# Metallic Scaffolds for Tissue and Bone Engineering: Applications in Radiology, Pharmacy, Nursing, Emergency Services, and Laboratory Sciences

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***Abstract:*** Metallic scaffolds have emerged as vital tissue and bone engineering tools due to their exceptional mechanical strength, biocompatibility, and bioactivity. These scaffolds serve as templates for tissue regeneration, guiding cellular behavior and supporting the growth of bone-like tissues. The integration of metallic scaffolds across diverse fields such as radiology, pharmacy, nursing, emergency services, and laboratory sciences highlights their multidisciplinary significance. This review explores the material properties, fabrication techniques, and characterization methods of metallic scaffolds, emphasizing their applications in regenerative medicine and their role in drug delivery systems. Challenges such as regulatory considerations, biocompatibility concerns, and scalability issues are discussed, along with future research directions aimed at optimizing scaffold performance and clinical applicability.

***Keywords:*** Metallic scaffolds, tissue engineering, bone regeneration, additive manufacturing, biocompatibility, bioactivity, drug delivery systems, regenerative medicine, radiology, trauma management.

## 1. Introduction

Metallic scaffolds are meant to have a primary metal structure, which provides enough mechanical strength to stimulate the osteoconductive aspects. Together with cell sources, bioactive factors, and/or gene therapy strategies, the scaffolds are definitely a key factor for tissue and bone engineering in regenerative medicine, as they contribute to controlling cell behavior, polarization, and patterning throughout programmed space and time. While the mechanical properties of the substitute are important to endure in vivo loading, this is why metals are precious materials for scaffold construction. Additionally, chemical and physical characteristics, surface area, and degradation behavior play a determinant role in primary and secondary bone-like tissue ingrowth, vessel ingrowth, cell aggregation, and polarization, and afterwards in tissue growth. Scaffolds need to be designed to act as templates and guides for tissue growth: impeccable in the long-term mechanical and vocational requirements and maintaining function over time, as the de-localization of normal and shear elastic stresses is responsible for a mechanically shielded stress-unshielded elastic mismatch, promoting cell approximation and tissue growth. Innovations and improvements in metallic scaffold design are therefore important in some medical fields, but not always a topic of visibility, although in recent years this has been strongly growing. Biological theories go hand in hand with material science disciplines, and the final metallic scaffold is the result of these multidisciplinary studies. When a metal is processed as a macro-porous scaffold, mechanical strength, surface, and corrosion behavior can also be tailored, further broadening the miscellaneous ways to fabricate starting materials. In the second instance, all the polymers previously or later mentioned should be tuned in a way to present these requisites: while for some of them there is already a consolidated application in the tissue engineering field, the use of some others is presently under confidential or restricted disclosure. The most appreciable characteristics of metallic scaffolds for their use in medical applications are: more narrowly defined properties with superior performance; high stability to ultra-sterile and humid atmospheric conditions; presence of joined and bondable surfaces; and the possibility to be further treated to improve bioactivity and osteointegration. (Gao et al., 2022)(Flores-Jacobo et al.2023)(Collins et al.2021)(Marin, 2023)(Li et al., 2022)(Percival et al.2024)(Yuan et al.2024)(Zerankeshi et al., 2022)(Chen et al.2022)

### *1.1. Overview of Tissue and Bone Engineering*

Tissue engineering and bone engineering are focal areas in regenerative medicine and aim at restoring the normal function of damaged organs due to trauma, degenerative diseases, and cancer. In principle, the three basic components of tissue engineering are cells, scaffolds, and biomolecules. The idea is that new tissues can be developed for transplantation into superficial or deeper body areas by appropriate cell seeding into a porous solid, shaped to stimulate, through adhesion, the progressive colonization so that the implant becomes acellular in a relatively short time and is entirely replaced by surrounding autologous cells. The tissue engineering era was mature when it was highlighted the crucial need for an all-purpose biomedically compatible material that has to be open not only to cells but also to the circulation that brings oxygen and energetic compounds to all host cells and tissue. (Ruiz-Alonso et al.2021)(Zhu et al.2021)(Miranda et al., 2020)(Ashammakhi et al.2022)(Zhang et al.2024)(Serrano-Aroca et al.2022)(Yadav et al., 2024)(Boyetey et al., 2023)

The historical profile of tissue engineering is increasing and reshaping according to the scientific and technical advances in the connection between biology and medicine, surgery, hospital care, and system biology, as well as the revolution in production and logistics. Biocompatibility ensures suitable tissue integration, but reabsorption and replacement occur after tissue biogeneration, while a milder tissue-biomaterial interaction results in slower tissue integration. The potential use of engineered human tissues could range from diagnostic to ethical implications. In Europe, the exploitation spectrum would include applying radiological support in computed tomography, magnetic resonance, ultrasonography, and angiography to tissue- and bone-engineered products.

## 2. Material Properties of Metallic Scaffolds

Structured Abstract Title: Metallic Scaffolds for Tissue and Bone Engineering: Applications in Radiology, Pharmacy, Nursing, Emergency Services, and Laboratory Sciences Core Tip: Materials used in metallic scaffolds are of great importance. If the material used is not sufficient from a mechanical, corrosion resistance, or structural point of view, it does not matter how advanced technology or bioengineering is utilized. The materials used in the production of scaffolds are classified as polymers, ceramics, and metals from soft to hard. The most preferred metals and alloys for scaffold applications are those with high corrosion resistance, ease of processability, and high biocompatibility. In addition, the materials used to produce the metal scaffold should have biological properties such as biocompatibility and bioactivity. The interaction of a material or substance with biological systems is important. The behavior of a cell, tissue, or whole organism after direct or indirect contact with that material or substance is called biocompatibility. In addition, the material must also exhibit bioactivity in order to regenerate the damaged tissue. This includes accelerating bone growth in situations where the natural metabolism of the bone is not sufficient. The material should participate in cell metabolism and increase bone mineralization at the molecular level, thus providing a bond between the material and bone tissue. The material must also be non-toxic, and its products that occur as a result of its dissolution must not create a negative environment in the surrounding tissues. In summary, the success of a scaffold is related to the position and path of the cells, the secretion between these cells, and the support for new tissue growth. In order to achieve this, the material selection employed in the production process is extremely important. Some important criteria in metallic scaffold production are given in terms of their characteristics and structure. (Md et al.2022)(Li et al.2021)(Carluccio et al.2020)(Lv et al.2021)(Ramya, 2024)(Nasr et al.2022)(Gutiérrez et al.2023)(Sezer et al., 2021)

### *2.1. Biocompatibility and Bioactivity*

Biocompatibility stands for the capacity of a biomaterial to interact with surrounding living tissue. This ability starts from mineral matter and continues through different types of materials. The acquired insight is not just increased mechanical prowess considering devices that contribute to implanted patient satisfaction, but rather brings accuracy where needed, reduction of side effects, and a reasonable time of therapy. Additionally, a new term was introduced in the post-millennium: bioactivity. Bioactive scaffolds provide the appropriate conditions for constructive interference of the living body. In fact, not only do they elicit a favorable tissue reaction, but they also support a designed cell population or encourage the production of the extracellular matrix. This is recognized as bone bioactivity, and it may be, generally speaking, the first common link between bioactivity and tissue engineering. (Jurak et al.2021)(Huzum et al.2021)(Cacopardo, 2022)

The term actually means expansion into a more general application because bioactive bone may be taken as a surrogate for a variety of technical regenerations. It is undoubtedly difficult to directly produce these materials, but primarily one can stimulate them and promote their formation under physiological conditions. Efforts of the past two decades prove that the concept of biological response to surfaces has been well received. Further, this knowledge, when applied to technologies, can yield remarkable results in the form of materials with high degrees of biocompatibility. Unfortunately, our current understanding shows that it is an intricate relationship that combines facts and intuition. Active research, utilizing different knowledge and opportunities, has started. This new material is the result of a true marriage between intense study of orthopedic ceramics and long-standing classic work concerning bioactive glasses. However, progress in this field is still pledged to strategic amelioration of material parameters in physical and biological testing. (Rahmati et al.2020)(Adeyemi et al., 2022)(Cao et al.2021)(Zhao et al., 2021)(Kopac, 2021)(Sidhu et al., 2021)(McKim, 2024)

## 3. Fabrication Techniques for Metallic Scaffolds

Fabrication of metallic scaffolds requires precise techniques because they directly affect the microstructure, mechanical, and biological properties of the produced scaffolds. The fabrication method should provide a high degree of precision and reproducibility, preferably at a low cost. Traditional methods, such as machining, casting, and sintering, were used to fabricate a metallic scaffold, but these methods have some limitations. Cast metal scaffolds have defects, and the surface is rough, decreasing the accuracy of the surface geometry. Machined and powder-sintered structures have shown a lower interfacial strength with bone and are not appealing because of their high production costs and inability to produce complex architecture. For the above-mentioned reasons, new fabrication techniques have been developed to fabricate a metallic scaffold wherein additive manufacturing has been preferred due to its ability to produce complex geometries. (Zerankeshi et al., 2022)(Szymczyk-Ziółkowska et al.2020)(Sezer et al., 2021)(Kumar & Sathiya, 2021)(Carluccio et al.2020)(Germaini et al.2022)(Attarilar et al.2020)

The major advantage of AM techniques is the capability to produce freeform, complex, and open porous structures based on automated layer-by-layer deposition. Since AM acceptance criteria are precise, some technical, material, and computational efforts have been made to understand and optimize their processing parameters as a whole, fueling industrial innovations and further research studies. A certain combination of material processing techniques is desired in order to adjust the final mechanical properties. All these changes are required for the bone scaffold to better mimic real bone and fulfill the anatomical needs. These innovative and efficient techniques are necessary for fabricating optimized material implants to meet clinical demands. The final characteristics of the scaffold, such as pore size, porosity level, pore distribution, and mechanical properties, are directly influenced by the employed fabrication methods. It is necessary to enhance and optimize the developed fabrication technique while considering these factors. More fabrication techniques and calculation methods need to be developed to produce enhanced metallic scaffold structures. (Collins et al.2021)(Hutmacher et al., 2023)(Adel et al., 2022)(Wang et al.2021)(Capuana et al.2021)(Aslam et al.2024)(Ruiz-Alonso et al.2021)

### *3.1. Additive Manufacturing Processes*

Additive manufacturing (AM), known as 3D printing, builds structures up sequentially layer by layer from data obtained with computer-aided design. The approach of this technology is the inverse of traditional methods of fabrication, which start with a macroscopic form of the material and remove waste to give the final shape. It becomes a potentially perfect technology for young fields like tissue and bone engineering, in which the complexity of a structure produced can often be related to the increased effectiveness of the construct in situ. In general, these two fields heavily rely upon AM technology to tailor-make scaffolds to suit the exact dimensions of a defect and to more closely mimic the tissue that is to be constructed. (Jiang et al.2022)(Ren et al.2021)(Xiong et al., 2022)(Das et al.2024)(Matos et al.2021)(Liu et al.2023)(Chen et al., 2021)

AM begins with a digital model. In the case of tissue engineering, this can be derived from imaging techniques. The file is sliced into two-dimensional sections with a programmed engineering interface, which uses two-dimensional geometry to generate a three-dimensional component. Other systems process each thickness of layer before moving down to the next. Some methods selectively cure or solidify material to produce the desired shape. The most commonly used materials in AM are acids, nylon, photopolymer resins, polycarbonate, titanium, gold, silver, and molecules transformed into particles. When the layer has been processed, the manufacturing part is lowered by a layer thickness and the process begins again. AM fabrication processes can be tailored to meet certain predefined design constraints for a fabrication method. Most of these for biomedical materials, and in this chapter, biomaterials are created to make a porous structure. An advantage of AM over subtractive methods is the ability to produce structures with more complex geometries. This can be geometric features, such as thin-walled sections, that have to be included in such a way that only a limited number of subsequent process steps can be used. However, while the ability to tailor structures on a case-by-case basis is an advantage, the process does not currently lend itself to mass production or high throughputs because of the need to process each layer individually. Error or failure in the fabrication method can lead to catastrophic effects on the part and has led to reliability concerns in commercial applications. Further tendencies towards personalized medicine have lent themselves towards technologies of this nature where anatomy is best mimicked. For all these reasons, AM is becoming a focus for many researchers concentrated on simulated scaffold production. (Liu et al.2021)(Korium et al.2021)(Armstrong et al., 2022)(Alhashmi Alamer & Beyari, 2022)(Song et al., 2024)(Secor et al.2022)(Arjunan et al.2020)(Petrossian et al.2023)

## 4. Characterization Methods for Metallic Scaffolds

Scaffolds for tissue engineering require different characterization methods to evaluate. The methods fall into different categories for characterizing mechanical, structural, or biological properties since those facets define the utility and integration of a scaffold. The production of a scaffold defines the material and technique used, creating different structures and properties. Proper characterization techniques should target each property and match the appropriate aspect to the corresponding scaffold. Methods of characterizing different aspects of a metallic scaffold include porosity testing, surface topology assessment, microstructure analysis, and mechanical testing. (Lv et al.2021)(Suamte et al., 2023)(Zerankeshi et al., 2022)(Lutzweiler et al., 2020)(Zhang et al., 2020)

Porosity testing works to verify the amount, distribution, and function of open and closed porosity constructs. Surface topology characterizes the roughness and surface area to provide an impression of cell attachment. Microstructure analysis uses imaging for a visual assessment of the pore shape and distribution. The technique used for both surface characterization and microstructure is scanning electron microscopy. X-ray diffraction, contact and non-contact profilometers, and micro-CT are techniques used for porosity testing. Scaffold mechanical testing evaluates the mechanical properties like strength, resilience, and mass density. The tests include compressive, tensile, and fatigue tests, as well as bulk compressive modulus measures. A combination of these techniques and testing provides an ideal image to bridge the gap between qualitative porosity assessment and in vivo performance. Quality assurance relies heavily on the absorption rate determination. Mechanical characterization techniques provide valuable input data and offer several keys to successful design optimization. Their processes adapt scaffold performance to manufacturing techniques and material selections. In turn, enhanced scaffold engineering and performance lead to improved clinical efficacy, deterrence from failure, and, as a result, patient satisfaction. (Fu et al., 2021)(Wang et al.2021)(Wang et al.2021)(Huo et al.2020)(He et al.2020)(Xiang et al.2021)(Feng et al.2022)

### *4.1. Microstructural Analysis*

Microstructural analysis is of central importance in the study of metallic scaffolds and metallic materials in general. This is because microstructure ultimately defines a material's properties, including mechanical response, and knowing what the microstructure is and how to control it is critical in making biomaterials for medical devices. Some of the techniques specifically used to aid in understanding microstructural features that are important to scaffold performance include optical microscopy, including confocal and laser scanning microscopy, and electron-based microscopy methods, such as scanning electron microscopy or transmission electron microscopy. Investigations have often focused on the appearance of microstructural features, including grain size, phase, and grain boundary formation, either with respect to processing or in terms of subsequent heat treatment and the influence of test conditions.

Microstructural features such as grain orientation, phase distribution, and presence of oxide will all work to determine how a material behaves, and understanding what an appropriate microstructure should be is necessary for engineered design. For example, if the role of struts in a BMS is to buckle under the stress they experience, leading to a redistribution of force, the part of the microstructure that is of interest may be the structural consistency of the strut shape or porosity, or the local effect of surface conditions like roughness. There is the opportunity to build understanding and a database of material behavior under different conditions that can again lead to other models and nowcasting tools. Hence, by investigating what the microstructural influences are, it is possible that some relationships could be gathered to help point the way to better-designed materials and therefore better patient outcomes. (Mills et al., 2020)(Pipintakos et al., 2024)(Xing et al., 2022)(Wu et al.2023)(Lamelas et al.2024)

Within the human pool of talent that have not let themselves be set back by the magnitude of cellular complexity, there is a growing understanding of the role that some of the microscopically localized mechanical property and implant surface characteristics can give rise to different biological responses to function. By acknowledging that materials are part of mechanobiology, there is value in the continued emphasis required to achieve repeatable microstructural control. This is mostly critical in areas like scaffold design for tissue and bone engineering. For example, having control over the grain distributions or bond formation is highly valuable in a loosely defined material area, much like being able to design a sports facility for more than one sport with the same basic structure. (Pecci et al.2020)(Kanwar et al., 2022)(Collins et al.2021)(Aslam et al.2024)

## 5. Applications in Radiology

Radiologic imaging is the least devastating way of revealing the tested structures' defects. The test-redefined operations, e.g., opening the skull or other cavities, can then be done after obtaining a precise diagnosis. Using imaging to guide surgical operations has allowed minimally invasive procedures. In some cases, metallic scaffolds are crucial for imaging. They can be used as a medium to obtain the image while providing drastic differences in impedance or other relevant parameters for beams propagating through the human body. They work as perforated tweezers, which help to see and follow the very tip of the whole end on the level that has been separated from the others. (Burnstine-Townley et al.2020)(Veletic et al.2022)(Lu et al.2023)(Prosolov et al.2024)(Song et al.2024)

As medical images become the basis for the construction of subsequent models, e.g., 3D or radiosurgery planning, faster improvement and elimination of errors in medical imaging technologies are needed. It is of great importance since, for many branches of science and practice, one of the most valuable data sources is the data obtained as a result of imaging. In the field of medical imaging, they often contain more explicit information compared to the data collected from the patient in any other way. Perhaps it will be possible in the near future, based on the results of many years of progress in clinical image analysis combined with other databases, to create tools for medical procedures tailored to each patient individually and thus most efficiently and effectively influence the patient during an operation, both peri-operatively and after surgical treatment. (Wang et al., 2021)(Xie et al., 2021)(Bhattacharya et al.2021)(Suganyadevi et al.2022)(Sarvamangala & Kulkarni, 2022)

### *5.1. Imaging Techniques for Evaluation*

The researcher who develops metallic-based tissue and bone engineering scaffolds in the laboratory should consider future applications by personnel who operate within the clinical environment. Specifically, radiology professionals, medical dosimetrists, CT or MRI technologists, or any other group of individuals involved in patient contact need to work in conjunction with the operation of the imaging tools to facilitate accurate tracking of scaffold performance or integration within the implanted site. The images yielded through these different imaging techniques may be shared with the potential patient to display the potential success or failure of the implant. Finally, the research scientist should refer to literature that incorporates these imaging techniques for metallic scaffolds as a control reference. (Olăreț et al., 2021)(Patil et al.2024)(Kalidindi, 2024)(Kacprzak et al., 2023)(Xu et al.2024)(Reddy and Pranav2024)(Hu et al.2022)

Imaging is critical in the assessment of metallic scaffold placement accuracy, healing of associated tissue, or implant integration with surrounding bone. It allows for the assessment of gross scaffold features and porosity. The limitations of metallic scaffolds when evaluating them in a clinical setting are the artifacts created in a patient from image findings. The patient may create the artifact from body movements during imaging, or the high imaging capabilities of the scaffold may prohibit accurate visualization of surrounding tissue. Still, the information obtained from imaging can be superior and more informative when compared to traditional clinical examination. Improvements in imaging have been presented in the evolution of techniques from planar radiographs, ultrasound, to magnetic resonance imaging, and computed tomography scanning; all modalities are currently available to be used clinically. The resolution of the imaging obtained from each of these techniques is directly proportional to the in-depth information that can be detected from image capture within the patient. Patient imaging, which is typically completed for the assessment of metallic-based bone repair at an orthopedic clinic, is reviewed to illustrate the modality used and assessed limitations to plan for patient care and possible alterations in the surgical strategy. Referring to human imaging applications indicates to the reader the imaging techniques and desired resolution of patient images used to determine metallic scaffold integration and repair of a bone defect. Osteotomy models facilitate greater resolution when applied to imaging techniques, and assessment was made based on imaging modalities and parameter choices that are useful as a standard for animal models. Physician assessment is published in tables and figures showcasing the potential of certain imaging capabilities. It is recognized that a more personalized approach to imaging scaffolds could be achieved based on the relative resolution capability of the scanning and the radiopaque content of a metallic scaffold. (Pawelec et al.2021)(Meng et al.2023)(Laubach et al.2023)(Zhou et al., 2023)(Farazin and Mahjoubi2024)(Carluccio et al.2020)(Pallares et al.2022)

## 6. Applications in Pharmacy

Metallic scaffolds should also play a very important role in drug release systems. They can be manufactured as drug-eluting stents in angioplasty or special local drug delivery systems. Better tolerability, reduced systemic toxicity, drug-dose sparing, and minimizing drug side effects are some of the numerous advantages of using a drug delivery system. Local formulations can offer effective treatment for bone diseases. The prolonged residence of the therapeutic substance at the target organ may improve the effectiveness of the drug. Moreover, the incorporation of a bone tissue engineering approach in prosthetic implant design would be of great economic importance for industries. (Wang et al.2021)(Wang et al.2021)(Li et al.2022)(Aggarwal et al., 2022)(Bharathi et al.2022)(Ranakoti et al.2023)(Syed et al.2023)

In scaffolds, the drug release characteristics must be properly adjusted: zero-order delivery to provide very slow and uniform release of the drug over a long time period; pulsatile delivery to provide a repeated sequence of bursts of a drug; and potentially multi-sequential delivery to deliver two or more agents in a controlled manner. Other important considerations for developing more stable and effective drugs are discussed as improvements and advances. Case studies on existing local delivery systems for prosthetic bone implants show that such systems reaching the clinical study phase may sometimes be very far from true effectiveness. The translation of research development into clinical practice represents a challenge in terms of setting objectives in advance and developing a long-term strategy. A side product of the introduction of scaffolds in the pharmacy might be to create a new area of pharmacy based on scaffold design, and after testing, directly highlight potential vulnerabilities that can be recognized in various areas of bulk drug storage. Also, the two-way flow of information would support further drug design and regulatory processes. (Kunrath et al., 2023)(Berg & Frossard, 2021)(Nasr et al.2022)(Barik & Chakravorty, 2020)(Meng et al., 2022)(Ma et al.2021)

### *6.1. Drug Delivery Systems*

6. Discussion 6.1. Drug Delivery Systems Scaffold technology can also integrate as part of a system for drug delivery. Such systems can release the co-administered drug, modify the release of the drug on the scaffold surface, and modify the release of the drug from the scaffold bulk. Drugs may also stimulate responses from the implanted scaffold, such as the recruitment of cells to the scaffold. It is possible to release protein growth factors by a diffusion-controlled or erosion-mediated process so that the recruited cells can be stimulated to differentiate into the desired cell type by the progress of the protective effect of revascularization on the scaffold. Slowly absorbed polymeric units in scaffolds provide the opportunity to act as a source of drug delivery, thereby increasing efficacy. Questions that need to be considered in the design of such systems are the release profile desired, the kinetics and mechanism of the drug's release from the materials, the desired site of release, and the influence of the scaffold properties and type of interaction with the drug-loaded scaffold. Various scaffolds, like candidates, metals, and polymers, are adjustable by modifying degradation rates, mechanical properties, etc. Scaffolds signify a relatively new area of therapeutic intervention with the prospective benefits of localized rather than systemic effects, incorporating co-delivery of a rational number of drugs and a change of combination delivery over time. Scaffold technology is unique in design, offering a feasible solution to several biological problems and could be considered an integral part of the next generation of drug therapy. Given the recent advancements in nano-scaffold delivery systems, the local delivery of anti-inflammatory agents might result in safer, more effective pain reduction and cartilage repair in early osteoarthritis. In parallel, the assessment of anti-cancer drug-eluting orthopedic implants has shown to be positive in locally relevant outcomes. Local therapy offers a potential foothold toward improved clinical management of musculoskeletal malignancy by optimizing surgical outcomes, preventing micrometastases, and reducing the burden of distant treatment relegates such as cytotoxic chemotherapy. Thus, the lessons learned could be used as an out-of-the-box application in the quest to slow the progress of osteoarthritis. In one case study, a porous titanium scaffold containing beta-TCP was designed and manufactured via electron beam melted laser sintering. These biomaterials could offer a platform for growth stimulatory therapeutics as a combination strategy for traumatic injury and resultant cartilage damage. Handling issues related to devices that are not sterile are more complex than single-drug systems, which have been commercial for over 20 years. Initial results from pre-clinical efforts do show relevance and safety of this option, relatively speaking. However, challenges relating to device material biocompatibility, long-term controlled release, and regulatory status will need to be addressed. It also remains uncertain the potential for additive or interactive impact of a biological therapy. Successful commercial translation will require cooperative conversations between the sponsors across Clinical Development, Regulatory, and Surgical Devices centers to express the hurdles for future trial and evaluation of finalized products. While clinical trials with bone scaffold devices have shown success, no clinical trials have been run and reported to date with delivered therapeutics. There has been limited commercial interest in this proposition. As such, no clinical system has been given at this point in time. (Bharathi et al.2022)(Chauhan et al., 2023)(Collins et al.2021)(Li et al.2022)(Pavan Kalyan & Kumar, 2022)(Castillo-Henríquez et al.2021)(Osouli-Bostanabad et al.2022)

## 7. Applications in Nursing

Available evidence related to applications of metallic scaffolds is very poor and insufficient; only a few papers focus on topics relevant to nurses. In comparison with other studies comprising a medical background, nurses make a positive remark about metallic scaffolds as a material that promotes fast and proper tissue ingrowth, allowing the implant to heal properly and the patient to recover from the surgical procedure more effectively. A very limited number of studies have considered the potential application of bioresorbable metallic scaffolds in point-of-care surgery, where multidisciplinary specialists, nurses, and people working in the field of engineering would be actively involved. Most metal scaffolds are used in thoracic, orthopedic, anaplastic, and oncological surgeries, with the main focus on contact tissues. The most significant applications of biodegradable metallic scaffolds in clinical practice are, in particular, in radiology, physiotherapy, and professional assistants dealing with the diagnosis, treatment, and monitoring of patients' health—nurses and paramedics. (Chin, 2022)(Kiselevskiy et al., 2023)(Kazimierczak et al.2023)(Elgharbawy et al., 2024)(Gašparovič et al.2024)(Hassan et al.2024)(Astaneh & Fereydouni, 2024)

Nurses, in collaboration with doctors, particularly a multidisciplinary surgeon with knowledge in tissue engineering and regeneration with bioresorbable metallic scaffolds, could function as leading experts in intra-hospital and extra-hospital nursing practice. Nurses in both clinical and scientific work apply the theory of cell biology, tissue biology, physics, materials engineering, and chemistry in practice. From a clinical perspective, the nurse—in cooperation with a medical engineer—could also recommend prophylactic implantation in athletes, thereby making an important step, with the aim of proving that nursing, as well as tissue engineering related to medicine, contributes to the overall health of the individual. Generally, the intervention of metallic scaffolds is not recommended because the population needs education and training. There is an important issue concerning patient management and examination, leading from the "What to Know and What to Ask Before Intervention" if considering implanting bioresorbable devices. Overall, this nursing practice using absorbable metallic constructs can be translated and propagated using case studies in order to improve patient outcomes. (Carbone et al.2022)(Tolfo et al.2021)(Jesus & Balsanelli, 2023)(Serafini et al., 2024)(Lahmer et al.2021)(Aparecido et al.2024)(Bouchlarhem et al.2023)

### *7.1. Patient Care and Rehabilitation*

Replacing the inpatient stay after an injury and replacing the bone with faster and painless procedures will significantly contribute to enhancing the quality of life, patient mobility, and functional recovery times. The alignment of the use of metallic scaffolds in the care process of patients with the model of good nursing practice will result in the improvement of rehabilitation programs. Scaffolds used in the support field are seen as a source of pain relief; the action of the graft is visible immediately, comfortable, and pleasant for the patient. The function of nursing should become the real image of the possibilities offered by modern surgery in nursing actions. The optimum compromise between patient comfort and safety, and the performance of nursing care before and after a surgical operation should be made to provide patients with the best perspective of gait rehabilitation programs. Integrating into the patient care support system consists of personally informing the patient pre-surgery, during hospitalization, and in post-operative rehabilitation. In the comprehensive care process, the patient should be informed during ongoing care and support with the integrated adjacent fields in the medical field, a nursing process initiated and perfected based on integrated therapeutic education, quality of life guaranteed, and patient safety. The nurse must engage in continuous care and support through an educational program and provide responses tailored to the needs of each patient: patient integration and acceptance of the gain of support; the family is familiar with the process of supporting the patient. The clinic has successfully carried out the support programs after the metallic assistance for a long time, and the care programs include several complete recovery stories presented in the patient's book of recoveries. Many developments have the prospect of being accessible to a larger percentage of our population in the rehabilitation process, leading to a major revolution in the field of medical imaging, assisted tissue reconstruction with various grafts, and medication response programs, all based on metallic scaffolds. The people we address are those who have knowledge of the support and transfer to the established programs, and the benefits are tangible after the way the story of the recovery program is presented. (Van et al.2023)(Laubach et al.2023)(Wang et al.2021)(Haude et al.2023)

## 8. Applications in Emergency Services

In emergency services, metallic scaffolds have different but no less importance. The application of them in trauma or other more chronic situations can deliver an immediate and effective intervention, which is crucial in these areas. Metallic scaffolds play a unique role in helping to stabilize and heal not only hard but also soft tissues. The advantage of using scaffold technology in traumatology is a very quick way of delivering it directly to the place of injury or disease and facilitating re-interference by each person. The clinical application of bone tissue engineering relies on close cooperation between interdisciplinary teams, including engineers, paramedics, and other laboratory scientists. Engineering problems closely follow the medical application, resulting in options for rapid production of the metal scaffold and the design adaptations that are necessary for broad clinical application of preferred treatment for skeletal injuries and other skeletal deformities that can be treated by regenerative means. (Marin, 2023)(Collins et al.2021)(Hassan et al., 2023)(Gao et al., 2022)(Golchin et al.2021)

The use of metallic implants for the fixation of bone fractures is a common procedure in emergency care settings. Bone tissue is known to repair and regenerate, and during this repair process, it deteriorates in quality and weakens by over 50% compared to undamaged bone. The stress shielding, in turn, leads to long-term deterioration that can and often does result in secondary fractures and other orthopedic problems. The geometric design of the scaffolds can be applied to avoid negative stress shielding and eventually determine better scaffold integration with host bone. New metallic scaffolds for implantation during accident surgery could be crucial in stabilizing the biomechanically compromised injury site more adequately, thereby reducing the patient's time to ambulate with full loading as tolerated. The development of this technology is in its infancy due to the increasingly complex problems related to rapidly designing and customizing very specific and individual clinical fixes with rapid manufacturing techniques and scaling. Honeycombs have been used extensively and successfully for other applications ranging from reducing the weight of industrial construction, automobiles, electronic components, and improving crashworthiness. Honeycombs' rapid engineering readiness makes them attractive for a range of research and applications for injuries, especially in the construction of metal scaffolds with tailored design. (Li et al.2020)(Barber et al.2021)(Kim et al., 2020)(Meng et al.2023)(Yang et al.2021)

### *8.1. Trauma Management*

Metallic scaffolds may be of use in trauma patients who are treated either in the community, in the hospital setting, or to aid recovery following emergency surgery. They can be immediately recovered from bodily fluids at the trauma scene or during intervention and provided to the patient alongside other pharmaceutical, radiological, nursing, or emergency medicine management strategies. The immediate use of scaffolds not only aids the patient's recovery but ensures minimum loss of bone tissue following trauma and facilitates a return to pre-operative function. (Yang et al., 2022)(Kim et al., 2020)(Marin, 2023)(Ferrigno et al.2020)(Mneimneh & Mehanna, 2021)

It has been shown that the insertion of load-bearing devices as quickly as possible after trauma can improve outcomes for the patient. Of greatest pertinence for patients is the time from injury to surgical fixation of the knees, as reduction of this time has been clearly linked to a reduced risk of adult respiratory distress syndrome, and with shorter Intensive Care Unit and hospital stays following trauma. These time scales can be improved using drills rather than guides, which need to be used in trauma to rapidly assess internal structures. Following the application of a drill, a cylindrical scaffold would be added and penetrated, further stabilizing the bone. Scaffolds can be designed to include joints for rotation or areas of lattice to allow vascular or epithelial tissues to form. One of the greatest challenges facing this biomaterial tissue interface will be ensuring biocompatibility before final functional ability can be verified in a clinical trial setting.

Successful application of scaffolds in trauma has been reported in two unique case studies where the patients have shown no signs of infection. For example, if we placed a few hundred grams of bone through the tibial plateau, the bone would fail in its function. Such a force is an enormous force imposed by today's active patients. (Negut et al., 2020)(Halim et al.2021)(Laubach et al.2023)(Jiang et al.2020)(Laubach et al.2022)(Zurina et al.2020)(Mirhaj et al.2022)

## 9. Applications in Laboratory Sciences

Laboratory science applications have been contemplated and have had scaffold arrays included in the wide range of prior art investigations for the past 30 years. Metallic tissue scaffolds have seen an increase in use regarding the fields of orthodontics, orthopedic surgery, plastic surgery, maxillofacial surgery, dental surgery, and sports medicine. Unfortunately, the majority of tissue scaffold metallic devices are used as in vivo prostheses, and images obtained with them are primarily for diagnostic criteria. However, it is generally agreed upon that scaffolds are needed in these areas for the large animal and human in vitro testing presently imposed by testing and regulatory agencies. (Al et al.2023)(Thanigaivel et al.2022)(Al-Shalawi et al.2023)(Bandyopadhyay et al.2023)

Scaffolds have the capability of providing dynamic culturing of cells, and specific analyzers, just as most test gases are monitored continuously in modern in vitro exposure systems. Scaffolds assist in providing elements similar to functional tissues where a majority of in vitro techniques make measurements. The graduated attachment of a cell can be continually observed when a scaffold is placed on a microbalance. Experimental studies are usually comparisons to conventional cultures in petri dishes or other containers. The majority are looking at long-term cultures and the effects when two cell types are placed in close proximity. Consistent results based on scaffold studies are usually obtained after some physical modifications have been completed. To receive physical data, it would be beneficial if one could change cell culture systems at least once. The need for an interdisciplinary approach is emphasized as most aggressive biotechnology in vitro applications using tissue scaffolds have been with 2-D instead of 3-D measurements in attempting to evaluate exposure data. Ratios greater than 1 do give a false sense of security unless similar or equivalent tissue equivalents are used. (Collins et al.2021)(Suamte et al., 2023)(Lutzweiler et al., 2020)(Zhang et al., 2022)(Zhang & King, 2020)(Lett et al.2021)(Valdoz et al.2021)

### *9.1. In Vitro Testing and Analysis*

Metallic scaffolds as tissue or bone engineering constructs introduce tissue-like properties that can be analyzed in in vitro studies but are still rare in the literature. The classic first step to test the performance of a biomaterial or a scaffold is the analysis of in vitro assays either in the form of morphology or quantification applying live/dead or calcein/ethidium assays. Furthermore, the scaffold’s capacity to influence and guide cellular growth in accordance with its function of volume-filling must be investigated. Here, cell culture assays to assess the proliferation and viability of the host membrane environment or the migratory response are typically applied for various cells, including osteoblasts, fibroblasts, mesenchymal stromal cells, and osteoclasts/osteoblasts. Common parameters generally relate to protein analysis, such as DNA or total protein content. Importantly, the cytotoxicity of the matrix of choice must be proven.

However, the performance of potential matrix-mimicking materials should also be proven by functional analyses. Here, the mineralization per detail area owing to osteoblast-specific cells in response to direct contact or to cohesive has been successfully applied in recent years. This circumstance results in a 'tissue-engineered construct' that is reminiscent of a lesion-like area of the so-called gold standard. In conjunction with this, characterizing staining techniques to quantify the hard and soft tissue development seem to be more and more available. It would benefit future in vitro testing methodologies for healthcare or drug-oriented medical sciences to provide all possibly quantifiable metrics information about the new construct to develop a highly optimized test system. Hereafter, these improvements in alveolar cleft repair methodologies are fixed patient scenarios that are worth commercial patenting. This strategy would correlate the in vitro outcomes with the realistic implantation-related usefulness of the grids in the operating room. However, this study will also face several limitations with respect to making it difficult to compare the in vivo effects of the grid with cases where the operation is carried out without bone substitutes. Of course, weaker in vitro methods can be replaced by stronger in vivo tests. In vitro and standardized, reproducible cases can be treated with passage studies that are otherwise very different from each other. Indeed, imperceptible and very small changes need to be developed. Changes before and after chemical and physical processes in the laboratory can be examined in standardized ways. Usually, changing a complete type of implant could be examined. Permanent implants can be changed in an hour. Scaffolds are designed to be parallel to the flat bottom end of the well, plate, or scaffold holder, allowing the vacuum formers of the incubator’s gas exchange system to operate bulk bioreactors.

## 10. Challenges and Future Directions

The lack of biological integrity, test tracking, and standard normalization to allow comparability between studies has resulted in a scattered application of these scaffolds in the fields of diagnostics, radiology, pharmaceuticals, veterinary field, nursing, emergency services, and most predominantly the laboratory sciences. Barriers to integration in these fields include but are not limited to (1) metallic materials are typically not inherently biocompatible due to the foreign-body reaction, (2) scalability to standard manufacturing is required for actual regulatory compliance and allows sufficient dimensions for directly simulating a large animal model or human clinical condition, (3) stability under environmental conditions is required for acceptance of metal implants in the biomedical field due to regulatory requirements on standardized test environments and a vacuum level scanning electron microscopy chamber, (4) non-destructive time-lapsed patient/device analysis is required for translation to the medical diagnostics field in order to integrate into radiology, particularly for in situ radiological dose monitoring as it can be coupled to biomaterial degradation.

To promote future scientific innovation and development in the field of metallic bioabsorbable scaffolds, which are some 20 years behind the now widespread application of metallic fixed-body devices, specific directions for significant research areas were proposed. Despite the extensive application of this clinical technology, some potential translational barriers exist, which will especially challenge the successful translation of purely resorbable tissue-engineering substitute devices. These barriers are artifact-induced frustration and governmental funding restrictions in their use—favoring minimally invasive and explant-free funding relief for patent-holding device developers. Additional funding will be required for the case process development of potential entire body and organ replacement through the test pathway to market. Social and ethical considerations must also be made for a possible increase in the ceramic-coating technology of devices, possibly leading to the treatment and survival of older patients more quickly. Considerations in future research funds should extend to interdisciplinary research with trained ethicists addressing these concerns. Ethicists and the social sciences need to be included in these efforts.

### *10.1. Regulatory and Safety Considerations*

The pathways of regulatory clearance or approval for medical device components and biologics, such as scaffolds, are well delineated. The documentation on these regulatory pathways clearly indicates that clinical trials are important to develop evidence regarding patient safety and the performance of the medical device othese devices' uses and performance evaluationsr biologic. It is important to determine whether existing regulatory clearances for the metal scaffolds application are sufficient to cover the uses and performance evaluations of these devices. Indeed, the initial selection of a scaffold material must consider these regulatory aspects because a plethora of materials and material forms exist. Designing a scaffold for a specific clinical treatment is followed by producing a representative amount of the material and cleaning, packaging, labeling, and release onto the market. The important message at this stage is that the main goal of medical device development is to ensure good safety, efficiency, repeatability, and robustness for the end user, that is, the patient. A new regulatory path must be followed if the device is manufactured by a different process or company. The primary aim of any medical device or product is to ensure safety and set the degree of success in the patient population targeted; subsequently, mass production and market share are important. Risk analysis is an important tool, and hospitals can demand this information from manufacturers to best adapt the device for the hospital facilities, safety, and patient treatment.

Research projects are the main push for the development of new antimicrobial scaffold materials, including metal scaffolds. In essence, choosing the clinical aspects for development is the driving force prior to scaffold design. The Research Ethics Committee is an important part of the regulatory framework of each country, monitoring patient treatment in a hospital under a specific clinical study to ensure their safety and to demand adequate insurance for liability on any subsequent procedure or result. The main regulatory aspects are addressed; however, because ambient healthcare technology is constantly evolving, the procedures of medical ethics committees are beyond the scope of this review. In clinical practice, it is important to continuously monitor the performance of a scaffold and to ensure its regulatory clearance for use, or to monitor it continuously as part of the trial. If a substantial deviation from the initial proposal is detected, the effect on the patient may be reversed or at least minimized. Thus, close clinical follow-up in this practice is essential, even after approval of the material for clinical use.

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