MECHANOBIOLOGICAL INFLUENCES ON ENDOGENEOUS BONE TISSUE ENGINEERING STRATEGIES

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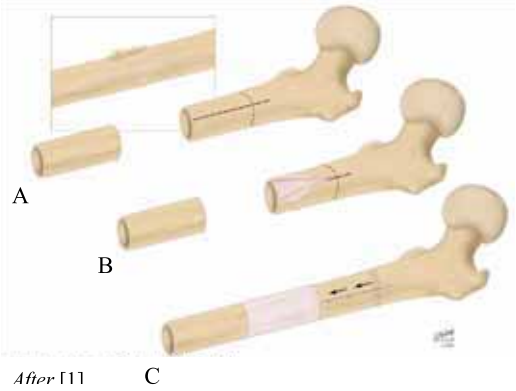
INTRODUCTION

In this study we implemented a previously developed surgical model [1, Figure] to quantify specific mechanobiological influences on endogeneous bone tissue engineering strategies.



After [11]

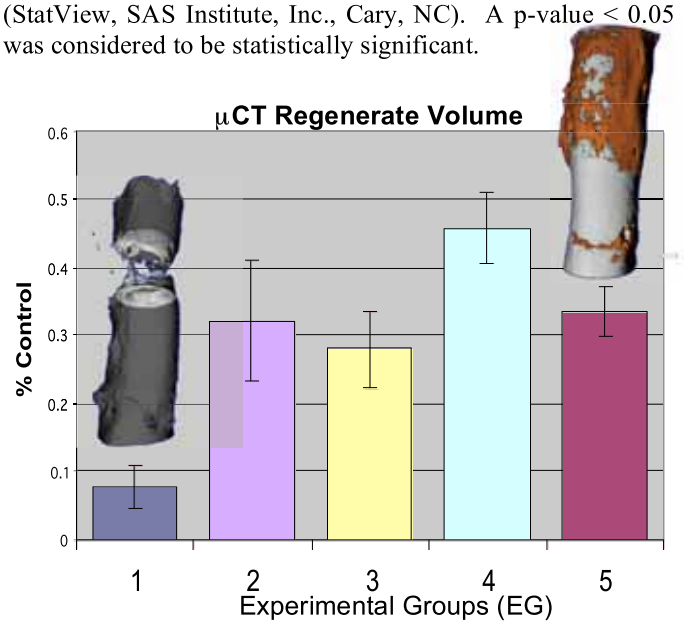
This surgical model allows for osteogenesis, osteoconduction and osteoinduction to take place *in situ*. The **periosteum** serves as a source of osteoprogenitor cells and osteoblastic precursors as well as a well-vascularized tissue bed. The periosteal sleeve also acts as a barrier to ingrowth of fibrous granulation tissue and allows for establishment of chemical gradients, *e.g.* of osteogenic substances, that otherwise could diffuse out to the surrounding soft tissue. In addition, use of vascularized and/or morcellized **bone grafts** may provide osteoblasts for *de novo* bone generation, a scaffold for osteoconduction and/or release of osteoinductive substances from the bony matrix of the host graft. Finally, an intramedullary nail provide mechanical stability for the entire construct. In implementing this model, we aimed to elucidate the influence of mechanics, availability of osteoprogenitor cells (from the periosteum), and autologous bone graft on density and spatial distribution of bone tissue regenerate.

METHODS

An ovine femur model was implemented with a critical size (2.6 cm) diaphyseal defect in skeletally mature, females (n = 35)[‡]. The periosteum was elevated circumferentially off the proximal femoral diaphysis adjacent to the defect. The healthy "donor" bone was then osteotomized (Fig A) and transported distally over a retrograde IM nail to fill the defect (Fig B), thereby creating a new defect around which the healthy periosteum was sutured to form a sleeve (Fig C). The entire construct was stabilized with a custom made, interlocking, retrograde IM nail. Five groups of 7 sheep were investigated. In the control group, no periosteal sleeve enveloped the defect. The sleeve alone enveloped the defect in a 2nd group. Autogenous cancellous bone graft was placed within the sleeve of the 3rd group. Vascularized bone chips were left adhering to the periosteum in the 4th group. Bone graft and adherent bone chips were included in the 5th group.

[‡]All animal protocols were approved by the IACUC.

Mean density and spatial distribution of bone regenerate were calculated from high-resolution (20 μm) μ-CT data sets (Scanco Medical, Bassersdorf, Switzerland). Inter-group differences were assessed using ANOVA and Fisher's protected least significant difference (PLSD) post-hoc tests (StatView, SAS Institute, Inc., Cary, NC). A p-value < 0.05 was considered to be statistically significant.



RESULTS AND DISCUSSION

All groups in which the periosteal sleeve was retained (EG 2-5, Fig.) exhibited significantly greater *volume of regenerate bone* within the defect zone than the group without periosteal sleeve (EG 1, Fig., $p<0.0001$). The addition of bone graft (EG 3) in the defect zone did not increase regenerate volume compared to the periosteal sleeve alone (EG 2). The addition of graft (EG 5) in the defect zone resulted in a significantly decrease in regenerate volume compared to the periosteal sleeve with adherent, vascularized bone chips (EG 4). However, the observed increase in regenerate with addition of adherent, vascularized bone chips (EG 4) was not statistically significant, as compared to the periosteal sleeve alone (EG 2). Currently we are measuring the spatial distribution of the regenerate as a function of distance from the blood supply as well as the neutral axis. These data will allow us to colocalize distance to blood supply as well as predominate modes of mechanical loading (via matrix deformation and/or fluid flow) to spatially-resolved regenerate density data.

CONCLUSIONS

For the first time to our knowledge, this experimental model provides a novel means to elucidate the relative influence of intrinsic and extrinsic factors on successful functional engineering of bone tissue replacements.

REFERENCES [1] Knothe U, Springfield DSS, *World J Surg Onc*, 2005. [2] Ritzman *et al. Trans ORS*, 2005.