

# Amifostine Demonstrates Significant Cytoprotection in an Irradiated Murine Model of Mandibular Distraction Osteogenesis

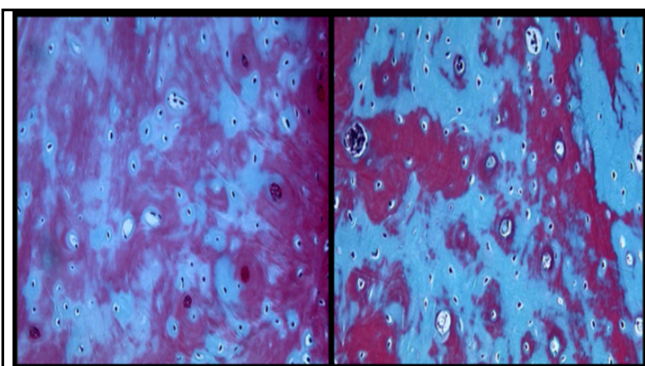
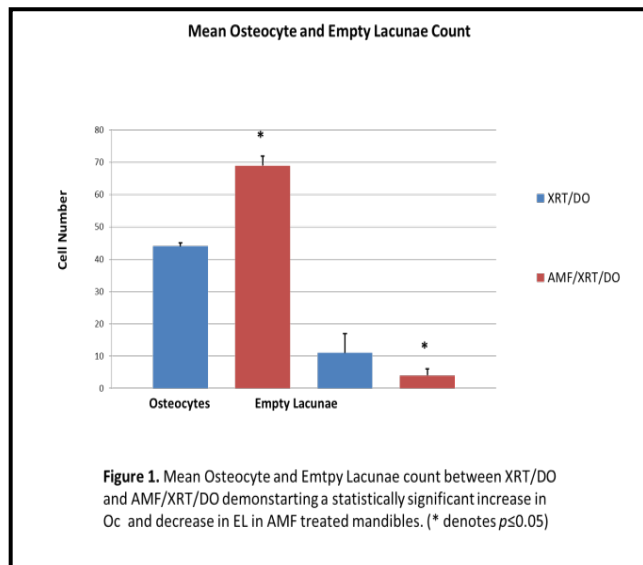
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## Abstract

**Background:** Head and neck cancer (HNC) clinical management requires adjuvant radiation (XRT) therapy. Our previous studies have demonstrated the deleterious effect of a human equivalent dose of radiation (HEDR) on a murine mandibular model of distraction osteogenesis (DO). Here, we use quantitative histomorphometry (QHM) to objectively measure the radio-protective effects of Amifostine (AMF) on the cellular integrity in an irradiated and distracted regenerate. We posit that AMF will protect osteocytes from the damaging effects of XRT.

**Methods:** 16 Sprague Dawley rats were randomly assigned into 2 groups: Group 1 (n=6) and Group 2 (n=10) received a HEDR given in 5 fractionated doses. Group 2 was given AMF 45 minutes prior to XRT. Both groups underwent a left mandibular osteotomy with bilateral fixator placement. Distraction to 5.1mm was followed by a 28-day consolidation period. All left hemimandibles were harvested, sectioned and stained. QHM was performed for osteocyte count (Oc) and empty lacunae (EL). Independent Samples t-test was used for group comparison with  $p < 0.05$  considered statistically significant.

**Results:** Complete bony bridging was observed in all AMF pre-treated animals, whereas the irradiated group exhibited some specimens with incomplete bridging. QHM analysis revealed a statistically significant higher Oc compared with irradiated mandibles (69 vs. 44 osteocytes,  $p=0.000$ ). There was also a corresponding decrease in the number of EL between the AMF-treated and irradiated groups (4 vs. 11 EL,  $p= 0.002$ ). (See Figures)



**Figure 2.** Left XRT/DO vs. Right AMF/XRT/DO. Oc and EL per high power field at 16X magnification demonstrating a robust proliferation in Oc and a decrease in EL in the Amifostine pre-treatment group

**Conclusion:** Our findings demonstrate the significant osseous cytoprotective capacity of AMF on distraction using XRT. The maintenance of bone forming cells resulting from AMF pretreatment was associated with an increase in bony union and a complete elimination in the incidence of fibrous union. We posit AMF's efficacy in the clinical arena may allow the successful implementation of DO as a viable reconstructive option for HNC in the future.

## References:

### Disclosure/Financial Support

Supported in part by NIH-R01 CA 125187-01 - Optimization of Bone Regeneration in the Irradiated Mandible (to Dr. Steven R. Buchman).

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.