IN BRIEF

Tissue Engineering Technologies in the Management of Bone Infections

E. Carlos Rodriguez-Merchan, MD, PhD; Alberto D. Delgado-Martínez, MD, PhD

Research performed at Department of Orthopedic Surgery, Hospital Universitario La Paz, Madrid, Spain

Received: 26 October2024 *Accepted: 31 December 2024*

Abstract

Osteomyelitis is a calamitous illness produced by microbial infection in deep osseous tissue. Its elevated recurrence percentage is a major defiance in management. Besides, microbial-mediated dysregulation of the osseous tissue immune microhabitat hinders the process of osseous regeneration, resulting in defective repair of the osseous defect. In spite of advancements in surgical approaches and medication employments for the management of infections of the osseous tissue within the most recent years, dares endure in clinical treatment. The creation and employment of tissue engineering materials have rendered new approaches for the management of infections of the osseous tissue. In the discipline of tissue engineering, we should center on utilizing materials science and engineering technology to create biomimetic 3D printed degradable frameworks with structure, layout, and mechanical attributes; accomplishing controlled liberation of antimicrobial medications via nanocarriers or scaffold surface coating technologies; and utilizing coaxial printing or gradient printing techniques to accomplish graded controlled liberation of antimicrobial medications and osteogenic active drugs.

Level of evidence: III

Keywords: Bone, Infection, Tissue engineering technologies, Treatment

Introduction

The objective of managing infections of the osseous tissue is to entirely remove the infection area, ensure coverage of the soft tissue, promote the consolidation of bone ends, and maintain the length and function of the affected extremity. After the full elimination of the infection area, osseous defects frequently happen, which are zones where infection is inclined to repeat. At present, there are various problems in the management of infections of the osseous tissue [Figure 1].[1] Current approaches for the treatment of infectious defects of the osseous tissue and for their repair are shown in [Figure 2].[2] Consequently there is a dire clinical necessity for a material that offers suitable antibacterial activity and facilitates the repair of osseous tissue.[3] The objective of this paper was to perform a review of the literature on the current status of tissue engineering technologies in the management of infections of the osseous tissue. To accomplish this objective, a search of the literature in PubMed was performed on September 18, 2024, using "bone infection engineering technologies 2023" and "bone infection engineering technologies 2024"as keywords. Of the 467 articles recognized (245 in 2023 and 222 in 2024), twenty specifically related to bone infection engineering technologies were chosen (inclusion criteria). The rest of papers did not fulfil this prerequisite (exclusion criterion) and were consequently excluded.

Main body

The dire challenge to be confronted is the election of a filling scaffold that mixes antimicrobial properties and osseous tissue-promoting capacities to avert secondary bone graft surgery and diminish the percentage of infection recurrence. The characteristics of an good restoration scaffold for infections of the osseous tissue are shown in [Figure 3].[4] Current existing materials for bone infection repair are displayed in [Figure 4].[5-8] The establishment methods of scaffolds for the repair of infection of the osseous tissue are shown in [Figure 5].[9-12] Composite scaffold systems for the repair of infections of the osseous tissue are displayed in [Figure 6].[13-16]

Corresponding Author: E. Carlos Rodriguez-Merchan, Department of Orthopedic Surgery, Hospital Universitario La Paz, Madrid, Spain

Email: hassaninalkaduhimi@gmail.com

THE ONLINE VERSION OF THIS ARTICLE ABJS.MUMS.AC.IR

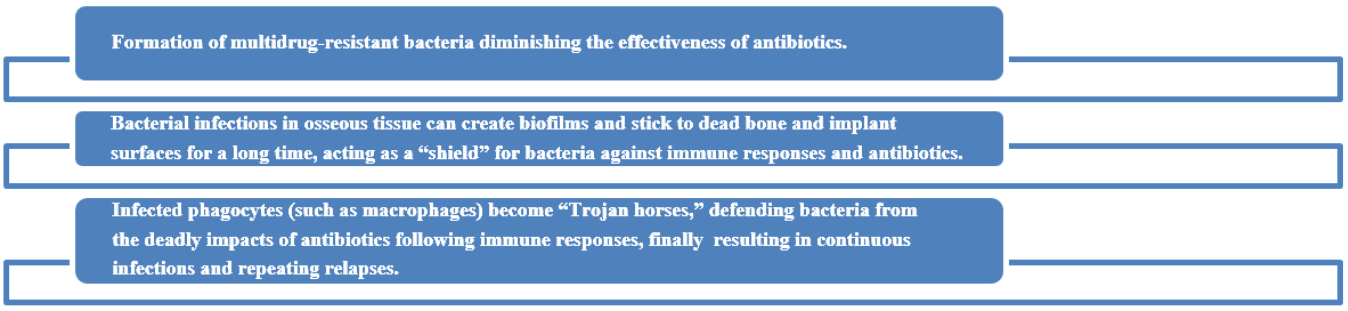

Figure 1. Main current problems in the treatment of bone infections

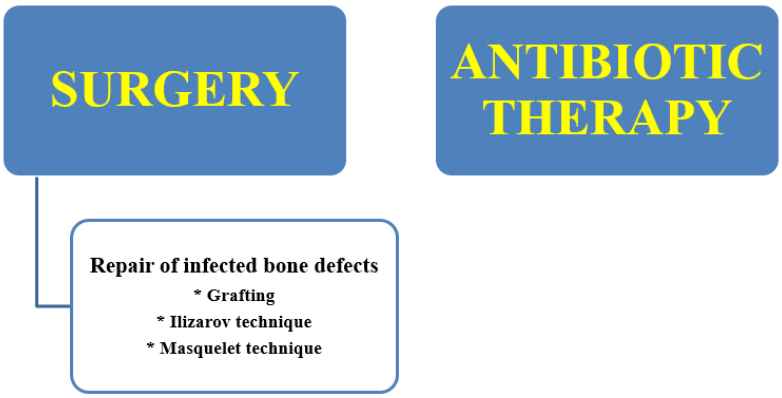

Figure 2. Main current clinical treatments for infectious bone defects and their repair

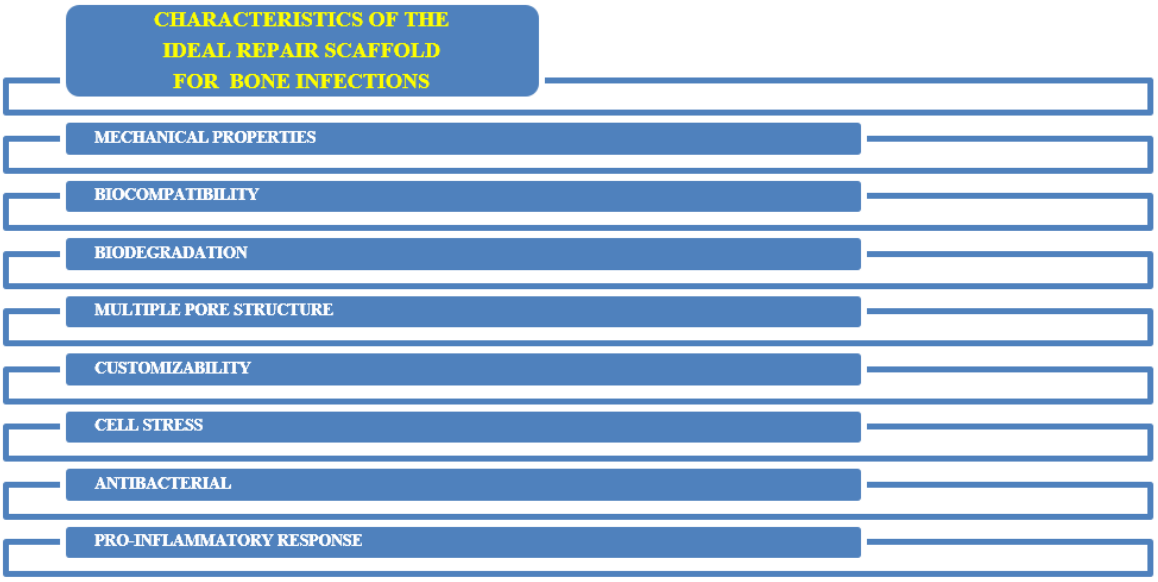

Figure 3. Characteristics of an ideal repair scaffold for bone infections

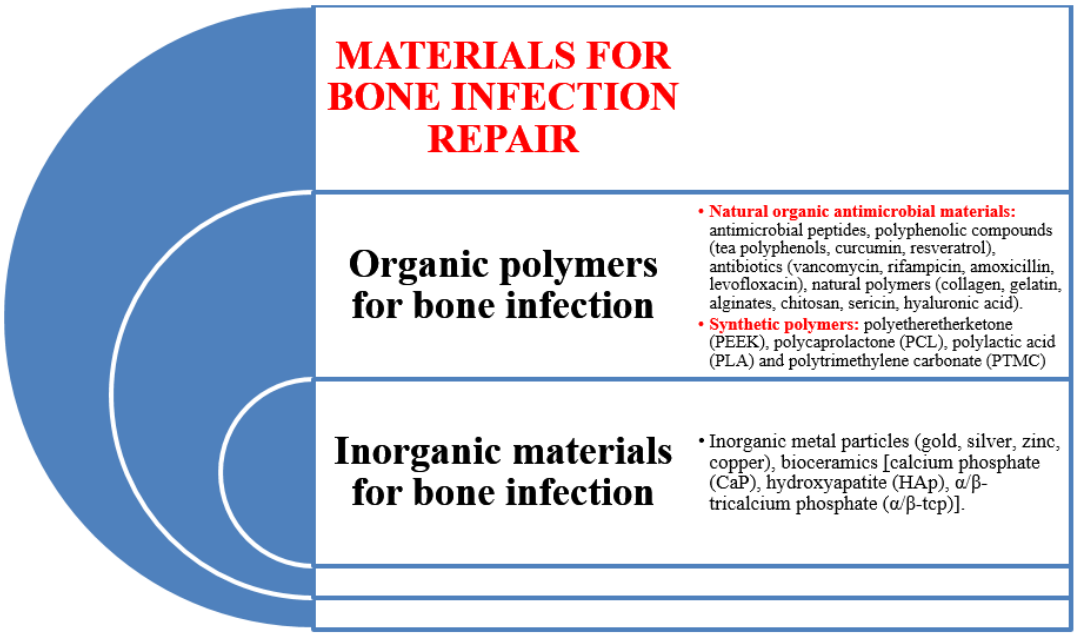

Figure 4. Current existing materials for bone infection repair

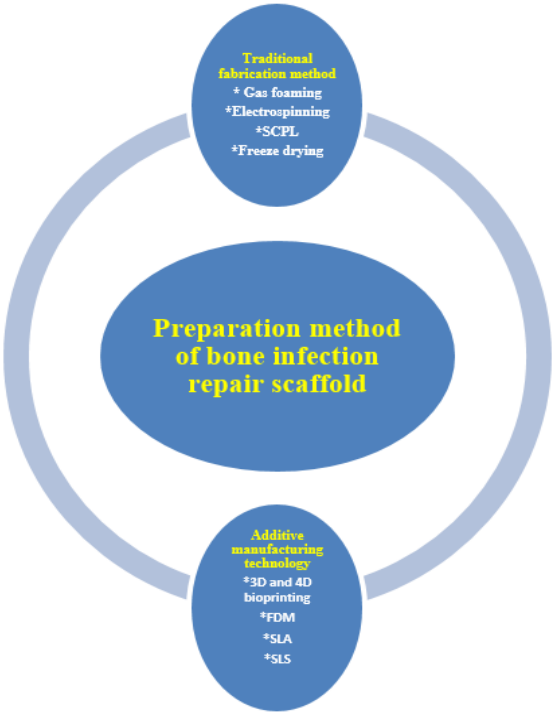

Figure 5. Preparation methods of bone infection repair scaffold. SCPL = Solvent casting/particle leaching; 3D = Three-dimensional; 4D = four-dimensional; FDM = Fused deposition modeling; SLA = Stereo lithography appearance; SLS = Selective laser sintering

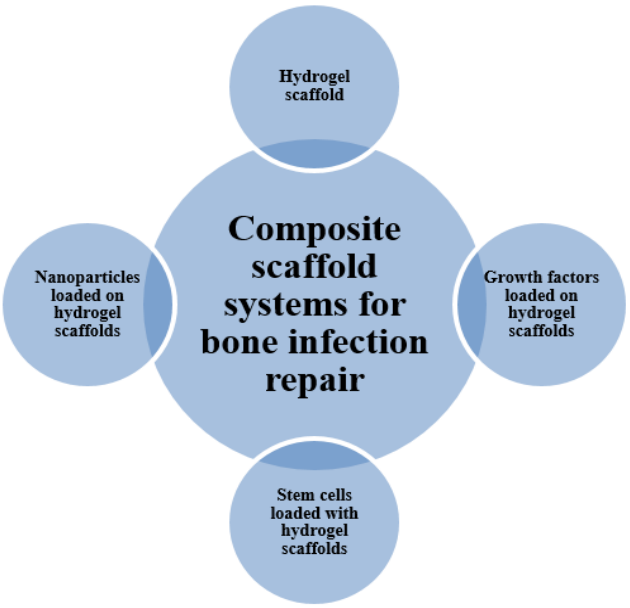

Figure 6. Composite scaffold systems for bone infection repair

The most usual technique for tissue engineering and culturing stem cells is using 3D scaffolds. Under adequate circumstances, cells multiply, differentiate, and liberate extracellular matrix (ECM) molecules, led by the three-dimensional space of the scaffold. This method yields an ideal therapeutic approach for tissue repair.[17] Solid bone tissue substitutes are shown in [Figure 7].[18,19]

The usage of polymeric biomaterials, either as pre-made solid scaffolds or injectable glues that can toughen *in situ*, has shown interesting results as a substitute for frequently utilized autografts and allografts.[19]

According to Ghassemi et al people working together is paramount for the success of any process of tissue regeneration.[20]

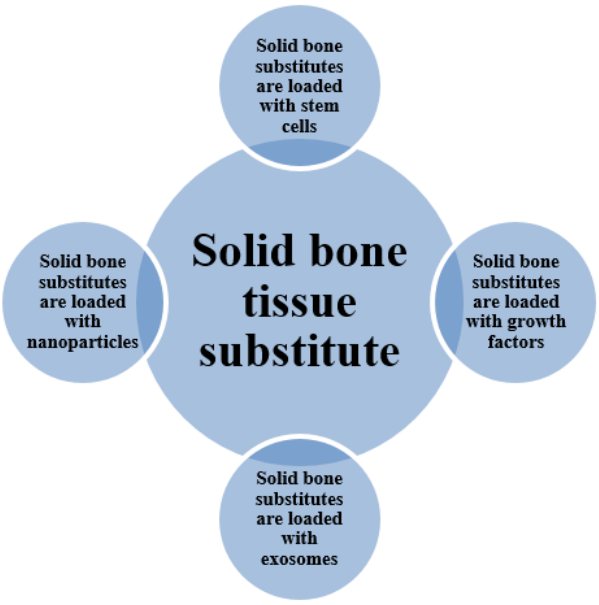

Figure 7. Solid bone tissue substitutes

Conclusion

In the management of osteomyelitis, the elimination of pathogenic bacteria is the principal factor to be considered. Even though numerous improvements in antimicrobial approaches for antibiotics in the last 50 years have been made, there has been no qualitative jump in the creation and employment of antibiotics, and the current clinical treatments have not essentially varied. In the discipline of tissue engineering, we should use materials science and engineering technology to create biomimetic 3D printed degradable scaffolds; accomplish controlled liberation of antimicrobial medications; and utilize coaxial printing or gradient printing techniques to accomplish graded controlled liberation of antimicrobial medications and osteogenic active drugs.

Acknowledgement

N/A

Authors Contribution: Authors who conceived and designed the analysis: ECR-M and ADD-M/ Authors who collected the data: ECR-M and ADD-M/Authors who contributed data or analysis tools: ECR-M and ADD-M/Authors who performed the analysis: ECR-M and ADD-M/Authors who wrote the paper: ECR-M and ADD-M/Other contribution: ECR-M and ADD-M

Declaration of Conflict of Interest: The authors do NOT have any potential conflicts of interest for this manuscript.

Declaration of Funding: The authors received NO financial support for the preparation, research, authorship, and publication of this manuscript.

Declaration of Ethical Approval for Study: Our institutions do not require ethical approval for reporting "In Brief" review articles.

Declaration of Informed Consent: The authors declare that there is no information (names, initials, hospital identification numbers, or photographs) in the submitted manuscript that can be used to identify patients.

E. Carlos Rodriguez-Merchan MD, PhD [1]
Alberto D. Delgado-Martínez MD, PhD [2]

1 Department of Orthopedic Surgery, Hospital Universitario La Paz, Madrid, Spain

2 Department of Orthopedic Surgery, Hospital Universitario de Jaén, Jaén, Spain

References

1. Masters EA, Trombetta RP, de Mesy Bentley KL, et al. Evolving concepts in bone infection: redefining "biofilm", "acute vs. chronic osteomyelitis", "the immune proteome" and "local antibiotic therapy". Bone Res. 2019; 7:20. doi: 10.1038/s41413-019-0061-z.
2. Masters EA, Ricciardi BF, Bentley KL, Moriarty TF, Schwarz EM, Muthukrishnan G. Skeletal infections: microbial pathogenesis, immunity and clinical management. Nat Rev Microbiol. 2022; 20(7):385-400. doi: 10.1038/s41579-022-00686-0.
3. Qin L, Yang S, Zhao C, et al. Prospects and challenges for the application of tissue engineering technologies in the treatment of bone infections. Bone Res. 2024; 12(1):28. doi: 10.1038/s41413-024-00332-w.
4. Zhou Z, Feng W, Moghadas BK, et al. Review of recent advances in bone scaffold fabrication methods for tissue engineering for treating bone diseases and sport injuries. Tissue Cell. 2024; 88:102390. doi: 10.1016/j.tice.2024.102390.
5. Zhou H, Zhu Y, Yang B, et al. Stimuli-responsive peptide hydrogels for biomedical applications. J Mater Chem B. 2024; 12(7):1748-1774. doi: 10.1039/d3tb02610h.
6. Zegre M, Barros J, Ribeiro IAC, et al. Poly (DL-lactic acid) scaffolds as a bone targeting platform for the co-delivery of antimicrobial agents against S. aureus-C.albicans mixed biofilms. Int J Pharm. 2022; 622:121832. doi: 10.1016/j.ijpharm.2022.121832.
7. Xue X, Hu Y, Wang S, Chen X, Jiang Y, Su J. Fabrication of physical and chemical crosslinked hydrogels for bone tissue engineering. Bioact. Mater. 2022; 12:327-339. doi: 10.1016/j.bioactmat.2021.10.029.
8. Zhan S, Guo AXY, Cao SC, Liu N. 3D printing soft matters and applications: a review. Int J Mol Sci. 2022; 23(7):3790. doi: 10.3390/ijms23073790.
9. Grenier J, Duval H, Lv P, et al. Interplay between crosslinking and ice nucleation controls the porous structure of freeze-dried hydrogel scaffolds. Biomater Adv. 2022; 139:212973. doi: 10.1016/j.bioadv.2022.212973.
10. Zhang X, He J, Qiao L, et al. 3D printed PCLA scaffold with nano-hydroxyapatite coating doped green tea EGCG promotes bone growth and inhibits multidrug-resistant bacteria colonization. Cell Prolif. 2022; 55(10):e13289. doi: 10.1111/cpr.13289.
11. Xulin H, Hu L, Liang Q, et al. 369 fabrication of 3D gel-printed β-tricalcium phosphate/titanium dioxide porous scaffolds for cancellous bone tissue engineering. Int J Bioprint. 2023; 9(2):673. doi: 10.18063/ijb.v9i2.673.
12. Mirasadi K, Rahmatabadi D, Ghasemi I, et al. 3D and 4D printing of PETG-ABS-Fe(3)O(4) nanocomposites with supreme remotely driven magneto-thermal shape-memory performance. Polymers (Basel). 2024; 16(10):1398. doi: 10.3390/polym16101398.
13. Rosenquist J, Folkesson M, Höglund L, Pupkaite J, Hilborn J, Samanta A. An injectable, shape-retaining collagen hydrogel crosslinked using thiol-maleimide click chemistry for sealing corneal perforations. ACS Appl Mater Interfaces.2023; 15(29):34407-34418. doi: 10.1021/acsami.3c03963.
14. Guo Y, Wang M, Liu Q, Liu G, Wang S, Li J. Recent advances in the medical applications of hemostatic materials. Theranostics. 2023; 13(1):161-196. doi: 10.7150/thno.79639.
15. Li Y, Liu Z, Zhao C, et al. A sustained-release PDGF-BB nanocomposite hydrogel for DM associated bone regeneration. J Mater Chem B. 2023; 11(5):974-984. doi: 10.1039/d2tb02037h.
16. Wassif RK, Elkheshen SA, Shamma RN, Amer MS, Elhelw R, El-Kayal M. Injectable systems of chitosan in situ forming composite gel incorporating linezolid-loaded biodegradable nanoparticles for long-term treatment of bone infections. Drug Deliv Transl Res. 2024; 14(1):80-102. doi: 10.1007/s13346-023-01384-x.
17. Liu X, Gaihre B, Park S, et al. 3D-printed scaffolds with 2D hetero-nanostructures and immunomodulatory cytokines provide pro-healing microenvironment for enhanced bone regeneration. Bioact Mater. 2023; 27:216-230. doi: 10.1016/j.bioactmat.2023.03.021.
18. Liu D, Liu J, Zhao P, et al. 3D bioprinted tissue-engineered bone with enhanced mechanical strength and bioactivities: accelerating bone defect repair through sequential immunomodulatory properties. Adv Healthc Mater. 2024:e2401919. doi: 10.1002/adhm.202401919.
19. Ghasemi F, Jahani A, Moradi A, Ebrahimzadeh MH, Jirofti N. Different modification methods of poly methyl methacrylate (PMMA) bone cement for Orthopedic Surgery applications. Arch Bone Jt Surg. 2023; 11(8):485-492. doi: 10.22038/ABJS.2023.71289.3330.
20. Ghassemi T, Ghoddusi J, Moradi A. Teaming up; a critical "must do" for clinically bone tissue engineering. Arch Bone Jt Surg. 2023; 11(6):376-377. doi: 10.22038/ABJS.2023.69762.3297.