A Quantitative Assessment of Tissue Engineered Bone

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Approximately 500,000 critical-sized bone defects are treated in the US annually. Autologous bone repairs are concomitant with high donor site morbidity and limited tissue availability. Alternatively, acellular allografts commonly develop microfractures and fail. We assessed the ability of adipose-derived stem cells (ASCs) to restructure xenograft and produce bone when surrounded by periosteum, an osteogenic tissue. We postulated that xenograft would be resorbed and replaced by new bone, with normal bone biomechanical properties.
Methods: Stem cells derived from adipose tissue harvested from three gfp^+ rats were expanded in culture. In each treatment group, a periosteal flap was raised bilaterally from the lateral surfaces of the tibias and wrapped around acellularized bovine bone (xenograft), collagen sponge, and 30 µL of cell culture media. Treatment groups (five Lewis rats each) were differentiated by media stem cell concentration: control (media-only), $1x10^4$, $1x10^6$, and $1x10^8$ ASCs/mL. After 28 days, all animals were scanned with microCT and samples were harvested. Samples obtained from each right leg were subjected to compression testing, while left samples were reserved for histology.
Results: MicroCT analysis revealed significant calcitic tissue deposition external to the xenograft, the volume of which was significantly greater for ASC treatment groups than controls or non-implanted xenograft ($p<0.001$, ANOVA). ANOVA revealed statistically significant differences among treatement groups for failure strength (FS) and Young's modulus ($p<0.001$). Native bone was significantly more elastic (4.81 GPa) than all other treatments (including non-implanted allograft bone). Non-implanted allograft bone was significantly more elastic (3.48 GPa) than allograft implanted with 10^6 stem cells. Native bone resisted compression more than all other treatments (FS=257.90 MPa), while non-implanted allograft exceeded the FS of implanted allografts, independent of stem cell presence (197.98 MPa). Histology revealed osteoclastic activity within the xenograft and osteoblastic deposition in the surrounding tissue.
Conclusions: Stem cell treatment groups had xenografts with lower failure strength and elasticity. This is likely due to widespread resorption in absence of bone deposition within the xenograft. Significant calcitic tissue deposition was observed external to the xenograft in stem cell treated groups. Although unexpected, these results demonstrate the importance of utilizing stem cells in bone tissue engineering.
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