Adipose Derived Stem Cells Enhance Vascularity in an Irradiated Murine Mandibular Fracture Model

Snider AE, Ettinger RE, Nelson NS, Donneys A, Ranganathan K, Rodriguez JJ, Buchman SR

Purpose: Bone regeneration is impaired after radiotherapy-induced vascular injury. Therapeutic enhancement of vascular response offers a solution for regenerating damaged vessels with resultant improvement in bone healing. There is evidence that tissue regeneration is stimulated with the use of cytokine-rich adipose derived stem cells (ASCs). We posit that use of ASCs will substantially enhance the quality of vascularity in an irradiated mandibular fracture model.

Methods: Lewis rats (n=37) were divided into 3 groups: mandible fracture (Fx), radiotherapy followed by fracture (XFx), and radiotherapy followed by fracture and adipose-derived stem cell treatment (XFxASC). All experimental groups underwent external fixator placement with surgical creation of a mandibular osteotomy. After a 40-day recovery period, animals were perfused and micro-CT vascular radiomorphometrics were obtained. The measured vessel metrics included volume fraction, number, thickness, and separation were assessed and statistically analyzed using ANOVA.

Results: A statistically significant three-fold increase in vessel volume fraction was seen in both Fx (p=0.001) and XFxASC treatment (p= 0.048) groups when compared to the XFx group. No statistically significant difference was seen in vessel volume fraction between control and ASC groups (p=0.28). Vessel thickness was also significantly higher in Fx (p=0.031) and XFxASC (p= 0.006) groups when compared to XFx groups. While not statistically significant, there were numerically distinctive improvements for vessel number and vessel separation when comparing groups. The XFx group had the expected lowest vessel number at a value of 0.15 mm^{-1}, the Fx group had the highest value of 0.49 mm^{-1}, and the XFxASC group exhibited an intermediate vessel number of 0.27 mm^{-1}. Vessel separation also demonstrated an expected trend with XFx displaying the most sparse vessel characteristics at a vessel separation of 44.9 mm and Fx group with increased vascular presence with a separation of 2.34 mm. Treatment with XFxASC group improved vessel separation from XFx with a value of 0.778 mm, a vascularity improvement that exceeded the Fx group.

Conclusion: Use of ASCs in fracture defects following radiotherapy improves the clinically relevant vascular metrics of vessel volume fraction and vessel thickness. Favorable trends were also noted with the metrics of vessel number and vessel separation. Our results support further study for the potential use of ASCs in restoring vascularity in irradiated bone.