Canine Mandibular Augmentation Using Autologous Bone Marrow Stromal Cells

Mankani MH, Kuznetsov SA, Huang K, Robey PG, Marshall GW
University of California, San Francisco; NIDCR, NIH.

Statement of Purpose: Transplants of culture-expanded autologous or allogeneic bone marrow stromal cells (BMSCs) form cortico-cancellous bone which demonstrates longevity in rodent animal models, supporting their eventual clinical role to restore atrophic bone. Up to now, the stability of these transplants in large animal models has not been evaluated. Given the propensity of autologous bone graft to undergo resorption over time, initiation of clinical studies utilizing autologous BMSC transplantation first requires a demonstration of long-term bone stability, especially when particulate scaffolds are used.

Methods: BMSCs from femoral bone marrow from 3 dogs underwent expansion in tissue culture. Autologous BMSCs were combined with 1 or 2 gram aliquots of hydroxyapatite/tricalcium phosphate (HA/TCP, 65%/35% relative ratio) particles (Zimmer) to create transplants, which were introduced onto the unilateral mandible as onlay grafts. The contralateral control mandibles were augmented with the HA/TCP particles alone, each the same volume as the BMSC- HA/TCP transplant. Quantitative CT (qCT) scans were obtained twice for each dog, both early after transplantation and prior to harvest. At intervals ranging from 17 to 19 months, transplants were harvested for histologic and mechanical analysis

Results: In all animals, BMSC-containing transplants formed significantly greater amounts of bone over their control counterparts (Figure 1 and 2) and maintained their volumes long-term (Figure 3), in contrast to BMSC-free transplants. Evaluation by qCT distinguished BMSC transplants from BMSC-free transplants (Figure 4). BMSC-associated bone exhibited stiffness and hardness similar to the adjacent normal bone.

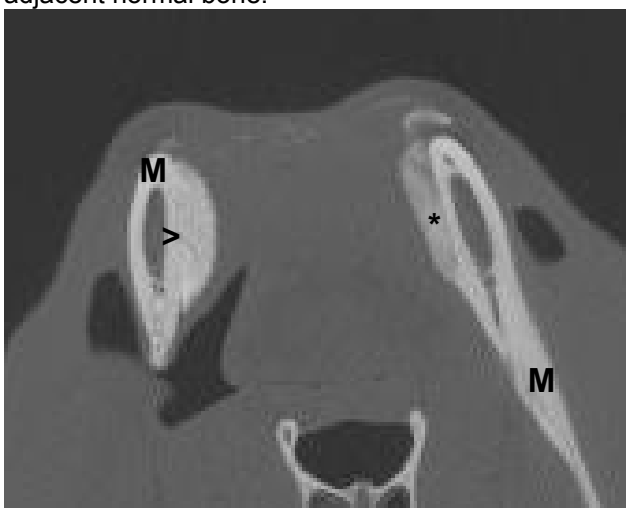

Figure 1: Representative BMSC/HA/CTP transplant (>) on mandible (M), with BMSC-free HA/TCP transplant (*) on contralateral mandible. BMSC transplant has greater volume and density.

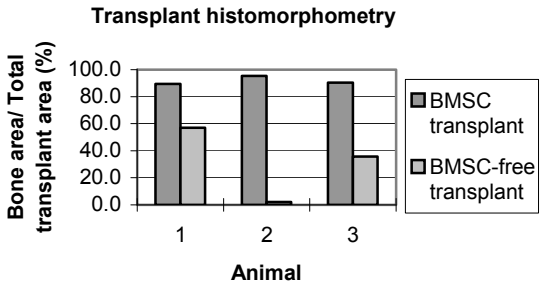

Figure 2. Bone in each transplant, by histomorphometry

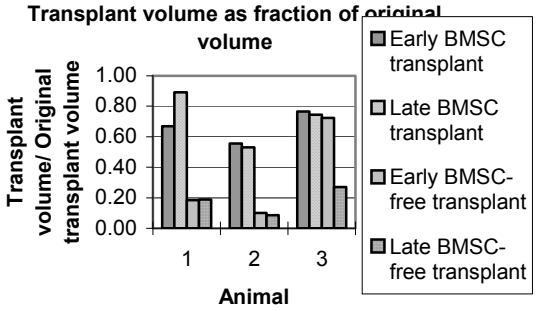

Figure 3. Volume of transplant at each CT scanning session, relative to original volume

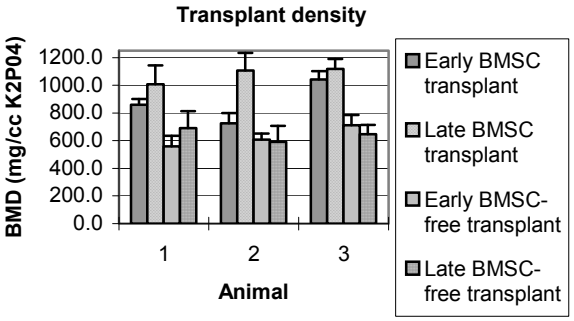

Figure 4. BMD of each transplant at each CT scanning session

Conclusions: Autologous cultured BMSC transplantation is a feasible therapy for mandibular augmentation. Autologous BMSCs with HA/TCP particles form cortico-cancellous bone and maintain their volume long-term, unlike HA/TCP scaffolds alone. This represents the first evidence in a large animal model that transplantation with autologous BMSCs can successfully augment the mandible long-term, and may eventually serve as a therapy for atrophic bone.