DEGRADATION AND REMOVAL OF THE GRAFT DELIVERY BAG COMPONENT OF MAGNIFUSE™ BONE GRAFT
In recent years, as surgeons have sought new ways to achieve healing while avoiding morbidity at an iliac crest donor site, numerous materials have been used in posterior fusion procedures. Demineralized bone allograft, an osteoinductive and osteoconductive grafting material, is commonly used in posterior fusions as a bone void filler or a bone graft extender. As surgeons have developed experience with such materials, their abilities have been prominent. Fiber based demineralized bone forms such as those of the Grafton™ products have shown enhanced osteoconductivity relative to particle based formulations.¹

Yet certain clinical issues remain for grafting products in posterior fusion:

- Graft migration can limit the healing capabilities of the graft²
- Certain carriers limit the cell access to the healing scaffold²
- Radiographic placement confirmation is very difficult for demineralized bone grafts⁴
- Intraoperative modifications to placement require that the graft be collected in a container and then re-applied

Magnifuse™ Bone Graft was developed to address such issues, while retaining the enhanced osteoconductivity relative to particle based formulations which are known from the Grafton™ fiber-based demineralized bone products.

Magnifuse™ Bone Graft is demineralized human allograft bone fibers combined with surface demineralized cortical bone chips, all contained in a bioresorbable polyglycolide mesh enclosure. It provides an osteoinductive, osteoconductive, radiopaque, repositionable graft (Figure 1).

The purpose of this document is to address the bioresorbable containment mesh used in Magnifuse™ Bone Graft: What it is, how it degrades, and where those degradation products go as the graft is being incorporated into the decorticated bony site.

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MESH CONTAINMENT BAG

The containment bag for Magnifuse™ Bone Graft is composed of multifilament threads of polyglycolic acid, woven together to create a porous covering having openings of approximately 0.5-1.0 mm. Such openings are small enough to contain the fibers and surface demineralized chips contained within, yet large enough to permit unrestricted cell access. Osteoblasts are approximately 15-20 microns in diameter.⁵ The mesh material is between 69% to 83% porous to allow easy vascular and fluid passage for removal of degradation products (Figure 2).

Figure 1: Magnifuse™ Bone Graft

Figure 2: PGA mesh used in Magnifuse™ Mesh bag. The strands of the mesh are multi-filament, providing extensive access by fluids.
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MATERIAL – PGA HISTORY

Polyglycolic acid (PGA), the material composing the mesh enclosure is a well-known bioresorbable polymer of glycolic acid, and was first introduced in the 1960's as Dexon®️, the first bioabsorbable suture material. PGA is also commonly used in other bioresorbable implants, including sutures, suture anchors and fracture fixation pins. When exposed to a water-containing environment (as in a surgical site) the PGA breaks down to glycolic acid by water through a hydrolysis reaction. The degradation product, glycolic acid, occurs naturally in the body during metabolism as hydroxyacetic acid. Since they occur naturally as a result of metabolism, the body has natural biochemical pathways to process them. The degradation products are further degraded biochemically to pyruvate, where they enter the Krebs cycle, and are ultimately reduced to water and CO2, then eliminated by excretion or respiration.

The PGA mesh is broken down to degradation products that may be metabolized in normal pathways of the body.

DEGRADATION OF PGA-BASED MESH

In Vitro Degradation:

In a laboratory experiment, samples of the mesh used in Magnifuse™ Bone Graft were tested for degradation profile in fluid solutions.

Prewedsgned PGA mesh was placed in an individual 50ml test tube containing 50ml of phosphate buffered saline (PBS, 10mM, pH=7.4). The tubes were kept in a water incubator that was maintained at 37°C. PBS was changed every 4 weeks. At predetermined degradation intervals, 1, 2, 4, 6, 8, 12, 16, 20 and 24 weeks, three (3) mesh samples were collected by centrifugation, washed with deionized water to remove residual buffer salts, and dried to constant weight with vacuum. Mass loss of the mesh was determined gravimetrically.

Results showed rapid loss of mass over the first 4-6 weeks (Figure 3). Mesh degradation reached the point by 4 to 6 weeks where it would no longer function to contain the grafting material. By 24 weeks, the material was almost completely degraded, and no longer resembled a mesh.

In vitro testing shows mesh bag breakdown in a fluid environment.

Figure 3: Mass loss over time as mesh material degrades in vitro. By 24 weeks, the mesh is almost completely degraded.

Figure 4: Photographs of degraded PGA mesh used in Magnifuse™ Bone Graft from left to right: 0, 1, 2, 4, 6, 8, 12 weeks after degradation in phosphate buffered saline. The mesh no longer functions to contain graft at 4 to 6 weeks, and is completely deteriorated by 12 weeks in this fluid environment.
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**In Vivo Degradation**

1) **Sheep Metaphyseal Defect Study:**

A study was designed as non-clinical investigation to evaluate the bone formation potential of a sheep derived allograft formulation contained in PGA mesh compared to autogenous bone graft in a critical sized sheep femoral defect. While they can demonstrate relative performance of materials, animal studies should not be interpreted as predicting human clinical performance.

- A critical sized cancellous defect (10mm in diameter by 18mm in depth) was created in the distal femur of sheep.
- Magnifuse™ DBM or autogenous bone recovered from the iliac crest were placed within the bone defects.
- The study was concluded at 13 weeks post-op.
- Evaluations of the implantation site included histological and histomorphometric analysis.

2) **Non-Human Primate Study**

Six skeletally mature rhesus monkeys underwent single-level posterolateral intertransverse process arthrodesis bilaterally at L4-5. The transverse processes of L4 and L5 were exposed, and a burr was used to decorticate bone from the transverse processes. Magnifuse™ Bone Graft, with its mesh container, was placed at the sites.

Following sacrifice at 24 weeks, histopathologic review of the implantation sites showed that there was no histologic evidence of residual mesh at this time point, and there was no histologic evidence of an inflammatory reaction at the interface between skeletal muscle and graft materials. While this demonstrates the resorption potential of the mesh container, the primate animal study is not indicative of clinical performance in humans.

**The mesh containment bag was fully resorbed and gone without signs of inflammation by 13 to 24 weeks in vivo.**

Figure 5: Histological analysis showed that the defect included new bone, but the containment mesh was not evident at 13 weeks in a sheep metaphyseal defect. (Lines show the original approximate boundary of the defect.)

Figure 6: Low magnification of fusion mass and transverse process (cross section). Examination at higher powers of all sections failed to reveal any traces of the mesh containment bag.
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SUMMARY

- The mesh bag material used in Magnifuse™ Bone Graft is made from materials that degrade in the presence of water, and have a long history of clinical use.\(^6,7\)
- Degradation is to glycolic acid, which has established metabolic pathways for breakdown and elimination from the body.\(^7,9\)
- The bag functions to deliver the graft to the surgical site, and is then removed over time.
- Benchtop studies suggest that the mesh bag loses coherency at approximately 4-6 weeks in a fluid environment.\(^3\)
- Histopathological examination of sections from implantation sites in animals show no evidence of inflammation and no evidence of remaining mesh material at 12-24 weeks.\(^3,10,11\)

REFERENCES

3. Data On File
10. Data on File
11. Data on File