Adult stem cells in bone regeneration: advantages and present limitations

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INTRODUCTION: Bone damage, due to either pathologies or trauma, is a common occurrence in orthopedics. While synthetic BGS have proven to be useful in non load-bearing applications, their success in treating extensive, segmental defects is impaired by their inability to participate in the cell-mediated remodeling process. Hydroxyapatite-based BGS remain within the body for extended periods and BGS based on the more soluble Tricalcium Phosphate (TCP) may experience significant dissolution prior to the ingrowth of bony tissue. In a recent study in sheep we evaluated the performance of implants of Skelite™, resorbable BGS based on Silicon-stabilized Tricalcium Phosphate, in promoting the repair of critical-sized demonstrating that a progressive resorption of the scaffold by osteoclasts was subsequently replacement with highly mineralized lamellar bone suggesting that these two processes are interrelated.

The objective of this study was to further investigate the simultaneous occurrence of new bone formation and Skelite scaffold resorption.

METHODS: To investigate the coupled mechanisms of bone formation and scaffold resorption, X-ray computed microtomography (microCT) and X-ray micro-diffraction with synchrotron radiation were performed on BMSC-seeded ceramic cubes. These were analyzed before and after implantation in immunodeficient mice for 2 or 6 months.

Experiments were performed at the European Synchrotron Radiation Facility (ESRF, Grenoble, France).

DISCUSSION & CONCLUSIONS: Areas of different segregated densities were instead observed, in the same scaffolds, once seeded with cells and implanted in vivo. The microCT data evidenced that all scaffolds showed a uniform density distribution before implantation. (Fig.1) A significant decrease in the density of the scaffold, together with major changes in scaffold chemical composition, were observed by micro-CT in areas immediately adjacent to where new bone had been deposited in agreement with the concept that Skelite scaffold resorption and bone formation are interrelated processes. With increasing implantation time, scaffold thickness significantly decreased while bone thickness increased.A detailed microX-ray diffraction analysis revealed that only in the contact areas between deposited bone and scaffold, the TCP component of the biomaterial decreased much faster than the HA component. This event did not occur at areas away from the bone surface, highlighting coupling and cell-dependency of the resorption and matrix deposition mechanisms. Moreover, in scaffolds implanted without cells, both the ceramic density and the TCP:HA ratio remained unchanged with respect to the pre-implantation analysis. The depletion of the TCP increases with the increase of implant time (Fig.2). The results of the scaffold implanted without preloading with cells demonstrate that the resorption is a cell-mediated mechanism.

In summary, we have shown that the Skelite™ implant is progressively resorbed through an active cell mediated process and that its resorption coincides with the formation of new bone.

Fig.1 *density distribution after 24 weeks of implant*

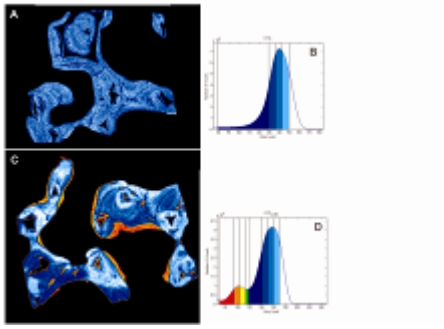

Fig.2 *scaffold resorption*