Providing an environment conducive to bone growth
An Environment Conducive to Bone Growth

Clinically Proven Technology
In a prospective, randomized, multi-center study of 213 patients (249 long bone fractures) that compared autogenous iliac crest bone graft (ICBG) to calcium phosphate (CaP)-collagen graft (Collagraft® Matrix) the authors concluded that composite grafts of CaP-collagen material and bone marrow aspirate are as effective and as safe as autogenous bone graft in the treatment of fracture defects of long bones.

Synthetic Carrier Delivers Biologic Elements
CopiOs® Bone Void Filler alone is an osteoconductive scaffold; the addition of autologous bone marrow aspirate (BMA) provides osteogenic cells and osteoinductive proteins necessary for bone growth.

CopiOs Bone Void Filler is Formulated to Provide Physical and Chemical Characteristics to Optimize Bone Healing

- An abundance of localized calcium and phosphate ions promotes bone formation.
- Acidic conditions for bone healing may preserve the solubility of osteoinductive proteins for bone healing.
- A high porosity collagen sponge scaffold or a high void volume paste provides the 3-D structure, which plays a key osteoconductive role in bone regeneration.
- Resorption concurrent with bone growth.
- Biocompatibility and safety.
- Excellent handling and ease-of-use.
**An Effective Autograft Alternative**

**CopiOs Bone Void Filler**
- *CopiOs* Bone Void Filler combined with bone marrow aspirate provides the three requisite properties for bone healing.
- Preclinical studies with *CopiOs* Sponge plus bone marrow aspirate show bone healing performance equivalent to autograft.
- Eliminates the need for a second surgical harvest procedure and associated complications including donor site morbidity.
- Readily available with consistent quality.

Autograft is widely regarded as the ideal construct for graft procedures, supplying osteoinductive growth factors, osteogenic cells, and a structural scaffold. However, autograft has its limitations: Requires a second surgical procedure which increases costs and is associated with:
- Longer OR and recovery times.
- Greater blood loss.
- Extended hospital stays.
- Limited bone supply and often issues with bone quality, especially in the elderly.
- Donor site morbidity.
- Major complications (25%-29%) have been reported including disabling chronic pain at the donor site.

**Two Convenient Forms for Interoperative Flexibility**

<table>
<thead>
<tr>
<th>Part Number</th>
<th>Sponge Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>00-1103-010-01</td>
<td>1cc (1cm x 2cm x 0.5 cm)</td>
</tr>
<tr>
<td>00-1103-010-05</td>
<td>5cc (2cm x 5cm x 0.5 cm)</td>
</tr>
<tr>
<td>00-1103-010-10</td>
<td>10cc (2cm x 5cm x 0.5 cm) x 2</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Part Number</th>
<th>Paste Volumes (when hydrated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>00-1103-020-01</td>
<td>1cc</td>
</tr>
<tr>
<td>00-1103-020-05</td>
<td>5cc</td>
</tr>
<tr>
<td>00-1103-020-10</td>
<td>10cc</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Part Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>00-1103-007-00</td>
<td>Bone Marrow Aspiration Needle</td>
</tr>
</tbody>
</table>
The Next Generation in Synthetic Bone Graft Materials

Abundance of Localized Mineral Promotes Bone Formation

- CopiOs Bone Void Filler is comprised of dibasic calcium phosphate and highly purified Type I bovine collagen.
- A unique mineral chemistry that is moderately soluble.
- Dibasic calcium phosphate provides 300 times more calcium and phosphate ions at equilibrium than either tricalcium phosphate (TCP) or hydroxyapatite. (HA) (Fig. 1)

Acidic Conditions for Bone Healing

- CopiOs Bone Void Filler provides a moderately acidic environment that promotes solubility of endogenous bone morphogenic proteins (BMPs). (Fig. 2)
- More soluble BMPs may remain available to bone healing processes in the early stages of bone growth.
- The concentration of BMPs in solution decreases substantially when HA or TCP is present. (Fig. 2)

![Fig. 1: Relative solubility of calcium phosphates](image)

<table>
<thead>
<tr>
<th>Mineral</th>
<th>% BMPs Left in Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (No Mineral)</td>
<td>100%</td>
</tr>
<tr>
<td>CaHPO₄ (DICAL)</td>
<td>76%</td>
</tr>
<tr>
<td>Ca₃(PO₄)₂ (TCP)</td>
<td>23%</td>
</tr>
<tr>
<td>Ca₅(PO₄)₃(OH) (HA)</td>
<td>15%</td>
</tr>
</tbody>
</table>

Fig. 2: Concentration of BMP in a calcium salt solution

Optimized Chemistry

Study model:
- Female, Long Evans rats (60-130 g).
- Bilateral subcutaneous ectopic implantations (diameter approximately 7mm).
- Mineral compositions with different pH values were implanted (using a collagen scaffold and osteoinductive protein mixture).
- Histology was compared to assess bone growth and healing potential.

Conclusion:
Comparatively, the acidic mineral compositions show more mature, higher quality bone formation and a greater quantity of bone at this time period in this particular study. Note: cortical rim formation in dibasic calcium phosphate histology slide (mineralization-dark spots, development of marrow-white spots, preliminary signs of vascularization-light pink spots).

![CopiOs Sponge Preclinical Product Performance Comparison (3 weeks)](image)
Osteoconductive Scaffolds Provide Key Role in Bone Regeneration

• Three-dimensional collagen scaffold sponge resembles human cancellous bone for guided bone regeneration.
• Sponge structure is approximately 93% porous with interconnecting, multi-directional pores ranging in size between 5-1000µm, which allow cell penetration and rapid, complete absorption of autologous fluids. (Fig. 3)
• Paste structure has high void volume. (Fig. 4)
• These osteoconductive attributes allow cellular attachment, nutrient and oxygen infiltration and vascularization throughout the graft material for bone healing.
• Sponge carrier technology wicks 7X its weight in autologous blood or bone marrow, localizing and retaining necessary cells and proteins at the defect for bone healing.

Timely Resorption Concurrent with Bone Growth

• Non-chemically cross-linked collagen provides strength and durability for the scaffold to persist until replaced by bone ingrowth.
• Rapidly incorporates into new bone and remolds by cell-mediated processes throughout the graft (as opposed to creeping substitution).
• As new bone growth occurs, the scaffold is resorbed. (Fig. 5)
• It resorbs more quickly than hydroxyapatite which is virtually insoluble.

Biocompatible and Safe

• Pre-clinical studies show CopiOs Bone Void Filler to be biocompatible and non-toxic.
• CopiOs Bone Void Filler was nonimmunogenic in animal studies.

Excellent Handling and Easy-To-Use

• Pliant when hydrated, so it can be easily molded into irregularly-shaped defects.
• CopiOs Sponge is easy to shape and cut.
• CopiOs Paste provides ease of graft placement in difficult to reach defects and for surgeons who prefer the handling properties of a putty/paste formulation.
• Stable in a fluid environment.
• CopiOs Sponge is radiolucent allowing for better imaging and less interference with visualization of the healing process than hydroxyapatite.
Pre-Clinical Performance

Study model:
- Skeletally mature New Zealand White rabbits (approximately 6 mos. old, 3-5 kg).
- Radial critical size segmental defect model (15mm).
- Evaluated use of autograft, CopiOs Sponge with bone marrow aspirate (BMA), and DePuy’s Healos Bone Graft Replacement with bone marrow aspirate. An unfilled defect was the negative control, and the contralateral limb was the control for mechanical strength.
- Mechanical, radiographic and histologic evaluations were completed.

Conclusion:
Pre-clinical studies with CopiOs Sponge plus bone marrow aspirate show bone healing performance equivalent to autograft.4

CopiOs Sponge with BMA was equivalent to autograft in failure torque and torsional rigidity testing.

![Mechanical performance at 11 weeks](image)

CopiOs Sponge with BMA was equivalent to autograft showing cortical rim formation at 11 weeks.

![Radiographic Analysis: 11 weeks](image)

CopiOs Sponge with BMA shows trabecular bone formation at 12 weeks equivalent to autograft.

![Histologic Analysis: at 12 weeks, 6x magnification](image)
Clinical Performance

Case 1
Post-op calcaneal osteotomy with subtalar fusion. Subtalar nonunion treated with CopiOs Sponge. Clinical union achieved 3-months post-op.¹

Case 2
Failed plafond fixation. Resulted in nonunion. Revised ankle arthrodesis and grafted with CopiOs Sponge.¹

Case 3
Periprosthetic fracture with failure of fixation. Fixation revised and nonunion treated with CopiOs Sponge.¹ Callus seen at 4 weeks.

Intended Use

CopiOs Bone Void Filler, in combination with autologous blood products such as bone marrow, is intended for use only for filling bone voids or gaps of the skeletal system (i.e., extremities, pelvis, and spine, i.e., posterolateral spine fusion procedures with appropriate stabilizing hardware) that are not intrinsic to the stability of the bone structure. These voids may be a result of trauma or creation by surgeon. CopiOs Bone Void Filler is intended to be gently packed into the void or gap and will resorb during the course of the healing process.
Surgical Technique

CopiOs Sponge and CopiOs Paste should be used in the OR in an aseptic surgical field. The bone void site should be adequately prepared to expose healthy bleeding bone to help promote future bone growth.

1. Determine the volume of the bone defect.
2. Select and open appropriate number of packages of CopiOs Bone Void Filler based on product volume/size to best fill the defect providing maximum contact with the bone surface. CopiOs Sponges may be cut to size with surgical scissors or a scalpel.
3. Aspirate or obtain locally autologous blood, bone marrow or other blood product in the following volume recommendations.

For CopiOs Sponge obtain a volume of blood or bone marrow equal to the volume of the defect.

For CopiOs Paste use the volumes in the table below to achieve a putty-like consistency.

<table>
<thead>
<tr>
<th>Product Size</th>
<th>Fluid Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>1cc</td>
<td>0.6cc</td>
</tr>
<tr>
<td>5cc</td>
<td>4.0cc</td>
</tr>
<tr>
<td>10cc</td>
<td>8.5cc</td>
</tr>
</tbody>
</table>

4. Hydrate CopiOs Bone Void Filler with the blood product obtained.

For CopiOs Sponge, place sponge(s) into a sterile mixing bowl and add the blood product to saturate.

For CopiOs Paste, transfer the compressed powder disc into the bowl and add the blood product. Add slightly more or less fluid to achieve desired putty handling characteristics. Mix thoroughly for 1-2 minutes until there are no dry spots.

5. Thoroughly irrigate the site of the bone defect.

6. Gently mold CopiOs Bone Void Filler into the defect. Avoid compressing the structure of the graft. As an alternative CopiOs Paste may be loaded into the barrel of an appropriate size sterile syringe and then extruded.

7. Secure filled defect with surrounding soft tissue and perform rigid fixation of bone void as needed. Optimal management of fractures or defects requires adequate alignment and stability.

CopiOs Bone Void Filler will resorb during the course of the healing process.


Manufacturer: Kensey Nash Corporation  ·  Distributor: Zimmer, Inc.

Contact your Zimmer representative or visit us at www.zimmer.com