

## **Engineered Bone from Bone Marrow Stromal Cells: a Structural Study by an Advanced X-ray Microdiffraction Technique**

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One of the most recent therapeutic strategies for the reconstruction of damaged large bony segments includes the tissue engineering approach. It takes advantage of the patient's own cells, which are isolated, expanded in vitro, loaded onto a bioceramic scaffold and reimplanted into the lesion site. Bone marrow stromal cells (BMSC) are the most commonly used cell type.

A structural characterization of the engineered bone is largely desirable. An important point is to evaluate if the BMSC extracellular matrix deposition on a bioceramic scaffold recapitulates the ontogeny of the natural bone development. Moreover the investigation of the interaction between the newly deposited bone and the scaffold results particularly interesting. Indeed the chemistry and the geometry of the scaffold used to deliver BMSC in the lesion site determine spatial organization of the new bone and the bone-biomaterial integration.

We investigated for the first time the local interaction between the newly formed mineral crystals in the engineered bone and the biomaterial by means of microdiffraction, using a set-up based on an X-ray waveguide. We demonstrated that the newly formed bone is well organized inside the scaffold pore, following the growth model of natural bone, and that there is a good adhesion with the scaffold. Combining Wide Angle (WAXS) and Small Angle (SAXS) X-ray Scattering with high spatial resolution, we were able to determine the orientation of the crystallographic c-axis inside the bone grains, and the orientation of the mineral crystals and collagen micro-fibrils with respect to the scaffold. Moreover from a quantitative analysis of both the SAXS and WAXS patterns the grain size appears to be compatible with the model for early stage mineralization.

**Keywords: SAXS, WAXS, bone mineralization**