DEMINERALIZED BONE MATRIX PROVIDES EQUIVALENT RESULTS TO AUTOGRAFT IN STANDARD POSTEROLATERAL FUSION MODEL IN ADULT RABBITS

W.R. Walsh, R. Oliver, Y. Yu, D.J. Bell, P. Pak and N. Russel
Surgical & Orthopaedic Research Laboratories and University of New South Wales
Prince of Wales Hospital, Sydney, Australia

Demineralized Bone Matrix Provides Equivalent Results to Autograft in Standard Posterolateral Fusion Model in Adult Rabbits

W.R. Walsh, R. Oliver, Y. Yu, D.J. Bell, P. Pak and N. Russel

Surgical & Orthopaedic Research Laboratories and University of New South Wales, Prince of Wales Hospital, Sydney, Australia

ABSTRACT

Achieving fusion between two bony segments represents a challenge to surgeons. Autograft is often considered the "Gold Standard" for fusion, but its use has well reported limitations including donor site morbidity, increased operative time and potential blood loss. Demineralized bone matrix (DBM) provides surgeons with an alternative to autograft, providing osteoinductive factors known to be involved in healing.

This study compared the *in vivo* results of a commercially available DBM (AlloFuse®, AlloSource®, Centennial, CO) to autograft and empty controls in a standard posterolateral fusion model in adult New Zealand (NZ) white rabbits.

The L5-L6 rabbit spine model of Boden et al.[1] was used in this study on 14 adult rabbits. Radiographic analysis, uniaxial tensile testing and peak load testing were performed at 6, 12 and 26 weeks following surgery.

The results of the study support the equivalence between autograft and DBM. The DBM was able to facilitate fusion with normal bone healing with time. Pre-clinical evidence suggests that AlloFuse DBM may provide a suitable alternative to autograft for routine bone grafting procedures.

Introduction

Achieving fusion between two bony segments represents a challenge to the surgeon as well as the patient. Improvements in surgical technique and patient selection, coupled with advances in our understanding of the cascade of bone healing, continues to improve patient outcomes.

Autograft is often considered the "Gold Standard" in fusion. The use of autograft has well reported limitations including donor site morbidity, increased operative time and potential blood loss. Demineralized bone matrix (DBM) provides surgeons with an off-the-shelf alternative to autograft, providing a complex cascade of osteoinductive factors known to be involved in healing.

This study compared the *in vivo* results of a commercially available DBM (AlloFuse, AlloSource, Centennial, CO) to autograft and empty controls in a standard posterolateral fusion model in adult New Zealand (NZ) white rabbits.

The purpose of this study was to evaluate the:

1. macroscopic and radiographic appearance of the fusion at 6, 12 and 26 weeks
2. fusion masses based on three dimensional computed tomography models at 6, 12 and 26 weeks
3. mechanical properties of the fusion at 12 weeks
4. histological appearance at 6, 12 and 26 weeks

* Stimublast™ is a registered trademark of AlloSource and is a product comprised of the same components and formulation as AlloFuse.

Methods

The L5-L6 rabbit spine model of Boden et al.[1] was used in this study *(Figure 1)* on 14 adult rabbits. This model duplicates the surgical technique, mechanical environment and biology of graft incorporation associated with a posterolateral inter-transverse process fusion in humans. The surgical model and experimental endpoints used in this study are identical to those reported recently by Walsh et al.[2]

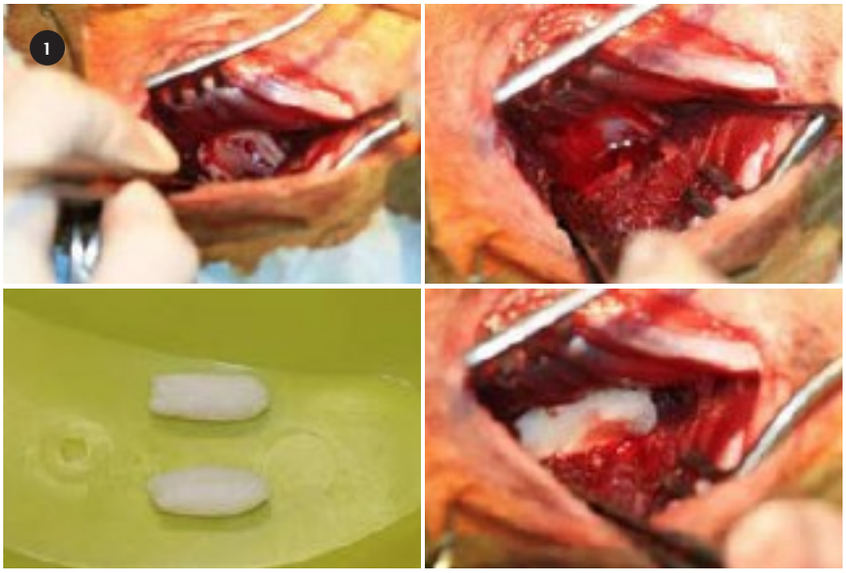


Figure 1. The transverse processes were exposed, decorticated and the DBM (1.5 cc per side) or autograft (1.5 cc per side) implanted.

Animals were euthanized at 6, 12 and 26 weeks following surgery. A sample size of n=3 per group was used at 6 and 26 weeks while n=8 per group was used at 12 weeks.

The endpoints included routine posteroanterior Faxitron (Faxitron Bioptics, Tucson, AZ) radiographs as well as computed tomography (CT). Three dimensional reconstructed views were created from CT data with Mimics software (Materialise, Belgium) using a threshold analysis technique. Images were examined in the axial, sagittal and coronal planes to assess the overall quality of the fusion mass.

Uniaxial tensile testing was performed at a displacement rate of 0.5 cm/min using an MTS 858 Bionix Testing Machine (MTS, Eden Prairie, MN) for the 12 week group only. Samples were dissected so that only the new bone formed between the vertebral bodies and the fusion mass participated to resist the tensile load.

The peak load, stiffness and energy to peak load were determined for all samples. The highest point of the graph was taken as the peak load. The stiffness in the linear region of the curve based on a linear regression was calculated. The energy was taken as the area under the curve to the peak load. Data was analyzed using analysis of variance (ANOVA) with Statistical Product and Service Solutions (SPSS) (IBM, Amonk, NY).

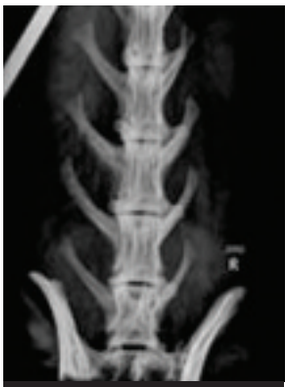
Samples were fixed in phosphate buffered formalin for a minimum of 48 hours. Spines in the 6 and the 26 week groups were fixed immediately following euthanasia. Spines in the 12 week group were fixed following mechanical testing. Spines were decalcified in 10% formic acid-phosphate buffered formalin at room temperature. The decalcified spines were sectioned in the sagittal plane for haemotoxylin and eosin (H&E) and tetrachrome staining. Stained sections were examined under light microscopy using an Olympus Microscope (Olympus, Japan). Histology was qualitatively assessed versus time at each time point and a summary written.

* Stimublast™ is a registered trademark of AlloSource and is a product comprised of the same components and formulation as AlloFuse.

Results

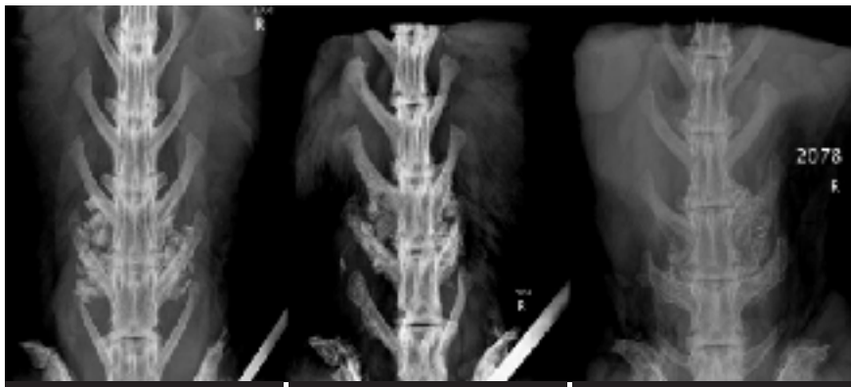
Radiographs revealed a progression of bone formation in the autograft and the DBM groups at both the 12 and 26 week time points. Fusion was achieved in both groups by 12 weeks, while the empty decorticated controls showed some reaction on the decorticated transverse processes without fusion. Three dimensional reconstructed CT images show similar results with clear evidence of bone formation in both the autograft and DBM groups at the 12 and 26 week time points. Mechanical properties of the autograft and DBM specimen showed increased stiffness and tensile strength as compared to the control.

Empty decorticated control



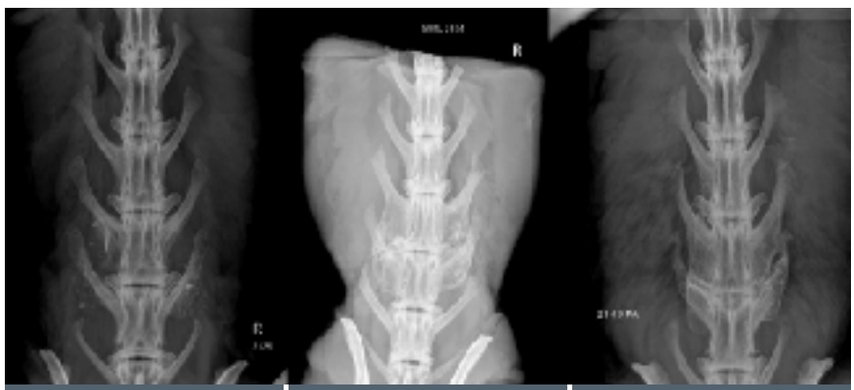
12 weeks

Autograft



6 weeks | 12 weeks | 26 weeks

AlloFuse



6 weeks | 12 weeks | 26 weeks

Figure 2. Radiographs show bone formation at the 12 and 26 week time points for both the autograft and DBM specimens.

The empty decorticated control did not show evidence of bone formation at the 12 week time point.

26 weeks CT - autograft | 12 weeks – empty decorticated defect | 26 weeks - DBM

Figure 3. Three dimensional reconstructed CT images show clear evidence of bone formation in both the autograft and DBM specimens. No bone formation appears in the control specimen.

* Stimublast™ is a registered trademark of AlloSource and is a product comprised of the same components and formulation as AlloFuse.

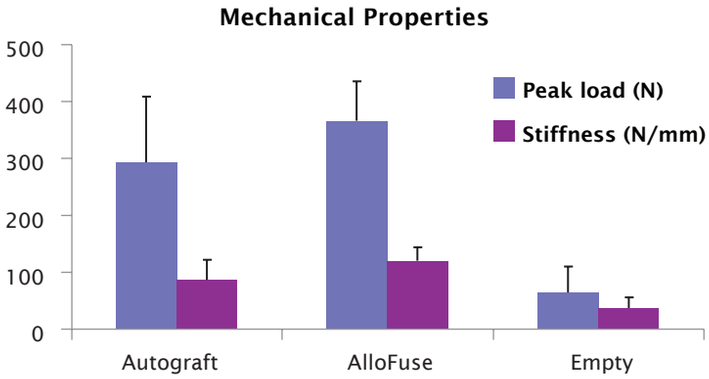
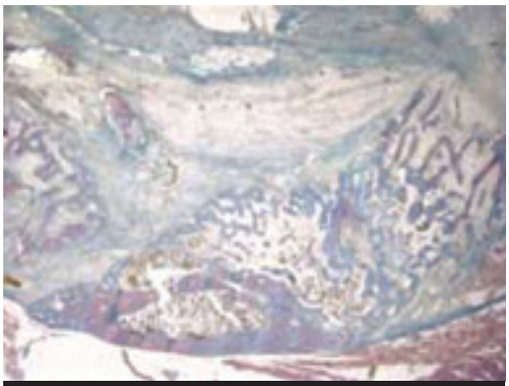
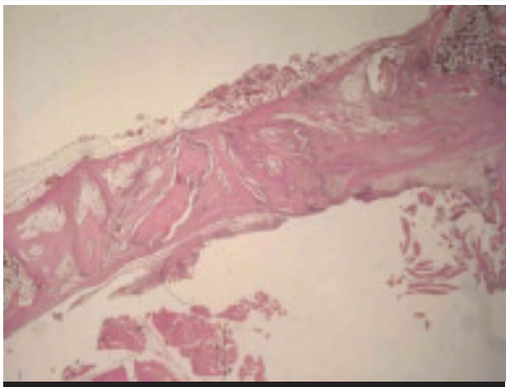


Figure 4. No statistical differences were detected between the tensile properties for fusions treated with autograft and DBM while both were superior to the empty decorticated controls.

Autograft

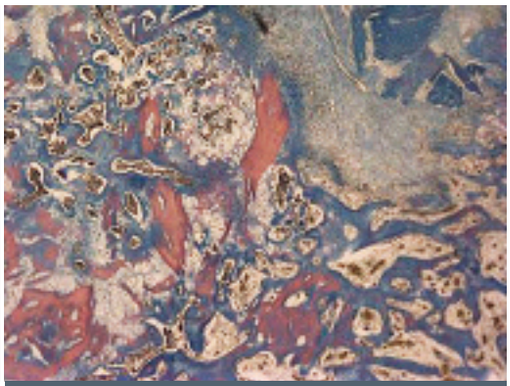


6 weeks

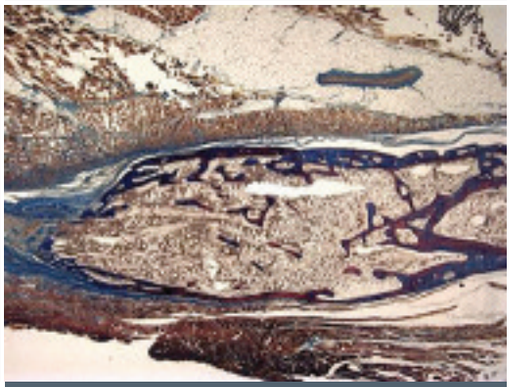


6 weeks

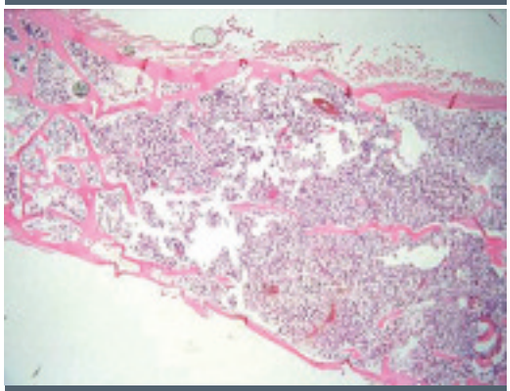
AlloFuse



6 weeks



6 weeks



26 weeks

Figure 5. Histology at 6 weeks: autograft and AlloFuse revealed new bone formation. Endochondral ossification was evident in the DBM group adjacent to the DBM particles.

Histology at 26 weeks: DBM shows a mature mass with a normal cortex and normal marrow space.

* Stimublast™ is a registered trademark of AlloSource and is a product comprised of the same components and formulation as AlloFuse.

Conclusion

The results of the current study support the equivalence between autograft and DBM. The DBM was able to facilitate fusion with normal bone healing with time. Pre-clinical evidence suggests that AlloFuse DBM may provide a suitable alternative to autograft for routine bone grafting procedures.

References:

1. Boden et al., Delivery of recombinant human bone morphogenetic protein-2 using a compression-resistant matrix in posterolateral spine fusion in the rabbit and in the non-human primate, 27(4): p. 353-60, Feb 15 2002.
2. Walsh, W.R., F. Vizesi, D. Michael, J. Auld, A. Langdown, R. Oliver, Y. Yu, H. Irie, and W. Bruce, beta-TCP bone graft substitutes in a bilateral rabbit tibial defect model [epub ahead of print] [Record Supplied By Publisher]. Biomaterials, 2007.

* Stimublast™ is a registered trademark of AlloSource and is a product comprised of the same components and formulation as AlloFuse.

6278 S Troy Cir
Centennial, CO 80111

MAIN 720. 873. 0213
TOLL FREE 800. 557. 3587
FAX 720. 873. 0212

allosource.org