In Vivo Evaluation of STRUCSURE™ CP for Augmentation of Segmental Defect Healing

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Statement of Purpose: Segmental bone defects are often associated with delayed healing or nonunion. The gold standard treatment for these clinically challenging defects is autograft, which has drawbacks of donor site availability and morbidity. STRUCSURE™ CP (Smith and Nephew, Memphis TN), a porous injectable calcium phosphate based bone graft substitute with indications for use in complex fractures and joint replacements, may also promote growth in segmental defects. In this study, the ability of STRUCSURE™ CP to augment segmental bone defect healing was evaluated in rabbit radii.

Methods: Full-thickness segmental radial defects 2.0 cm in length were created approximately 1.5 cm from the right carpus in male New Zealand White rabbits (approximately 3kg, 14-week-old), using a gas-powered dental drill. Defects were then filled with one of three treatments (n=5 per group): fresh morselized autograft (positive control), empty defect (negative control), and Smith & Nephew's STRUCSURE™ CP Macroporous Calcium Phosphate Bone Graft Substitute.
STRUCSURE™ CP implants were prepared according to the manufacturer's instructions by mixing the powder and liquid components for two minutes using a closed mixing and injection device.[1] Immediately following placement of the implants, the soft tissue and skin were sutured separately, and post-surgical radiographs were taken. Rabbits were sacrificed at four weeks and eight weeks, and the entire right forelimb was recovered. MicroCT images were taken, and radiographs were reconstructed with ImageJ software. Tissue samples then underwent decalcified histological processing and were stained with hematoxylin and eosin (H&E) and Goldner's trichrome. Using BIOQUANT imaging software, the amount of bone per defect area was quantified. A semi-quantitative scoring system based on the method of Karaoglu et al. was used to assess the bone quality.[2] The reconstructed radiographs were also analyzed for amount of bone formation and degree of remodeling using a semi-quantitative scoring system based on the method described by Karaoglu et al.[2] Data was analyzed using single-factor analysis of variance (ANOVA) followed by Student-Newman-Keuls post-hoc tests with a significance level of 5%.

Results: Defects treated with STRUCSURE™ CP had more increased bone per defect area in histological sections than the empty defect group at eight weeks (p=0.034) (Figure 1a). The amount of bone in the autograft group was also significantly higher than that in the empty defect group (p=0.031). By eight weeks, the autograft and STRUCSURE™ CP samples displayed almost complete bone filling of the defect site. Unexpectedly, the negative control group also had a considerable amount of bone present. The total radiographic scores for all three groups increased over time (Figure 1b). At four weeks, both the autograft

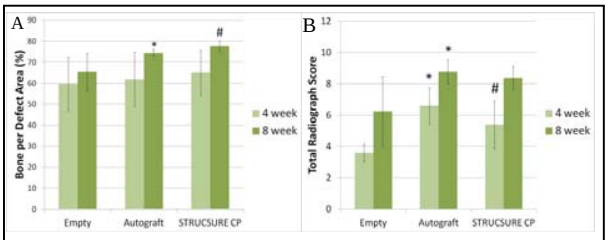

Figure 1. A.)Percent bone per defect area at four weeks and eight weeks. B.)Total radiograph score (out of 10) at four weeks and eight weeks. Data presented is mean ± standard deviation.* represents statistical difference in autograft compared to empty defect. # represents statistical difference in STRUCSURE CP group compared to empty defect.

(p=0.004) and STRUCSURE™ CP (p=0.028) groups had higher radiograph scores than the empty defect group. At eight weeks, the autograft radiograph score was significantly higher than empty defects (p=0.047), while the STRUCSURE™ CP group approached statistical difference from the empty negative controls (p=0.053). No differences in total radiograph scores were detected between the autograft and STRUCSURE™ CP groups. At four weeks, very little residual STRUCSURE CP implant material (0.2 ± 0.2 % per defect area) was evident by visual observation in histological sections, and by eight weeks no residual material was observed.

Conclusions: STRUCSURE™ CP provides an osteoconductive matrix to promote bone ingrowth into defects, improving quality and rate of bone healing over no treatment. In this study, the STRUCSURE™ CP material performed similarly to the positive control autograft group in a segmental defect model. Histological observations indicated that STRUCSURE™ CP had resorption at an appropriate rate to allow bone ingrowth and minimal inflammatory response. Although increases in total radiograph scores for STRUCSURE™ CP group were not statistically significant compared to the negative control group at 8 weeks, differences may have been detected if larger sample numbers had been used in the study. Another limitation possibly minimizing detection of significant differences was the unexpected degree of bone growth in empty defects, which may have been due to skeletal immaturity of young rabbits as well as the proximity of the ulna.

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References:

1. http://global.smith-nephew.com/cps/rde/xbcr/smithnephewls/STreference.pdf.
2. Karaoglu S. Injury 2002;33(8):679-83.