Restoration of Marrow Varies with Bone Graft Materials

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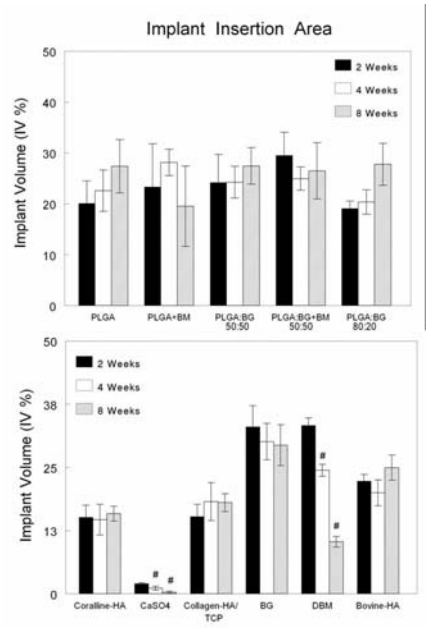
Statement of Purpose: Bone substitutes are used in sites that normally remodel once bony union has been achieved. As we have achieved a greater understanding of bone biology and bone healing, it has become desirable to identify materials that resorb as new bone is formed, thereby facilitating the restoration of normal bone contours and biomechanics. Of equal importance is the restoration of the marrow cavity. However, relatively little is known about the consequences of these materials to marrow restoration.

This study was based on the hypothesis that bone graft substitute materials of different chemical compositions and structural properties will support osteogenesis to a comparable extent but will vary in their rate of resorption, impacting the rate of marrow cavity restoration. To do this, we took advantage of the rat tibial marrow ablation model. In this model, ablation of the tibial marrow induces endosteal bone formation. The medullary canal fills with new bone via a well-documented process [1,2,3]. In the absence of any implant material, bone remodeling begins approximately 21 days post-ablation and the marrow cavity is restored by 28 days. The rate of bone formation is affected by the chemical and physical properties of materials within the marrow cavity. Because implants are placed only in the proximal tibia, the distal tibia marrow cavity provides an internal control. Using this model, we were able to detect differences in bone formation and bone remodeling due to the bone graft material used.

Methods: Skeletally mature male "Sabra" rats 3-months of age were used. Because the materials had very different densities and shapes, equal volumes were inserted in each case. All materials were used as provided by the manufacturer for clinical use, but in some cases, it was necessary to crush larger pieces and then use only particles less than 850 μm in diameter. Bone marrow was obtained from syngeneic rats. Following marrow ablation of the right tibia, the rats were grafted with the following materials (24 rats per implant type): poly-lactide-polyglycolide (75:25) granules (PLGA, OsteoBiologics, Inc., San Antonio, TX), PLGA mixed with bone marrow (PLGA-BM), PLGA fabricated with Bioglass® (PLGA+BG 50:50), PLGA+BG mixed with bone marrow (PLGA+BG+BM), PLGA+BG 80:20, coralline hydroxyapatite (HA, Interpore 200®, Biomet, Inc., Warsaw, IN), calcium sulfate (Osteoset®, Wright Medical Inc., Memphis, TN), collagen/tricalcium phosphate composite (Collagraft®, Zimmer, Inc., Warsaw, IN), Bioglass® (BG, Perioglas®, US Biomaterials, Alachua, FL), demineralized bone matrix (DBM, LifeNet, Inc., Virginia Beach, VA), and de-organified bovine bone granules (bovine-HA, Bio-Oss®, Geistlich, Switzerland). A control group of 8 rats were ablated but left untreated. At 2, 4 and 8 weeks post-ablation (8 rats/implant type/time), tibia were processed for histomorphometry.

Results: New bone formation varied with implant type. Control tibias had almost 30% TBV at 2w. This decreased to <5% by 4w, and by 8w, the marrow cavity was completely restored. Only tibias implanted with coralline-HA had less %TBV than controls at 2w; CaSO4 supported 40% TBV. Sites receiving PLGA, PLGA+BG, CaSO4, and DBM exhibited reduced %TBV at 4w. In sites treated with CaSO4 and DBM, %TBV was further reduced at 8w.



PLGA implant materials were reduced over 8w (Fig 1, top). In contrast, CaSO4 was gone by 2w and DBM was >50% resorbed at 8w (Fig 1, bottom).

Endosteal bone formation was induced in the distal canal but no implants were present. In the control animals, TBV was 20% at 2w and this was gone at 8w. PLGA+BG and CaSO4 caused >45% fill with trabecular bone. While the stimulatory effect of the other materials was not as great, BG, DBM and bovine-HA all caused greater bone formation than was seen in controls. In all cases, new bone was reduced to control levels by 4w and was gone by 8w.

Marrow was reestablished with all implant materials. However there were material-dependent differences in the rate at which marrow matured, based on the number of fat cells. This was true in the implant sites as well as in the distal canal.

Discussion. This study shows that bone graft substitute materials of a variety of types support new bone formation in sites that are predisposed to form bone. Moreover, their presence in those sites can stimulate bone formation at sites distal to the implant, in some cases to a greater extent that would occur without the implant material. The results also show that some materials retard the healing process, including remodeling and restoration of marrow. This needs to be considered when planning the course of regenerative treatment and the insertion, as well as loading, of osteo-integrative implants. Our results are supported by those of Valimaki et al. [4] showing that BG spheres increased medullary bone formation 2.5 fold over than seen in control rats, but delayed recovery of pQCT strength strain index of the bones. This suggests that in the presence of some materials, bone healing may require longer times before external forces can be applied.

References : (1) Sela J et al. Biomaterials 1995 16:1373-80 ; (2) Braun G et al. Clin Oral Implants Res 1995 6:1-13 ; (3) Stoumboudi MT et al. Acta Anat 1995 152:110-8 ; (4) Valimaki VV et al. Bone 2006 38:432-443.

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