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**3D bone-like scaffolds containing smart nanomaterials
to treat osteoporotic fractures**

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Osteoporosis is a worldwide spread disease and its incidence is continuously growing as the population ages; it results in bone loss and decreased bone strength that lead to an increase in the risk of low-energy fractures. Antiresorptive agents such as bisphosphonates are mainstays of the therapy for osteoporosis but some concerns on their possible adverse effects were raised.

From an overall perspective, the ultimate solution is still to be found and thus, in the frame of the ERC BOOST, we are working on the development of a biomimetic scaffold engineered to be used in case of osteoporotic fractures.

Healthy and osteoporotic bone geometries are obtained from tomographic scans of human bone tissues discarded during surgical interventions (following ethical approval by Istituto Ortopedico Rizzoli-Italy). A multi-material platform able to combine different rapid prototyping techniques has been developed in order to meet all the constraints related to the features of the materials to be processed and the degree of versatility and resolution

needed. To this aim, the STL file derived by the tomographic analysis of bone samples is used to process the optimised biomaterials in order to fabricate the smart scaffolds, reproducing as close as possible the 3D architecture and chemistry of healthy human bone tissue. Type I collagen, at different concentrations, was used as a matrix to mimic bone chemistry whereas mesoporous bioactive glass/nano-hydroxyapatite were embedded within the collagen fibers. Growth factors (IGF and β -TGF) were encased in the scaffold struts using several approaches in order to simulate the growth factors stored in the extracellular matrix, and their retained activity was assessed.

The fabricated scaffolds will be tested into bioreactors by means of a co-culture of osteoblasts and osteoclasts in order to define the influence of both chemical and topographical stimuli on the osteoblast-osteoclast coupling. The proposed approach will allow us to decode how biomaterial chemistry and topography at any scale (macro-, micro- and nano) influence the multifaceted coupling process of bone resorption and formation, with particular focus on the cell cross-talk between osteoclasts and osteoblasts.

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