

## 3D PRINTED GELMA/HYDROXYAPATITE SCAFFOLDS FOR ENGINEERING BONE-LIKE TISSUE: A POWERFUL TOOL TO PRECLINICALLY VALIDATE NEW PROSTHETIC DEVICES

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To reduce the need of revision surgeries of bone implants ascribed to loosening phenomena/implant instability, functional coatings are under investigation, requiring standard/reproducible procedures for their preclinical evaluation in a physiological-mimicking environment. In vitro bone tissue models represent a powerful tool for predictive in vitro screening, resulting in a reduction of animal experimentation in agreement with 3Rs principle.

In this perspective, this work was aimed at developing a 3D-printed bone tissue-like through micro-extrusion additive manufacturing of scaffolds from a purposely-engineered bio-ink. Bio-ink formulation was developed by combining gelatin methacryloyl (GelMA, 7%w/V) as polymeric component and inorganic rod-like nano-hydroxyapatite (nHA, 3%w/V) to mimic the bone mineral content. nHA addition did not alter bio-ink thermo-responsiveness as demonstrated by unchanged gelation onset temperature (i.e., 24°C) and kinetics. Differently, differences in the storage modulus before and after irradiation at 365nm ( $\Delta G'$ ) showed remarkably higher values for GelMA/nHA compared to GelMA (i.e.,  $\Delta G' = 5.3\text{kPa}$  vs.  $3.7\text{kPa}$ ), suggesting the role of nanoparticles as reinforcement filler. By exploiting ink thermo-responsiveness and photo-crosslinking ability, GelMA/nHA formulations were micro-extruded in mild conditions into model square meshed structures with high shape fidelity. Subsequently, printed geometry was refined to morphologically reproduce the cortical/cancellous bone tissues and to maximize cell response. 3D scaffolds (i.e., 25 layers in cylinder-shape constructs with 400  $\mu\text{m}$  pore size) were mechanically characterized showing adequate properties for bone tissue engineering/modelling. Murine fibroblasts (3T3) were preliminarily included in the bio-ink to obtain cellularized constructs. Cell viability tests evidenced the absence of cell damages induced by shear stresses during scaffold fabrication.

### References

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