ReproBone Synthetic Bone Graft Substitute
(Applications and Market information)

ReproBone

Cancellous Bone
ReproBone is a porous, resorbable ceramic bone graft substitute

- 60% Hydroxyapatite, 40% b-Tricalcium phosphate, similar to the mineral component of human bone
- Controlled resorption,
- Ultra porous, typically 200-800um pores
- Highly interconnected pores, similar to cancellous bone for rapid and unrestricted bone ingrowth,
- Microporous to allow nutrient transfer
- Osteoconductive
- Synthetic and reproducible, reliable consistent performance
- Bioactive, fully biocompatible
- Reduces/eliminates need for autograft or allograft
- Can be used as a bone graft extender to supplement autograft
- Easy to use, no chemical mixing of components
- Can be mixed with bone marrow aspirate or platelet concentrate to provide an additional biological boost
- Cost effective treatment with economical product
ReproBone – Areas of Application

- Orthopaedics and Traumatology
- Joint revision surgery (arthroplasty)
- Spinal and Neurosurgery
- Dental Implantology and Periodontology
- Maxillofacial Augmentation and Reconstruction

ReproBone is designed to provide an optimal environment for the ingrowth of new bone. The fully interconnected porous matrix is similar to the trabecular structure found in human cancellous bone and mimics both its chemical composition and structure.

ReproBone has typical cell diameters ranging from 200um to 800um with each cell having multiple interconnections to neighbouring cells. This ultra porosity plays a vital role in providing an optimal material allowing the unrestricted ingrowth of new bone.
Traumatology and Orthopaedics

• Areas include pelvis, long bone and extremity defects.

• Epiphyseal and diaphyseal simple and comminuted fracture reconstruction

• Filling after removal of other osteosynthesis materials

• Delayed or non-union

• Pseudarthrosis, arthrodesis and osteotomies

• Treating bone defects

• Benign bone lesions, bone cysts, and acting as a bone graft extender where large amounts of autograft are required eg. tumor resection.

• Note: In all cases, ReproBone is a “cancellous, non-load bearing, bone graft” only and if it is used where there is the possibility of a load being applied, or of movement, the defect must always be fixed with rigid fixation.
Traumatology and Orthopaedics

Main Competitors:

Demineralised Bone Matrix (Various suppliers)

Allograft & Freeze Dried Allograft (Various suppliers & national tissue banks)

Pro-Osteon (Interpore-Cross)
Vitoss (Orthovita)
Triosite (Zimmer)
Endobon (Biomet)
Osteoset (Wright Medical)
Novabone (Novabone)
Chronos (Synthes)
MBCP (Biomatlante)

(See chart for further information)
Hip & Knee Surgery

- Prosthesis revision surgery

- Impaction grafting or cemented revision of failed total joint arthroplasty

- Cup roof filling in joint arthroplasty
  Fills gaps between the synthetic prosthesis and the host bone providing a scaffold for the host bone to assist in full contact with the outer surface of the prosthesis
Spinal and Neurosurgery

- Spinal Fusion,
  Used as a bone graft extender with autograft. Also used as a bone graft scaffold alone when mixed with bone marrow aspirate or platelet concentrate. The product is packed inside rigid spinal cages.
Dental Implantology and Periodontology

- Sinus lift procedures.
  The sinus floor augmentation increases the amount of bone in the upper molar area for placement of dental implants. After the upper molars are removed, the bone above will no longer be under usual loading and will slowly resorb down towards the jawbone ridge. Over time the bone in this area may become so thin that there is no longer enough bone to place an implant.

- Alveolar ridge augmentation or reconstruction before implant placement
  Similar procedure but enhancement of the alveolar ridge to maintain bone height under bridgework or to encourage the formation of sufficient bone to later insert a screwed implant.
• Alveolar ridge augmentation around implants with immediate implantation
  Non structural filling around screwed implants where there is already sufficient bone to hold the implant in immediately but requires cosmetic filling around the area of the implant.

• Filling of extraction sockets
  Root socket filling and socket filling in preparation for later surgery or to prevent resorption.

• Defect filling due to periodontal disease, trauma, cyst removal etc.

• **Main Competitors**
  Bio-Oss (Geistlich) Bovine based product
  Grafton (Osteotech) DBM allograft product
  Perioglas (Novabone) Non-porous Bioglass beads
  Emdogain (Straumann) Biology based protein mixture, can be mixed with bone substitutes.
General Surgical Application of ReproBone

- Implant should preferably first be soaked in either BMA (bone marrow aspirate), PRP (Platelet rich plasma) or blood. This gently coagulates the granules together and helps placement into the defect. The BMA or PRP also provides an additional biological boost.

- If using as a bone graft extender mix well with autograft

- Implant the product into the defect (or in the case of spinal fusion fix into the rigid cage), maximising the bone-implant interface

- Granules may be gently tamped into place

- A membrane should be used where appropriate to prevent soft tissue ingress (guided tissue regeneration)

- Secure the site
Alternative Materials - Autograft

Autograft, the patient's own harvested bone, is often referred to as the gold standard but has some significant drawbacks.

- Morbidity associated with harvest site (typically iliac crest)

- Additional patient discomfort, significant pain from autograft harvesting. Discomfort is not uncommon even years after surgery.

- Insufficient supply / limited quantity available to harvest, sometimes need to be supplemented, ReproBone ideal for this.

- Additional cost of theatre time and extended hospital stay due to secondary bone harvesting operation
Alternative Materials - Allograft

Allograft is used widely but has significant drawbacks and the cost of maintaining a bone bank can be high.

- Quality is often inconsistent and performance varies due to variety of donor and quality of the bone.
- Potential shortage of supply
- Possible risk of disease transmission
- Cost and effort in maintaining bone bank
- Synthetic products have similar performance
- Freeze dried allograft required special preparation before surgery
Alternative Materials - DBM

Demineralised Bone Matrix is usually in the form of a putty. However, it does not provide a porous scaffold, and does not provide longer term bone support such as may be required for some dental / periodontal applications.

- Potential risk from disease transmission / sterility as it is derived from a human source
- Batch to batch variability
- Potential for immunogenic response
- Weakly osteoinductive but no real osteoconductivity
Alternative Materials - Other Synthetic Products

There is a variety of synthetic products available which can be characterised by their composition. Calcium Sulfate (CaSO$_4$) materials resorb very quickly in 1-3 months, usually in the form of dense pellets providing little or no osteoconductive scaffold and can potentially resorb before the defect is stabilised by bony ingrowth.

Pure Hydroxyapatite having a calcium to phosphorus ratio (Ca/P) of 1.67 takes many years to resorb and is now used only in cases where a long term bone scaffold is required, for example in maintaining ridge augmentation under bridgework.

TCP (Ca/P 1.50) and HA/TCP combinations are similar in performance, although in 60/40 HA/TCP the intermediate Ca/P of 1.60 provides what is widely regarded as a more controlled resorption profile reducing the potential for implant resorption before healing, and does not provide an excess local concentration of degradation products at the implant site. The difference in performance between these products is mainly due to differences in porous structure of the products. Generally a more open interconnected porosity will encourage better vascularisation and faster bone ingrowth.
ReproBone – Key Advantages

An extensive research programme led by Ceramisys has resulted in ReproBone, an ultra-porous resorbable bone graft substitute with a proven biocompatibility.

- One of the most significant and unique points is the similarity of the controlled porous structure to that of natural cancellous bone

- 60% Hydroxyapatite 40% beta tricalcium phosphate composition provides controlled resorption.

- Rapid bone ingrowth throughout, and around, the ultra porous granules without restriction by the material.

- Highly microporous (10um - 0.1um) allows for fluid/nutrient transfer to feed the ingrowing tissues, and allows the complete wicking of fluid throughout, during surgery.

- Easy to handle, the product once wetted with the patients blood will gently cling to itself and the instruments and does not easily migrate around the implant site during surgery.
ReproBone – Advantages

- The volume available for regrowth is not significantly limited by the speed of resorption as the total volume actually occupied by the HA/TCP material when in-situ is only around 10% for granules. ie. the volume immediately available for bone ingrowth and vascularisation is approx 90%

- Composition similar to mineral part of bone and is eventually completely remodelled in a controlled way. No need for very fast resorption as product is ultra porous. See above point

- Provides longer and better osteoconductive support compared to calcium sulfate and pure TCP based products, whilst the ultra high porosity ensures that the more controlled resorption profile does not delay the healing process

- Sterile synthetic material eliminates risk of disease transmission
Product Positioning

The unique features are:

- Similarity of the porous structure to that of human cancellous bone
- The ultra-high level of porosity and interconnectivity promoting maximum bone ingrowth
- Complete resorption and more controlled than calcium sulphate pellets and packs into the defect better. It also provides osteoconduction inside the granules.
- It is completely synthetic and sterile compared to potential risks associated with DBM or allograft
- Interconnected porosity is greater than seen in other synthetic products
- High integral strength, the granules do not dust or crumble when handled compared to many other synthetic granules
- Advanced manufacturing provides cost effective product
The information provided is indicative of some comparative hospital prices only, and will vary according to market studied.

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### Product Comparison table

* 5= highest, 0= Lowest

<table>
<thead>
<tr>
<th>Company</th>
<th>Trade Name</th>
<th>Appearance</th>
<th>Composition</th>
<th>Porosity inside granules</th>
<th>Ease of application</th>
<th>Resorption rate</th>
<th>Indicative Cost only</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceramisys</td>
<td>ReproBone Blocks, Granules &amp; cylinders</td>
<td>60:40 HA/TCP</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>100% synthetic, controlled resorption, ultra high porosity</td>
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</tr>
<tr>
<td>Interpore Cross</td>
<td>Pro Osteon 200(R) Blocks &amp; Granules</td>
<td>HA surface with calcium carbonate interior</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>Coral Derived, fully interconnected, around 60% porous</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pro Osteon 500(R) Granules</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthovita</td>
<td>Vitoss Cortoss Granules and cylinders</td>
<td>Tri-calcium phosphate</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td>Ultra high porosity</td>
<td></td>
</tr>
<tr>
<td>Synthes</td>
<td>Chronos Block &amp; granules</td>
<td>Tricalcium phosphate</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>Ultra high porosity</td>
<td></td>
</tr>
<tr>
<td>Zimmer</td>
<td>Triosite Granules &amp; block</td>
<td>HA/TCP</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>Some porosity</td>
<td></td>
</tr>
<tr>
<td>Zimmer</td>
<td>Collagraft Strips</td>
<td>TCP with collagen</td>
<td>-</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td></td>
<td></td>
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<tr>
<td>Biomatlante</td>
<td>MBCP Granules wedges &amp; Blocks</td>
<td>HA/TCP</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>Some porosity</td>
<td></td>
</tr>
<tr>
<td>Teknimed</td>
<td>Ceraform Blocks &amp; granules</td>
<td>HA/TCP</td>
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<td>4</td>
<td>2</td>
<td>3</td>
<td>Some porosity</td>
<td></td>
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<tr>
<td>Synthes (Norian)</td>
<td>SRS Cement paste</td>
<td>Calcium Phosphate with mixing solution</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>Limited indications, pre-mixing required</td>
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<tr>
<td>J&amp;J (Deputy)</td>
<td>Alpha BSM Cement putty</td>
<td>Calcium phosphate</td>
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<td>2</td>
<td>1</td>
<td>3</td>
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<td></td>
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<tr>
<td>Stryker</td>
<td>Bonesource Cement Putty</td>
<td>Calcium Phosphate with mixing solution</td>
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<td>2</td>
<td>1</td>
<td>3</td>
<td>Pre-mixing required</td>
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<tr>
<td>U.S. Biomaterials</td>
<td>Novabone Perioglas Dense Granules</td>
<td>Bioglass</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>No osteoconduction inside the granules</td>
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<td>Wright Medical</td>
<td>Osteoset Dense Pellets</td>
<td>Calcium sulfate</td>
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<td>4</td>
<td>5</td>
<td>4</td>
<td>No osteoconduction inside the granules</td>
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<tr>
<td>Encore</td>
<td>Stimulan Dense Pellets</td>
<td>Calcium Sulfate</td>
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<td>4</td>
<td>5</td>
<td>3</td>
<td>No osteoconduction inside the granules</td>
<td></td>
</tr>
<tr>
<td>Smith &amp; Nephew</td>
<td>Jax Granules</td>
<td>Calcium Sulfate</td>
<td>0</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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