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**Endothelial Progenitor Cells for Healing and Angiogenesis  
in a Segmental Bone Defect Model:  
A Comparison with Mesenchymal Stem Cells**

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**Purpose:** Fracture healing requires a coordinated coupling between osteogenesis and angiogenesis. The purpose of this study was to compare the effects of two types of stem/progenitor cells on the healing of critical sized bone defects in a rat model. Endothelial progenitor cells (EPCs), a novel cell type with previously demonstrated effects on angiogenesis in animal models of vascular disease, were compared to both a control group of no cell therapy, and a treatment group of mesenchymal stem cells (MSCs). The hypothesis was that EPCs would demonstrate both superior bone healing and angiogenesis, when compared to the control group and MSC group.

**Methods:** EPCs and MSCs were isolated from the bone marrow of syngeneic rats by differential culture and grown ex vivo for 10 days. Subsequently the cells were harvested, seeded on a gelfoam scaffold, and implanted into a 5mm segmental defect in a rat femur that had been stabilized with a plate and screws. Bone healing was assessed radiographically and by microCT. Angiogenesis was assessed by histology and physiologically, using laser doppler to assess blood flow in the bone and soft tissues.

**Results:** The EPC group demonstrated radiographic evidence of healing of the bone defect as early as 2 weeks, and all specimens were radiographically healed at 6 weeks. Both the control group and the MSC group showed no radiographic evidence of healing at 10 weeks. MicroCT comparison of the EPC group versus the control group showed significantly greater bone volume and density at the defect site ( $p < 0.001$ ). More blood vessel formation was observed in the EPC group versus the control group on histology at 2 weeks. Laser Doppler assessment showed significantly more soft tissue and bone blood flow at 2 and 3 weeks in the EPC group versus the control group ( $p = 0.021$ ).

**Conclusions:** EPCs are effective as cell-based therapy for healing critical sized bone defects in a rat model. EPCs are superior to mesenchymal stem cells in this model. EPCs demonstrate superior angiogenesis over controls in a rat model of fracture healing. These results strongly suggest that EPCs are effective for therapeutic angiogenesis and osteogenesis in fracture healing.