ID contributo: **117** Tipo: **Presentazione orale**

Scaffold multi-scala bioispirati stampati in 3D per la rigenerazione ossea: valutazione strutturale, fluidodinamica e biologica

mercoledì 3 settembre 2025 10:15 (15 minuti)

Osteoporosis and other bone-related diseases pose a critical challenge for modern healthcare systems, necessitating innovative and patient-specific treatment strategies. Bone tissue engineering has emerged as a promising solution, with the development of bio-inspired, 3D-printed scaffolds designed to mimic the complex hierarchical architecture of bone at multiple scales. However, existing scaffold designs often fail to accurately replicate bone's multi-scale organization, leading to suboptimal mechanical properties, insufficient cellular colonization, and inadequate fluid-dynamic conditions for nutrient transport.

Objectives

In particular, current scaffolds either focus on large-scale porosity, neglecting the intricate canalicular structure, or lack mechanical strength due to excessive porosity. Our work addresses this gap by developing a novel, hierarchically structured scaffold that integrates both macro- and micro-architectural features to optimize biological and mechanical performance.

Methods

This study introduces two distinct scaffold architectures: (i) a regular lattice-based scaffold with uniform lacunae and canaliculi distribution, and (ii) a biomimetic scaffold inspired by the canalicular network, generated using a Delaunay triangulation-based approach to better mimic the anisotropic and interconnected nature of bone porosity. These designs were implemented using computational modeling tools such as Autodesk Inventor Pro and Open CASCADE, followed by high-precision fabrication via two-photon polymerization using IP Visio resin. The regular scaffold exhibits a periodic cubic arrangement of lacunae, while the Delaunay-based scaffold presents a more heterogeneous structure with interconnected pores, enhancing its similarity to native bone tissue.

Results

To ensure scaffold fidelity and reproducibility, synchrotron-based imaging and deep-learning segmentation techniques (U-Net architectures) were employed for structural analysis. Fluid-dynamic analyses were conducted to assess wall shear stress (WSS) distribution within the scaffold microstructure, providing crucial insights into its biomechanical environment. Computational fluid dynamics (CFD) simulations performed using ANSYS Fluent revealed that the Delaunay-inspired scaffold exhibited a more favorable WSS distribution, closely matching physiological conditions necessary for osteocyte mechanotransduction. The regular scaffold, on the other hand, appears to potentially limit nutrient diffusion and cellular viability.

Experimental validation was performed through mesenchymal stem cells (differentiated into osteoblasts) seeding and in vitro culture, with scaffolds analyzed post-cellularization using optical and scanning electron microscopy. The regular scaffold exhibited highly reproducible geometries with well-defined porosities, while the Delaunay-based scaffold demonstrated enhanced cellular infiltration and interconnectivity, suggesting superior biointegration potential. Synchrotron-based imaging confirmed the presence of mineralized nodules within the Delaunay-based scaffold after 21 days of culture, supporting its potential for bone tissue regeneration.

Additionally, scaffold porosity was quantified, revealing that the Delaunay-based structure had a total porosity of 75%, compared to 60% for the regular scaffold, effectively balancing mechanical integrity and permeability. Our work provides a novel solution by combining hierarchical structuring with bioinspired canalicular networks, ensuring enhanced cellular viability, nutrient diffusion, and mechanical stability.

Based on the combined structural, biological, and fluid-dynamic assessments, the Delaunay-based scaffold configuration was identified as the most promising design, balancing mechanical support with optimal con-

ditions for cellular activity. Future work will focus on refining imaging techniques to monitor bone matrix deposition and further optimizing scaffold architectures to improve osteoconductivity and regenerative outcomes. In addition, further studies will explore dynamic culture conditions, where mechanical stimulation could be introduced to enhance osteogenic differentiation and scaffold maturation.

Conclusion

This study highlights the transformative potential of bio-inspired, hierarchically structured scaffolds in advancing bone tissue engineering. By integrating advanced fabrication, imaging, and computational modeling, this research paves the way for personalized scaffold solutions tailored to individual patient needs, ultimately enhancing treatment efficacy for bone regeneration in clinical applications. The combination of hierarchical structuring, optimized fluid dynamics, and synchrotron-aided assessment represents a cutting-edge approach in biomaterial design, addressing critical limitations in the current state-of-the-art and providing a robust foundation for future developments in regenerative medicine.

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Classifica Sessioni: Biomeccanica

Classificazione della track: Biomeccanica