

“Bioinspired Bone-like Hydrogel Scaffolds for Bone Tissue Regeneration via Multiphoton Lithography”

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Bone-related disorders affect millions of people worldwide, necessitating advanced solutions for bone tissue engineering and regeneration.ⁱ Traditional 3D printing methods struggle to replicate the complex trabecular structure and composition of cancellous bone, highlighting the need for innovative approaches. The composition of bone includes an organic phase (collagen/cells), an inorganic phase (hydroxyapatite/metals) and water.ⁱⁱ

The purpose of this study is to fabricate bone-like scaffolds with the desired structure and composition to promote bone regeneration. Gelatin methacrylate -a natural biodegradable material derived from hydrolyzed collagen- metal ions and hydroxyapatite are used in this study, for the resemblance of organic and inorganic phase.ⁱⁱⁱ Multiphoton lithography and more specifically 2PP is employed to fabricate intricate scaffolds followed by a hydrogel infusion process for metal ion incorporation and a mineralization procedure for the formation of hydroxyapatite.^{iv} Biocompatible GelMA scaffolds successfully fabricated with various complex structures (e.g., square lattices, Triply Periodic Minimal Surface - TPMS structures) using FDA-approved photosensitive molecules (Eosin Y/Bengal Rose) and effectively infused with metal ions (zinc/iron), while hydroxyapatite formation was achieved on both the surface and within the hydrogel scaffolds.

This research demonstrates the feasibility of using multiphoton lithography for the creation of complicated hydrogel scaffolds, while the post-fabrication modification provides several desirable characteristics such as antimicrobial properties and osteogenesis, ideal for bone regeneration applications.

ⁱ Phillips, M., & Joshi, K. (2008). Bone disease. In *Orthopaedic bone cements* (pp. 3-40). Woodhead Publishing.

ⁱⁱ Selim, M., Mousa, H. M., Abdel-Jaber, G. T., Barhoum, A., & Abdal-hay, A. (2024). Innovative designs of 3D scaffolds for bone tissue regeneration: Understanding principles and addressing challenges. *European Polymer Journal*, 113251.

ⁱⁱⁱ Qu, H., Fu, H., Han, Z., & Sun, Y. (2019). Biomaterials for bone tissue engineering scaffolds: A review. *RSC advances*, 9(45), 26252-26262.

^{iv} Zyla, G., & Farsari, M. (2024). Frontiers of Laser-Based 3D Printing: A Perspective on Multi-Photon Lithography. *Laser & Photonics Reviews*, 2301312.