

Deferoxamine Augments Vascularity and Prevents Osteocyte Depletion Following Radiotherapy in a Mandibular Pathologic Fracture Model

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Objective: The effects of radiation on bone formation and healing are mediated through the mechanisms of vascular damage, direct cellular depletion and diminished function of osteocytes. Over time, this accumulated damage predisposes patients to the debilitating problem of late pathologic fractures and non-unions. Here we employ the use of Deferoxamine (DFO), an angiogenic enhancing therapy, to bolster the vascular response during bone healing in this setting and posit that the untoward effects of radiotherapy on vascular density and osteocyte count can be mitigated with the addition of DFO.

Methods: 12 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. A 40-day healing period was allowed prior to vessel perfusion, μ CT and histologic processing. Mandibles were dissected and gross union was assessed. Union was defined as bony bridging and the absence of motion across the fracture site. Outcome data was analyzed with ANOVA, and $p \leq 0.05$ was statistically significant. The DFO group was compared with two other groups: fracture-Fx and radiated fracture-X/Fx (n=12,12).

Results: Vascularity: The DFO treated group demonstrated a significant restoration to control level Vessel Volume when compared to X/Fx ($p=0.029$). Vessel Number, Thickness and Separation also showed significant restorative effects.

Histomorphometry: Histology revealed a significant restoration to control level osteocyte count ($p=0.000$); and a corresponding decrease in empty lacunae ($p=0.000$) when comparing X/Fx/DFO to X/Fx.

Bony Union: While Fx mandibles demonstrated 100% bony union, X/Fx mandibles only demonstrated 25% union. The X/Fx/DFO group demonstrated 67% bony union.

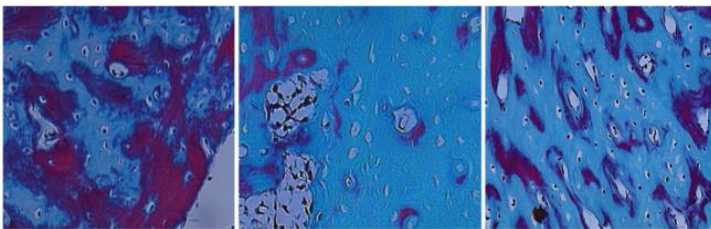


Figure 2: From left to right, Fx, X/Fx, and X/Fx/DFO. Digital photograph at 16X magnification demonstrating Deferoxamine-treated restoration of osteocyte count. Note the abundant robust osteocytes within lacunae in both the Fx and X/Fx/DFO groups.

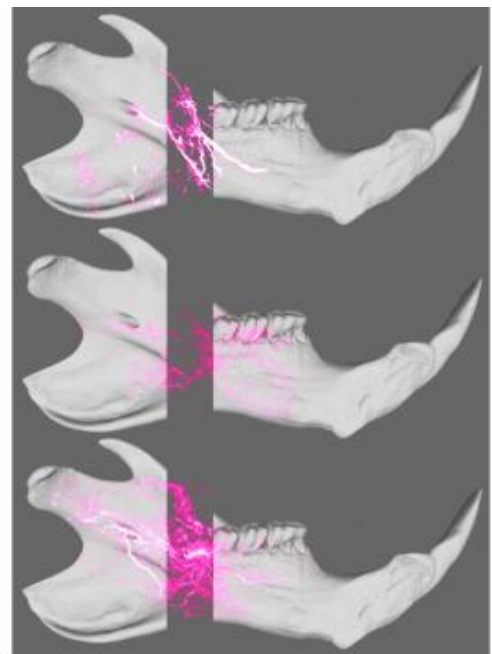


Figure 1: Reconstructed microangiograms depicting the efficacy of DFO in augmenting vascularity in radiated fracture. From top to bottom: Fx, X/Fx, X/Fx/DFO

Conclusions: We observed a complete restoration of vascular density and osteocyte count with the addition of DFO. The most consequential finding was a 42% increase in bony unions in a model where healing was not routinely observed.

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