BONE FORMATION THROUGH OSTEOINDUCTION SUPPORTED BY A NEW FORM OF DEMINERALIZED BONE AS DEMONSTRATED IN THE ATHYMIC RAT

Data on File
Osteotech Inc.
51 James Way, Eatontown, NJ 07724

SUMMARY

A novel form of human bone allograft was constructed by forming milled, elongate demineralized fibers into a freeze-dried, flexible 'Bone Sheet'. Over the course of two separate experiments, three formulations of the Bone Sheet were implanted intramuscularly and subcutaneously into athymic rats, along with human demineralized bone matrix powder (hDBM), hDBM Fibers (Fibers), and rat demineralized bone matrix powder (rDBM). Devitalized forms of each implant type were used as negative controls. Implant materials were retrieved at 28 days and analyzed histologically. Results showed that the Bone Sheets, Fibers, hDBM, and rDBM demonstrated an osteoinductive response.

INTRODUCTION

A new demineralized allograft implant form was developed in order to address a principal limitation of particulate bone: possible migration from the site. It is also believed that by providing a contiguous mass of DBM, the osteoconductive portion of new bone formation stimulated by these implants may be guided along the matrix to improve the chances for successful bony bridging.

This new graft is in the form of a flexible sheet several millimeters in thickness and may prove to be useful for filling a skeletal defect when there is concern of implant wash-out or migration. This study was performed to assess the osteoinductivity of this material when implanted in rodents. The response was compared with other forms of human and rat DBM. In order to separate the osteoinductive response from any osteoconductive effects, the test articles were implanted ectopically (intramuscular and subcutaneous). The athymic rat was selected as the animal model to reduce the potential for cross-species incompatibility to human tissue implants.

TEST ARTICLE PREPARATION

The raw material for the sheets was produced by milling cortical shafts into elongate fibers, followed by a demineralization reaction utilizing hydrochloric acid. The wet fibers were then formed into a sheet and lyophilized. The human and rat DBM powders were produced using standard Osteotech demineralization procedures and classifying the lyophilized powder to a range of 100-500 microns. An additional test article was prepared by lyophilizing fibers that had been demineralized but had not been formed into a sheet. Negative controls were prepared by devitalizing Bone Sheets, Fibers, hDBM, and rDBM using a 4N guanidine hydrochloride extraction.

IMPLANTATION

Intramuscular implants were performed by placing test articles between bluntly dissected semimembranosus and adductor magnus muscle groups of the hind limb. Subcutaneous implants were inserted at the thorax and placed so that they rested between the medial forelimb and chest. Each animal received two intramuscular or two subcutaneous implants.

RESULTS

All devitalized implants showed no new bone formation and no osteoblastic activity. In general, the Bone Sheets, Fibers, and powder materials all showed significant new bone formation and osteoblastic activity. A consistent observation was the great variation in neovascularization induced by the implant materials. The variation appears not to be linked to the type of implant, although one of the Bone Sheet formulations did demonstrate extensive vascularization quite consistently. At least one implant type (rDBM) was relatively more osteoinductive in intramuscular sites but demonstrated no bone formation in subcutaneous sites, indicating that the intramuscular model may be a more useful indicator of osteoinductive potential.

In some animals no new bone formation was noted at either treatment site, suggesting differences between animals in their ability to respond to the implants. It is possible that these animals may not have been competent in the formation of ectopic bone and therefore these animals were excluded from some portions of data analysis.

CONCLUSIONS

The athymic rat ectopic bone formation model, especially when used with intramuscular placement, presents the full range of bone formation responses from none for devitalized materials to highly responsive for rDBM and inductive formulations of human demineralized bone. The results demonstrate an osteoinductive response is elicited by Bone Sheets, Fibers, and hDBM powder. The conclusion drawn from this study is that a flexible Bone Sheet formed from human demineralized bone fibers can demonstrate an osteoinductive response that is similar to the response induced by particulate human DBM.