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Magnetic Scaffolds for Targeted Drug Delivery in Bone Tissue Engineering

Matteo Bruno Lodi[1*], Alessandro Fanti[1]

[1]Department of Electric and Electronic Engineering, University of Cagliari, Cagliari, Italy

matteob.lodi@unica.it, alessandro.fanti@diee.unica.it

The goal of bone tissue engineering is the development of tools and devices capable of favoring and selectively elicit the physiological process of bone healing to repair or regenerate an injured area. Bone scaffolds are instruments that use exogenous and extrinsic factors to induce a therapeutic action to facilitate the healing process. Primarily they have a structural function, but they should also create optimal conditions for cell migration, adhesion, and differentiation. Many research efforts have been spent to turn scaffolds into therapeutic devices, i.e. functional objects that aim to minimize tissue rejection and allow integration of prosthetic implants by acting on the physical phenomena involved in bone reparation and regeneration.

This clinical neediness lead to the investigation of the bone scaffold functionalization with Magnetic Nanoparticles (MNPs) to obtain a remotely controlled functional object. A so-called magnetic scaffold is a nanocomposite material with strong saturation magnetization ($5 \div 20$ emu g^{-1}), which is implanted in the injured bone and can be exploited as an attraction site for some recent magnetic carriers of bioactive molecules. Indeed, MNPs bio-conjugated to proteins such as Vascular Epithelial Growth Factor (VEGF) or Transforming Growth Factor β (TGF- β) have been synthetized. Both these biomolecule are known to promote angiogenesis, which in turns allows to increase the survival rate of bone progenitor cells host by the scaffold, but also to act as a chemoattractant able to promote the migration of mesenchymal stem cells, which would differentiate into osteoblasts and ensure the production of new bone. The functionalized MNPs can release the proteins only if a temperature of 42°C is reached, since the protein linker, which tether it to the particle surface, collapse by thermal degradation. Therefore, for bone tissue engineering application, these particular bio-agents or magnetic shuttles can be employed to deliver very specific signaling agents at the site where the magnetic scaffold is implanted (i.e. the injured area) under the action of an external static magnetic field. Then, by applying a radio-frequency magnetic field, the temperature at the scaffold and the MNPs site is increased up to the threshold value and the biomolecules is released in order to increase the rate of bone healing process.

This work deals with the mathematical modelling of the non-linear magnetization properties of magnetic scaffolds, with the calculation of the force exerted on the MNPs and the description of the related transport process of the growth factor delivery in a static magnetic field. After the delivery of MNPs to the scaffold, the release of growth factor from them is simulated carefully solving the transient Bio-Heat equation during the RF-exposure phase. This is done relying on a recent and non-linear numerical framework employed for bone tumor hyperthermia. Finally, the bone healing process is simulated to investigate the effects of the magnetic delivery of VEGF and TGF-β on the bone healing process. The innovative technique under analysis is compared to traditional drug delivery strategies. The performance of the drug delivery strategy is assessed in terms of lamellar bone homogeneity and considering the mechanical properties of the newly formed bone tissue. The model is implemented in COMSOL Multiphysics.

The proposed mathematical model is the first semi-quantitative description of the possible improvements due to the employment of novel magnetic scaffolds in magnetically targeted drug delivery for bone tissue engineering applications.