Calvarial Reconstruction with BMP-2: Concomitant Treatment with Bone Marrow Cells

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Abstract

Background: While bone morphogenetic protein-2 (BMP-2) demonstrates promise as a therapy for calvarial bone regeneration, its application remains controversial due to concern for side effects such as heterotopic ossification or malignant transformation. Meanwhile, bone marrow cells (BMCs) have demonstrated therapeutic promise, but therapies remain to be optimized. The aim of this study was to augment the efficacy of bone marrow cell mediated bone regeneration through application of a low dose of rhBMP-2.

Methods: Subtotal calvariectomy defects measuring 7.5 x 7.5 mm² were created in 12-week old New Zealand White rabbits. Defects were reconstructed in one of three groups: Group 1, acellular dermal matrix (ADM) soaked in PBS overnight [ADM/PBS, n=3]; Group 2, ADM soaked overnight in DMEM with 150,000 bone marrow cells from the femur of a New Zealand White rabbit [ADM/BMCs, n=3]; and Group 3, ADM and BMCs with 1.78μg of BMP-2 applied by ink-jet based biopatterning [ADM/BMCs/BMP-2 n=3]. Animals underwent serial CT imaging at 0, 2, 4 and 6 weeks postoperatively, followed by euthanization and histological analysis. CTs were reconstructed utilizing Amira software (Visage Imaging, San Francisco, CA, USA), and areas of translucency were calculated using ImageJ (NIH) to determine change in defect area relative to time zero (baseline value).

Results: At 6 weeks compared to time zero, ADM/PBS resulted in 45.2% healing (standard deviation 30.1%), and ADM/BMCs resulted in 54.1% healing (standard deviation 12.7%). Treatment with ADM/BMCs/BMP-2 resulted in 78.6% healing (standard deviation 11.6%); there was no significant difference between groups (Figure 1). Histologically, bone in each group was similar, consisting of islands of compact, cellular bone.

Figure 1. Percent Defect Healing
**Conclusions**: Compared to treatment with ADM/PBS only, addition of BMCs for reconstruction of an acute calvarial defect trended toward better results, and addition of BMP-2 to this regimen further optimized outcomes. Combination cell/growth factor therapy may enable successful reconstruction of calvarial defects without side effects related to higher dose.

**Disclosure/Financial Support**: Nothing to disclose

Dr. Losee receives financial support for other research projects from Medtronic