

Deferoxamine Decreases Non-Unions and Restores Bone Quality and Biomechanical Strength in Pathologic Fracture Healing After Radiotherapy

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Objective: Adjuvant radiotherapy for head and neck cancer patient management continues to be paralleled with costly and devastating bone related pathologies. Most detrimental is the development of non-unions secondary to pathologic fractures. A pharmacologic means to prevent these pathologies would be highly desirable. Deferoxamine (DFO), an angiogenic therapy, augments vascularity and subsequently enhances fracture healing when injected into a fracture callus. We posit that the untoward effects of radiotherapy on bone quality, mechanical strength and non-union formation can be mitigated with this powerful angiogenic therapy.

Methods: 15 rats received fractionated radiotherapy to left hemi-mandibles. After recovery, fracture repair ensued with external fixator placement and mandibular osteotomy. DFO was injected into the callus site every other day from post-operative days 4-8. After a 40-day healing period, mandibles were dissected and gross union was assessed. Union was defined as bony bridging and the absence of motion across the fracture site. Fracture site integrity was assessed via μ CT and biomechanical testing. Data were analyzed with ANOVA and $p \leq 0.05$ was statistically significant. The DFO group was compared with two different groups: non-radiated fracture-Fx and radiated fracture-X/Fx (n=5,15).

Results: μ CT: DFO group demonstrated a significant restoration to control level Bone Volume Fraction when compared to X/Fx ($p=0.000$). Three other radiomorphometrics also showed significant restorative effects. *Biomechanical Testing:* A significant restoration to control level Ultimate Load was observed when comparing X/Fx/DFO to X/Fx ($p=0.003$). Yield, Stiffness and Failure Load also showed significant restorative effects. *Bony Union:* While Fx mandibles demonstrated 100% bony union, X/Fx mandibles only demonstrated 20% union. The X/Fx/DFO group demonstrated 67% bony union.

Conclusions: Bone quality and biomechanical strength were significantly restored with DFO from radiation levels. The most consequential finding was a 47% increase in bony unions within a model where healing was not routinely observed.

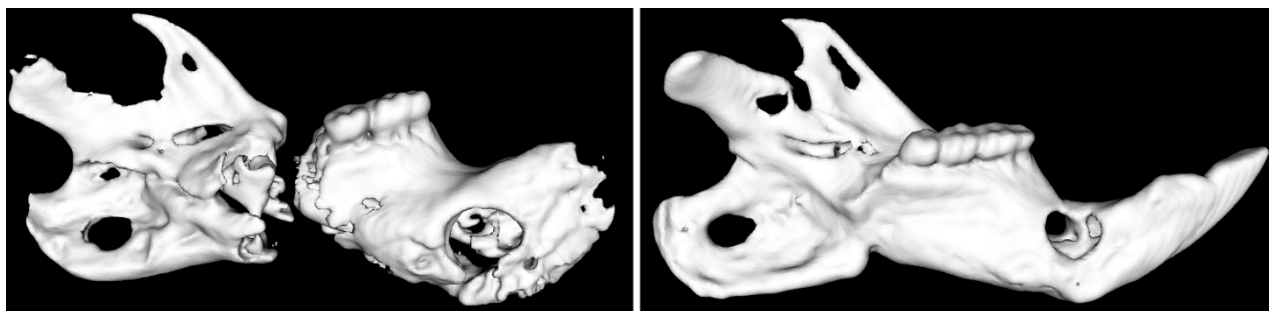


Figure 1: The μ CT image depict selected untreated (L) and DFO treated (R) mandibles, demonstrating the effectiveness of DFO treatment in restoring bone quality.

Disclosure/Financial Support

Funding Support provided by NIH RO1 CA 12587-01 to S. R. Buchman

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