ReadiGRAFT® BLX DBM Fibers & Cancellous

Engineered to provide Osteoinductive potential and an Osteoconductive scaffold

Demineralized cortical fibers provide potential growth factors necessary for bone healing and growth.

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Saving Lives. Restoring Health. Giving Hope.

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Introduction

ReadiGRAFT BLX DBM Fibers & Cancellous is a proprietary mix of demineralized cortical fibers and mineralized cancellous chips. This mix is specifically engineered to maintain osteoinductive potential and osteoconductive properties of the graft. The graft provides the surgeon the operative flexibility to customize hydrating options to fit patient's needs. It is a safe and effective choice in a clinical setting and offers lower supply cost than processed DBM's (with carrier) and growth factors (rhBMP, Infuse®).

ReadiGRAFT BLX DBM Fibers & Cancellous utilize key LifeNet Health technologies. The cortical fibers are demineralized with the patented and proprietary PAD® process. This process targets optimal residual calcium levels without damaging the grafts inherent osteoconductive and osteoinductive potential.[1,2,3,4,5] Additionally the graft is processed with Allowash XG®, a cleaning and sterilization process that provides a sterility assurance level of 10^{-6}.

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Features & Benefits

Optimal Scaffold for Cellular Attachment

- The natural interconnected porous architecture of cancellous bone and the increased surface area of demineralized cortical fibers provide an optimal scaffold for cellular attachment and proliferation and vascular in-growth.

Contains Natural Growth Factors

- The cortical fibers are demineralized using LifeNet Health's patented and proprietary PAD process. This process carefully exposes natural growth factors trapped within the cortical bone while maintaining the inherent osteoinductive potential.

100% Natural Bone Matrix

- ReadiGRAFT BLX DBM Fibers & Cancellous is comprised of 100% natural bone matrix which is remodeled naturally during the bone healing process. It contains no fillers or carriers commonly used in bone putties, pastes, and gels.

Customizable Hydration

- Absorbs and retains bioactive fluids like blood, Platelet Rich Plasma (PRP), and Bone Marrow Aspirate (BMA). This allows the surgeon to customize the hydration option to fit patient's needs.

Osteogenic Potential

- Bone marrow aspirate (BMA) and autologous tissue may contain bone forming cells and osteoprogenitor cells. These osteogenic components may be combined with ReadiGRAFT BLX Fibers & Cancellous.

Rehydration Guide:

1. When ready to begin hydration; remove foil stock lid from plastic tray containing demineralized fibers & cancellous chips
2. Mix the graft with the desired hydration fluid directly in the plastic tray containing graft material. After mixing fluid and graft material in plastic tray; five minute incubation time is recommended as the freeze dried bone material absorbs and retains the hydration fluid.
    - The graft may be hydrated with the following options
        * Bone Marrow Aspirate (BMA)
        * Platelet Rich Plasma (PRP)
        * Whole Blood
        * Saline
        * Antibiotic Solution
        * Other
    - It is recommended to use 1 cc of hydrating fluid per 1 cc of the graft.
    - When BMA, PRP, or Whole Blood are used; allow the combination of fluid and graft to clot. This will improve handling and containment of graft at surgical site.
3. The graft material may be mixed with any amount of autologous tissue collected during the procedure
    - The autologous bone may be passed through a bone grinder prior to mixing with graft.
    - The grinding of autologous tissue will complement the handling and packing characteristics provided by the DBM fibers.
4. The graft is now moldable and ready to be implanted in the surgical space.

Clinical Examples

ReadiGRAFT BLX DBM Fibers & Cancellous is a specifically engineered graft matrix providing the porosity, surface area, and osteoinductive potential necessary for bone healing and growth. It should be used as a bone void filler for defects in the skeletal system (e.g. CMF, extremities, spine, and general orthopedics). These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone.

Spine

Posterolateral Fusion

- Pack graft material around the screws and wires implanted in the pedicles and between transverse processes in the back of the spine.

Interbody Fusion

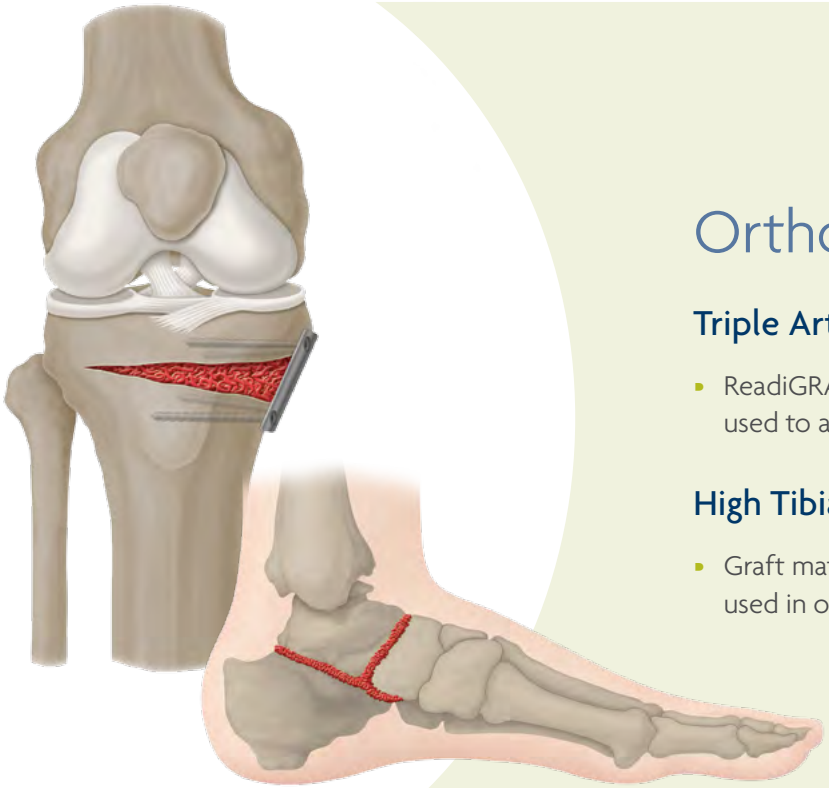
- Pack graft material in and around allograft implant; filling allograft void and packing into space.

Cranio-maxillofacial

Reconstruction of Mandible

- Pack graft material into void in mandible created due to tumor resection
- Graft material may be packed around a rib implanted due to significant traumatic injury

See disclaimer on page 8.



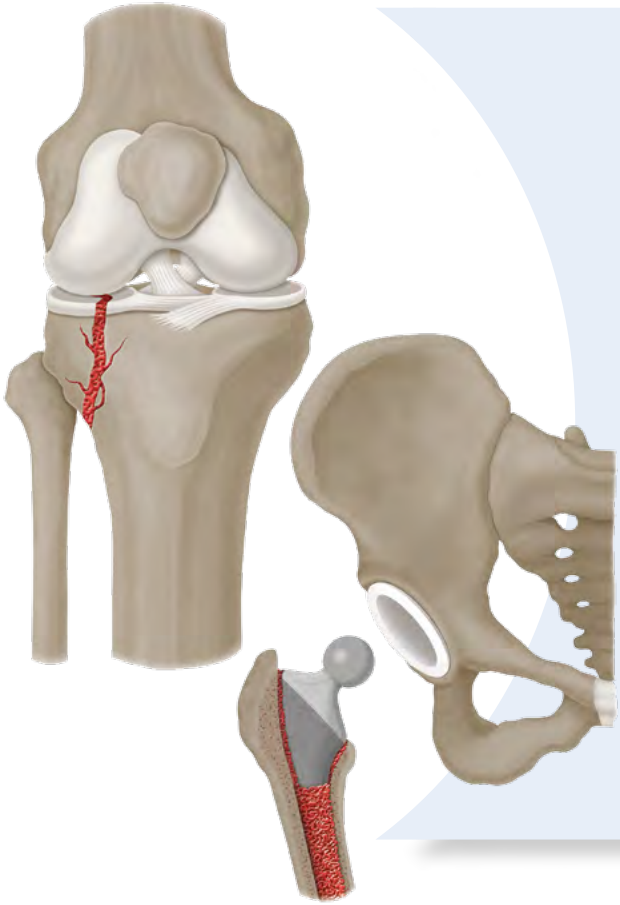
Orthopedics

Triple Arthrodesis Procedure

- ReadiGRAFT BLX DBM Fibers and Cancellous may be used to augment a triple arthrodesis procedure

High Tibial Osteotemy

- Graft material is used to augment wedges and hardware used in osteotemy procedures in the knee



Orthopedics

Hip Revision

- Osteoinductive potential of graft will complement bone growth and incorporation of implanted stem

Trauma – Tibial Plateau Fracture

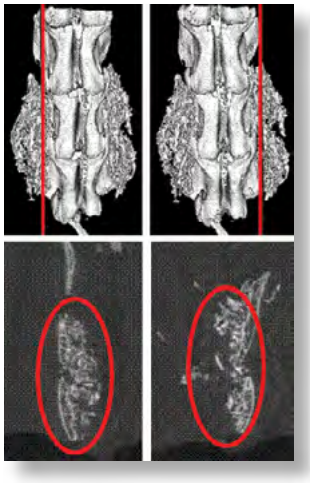
- Graft material is used to augment fracture of bone prior to fixation with plate and screws

Proven Performance in an Animal Fusion Model

Radiography:

The DBM fibers/cancellous chip induced a 100% fusion rate, with four out of the six animals demonstrating bilateral fusion. A representative radiographic image is shown in Figure 1.

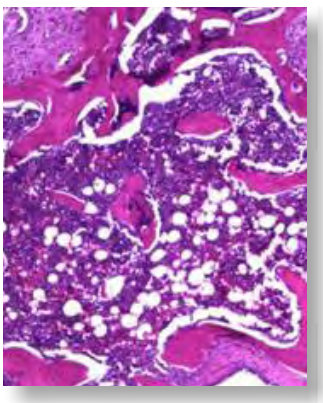
Figure 1: Representative radiograph image with the fusion masses highlighted in red.



MicroCT:

Similar to the radiography, a 100% fusion rate was observed, with five out of the six animals had bilateral fusion. Representative MicroCT images showing dense fusion mass are shown in Figure 2.

Figure 2: Representative MicroCT Images showing bilateral fusion. Top row - the red line indicates the plane of the cross sectional image. Bottom row - cross sectional image of the image above with the red circle highlighting the fusion mass.



Histology:

Complete spinal fusion was seen in all samples. The DBM fibers proved to be osteoinductive, inducing new bone and bone marrow formation (Figure 3). Histology samples showed new bone and bone marrow formation (Figure 3).

Figure 3: Representative histology of DBM fibers explant fusion mass, H&E stained, which shows new bone and bone marrow formation.

Conclusion

The bone void filler containing DBM fibers and cancellous chips showed successful spinal fusion in the athymic rat PLF model. A 100% fusion rate was observed in both radiography and MicroCT. Additionally, histology analysis indicated that the amount of new bone was directly related to the amount of DBM fibers present, indicating the importance of the osteoinductive potential of the DBM fibers in spinal fusion.

**Data on file at LifeNet Health.

Clinical Compendium

1. Effect(s) of the demineralization process on the osteoinductivity of demineralized bone matrix. *Zhang M, Powers R M, and Wolfinbarger L. J Periodontol 1997; 68:1085-1092*

   "The effects of variable residual calcium levels, variable particle sizes, and donor age and gender were studied using a tissue culture based bioassay (in vitro) as well as an athymic mouse (in vivo) bioassay."
   "...bone demineralized to levels of approximately 2% residual calcium provided for maximum osteoinductive potential in both assay systems."

2. The affects of residual calcium in decalcified freeze-dried bone allograft in a critical-sized defect in the Rattus norvegicus calvarium. *Turonis JW, McPherson JC 3rd, Cuening MF:. J Oral Implantol. 2006;32(2):55-62*

3. Effects of Varying degrees of Allograft Decalcification on the Cultured Porcine Osteoclast cells. *Herold RW, Pashley DH, Cuening MF J Periodontol. 2002 Feb; 73(2):213-9*

   "In this in vitro model, porcine osteoclasts show significantly more resorptive activity as measured on calcium phosphate-coated disks in the presence of 2.41% residual calcium in DFDBA than in other DFDBA residual calcium levels."

4. Enhancement of osteoblast proliferation in vitro by selective enrichment of demineralized freeze-dried bone allograft with specific growth factors. *Mott DA., Mailhot J, Cuenin MF, Sharawy M, Borke J; J Oral Implantol 2002;28(2):57-66*

5. BMP depletion occurs during prolonged acid demineralization of bone: characterization and implications for graft preparation. *Pietrzak WS, Ali SN, Chitturi D, Jacob M, Woodell-May JE. Cell Tiss. Bank 2007 (Published on line)*

6. DBM Fibers and Cancellous Bone Induce Spinal Fusion in the Athymic Rat PLF Model. *Triplett S, Gonzales K, Chen S. LifeNet Health, 68-20-031.01*

   "The bone void filler containing DBM fibers and cancellous chips showed successful spinal fusion in the athymic rat PLF model. A 100% fusion rate was observed in both radiography and MicroCT. Additionally, histology analysis indicated that the amount of new bone was directly related to the amount of DBM fibers present, indicating the importance of the osteoinductive potential of the DBM particles in spinal fusion."

7. Perioperative and long-term complications of iliac crest bone graft harvesting for spinal surgery: a quantitative review of the literature. *Gupta AR, Shah NR, Patel TC, Grauer J. International Medicine. 2001, 8(3), 163-166.*

   "Iliac crest bone graft harvesting for spine surgery has significant associated morbidity with close to one third of patients experiencing donor site pain two years postoperatively. Recognition of this morbidity may encourage research and development of alternative graft material."

8. Influence of irradiation on the osteoinductive potential of demineralized bone matrix. *Weintroub S, Reddi AH. Calcif Tissue Int. 1988, 42(4), 255-60.*

   "Samples of demineralized bone matrix (DBM) were exposed to graduated doses of radiation (1-15 Megarad) utilizing a linear accelerator and then implanted into the thoracic region of Long-Evans rats...The dose of radiation (2.5 Mrad) currently used by bone banks for sterilization of bone tissue did not destroy the bone induction properties of DBM. Furthermore, radiation of 3-5 Mrad even enhanced bone induction."

9. Fixation of tibial plateau fractures with synthetic bone graft versus natural bone graft: a comparison study. *Ong JC, Kennedy MT, Mitra A, Harty. Ir J Med Sci. 2012, 181(2), 247-52.*

   "Maintenance of knee flexion was found to be better in the allograft/autograft group when compared between the groups...Use of autologous/allogenic bone graft allows better recovery of long-term flexion, possibly due to reduced inflammatory response compared with synthetic bone composites."

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Freeze Dried Code	Description
DF-1002	2 cc
DF-1003	5 cc
DF-1006	10 cc
DF-1004	15 cc
DF-1005	30 cc

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LifeNet Health helps to save lives, restore health and give hope to thousands of patients each year. We are the world's most trusted provider of transplant solutions, from organ procurement to new innovations in bio-implant technologies and cellular therapies—a leader in the field of regenerative medicine, while always honoring the donors and healthcare professionals that allow the healing process.

*This guide is provided as an educational tool and clinical aid to assist properly licensed medical professionals in the usage of specific LifeNet Health grafts. As past of this professional usage, the medical professional must use their professional judgment in making any final determinations in product usage and technique. In doing so, the medical professional should rely on their own training and experience and should conduct a thorough review of pertinent medical literature.

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