

Purpose: Radiation therapy is known to be detrimental to bone and soft tissue repair, resulting in an unacceptably high incidence of devastating wound healing complications as well as the associated morbidity of late pathologic fractures and non-unions. Our global hypothesis is that the pathologic effects of radiation on bone formation and healing are mediated through a mechanism of direct cellular depletion as well as diminished function of the cells responsible for the generation and maintenance of osteogenesis. We posit that transplanted bone marrow stromal cells (BMSCs), a type of mesenchymal stem cell, will provide sufficient cellular replacement and increased cell signaling to enhance the generation and quality of new bone during DO.

Methods: 21 male isogenic Lewis rats were randomly split into three groups. Group 1, XRT/DO (n=6) and Group 2, BMSC (n=7) underwent 5 day fractionated XRT of the left mandible at 7 Gy per day. Group 3, DO (n=8), received no radiation. All animals were allowed to recover for two weeks, then underwent mandibular distractor placement. The BMSC group received a Surgifoam scaffold loaded with 2 million BMSCs intra-operatively placed within the distraction gap. All groups were then distracted at 0.3mm every 12 hrs to a total distance of 5.1mm. The regenerate was allowed to consolidate for 40 days after surgery was completed, after which tissue was harvested and underwent analysis both grossly and with micro-CT.

Results: Union quality of mandibles from each group were graded on a 4 point Likert scale. BMSC mandibles union quality was significantly higher than XRT/DO mandibles and demonstrated no difference to non-radiated DO animals. The radiomorphometric parameters for bone mineral density (BMD) and bone volume fraction (BVF) were also significantly improved by BMSC replacement therapy and again the treated group showed no difference when compared to non-irradiated animals.

Conclusion: Stem Cell therapy successfully reversed much of the damage to radiated mandibles allowing successful DO in our murine model as measured by rate of union, BVF and BMD. Our results show that the administration of BMSCs intra-operatively to the distraction gap can rescue the ability for irradiated bone to undergo distraction osteogenesis, thereby producing a solid, bony union with improved parameters of bone quality in an otherwise nonfunctional mandible.

