

IN VIVO OSTEOINDUCTIVITY ASSESSMENT OF A DBM-BASED CARRIER

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Abstract

The osteoinductive potential of a proprietary DBM-based Accell® carrier (IsoTis OrthoBiologics, Inc., Irvine, CA) was assessed in the athymic mouse muscle pouch assay. Histological sections of the implant sites were obtained at 28 days post-implantation and analyzed for new bone formation. Corresponding alkaline phosphatase levels associated with the explants were also measured. All animals implanted with the Accell carrier demonstrated robust bone formation at 28 days through either the intramembranous pathway, endochondral pathway or a combination of both.

Introduction

IsoTis OrthoBiologics' second generation Accell technology provides a highly osteoinductive demineralized bone matrix (DBM) carrier that is also used as the delivery vehicle for DBM particles, thereby eliminating the need for an inert carrier. An inert carrier is added to first generation DBM grafts as a mechanism to keep particulate DBM contained at the surgical site. The inert carrier is present strictly for handling and graft containment purposes and does not provide additional osteoinductivity.

Because of differences in bone forming characteristics between individual donors and tissue banks, measurement and confirmation of osteoinductivity plays an imperative role in predicting the success of the DBM implant.¹ Realizing the importance of assuring the bone forming potential of their grafts, IsoTis tests every lot of DBM in a quantitative *in vitro* assay. Only DBM that reaches a threshold alkaline phosphatase level compared to a positive and negative control is used in the production of their implants. Alkaline phosphatase is a by-product of mesenchymal stem cells differentiating into osteoblasts, bone-forming cells. Additionally, the osteoinductivity of the Accell carrier derived from DBM particles has been confirmed using the

classic Urist model, which represents a well accepted method for measuring bone forming potential.²

Materials and Methods

Employing the classic Urist model that assesses osteoinductive potential, the Accell carrier was implanted into quadriceps muscle pouches of six athymic mice that were sacrificed 28 days post-implantation. Histological sections stained with hematoxylin and eosin were prepared from each explant and analyzed for new bone formation. Levels of alkaline phosphatase associated with the explants were also assessed. All implantations and analyses were performed by an independent laboratory.

Results

The Accell carrier was found to be osteoinductive based on both histological and quantitative alkaline phosphatase levels. Histologically, new woven bone was seen in all six animals. Four out of six animals showed robust new woven bone being formed primarily through the intramembranous pathway surrounding healthy fatty marrow (Figures 1-2). The remaining two animals showed new woven bone formation through both the intermembranous and endochondral pathways (Figures 3-4). A high alkaline

phosphatase level in all explants further supported the osteoinductivity of the Accell carrier and was consistent with the histological findings.

Conclusion

When used as an alternative to inert carriers for DBM particles, the Accell DBM-based carrier provides an osteoinductive substitute resulting in a graft that is 100% osteoinductive. Further experiments are required to quantify the increased bone forming potential of the final product that results when the osteoinductive Accell carrier is combined with DBM particles.

References

- 1 Blum N, Moseley J, Miller L, et al. Measurement of bone morphogenetic proteins and other growth factors in demineralized bone matrix. *Orthopedics* 2004;2:161-5.
- 2 Urist MR. Bone: formation by autoinduction. *Science* 1965;150:893-9.

FIGURE 1

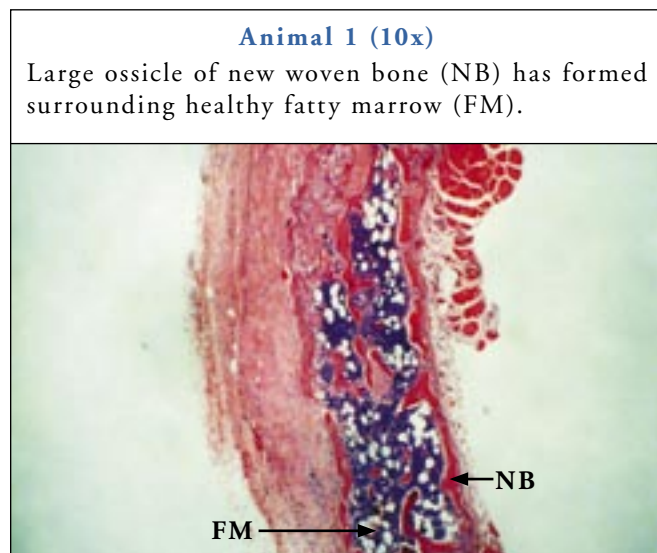


FIGURE 2

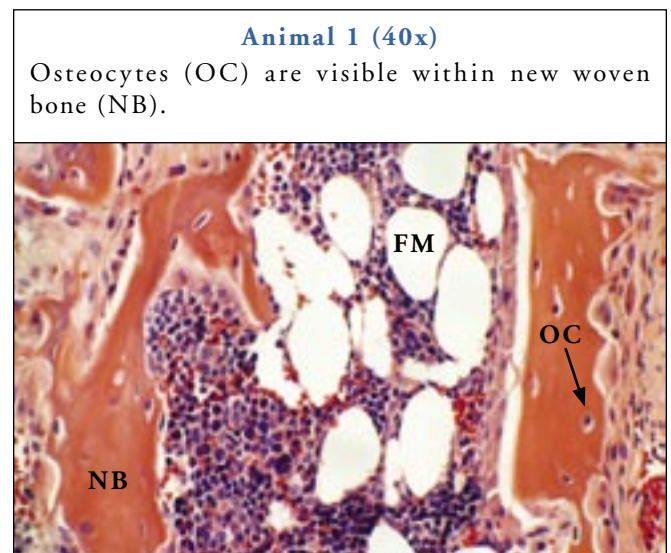


FIGURE 3

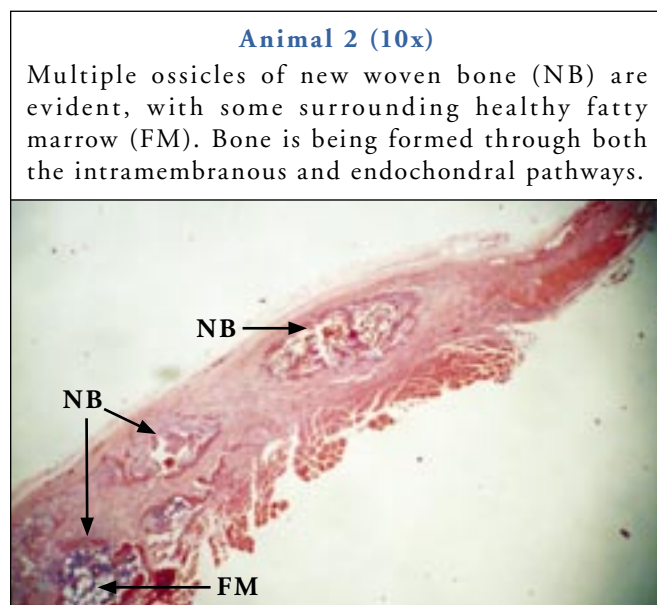


FIGURE 4

