Manufacturing approaches for hierarchical scaffolds for functional bone tissue regeneration

Mariana Ionita[1,2,3], Elena Alina CHITICARU[1,2], Alin Georgian TOADER [1,2],, Raluca DOBRISAN [1,2]

[1]Faculty of Medical Engineering, National University of Science and Technology Politehnica Bucharest, Bucharest, Romania
[2]Advanced Polymer Materials Group, National University of Science and Technology Politehnica Bucharest, Bucharest, Romania
[3]eBio-Hub ResearchCentre, National University of Science and Technology Politehnica Bucharest-Campus, Bucharest, Romania

Contact@mariana.ionita@upb.ro

The fabrication of scaffolds that replicate the anisotropic and hierarchical lamellar organization of native bone, together with its extracellular matrix, remains one of the central challenges in bone tissue engineering [1]. Achieving a precise biomimetic architecture that reproduces both the structural and functional complexity of bone is essential for successful integration and regeneration. In this context, advanced manufacturing technologies such as 3D printing and electrospinning have opened new possibilities to design scaffolds with controlled porosity, orientation, and composition, enabling better cell adhesion, proliferation, and differentiation. Hybrid manufacturing strategies that integrate electrospinning with 3D bioprinting represent a particularly promising direction. These approaches allow the creation of multiscale scaffolds with spatially controlled gradients in mechanical stiffness, biochemical composition, and topographical cues [2]. Such architectures can guide cellular alignment and direct tissue maturation, while also allowing the incorporation of bioactive agents or cells with high spatial accuracy. In parallel, the emergence of dynamically evolving materials—capable of modifying their structure, mechanical response, or drug release profile in response to physiological stimuli such as pH, enzymatic activity, inflammation, or mechanical loading—has further advanced the field toward the development of adaptive scaffolds.
Each of these technological advances exploits different aspects of biomaterials, revealing their versatility and transformative potential. Among these, graphene and its derivatives have emerged as outstanding nanomaterials for regenerative medicine. Initially appreciated for their exceptional mechanical strength, surface area, and electrical conductivity, graphene-based materials have since demonstrated unexpected biological functionalities, including [3] osteoconductive and osteoinductive properties. These findings position graphene not only as a structural enhancer but also as a bioactive component capable of stimulating bone formation and mineralization.

The advent of 3D and 4D printing has further expanded the potential of graphene by enabling its incorporation into functional bioinks. Nevertheless, the development of inks that combine high print fidelity, mechanical stability, biocompatibility, and mineralization capacity remains a key challenge. In this regard, graphene has once again proven to be an effective solution for formulating advanced composite inks and scaffolds, facilitating the design of hybrid systems that merge structural integrity with biological performance. The integration of graphene-based materials into hybrid biofabrication strategies therefore represents a powerful approach toward next-generation bone substitutes that are not only biomimetic and mechanically robust but also biologically active and responsive to the physiological environment

Acknowledgments: The authors would like to thank for the financial support provided by a grant from the Ministry of Research, Innovation, and Digitization, Romania's National Recovery and Resilience Plan, under the project titled "Advanced & Personalized Solutions for Bone Regeneration and Complications Associated with Multiple Myeloma", with reference CF 213/29.11.2022 and contract number 760093/23.05.2023.

References

[1] Cojocaru E, Oprea M, Vlăsceanu GM, et al. RSC Adv. (2024);14(44):32517-32532.

[2] Șelaru, A., Herman, H., Vlăsceanu, G. M., et al. (2022). International Journal of Molecular Sciences, 23(1)

[3] Chiticaru, E. A., & Ionita, M., (2022).. FlatChem, 35: 100417.