

Design of nano-micro composite scaffolds for bone tissue regeneration: process/structure/property relationships

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INTRODUCTION: Porous biodegradable scaffolds are essential for tissue engineering application since they should provide the adequate three-dimensional structure for cellular attachment and tissue development. In particular, the design of pore architecture on the micrometric scale (i.e., pore size and shape, interconnectivity and pore anisotropy) is mandatory for controlling neo-tissue formation determining the success of the tissue engineering approach. The current macro- or micro-fabrication techniques are partially unable to recreate sophisticated structures that could mimic the complexity of the ECM, taking into account that all living systems are governed by molecular events at nanometer scales.

In this context, recent paradigm moves towards the new fabrication techniques able to develop micro and nano-structured platforms which assure an optimal balance in terms of cell recognition, mass transport properties and mechanical response in order to reproduce the morphological and functional features of natural tissues at the microscopic and nanoscopic level.

Here, different techniques to emboss a controlled pattern of porosity in biodegradable polymers (i.e., phase inversion/salt leaching, electrospinning) are reviewed, highlighting process–structure–property relationships in order to develop hierarchically organized platforms for a wide range of tissue engineering applications.

METHODS: Several composite scaffold typologies have been considered to combine polymer matrices with one or more reinforcement systems in different forms – particles¹ and long fibres². Composite tubular scaffolds were obtained through the winding of PLA fibres (75/24 dtex) pre-impregnated into PCL solution (20/80 wt/wt) bath containing, in turn, salt crystals, 212-300 µm in size, Hyaff11® particles (FAB, Abano Terme, Italy) and/or tricalcium phosphate powder, on a rotating mandrel. Electrospun membranes from a polymer solution of PCL (MW 65kDa) and Gelatin (Type B from calf skin) in trifluoroethanol (TFE) were developed by a home-implemented equipment. All platforms were characterized: I) morphologically by SEM/FESEM/ESEM microscopy and quantitative pore analyses, II) chemically by contact angle, IR spectroscopy and degradation in vitro tests and III) biologically by the evaluation of mesenchymal cells (MSC) response.

RESULTS: The integration of PLA microfibrils improves the mechanical response of the scaffolds partially limited by the high pore volume fraction, needful for the accommodation of bone cells and their maintenance, so matching the mechanical behaviour of trabecular bone. The addition of calcium phosphate particles drastically improves the bioactive response of scaffolds. The presence of highly hydrophilic Hyaff11® positively contribute to growth factor entrapment/release as well as to cell recognition, as confirmed by preliminary evaluation of the attachment and MSC cell proliferation, adumbrating the potential in vivo success of tubular scaffolds. As for electrospun membranes, the morphology nano-texture firstly contributes to cell material interaction by offering an higher surface for binding sites to cell membrane receptors. Moreover, the presence of gelatin improves the less cell affinity with hydrophobic PCL exposing many integrin sites able to favor cell adhesion and differentiation, so creating a favorable environment which reproduce the chemical cues of natural extracellular matrix.

CONCLUSIONS: The sage mixing of materials with different properties contributes to finely control the structural properties, degradation profile and cellular events, guiding new tissue in-growth by the gradual transmission of biochemical and biophysical signals, moving towards a true mimicking of natural ECM functions.

REFERENCES:

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