventing the degeneration of adjacent segments.[76,77] Commonly used materials for these implants include titanium and its alloys, 316L stainless steel, and Co–Cr alloys, known for their high wear resistance. 3D printing techniques such as SLM and EBM have revolutionized spinal implant design by fabricating porous, biomimetic structures that improve osseointegration and reduce stress shielding.[13,78]

4.2.3. Joint implants

Joint implants are designed to restore mobility and relieve pain in patients suffering from degenerative diseases such as osteoarthritis, joint trauma, or inflammatory disorders. Hip and knee prostheses are the most widely used implants in orthopedic surgery. A hip implant consists of several key components, including the femoral head, femoral stem, neck, and acetabular cup, which together mimic the natural mechanics of the joint. During surgery, the acetabular cup replaces the damaged hip socket while the femoral stem is securely anchored in the femur, ensuring optimal stability and functional movement. Knee implants are composed of essential components such as the femoral component, tibial component, patellar component, and a polyethylene articulating surface.[13] These structures are specifically designed to support mechanical loads and provide smooth, stable articulation. Titanium and its alloys are widely favored as the implant material for their lightweight nature and high mechanical strength, while Co–Cr alloys are employed for their robustness and wear resistance.[79]

4.3. Essential tools and strategies for biomimetic implant development

AM plays a central role in designing bone implants that are tailored to patients' biomechanical and anatomical needs. One of the key benefits of AM in implant fabrication is personalization. The use of medical imaging, such as computed tomography (CT) scans and magnetic resonance imaging (MRI), allows for precise anatomical data acquisition, ensuring that the fabricated prosthesis matches the patient's skeletal structure. This high level of customization reduces surgical complications and enhances patient outcomes.[80]

A second major contribution of AM is the ability to design porous structures that mimic the natural trabecular architecture of bone. These porous architectures promote osseointegration, thereby reducing the risk of implant loosening and mitigating stress shielding by adjusting the elastic modulus of the implant. Widely used designs include regular, random, gradient, and topologically optimized lattice structures, which can be tailored to exhibit graded porosity in denser bone regions. These approaches significantly improve the mechanical compatibility between implant and host bone, ensuring long-term stability.[81] Furthermore, AM facilitates the development of implants with optimized surface properties, making them suitable for bioactive coatings such as Hap.[82]

In addition to material selection and structural optimization, several advanced tools and methodologies contribute to the success of AM-fabricated implants. High-quality 3D modeling, enabled by software such as nTop, SolidWorks, and AutoCAD, ensures precise control over implant geometry and internal architecture. Numerical simulations, including FEA and CFD, further optimize implant performance before fabrication, reducing failure risks and improving patient outcomes.[81] The overall workflow of biomimetic implant fabrication using AM is illustrated in Figure 11.

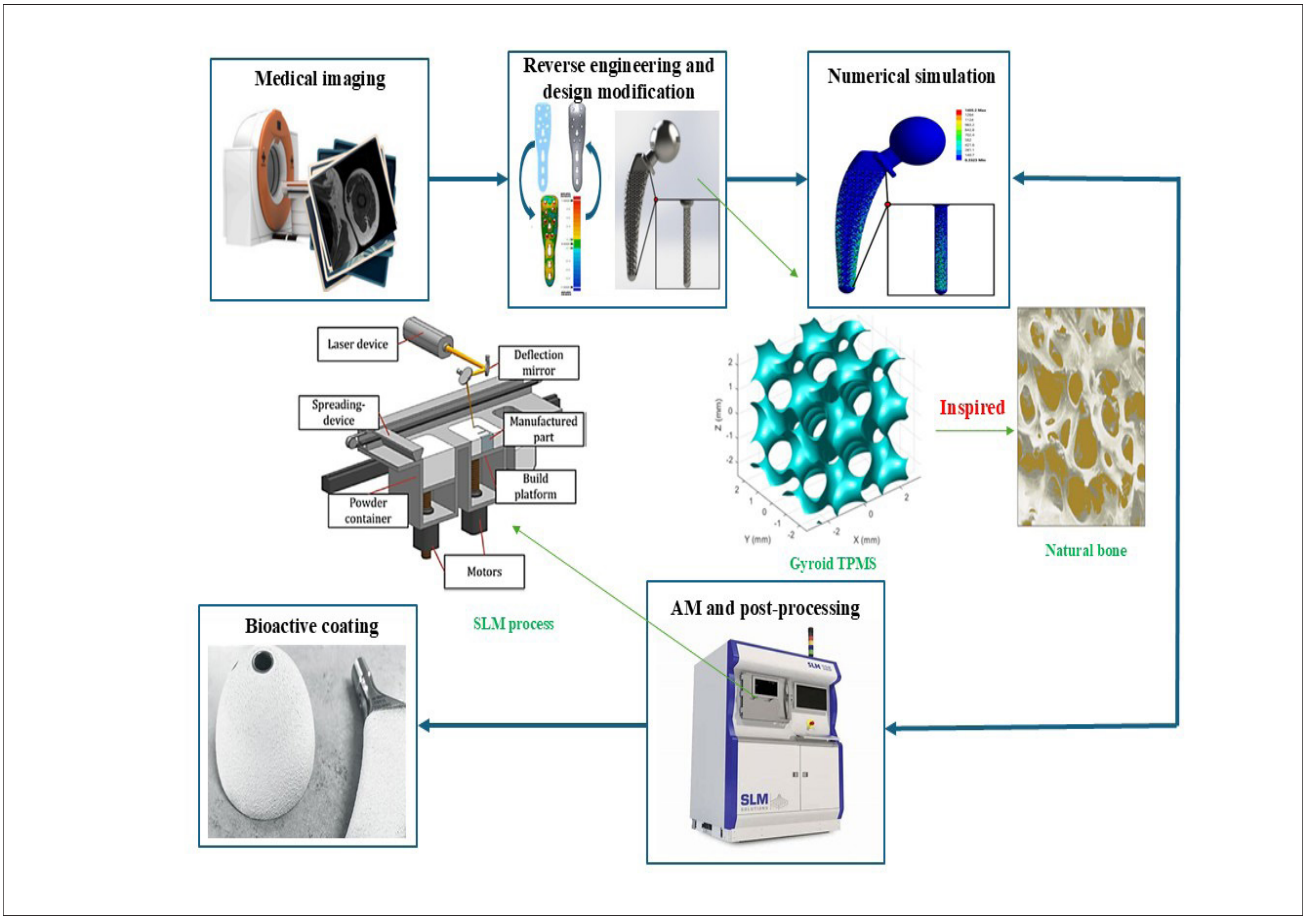

Figure 11. Workflow of biomimetic implant fabrication using AM. Abbreviations: AM, additive manufacturing; SLM, selective laser melting; TPMS, triply periodic minimal surfaces.

4.3.1. Importance of biocompatibility and osseointegration

Biocompatibility refers to the ability of a material to function effectively within a biological environment without triggering adverse reactions such as inflammation, immune rejection, or toxicity, while simultaneously supporting tissue repair and regeneration.[83] It is crucial for the long-term success of implants, as the material must not only integrate harmoniously with the surrounding tissues but also promote healing and functional restoration. The choice of biomaterials plays a pivotal role in ensuring biocompatibility. Titanium alloys, for instance, are highly valued for their exceptional strength-to-weight ratio, corrosion resistance, and low elastic modulus, which helps minimize mechanical mismatch with surrounding tissues. Their surface chemistry further enhances biocompatibility by forming a stable oxide layer that promotes cellular adhesion and proliferation, while reducing inflammation.[84]

Equally critical is osseointegration, a complex biological process that ensures stable and functional integration of an implant with living bone. This process is facilitated by surface modifications, such as bioactive coatings of HAp or titanium oxide, which enhance protein adsorption, cellular adhesion, and subsequent bone-implant bonding.[85,86] The dynamic interplay between biocompatibility and osseointegration ultimately determines an implant's stability, durability, and functional performance. Neglecting these factors can lead to complications such as implant loosening, inflammatory responses, and mechanical failure. Poor biocompatibility may trigger immune reactions that inhibit osseointegration, while insufficient osseointegration can weaken bone–implant bonding, elevating stress at the interface and jeopardizing structural integrity. Therefore, optimizing both biocompatibility and osseointegration is essential for ensuring the longevity and clinical success of orthopedic and dental implants.[13]

4.3.2. Patient-specific implants and customization

The shift toward patient-specific implants has revolutionized biomedical engineering, moving beyond standardized "one-size-fits-all" solutions to highly individualized devices. This approach relies heavily on advanced medical imaging techniques such as CT scans and MRIs, which generate high-resolution digital imaging and communications in medicine (DICOM) data used to reconstruct digital models of patient anatomy. These models serve as the foundation for CAD modeling, enabling precise digital reconstruction of patient-specific anatomical structures.[87] Furthermore, specialized software like nTop utilizes these medical imaging outputs to generate highly optimized lattice structures for AM. The integration of AM with computational modeling facilitates the creation of complex, patient-specific implants, improving biomechanical compatibility, enhancing load distribution, and reducing postoperative complications. Conversely, neglecting patient-specific considerations in implant design can lead to misalignment, instability, and discomfort, potentially compromising biomechanical function and necessitating additional surgical interventions for the associated complications.[13] **Table 5** provides an overview of the commonly used software for the design, simulation, and manufacturing of AM-based metal orthopedic implants.

4.3.3. Lattice structures

Lattice structures in metallic bone implants represent a transformative approach in biomedical engineering, enabling implants to better mimic natural bone properties, enhance osseointegration, and fulfill the mechanical demands of load-bearing applications. These structures can be categorized into four types—regular, random, gradient, and topological distribution structures—each offering unique features that enhance biomimetic capabilities.

Regular lattice structures, such as cubic, diamond, and octet-truss, offer uniform mechanical properties and favorable strength-to-weight ratios, making them suitable for implants requiring even load distribution.[88] However, their simple geometry limits their ability to mimic the complex, irregular architecture of natural bone, which adapts to mechanical stimuli. This mismatch can cause stress shielding. Cubic lattices are easy to manufacture and ensure isotropic mechanical performance. Diamond lattices provide better deformation resistance and strength—ideal for high-load applications like hip prostheses. Octet-truss structures perform well under dynamic loading, thereby improving clinical outcomes.[89]

Random lattice structures, exemplified by Voronoi-based designs, incorporate irregular, heterogeneous patterns that more accurately reflect the trabecular structure of natural bones. This variability enhances load transfer while fostering a favorable microenvironment for cellular proliferation, vascularization, and nutrient diffusion—processes essential for bone regeneration and integration with host tissue.[90,91]

Moreover, they can reduce the likelihood of implant failure by distributing stress more effectively during mobilization and daily activities.

Gradient lattice structures further elevate the biomimetic capabilities of implants through the incorporation of spatial variations in porosity and strut thickness. Such designs allow implants to replicate the mechanical behaviors of both cortical and cancellous bone, ensuring site-specific functionality. This capability not only enhances compatibility but also provides a

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Table 5. Key software tools for additive manufacturing of metal bone implants

Software package	Company	Primary application	Use in metal orthopedic implants	Advantages	Limitations
SolidWorks	Dassault Systèmes	CAD design	Design of orthopedic implants and prosthetics	User-friendly, parametric modeling; integrates with simulation tools	Limited advanced simulation capabilities
nTopology	nTopology Inc.	Generative design	Lattice structures for porous implants, topology optimization	Advanced lattice and topology optimization, ideal for AM	Steep learning curve; may need additional simulation software
Abaqus	Dassault Systèmes	FEA	Structural and biomechanical simulation of implants	Advanced material models, excellent for stress–strain analysis	Requires expertise; high computational cost
ANSYS	ANSYS Inc.	FEA and multiphysics simulation	Fatigue and mechanical performance analysis	Industry-leading multiphysics supports	Expensive licenses; requires powerful hardware
COMSOL Multiphysics	COMSOL Inc.	Multiphysics simulation	Bone–implant interaction modeling; heat transfer in AM	Versatile for biomechanical and thermal studies	Computationally intensive; requires deep expertise
Materialise Mimics	Materialise NV	Medical image processing	3D reconstruction from CT/MRI for patient-specific implants	Precise anatomical modeling; ideal for personalized implants	Limited CAD capabilities, focused on image processing
Materialise Magics	Materialise NV	3D printing preparation	Mesh editing and STL preparation for metal AM	Advanced AM preparation tools	High cost; lacks FEA capabilities
3D Slicer	Open Source	Medical image processing	Patient-specific implant design and preoperative planning	Open-source; strong imaging and segmentation tools	Not designed for CAD or FEA
Fusion 360	Autodesk	CAD and CAM	Design and manufacturing optimization of implants	Cloud-based; integrates CAD and CAM	Limited advanced FEA features
HyperMesh	Altair Engineering	Mesh preprocessing for FEA	High-quality meshing for implant simulations	Optimized meshing; supports multiple solvers	Steep learning curve; complex interface
nTop Platform	nTopology Inc.	Computational design	Advanced lattice structures for implants	Optimized for metal AM	Requires high computational power
Optistruct	Altair Engineering	Structural optimization	Lightweight, topology-optimized implants	Advanced simulation and optimization	Limited multiphysics coverage
Simpleware	Synopsys	Image processing and FEA meshing	Converting CT/MRI data to FEA-ready models	Excellent segmentation and meshing	Expensive; requires additional FEA software
Morpheus	Biovia (Dassault Systèmes)	Computational materials science	Material behavior and surface coating analysis	Good for metal biomaterials and coatings research	Not a full CAD or meshing tool

Abbreviations: AM, additive manufacturing; CAD, computer-aided design; CAM, computer-aided manufacturing; CT, computed tomography; FEA, finite element analysis; MRI, magnetic resonance imaging; STL, standard tessellation language.

smooth transition between stiff and compliant areas, thereby mitigating mismatch in elasticity and lowering the likelihood of implant failure under typical loading conditions.[92] Recent studies have confirmed that graded porosity can significantly improve the overall performance of bone implants by enhancing their mechanical strength and reducing the risk of periprosthetic fractures.[92]

Topological distribution structures utilize advanced optimization algorithms to strategically allocate material based on loading conditions and performance requirements. This innovative design process produces highly efficient geometries that balance mechanical strength with lightweight characteristics, thereby enhancing the structural integrity and fatigue resistance of bone implants.[93] A notable example involves the use of triply periodic minimal surfaces (TPMS), such as gyroid, diamond, Neovius, and primitive structures.[94] These periodic surfaces facilitate effective stress distribution and adaptability to physiological loads, while their high degree of interconnected porosity supports fluid transport and cellular anchorage.[95] Such advancements are critical not only for mechanical performance but also for promoting effective osseointegration, which is fundamental to the bone healing process.

An overview of the four major categories of lattice structures used in metallic bone implants—regular, random, gradient, and topological—is provided in **Figure 12**, illustrating their distinct geometrical designs. Their implications for biomimetics are profound: by closely mimicking the micro-architectural characteristics of natural bone, these designs significantly enhance biological compatibility and functional efficiency. With ongoing progress in AM, the ability to fabricate highly intricate porous metallic lattices holds great promise for patient-specific, optimized implants that promote rapid recovery, seamless osseointegration, and improved long-term clinical outcomes.[96]

4.4. Recent advancements in the optimization of personalized bone implant design

Recent advancements in the optimization of personalized metallic bone implant design (**Table 6**) mark a major shift away from standardized solutions in favor of intelligently engineered, highly individualized, and biologically integrated devices. This transformation is enabled by the convergence of AM, bioinspired architectures, multiscale modeling, advanced surface treatments, and AI. Together, these technologies allow for the design of metallic

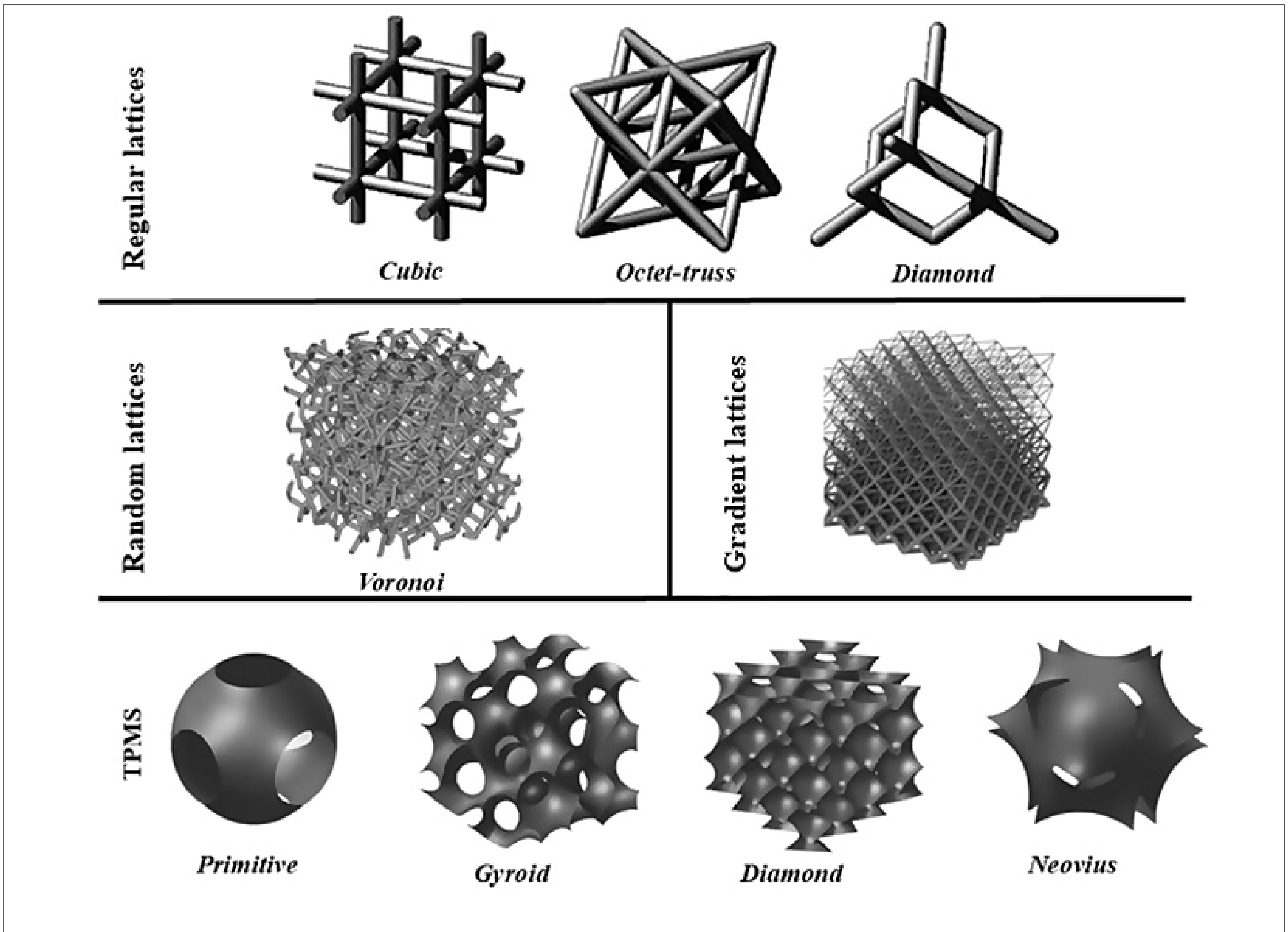

Figure 12. Types of lattice structures for metallic bone implants. Adapted from ref.[89]. Abbreviation: TPMS, triply periodic minimal surfaces.

Table 6. Recent advances in personalized metallic bone implant design

References	Innovation area	Key contribution
97–99	Anatomical personalization	Patient-specific implants based on imaging data, enabling improved biomechanical restoration
100,101	Multiscale architecture and surface design	Integration of macro–micro–nano porosity and optimized surface topography to enhance osseointegration
93,102,103	Biomimetic structures	Elastic modulus adaptation to reduce stress shielding and enhance implant fixation
104,105	AI-driven geometric optimization	Application of machine learning and genetic algorithms for automated implant design
106,107	Personalized surgical techniques	Patient-specific osseodensification protocols to improve primary stability
108,109	Targeted clinical validation	Customized implants shown to restore joint mechanics more accurately than standard models

Abbreviation: AI, artificial intelligence.

implants optimized in terms of geometry, porosity, surface roughness, and mechanical properties, to better match the biological and mechanical complexity of the patient. The central driver of this personalization is the direct use of medical imaging data to generate 3D digital models tailored to individual anatomy. For example, Caiti *et al.*[97] showed that the use of patient-specific metallic fixation plates in osteotomy procedures leads to better biomechanical restoration. Similarly, Milovanović *et al.*[98] demonstrated the clinical effectiveness of personalized titanium mandibular implants, while Wang *et al.*[99] emphasized the relevance of modular hemipelvic endoprostheses for reconstructing complex bone defects. These examples illustrate how morphological conformity, intraoperative adaptability, and modularity have become key decisive factors in clinical success.

At the microstructural level, the work of Martinez-Marquez *et al.*[100] and Deng *et al.*[110] demonstrated that metallic implants with multiscale architectures—combining macro-, micro-, and nanoporosity—promote cell adhesion, vascularization, and osseointegration, even without bioactive coatings. These advances reinforce the concept that internal architecture alone, if properly controlled, can induce a favorable biological response. Furthermore, Wähnert *et al.*[101] highlighted the role of surface topography in peri-implant bone remodeling, ultimately influencing long-term secondary stability. Bioinspired metallic lattice structures, such as trabecular-like networks or TPMS, play a central role in this strategy. Chao *et al.*[93] and Maietta *et al.*[102] showed how such architectures reduce stress shielding by locally adjusting the implant's elastic modulus while maintaining mechanical robustness. Rogala *et al.*[103] also proposed a multi-spiked endoprosthesis that mimics trabecular interdigitation, enhancing primary fixation in complex joint reconstruction. These architectures, further enhanced by graded porosity, facilitate smoother mechanical continuity between implant and host bone.

AI actively contributes to this evolution. Two studies used machine learning techniques and genetic algorithms to automate the design and optimization of metallic implants, particularly lattice geometries, based on biomechanical and biological criteria.[104,105] These tools allow for the rapid exploration of thousands of geometric configurations, while simultaneously considering clinical and manufacturing constraints. On the surgical side, personalized techniques extend into intraoperative protocols. Mello-Machado *et al.*[106] and Olmedo-Gaya *et al.*[107] demonstrated that patient-specific osseodensification protocols enhance bone compaction around the implant, improving primary stability. Additional clinical studies by Dong *et al.*[108] and Kim *et al.*[111] confirmed that customized implants, such as tibial components or femoral head prostheses, restore joint mechanics more physiologically than standard models, reducing misalignments and supporting functional rehabilitation. Kang *et al.*[109] further demonstrated the benefits of topological optimization in improving postoperative outcomes for talar implants.

Despite these remarkable advances, several challenges remain. Long-term validation of these personalized implants is still limited to small patient cohorts, and the lack of interoperability between medical imaging, modeling, mechanical simulation, and 3D printing software hinders the full automation of the design workflow. Additionally, the high cost of metallic materials, advanced fabrication equipment, and post-processing treatments continues to restrict large-scale clinical adoption. The absence of standardized biological and mechanical evaluation protocols, both *in vitro* and *in vivo*, also limits the ability to reliably compare outcomes across different studies. Overcoming these barriers requires long-term multicenter clinical trials with standardized assessment criteria, development of integrated software platforms for seamless workflow management, and deeper incorporation of AI tools into the modeling, simulation, and quality assurance. The future of personalized metallic implantology thus lies in the development of smart implants equipped with sensors for real-time physiological monitoring, the deployment of 5D and 6D printing technologies for enhanced fatigue resistance and geometric fidelity, the integration of gradient mechanical structures for localized stiffness tuning, and fully AI-guided surgical planning synchronized with design and manufacturing. By closing the loop between design, production, implantation, and clinical monitoring, these innovations aim to significantly improve patient outcomes and usher orthopedic and dental implantology into the era of precision medicine.

5. Advanced numerical simulation of biomimetic metallic bone implants: from classical tools to multiphysics coupling

5.1. Finite element analysis

FEA is an essential approach in the design and evaluation of metallic biomimetic implants, enabling the prediction of mechanical behavior under different physiological loads before manufacturing. This technique optimizes the internal structure of implants, improves osseointegration, and reduces the risk of long-term complications. However, simulation outcomes still require experimental validation. The modeling process typically proceeds from mesh generation to the application of boundary conditions and physiological loads. Digital models, often derived from medical imaging, are segmented using Mimics and then further processed with software such as ANSYS, ABAQUS, nTopology, and SolidWorks. Accurate meshing is essential to avoid prediction errors and inefficiencies in numerical calculations. Equally important is the correct assignment of material properties: Ti–6Al–4V remains the benchmark alloy for metallic implants, while composites such as HAp-reinforced polyether ether ketone (PEEK) are increasingly investigated to improve bone integration and reduce excessive stiffness. FEA simulations evaluate parameters such as von Mises stresses, displacement, stiffness, safety factor, and fatigue behavior.[112] A key determinant in implant biomechanics is porosity, as natural bone is inherently porous and heterogeneous. Comparative analyses of lattice structures provide valuable insights into stress distribution, stress-shielding mitigation, and overall implant performance.

Caouette *et al.*[113] demonstrated that a biomimetic carbon fiber femoral stem coated with HAp considerably reduced stress shielding compared with a Ti–6Al–4V titanium stem, while maintaining micromovements below the threshold critical for osseointegration. Similarly, Ceddia *et al.*[114] explored the benefits of carbon fiber composites in femoral stem design through topology optimization and FEA. The study revealed that a carbon-fiber-reinforced femoral stem exhibited a significant stress reduction from 987 to 509 MPa, along with a 30% weight reduction, contributing to a more homogeneous load transfer and decreased risk of bone resorption (**Figure 13**). Rezapourian *et al.*[115] studied different biomimetic topologies using FEA, revealing that the structure inspired by haversian canals (model D9) achieved an elastic modulus of 20.18 GPa and a porosity of 37.26%, favoring homogeneous stress distribution. A comparative study by Munteanu *et al.*[116] evaluated a femoral stem topologically optimized by AM against conventional Ti–6Al–4V implants. Their results show a 15% reduction in mass, a decrease in maximum stress to 349.1 MPa, and improved osseointegration due to controlled porosity, all of which reduces stress shielding while maintaining the required mechanical strength.

The study by Zhang *et al.*[80] showed that incorporating porosities ranging from 66.1 to 79.5% in Ti–6Al–4V implants provides an optimal compromise between mechanical strength and biological performance, with compressive strengths of between 36 and 140 MPa, values consistent with both trabecular and cortical bone. These results align with Alemayehu *et al.*,[117] who analyzed the influence of pore size on the stress distribution and mechanical stability of biomimetic dental implants made from Voronoi structures, with porosity ranging from 70 to 95%. Using nTopology and Creo Parametric, this study revealed that increasing pore size reduces mechanical stress, with von Mises values dropping from 305.93 MPa for a 1 mm pore to 161.16 MPa for a 2.5 mm pore (**Figure 14**). However, the micromotion increased to 17 μm for 2.5 mm pores, which could compromise the initial stability of the implant (**Figure 15**). An optimal pore size of 2 mm was thus identified as a good compromise between mechanical strength and biomimetic integration. In the same context, Simoneau *et al.*[118] and Mehboob *et al.*[119] studied the effect of porosity on orthopedic implants and confirmed the importance of striking a balance between strength and flexibility. Mehboob *et al.*[119] specifically analyzed cubic, diamond, and body-centered cubic (BCC) structures, with porosities ranging from 20 to 90%, using ABAQUS 6.17. Their simulations showed that porosity has a direct influence on implant stiffness and strength, with an optimal porosity of 47.3% replicating the mechanical properties of cortical bone. Taken together, these studies demonstrate that porosity plays a decisive role in the design of biomimetic implants, where a balance between mechanical strength, flexibility, and osseointegration

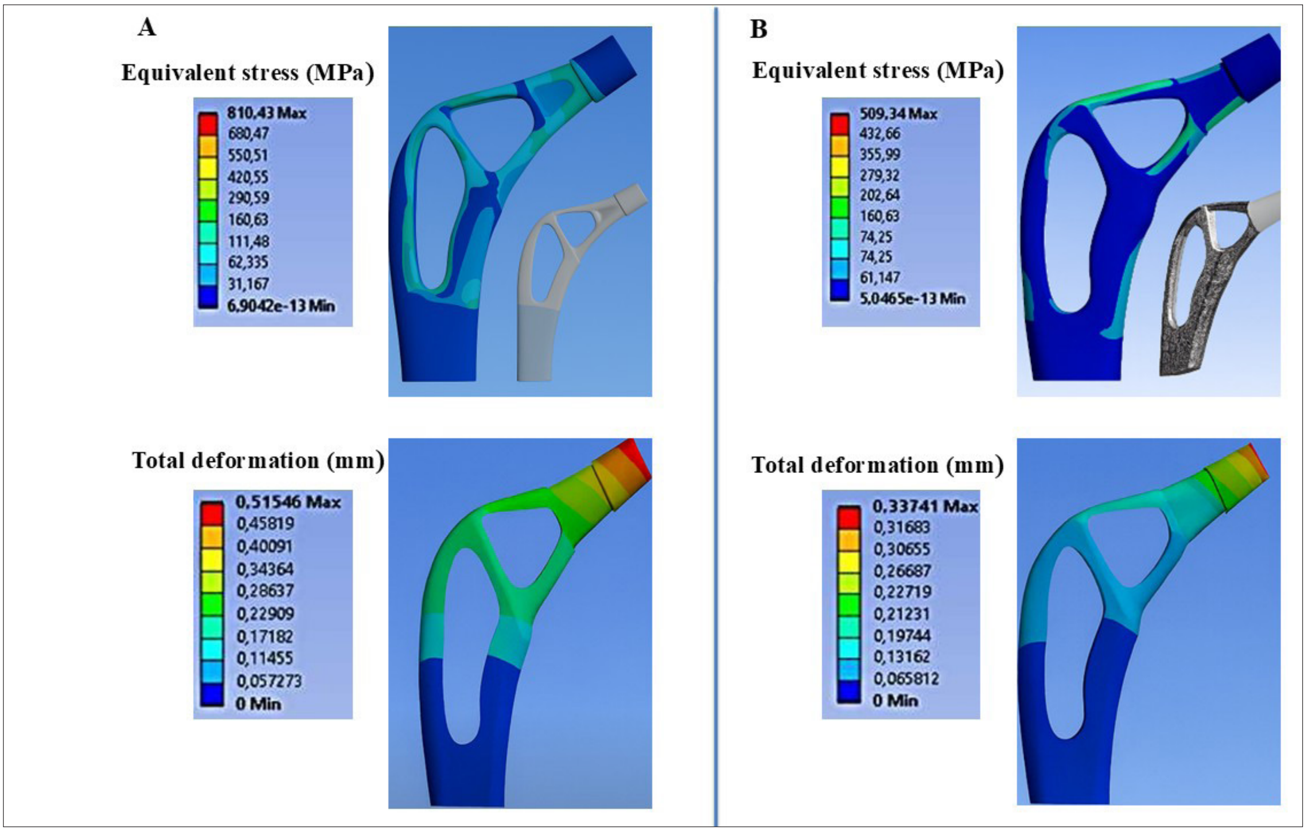

Figure 13. Results of Von Mises stress and total deformation for the topologically optimized stem: (A) titanium and (B) composite material. Adapted from ref.[114]. Abbreviation: FEA, finite element analysis.

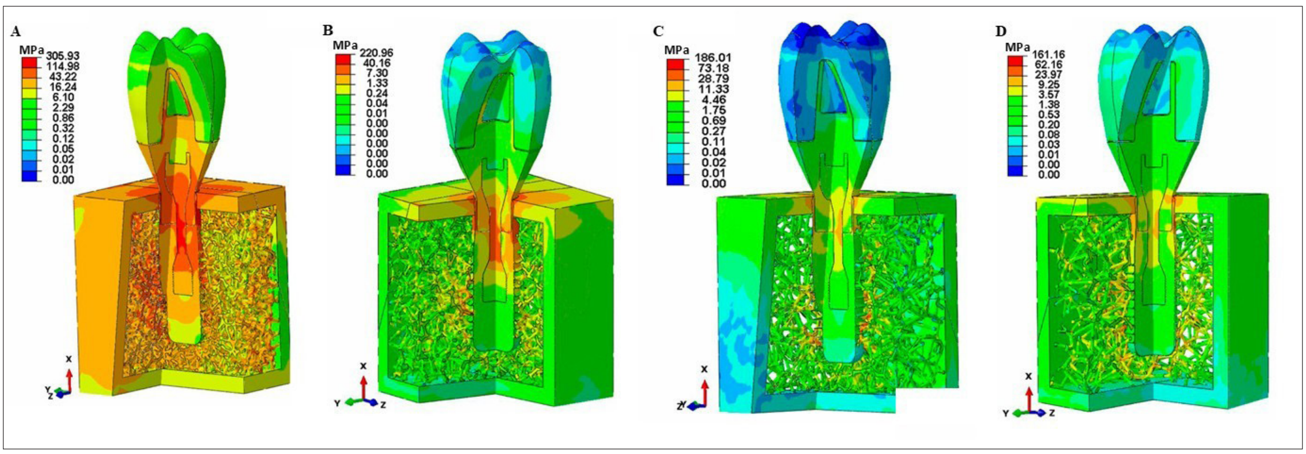

Figure 14. Maximum von Mises stress distribution in double-sliced assembled implant sections for four biomimetic VTB models. (A) VTB10. (B) VTB15. (C) VTB20. (D) VTB25. Adapted from ref.[117]. Abbreviation: VTB, voronoi trabecular bone.

is essential to improve bone compatibility and reduce undesirable effects such as stress shielding.

Pei *et al.*[120] explored homogeneous, quasi-homogeneous, and heterogeneous Ti–6Al–4V implants fabricated by SLM. FEA demonstrated superior stress distribution in the quasi-homogeneous implants compared with the other models (**Figure 16**). Li *et al.*[121] compared biomimetic implants made of PEEK/n-HAp/Carbon fibers, PEEK/HAp, and Ti–6Al–4V for mandibular reconstruction. Their study showed that Ti–6Al–4V, although more rigid, offers more stable fixation and improved osseointegration, while PEEK-based implants absorb loads better but present an increased risk of deformation and micromovements, which can compromise their stability and promote bone

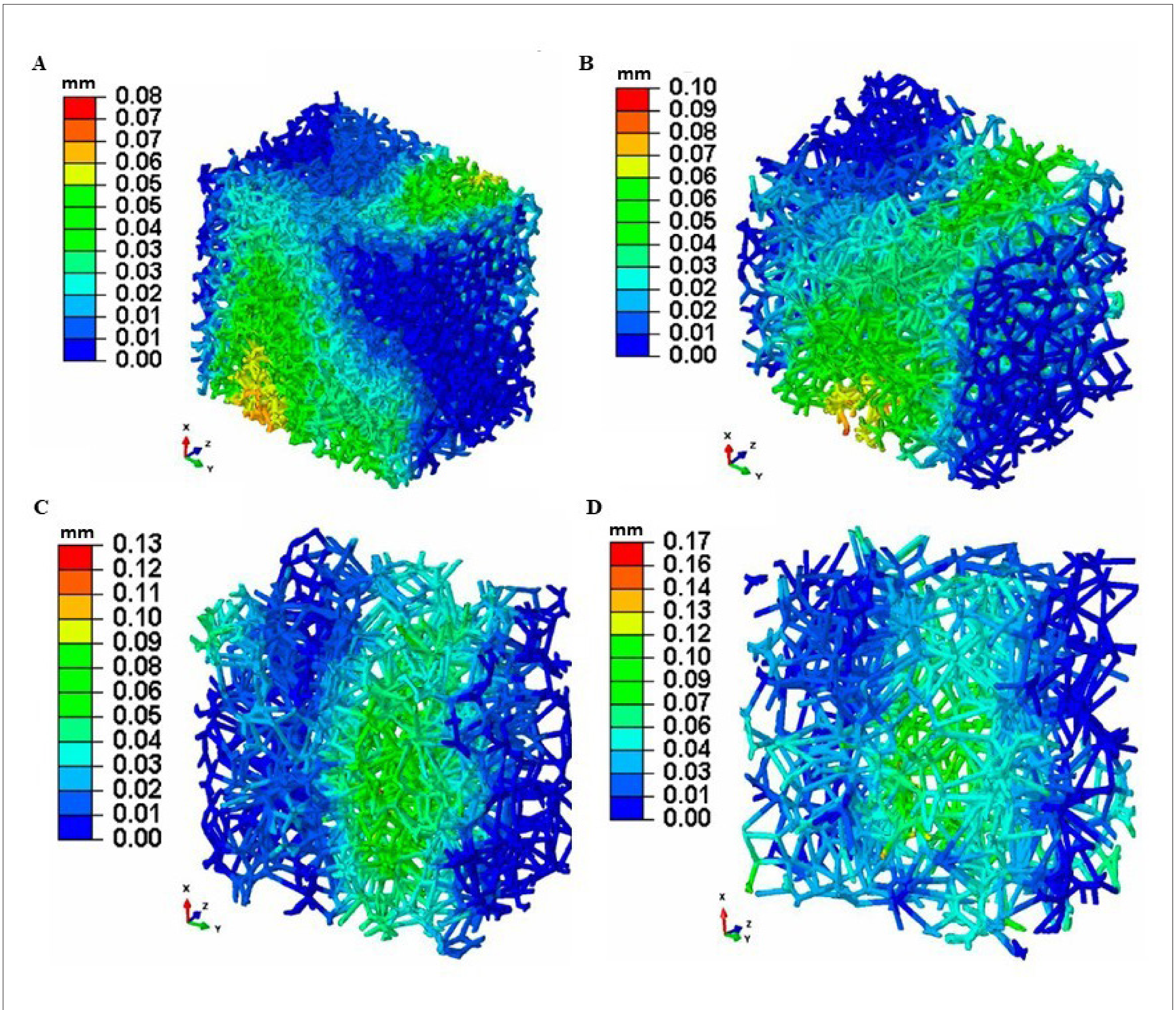

Figure 15. Displacement magnitude contour plots for biomimetic VTB structures with different pore sizes. (A) VTB10. (B) VTB15. (C) VTB20. (D) VTB25. Adapted from ref.[117]. Abbreviation: VTB, voronoi trabecular bone.

resorption. Despite their lightweight and biological compatibility, PEEK implants need further optimization to improve their osseointegration.

FEA has also been widely used to compare different biomimetic structures and architectures in the design of orthopedic implants. Mehboob *et al.*[119] analyzed several geometries of lattice structures and showed that cubic structures offer high compressive strength but anisotropic behavior, while diamond structures have lower stiffness. BCC structures, on the other hand, represent an optimal compromise between rigidity and flexibility, ensuring better biomechanical adaptation and a more even distribution of physiological stresses. Chatzigeorgiou *et al.*[122] studied the impact of TPMS structures on stress distribution and the reduction of stress shielding in the context of partial femur replacement. Their multiscale approach—incorporating a global model and a local model based on bone anatomy—demonstrated that primitive structures significantly improved stress distribution, while gyroid structures reduced stress concentration zones (**Figure 17**). Soro *et al.*[123] also used FEA further showed that gyroid TPMS in Ti-25Ta implants effectively reduced stress shielding, ensuring better mechanical adaptation to physiological conditions. In addition, Salaha *et al.*[124] compared gyroid and Voronoi structures applied to hip implants and found that the Voronoi implant provided better stress dissipation and reduced mass while maintaining even load distribution on the bone. This study also highlighted titanium alloy

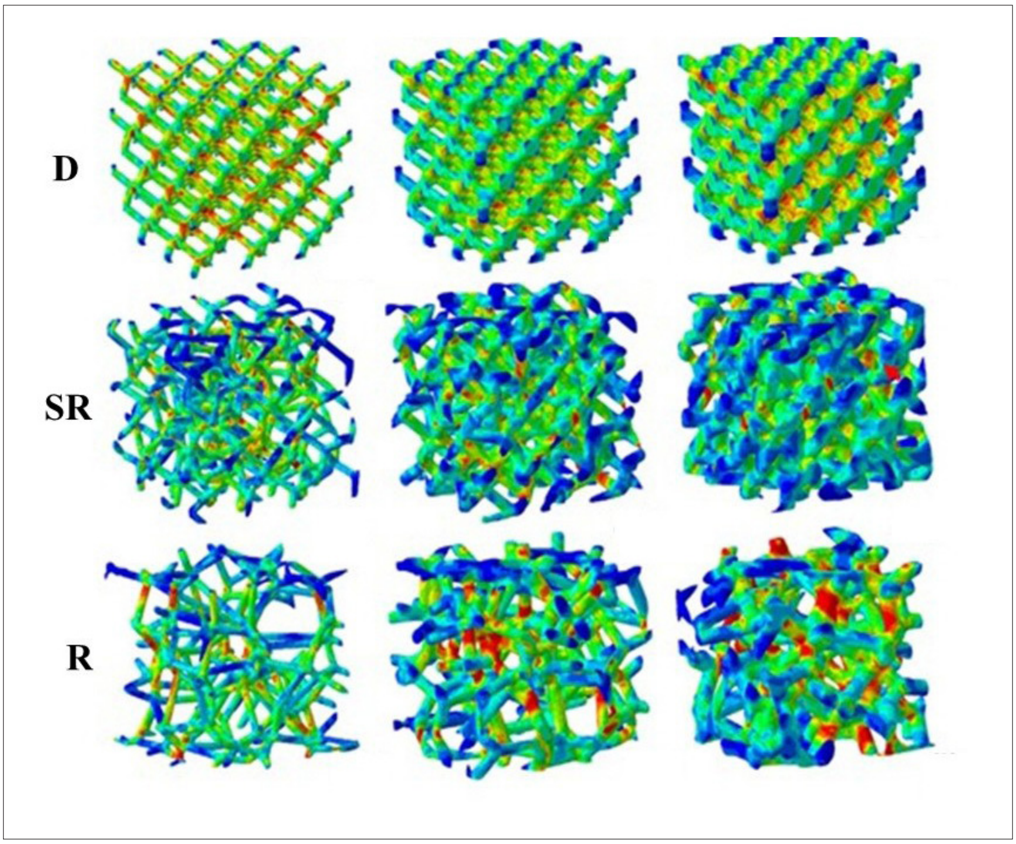

Figure 16. Compressive mechanical testing and FEA simulation results of three structural designs: D = Deterministic regular lattice structures, SR = Semi-random lattice structures, and R = Random lattice structures. Each category includes three parametric variations (different pore sizes and relative densities) to illustrate the effect of structural variation on stress distribution. Adapted from Pei *et al.*[120] Abbreviation: FEA, finite element analysis.

Ti–6Al–4V as the most suitable material due to its high strength and biomechanical compatibility, although magnesium alloys may offer lightweight alternatives for minimizing bone stresses.

5.2. Computational fluid dynamics

CFD has emerged as a powerful numerical tool for investigating the biological performance of lattice-based metallic implants, particularly in the context of osseointegration. Unlike purely mechanical simulations, CFD enables the modeling of interstitial fluid flow, wall shear stress (WSS), and nutrient transport through complex porous architectures. These parameters are critical for regulating cellular behaviors such as adhesion, proliferation, osteogenic differentiation, and vascularization, all of which are essential for successful implant integration.

Numerous studies have highlighted the strong influence of internal geometry, especially TPMS structures, on local fluid dynamics and permeability. Ali *et al.*[125] demonstrated that gyroid and diamond architectures produce more homogeneous WSS distributions and greater permeability than conventional topologies, thereby enhancing the osteogenic response. Karuna *et al.*[126] further showed that introducing a porosity gradient within TPMS implants improves nutrient transport and reduces regions of low shear stress, a key factor in preventing cellular stagnation and hypoxia. Similarly, Lai *et al.*[127] emphasized the role of curvature and geometric connectivity in shaping both local flow behavior and internal stress gradients within porous implants. Pei *et al.*[120] used CFD to compare the permeability of three types of Ti–6Al–4V lattice structures (homogeneous, quasi-homogeneous, and heterogeneous), demonstrating that the quasi-homogeneous configuration offers an optimal trade-off between mechanical integrity and fluid diffusion, thus promoting a more favorable environment for bone ingrowth and long-term osseointegration. These findings underline the importance of designing implants with fluid-conductive architectures that not only meet mechanical requirements but also create microenvironments conducive to tissue regeneration and angiogenesis. CFD results are thus becoming key design

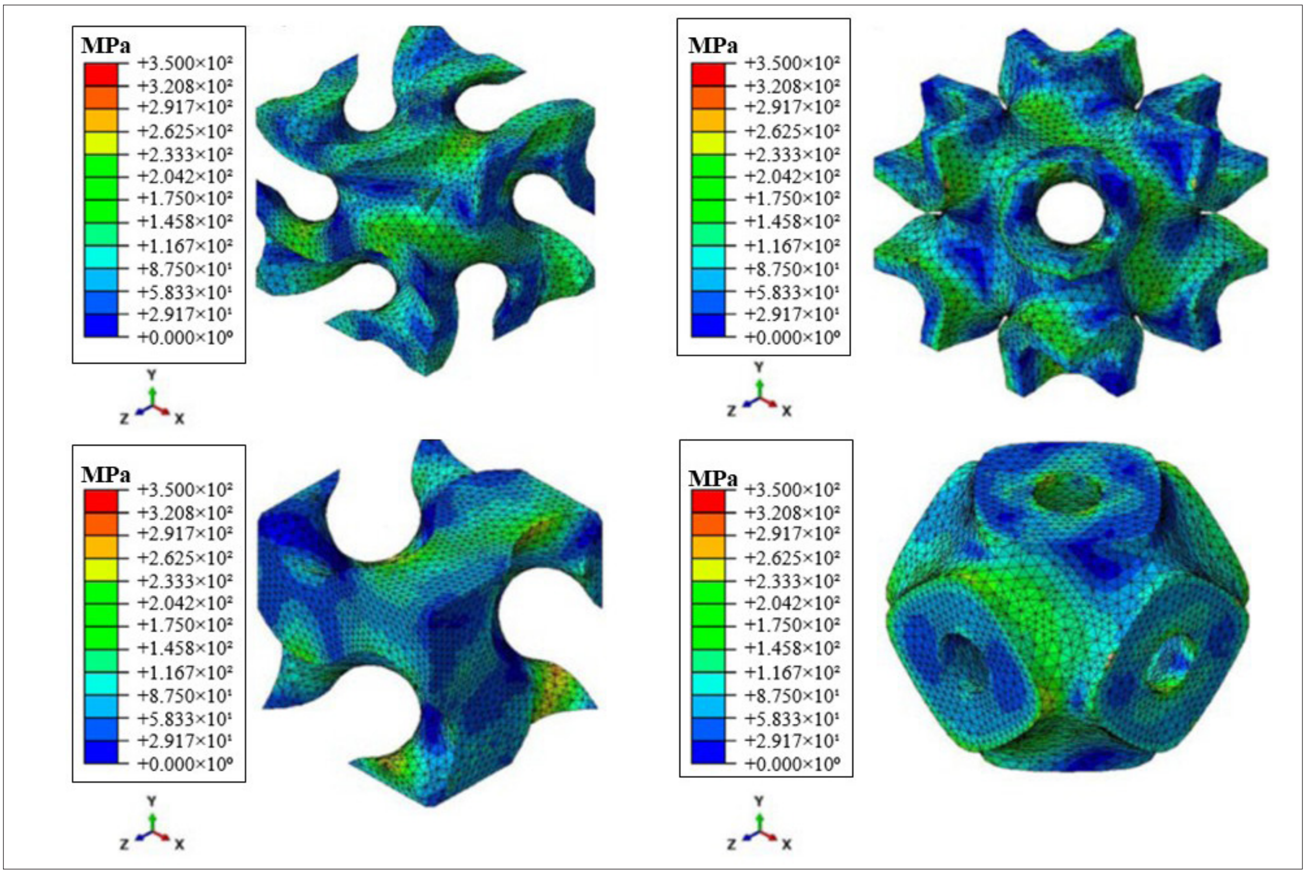

Figure 17. Von Mises stress contours for gyroid sheet, IWP sheet, gyroid skeletal, and primitive sheet unit cells. Adapted from ref.[122].

parameters, integrated early into the digital workflow of next-generation biomimetic implants.

5.3. Integration of multi-field coupling models for physiological accuracy

To better reproduce the complex physiological environment surrounding metallic bone implants, recent studies have adopted multiphysics simulation models that couple several physical domains—mechanical, thermal, chemical, biological, and electromagnetic—within a single computational framework. These models are particularly relevant for porous or lattice implants fabricated by AM, where multiple physical phenomena interact simultaneously and influence implant performance. **Figure 18** illustrates a typical multiphysics workflow, combining structural analysis, fluid dynamics, and topology optimization with additional coupled processes such as thermal conduction, chemical degradation, ion transport, and electromagnetic behavior under MRI exposure.

A pioneering example is provided by Ma *et al.*,[128] who developed a triply coupled framework integrating FEA, CFD, and topology optimization. Their model simultaneously assessed mechanical stability and interstitial fluid transport in TPMS-based implants. The results revealed optimal pore arrangements that improved both structural strength and permeability—key prerequisites for osseointegration, nutrient delivery, and cellular proliferation. In another domain, Jin *et al.*[129] investigated the mechanical-chemical degradation of biodegradable magnesium-based implants. Using time-dependent FEA, they modeled progressive implant resorption and its impact on local stress redistribution and bone remodeling, showing how degradation rates affect stress shielding and peri-implant bone health. Such models are critical for tailoring degradation kinetics to the natural healing timeline.

From the manufacturing perspective, Medina-Gálvez *et al.*[130] introduced a thermo-mechanical simulation to predict microstructural transformations in Ti-6Al-4V implants during SLM. Their study highlighted the influence of thermal gradients, cooling rates, and energy input on the formation of martensitic α′ phases and residual stresses, both of which have a major impact on implant fatigue resistance and biological response.

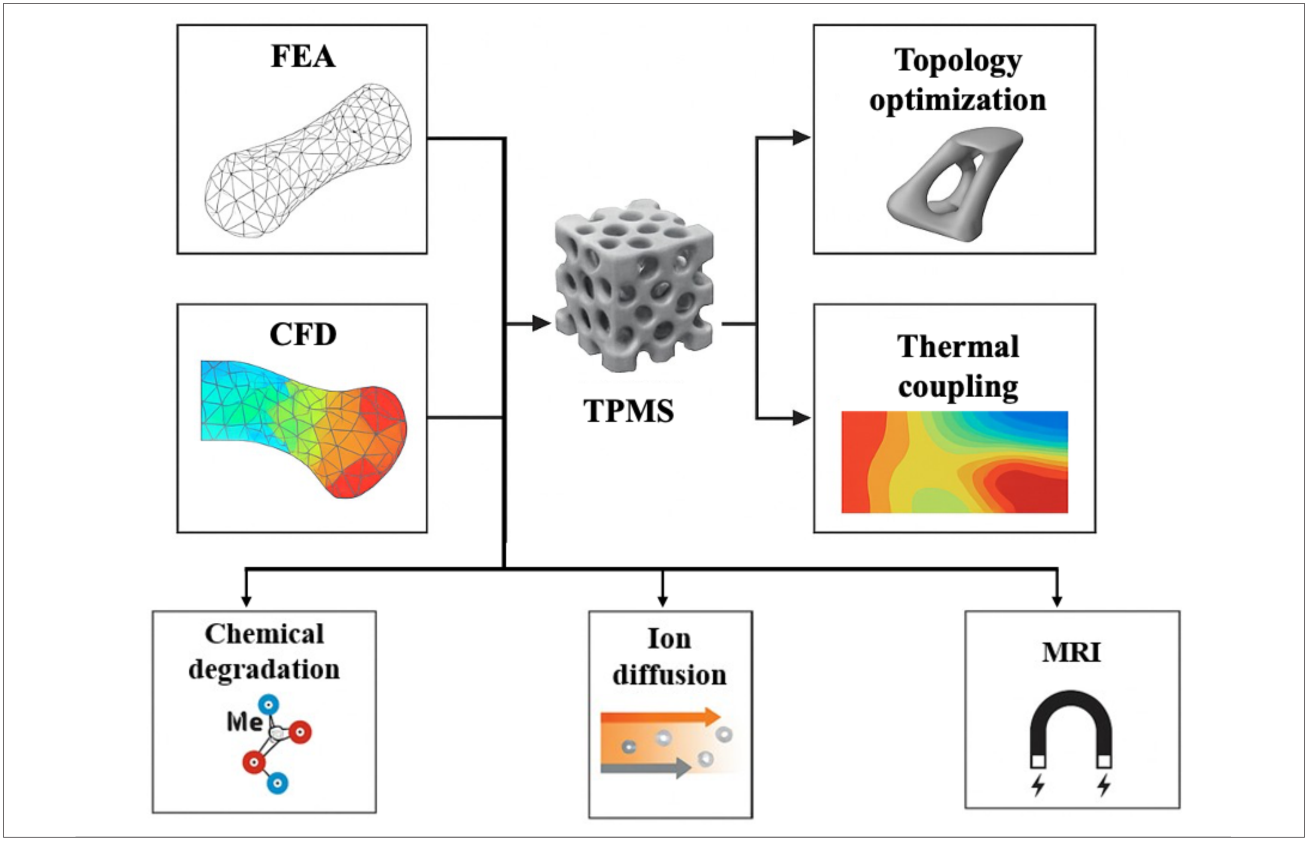

Figure 18. Schematic of a multiphysics simulation workflow for metallic bone implants. Abbreviations: CFD, computational fluid dynamics; FEA, finite element analysis; MRI, magnetic resonance imaging; TPMS, triply periodic minimal surfaces.

At the interface level, Ogawa *et al.*[131] and Rappe *et al.*[132] proposed chemical–mechanical–diffusive models to simulate metallic ion release through corrosion and subsequent tissue diffusion. These simulations revealed potential local inflammatory responses, linking surface degradation mechanisms to implant biocompatibility and safety. By including variables such as pH, oxide film behavior, and stress-assisted corrosion, these models offer a predictive understanding of long-term performance. For experimental validation, Hafidz *et al.*[133] integrated surface acoustic wave sensors into AM implants to measure real-time thermal and mechanical conditions during loading. The data validated predictions from a thermomechanical simulation, confirming temperature distributions and stress fields within the implant. This work demonstrates the synergy between *in silico* modeling and sensor-based monitoring for implant reliability. Lastly, Makarov *et al.*[134] employed an electromagnetic–thermal model to simulate radiofrequency-induced heating of metallic implants during MRI exposure. Their results identified hotspots and temperature elevations near implant surfaces, which are crucial for ensuring patient safety and adherence to MRI standards.

Altogether, these studies exemplify the transition from simplified, single-physics models to integrated, multiphysics computational tools that are not only more physiologically realistic but also vital for optimizing implant design, function, durability, and clinical safety under patient-specific conditions. They pave the way for next-generation, smart biomedical implants with predictive, personalized, and feedback-enabled capabilities. Considering this growing body of research, it becomes increasingly clear that the adoption of multiphysics coupling in numerical simulations is not merely an enhancement but a necessity for the rational design of metallic bone implants. These models enable researchers and clinicians to bridge the gap between mechanical reliability, biological integration, and patient-specific variability. In our view, the integration of such advanced computational strategies, especially when validated by real-time experimental data, will play a pivotal role in the future of implant development. They not only allow for predictive insight into failure modes and biological outcomes but also facilitate regulatory compliance and clinical translation. Ultimately, multiphysics modeling should become the gold standard in the simulation pipeline for next-generation implants, particularly those leveraging the full potential of AM and biofunctionalization.

6. Conclusion and future perspectives

AM has fundamentally transformed the landscape of bone implantology by enabling the fabrication of personalized, structurally optimized, and biomimetic metallic implants that closely replicate the complex architecture and mechanical behavior of native bone. This review has systematically explored the current technological, clinical, and biological advances that support the emergence of AM-based implants, focusing on key manufacturing processes such as SLM and EBM, the selection and optimization of advanced biocompatible materials like Ti-6Al-4V and cobalt-chromium alloys, and the compelling *in vivo* and clinical data highlighting their mid-term reliability and success in orthopedic applications.

Biomimetic design strategies—including the incorporation of graded porosity and topologically optimized lattice architectures—have demonstrated significant benefits in enhancing osseointegration, reducing stress shielding, and promoting a favorable biomechanical environment at the bone–implant interface. Simultaneously, patient-specific customization, enabled by high-resolution CT and MRI imaging, DICOM segmentation, and advanced CAD modeling, allows implants to be anatomically tailored while integrating bioinspired mechanical behavior. Numerical simulation tools, such as FEA and CFD, play an essential role in preclinical evaluation, offering predictive insights into stress distribution, fluid flow, fatigue performance, and structural stability under physiological loads. Emerging multiphysics coupling models that integrate mechanical, thermal, chemical, and biological domains have further revolutionized the predictive design pipeline, offering highly realistic simulations of *in vivo* conditions, including degradation kinetics, nutrient diffusion, corrosion, and remodeling dynamics. Despite these breakthroughs, several barriers continue to limit widespread clinical translation: the high cost of metal powders and AM equipment, the lack of universal standards for testing and validation, fragmented digital workflows, limited clinician training in AM technologies, and insufficient long-term clinical evidence, particularly for weight-bearing applications in younger and active patients.

Looking forward, the future of AM metallic bone implants lies in the convergence of multiple innovations: the integration of AI and digital twin technologies for real-time process optimization and automated implant design; the development of smart, sensor-integrated implants capable of postoperatively monitor strain, temperature, and biological markers; and the adoption of advanced manufacturing paradigms such as 5D and 6D printing, which combine multi-axis deposition, smart materials, and biofunctional gradients to produce next-generation adaptive implants. Furthermore, sustainable approaches must be prioritized, including the use of recyclable metal powders, streamlined post-processing protocols, and scalable manufacturing workflows to make these advanced solutions accessible to broader healthcare systems. In conclusion, AM—when synergized with biomimetic architecture, patient-specific customization, predictive multiphysics simulation, and intelligent clinical feedback systems—holds the potential to redefine the standard of care in skeletal reconstruction. It offers not only a path toward superior mechanical performance and biological integration but also ushers in a new era of intelligent, regenerative, and truly personalized orthopedic and dental implantology, where the implant becomes a dynamic interface between engineered precision and living biology.

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Conflict of interest

The authors declare no competing interests.

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