



Enhancing Ceramic Scaffolds with Bone Marrow Aspirate

Osteoinductive synthetic ceramic bone substitutes offer alternatives to autograft and allograft use. Osteoconductive materials commonly used as bone substitutes include hydroxyapatite (HA), β -tricalcium phosphate (β -TCP), calcium carbonate, and calcium sulfate. HA (ProOsteon®, OsteoGraf®) is generally considered non-resorbable. β -TCP (TheriLok™, Vitoss®, Conduit™) is resorbed by cellular activity - usually on a scale of months. Calcium carbonate and calcium sulfate (OsteoSet®) resorb mainly via chemical dissolution and thus disappear from a defect site rapidly. Resorption, both cellular and physical, is influenced by local circulation and/or increased implant surface area. Ceramics are often manufactured as grafts with porosities that facilitate cellular penetration and bone ingrowth. These porosities can also influence implant resorption due to increased surface area.

Ceramic bone substitutes have chemical compositions that facilitate the deposition of bone. They are effective as grafts when there is good contact between the graft and the surrounding bone. When bony contact is limited, as in the case of non-contained defects, large voids, or in spinal applications, healing can be improved by combining autologous bone marrow aspirate (BMA) to ceramic bone grafts. Muschler (1997) showed that BMA includes a viable population of connective tissue progenitor cells (CTPs), which can differentiate into osteoblasts. Grafts effectively combined with BMA are both osteoconductive and osteogenic. Seeding efficiency is influenced by surface chemistry and the porosities of the graft material. β -TCP has been shown to be more favorable for CTP attachment as compared to calcium sulfate or calcium carbonate.

Porosity also plays a major role in the effective seeding of a scaffold. Products with little or no porosity (OsteoSet®) or with a closed porous network (Conduit™), do not allow for BMA to penetrate into the scaffold. In the case of these latter two products, the healing effects of BMA are greatly limited.

TheriLok™ has been specifically designed with a porous network that promotes efficient BMA dispersion and cellular attachment throughout the graft. Clinical use of porous β -TCP combined with BMA has shown promising results. In a study by Guyer (2003), 25 patients underwent spinal fusion procedures using β -TCP with BMA on one side and autograft on the opposing. At 6 months, β -TCP with BMA showed better healing than autograft in 54% of the patients as judged by CT data.

Results in the spine have been mixed for other synthetic grafts combined with BMA. Boden (1999) showed no fusion (0/14) in a rabbit posterolateral lumbar L5-L6 fusion model treated with 3cc coralline HA combined with 1.5cc BMA. In anterior cervical fusion cases, porous HA showed clinical success (69 of 76 patients benefited) when combined with BMA and used to fill a cage (Papavero, 2003). Healos® (HA and type I bovine collagen) combined with BMA has shown results similar to autograft when used for interbody fusion (Griffith, 1999). Clinical use has shown similar success for Healos® when used for posterolateral spinal fixation procedures (Grosse, 1999).

Summary

- TheriLok characteristics
 - Porosity and pore size has been optimally defined to allow rapid bone ingrowth.
 - Graft has been designed to facilitate controlled material resorption – this provides a structure for new bone and long-term remodeling.
 - Graft has been designed with unique macro architecture to facilitate product interlocking – the more stable the graft, the better quality bone ingrowth
- Use of bone marrow aspirate (BMA)
 - Technique is of utmost importance. It is likely that the variation in healing effects of BMA as seen in the literature can be attributed to technique and/or model.
 - Increasing BMA volume from a single location does not increase the number of CTPs but dilutes the concentration by taking more peripheral blood. An aspiration volume of 2 cc or less from a location can yield maximal concentration of progenitor cells.
 - To get a higher volume of BMA with a high concentration of CTPs, aspirates can be taken from multiple locations on the iliac crest. For instance, 5 holes with a total of 2 x 2cc aspirates from each location can yield ~20cc of BMA.

Selected References

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THERICS Products: Comparison vs. VITOSS™

	Therics Synthetic Bone Fillers	Vitoss™ (Orthovita, Inc.)
Product Form	Granules, interlocking shapes, wedges, struts, channeled cylinders and disks	Granules, strips, and cylinders
Indications	FDA cleared for use as bone void filler	FDA cleared for use as bone void filler
Composition	β-Tricalcium phosphate	β-Tricalcium phosphate
Porosity	53-70%	80-90%
Pore Size range	7 – 900 μm	7 – 1000 μm
Resorption	6 – 12 months	3 months*
Surgeon Utility	Excellent – many shapes and sizes	Limited
Comparative Cost	<i>Lower</i>	<i>Higher</i>

* From Orthovita literature

Points to discuss with users of Vitoss™

Resorption

- Vitoss™ has a very high porosity and therefore it resorbs very quickly. Subsequently, the bone has no graft structure for long-term remodeling. This may affect quality of the healed bone. Emphasize to the surgeon that fast is not good for bone healing.
- Therics products are approximately 60% porous and are designed for controlled resorption (over a 12 month period). This feature is designed to lead to higher quality bone formation (i.e., it is stronger)**. Emphasize to the surgeon that bone needs a structure on which to heal and remodel.

**Stronger - defined as mechanical properties of healed tissue through pre-clinical testing of TheriLok™ vs. Orthovita's Vitoss™ (data – Therics, Inc.)

Product Forms/handling

- Vitoss™ is also only available in granules, strips, and cylinders thereby limiting the surgeons' options.
- Therics products handle very well and are designed to be stable during packing into a surgical site. TheriLok™ crosses are designed to interlock and help keep the material in its intended location, with minimal migration. Have the surgeon handle the material to demonstrate superior handling characteristics.
- Therics products also come in multiple shapes and sizes, thereby providing the surgeon maximum utility. For example, tell the surgeon how wedges can be used for backfilling of the iliac crest or realignment in foot surgery. Explain how TheriLok™ can be mixed with blood, bone marrow, or other bone growth promoters and placed, for example, (depending on the preferences of the surgeon) within the area of the spinous process in standard fashion for the indicated fusion.

Wicking Characteristics (for blood and bone marrow)

- Therics products have excellent wicking ability since the porosity, pore size and architecture are precisely controlled to promote rapid blood and bone marrow wicking. Emphasize to the surgeons that the channels designed into Therics implants may improve nutrient delivery.

Price

- Vitoss™ is more expensive than Therics products for all available sizes.

Summary

The Key points to emphasize on every call:

- **Resorption:** Therics ability to precisely control the architecture and porosity make it the only manufacturer in the industry to control resorption. This feature leads to higher quality bone formation (i.e., it is stronger*)
- **Porosity:** Vitoss™ has a very high porosity and resorbs much more quickly than Therics products. Subsequently, the bone has no graft structure for long-term remodeling.
- **Wicking:** Therics excellent wicking characteristics allow the surgeon to integrate blood or marrow quickly and completely through the implant structure.
- **Product Range of Shapes and Applications:** The wide variety of shapes and sizes of the Therics product line allows the surgeon unique flexibility of choice and can reduce surgical time.

*Stronger - defined as mechanical properties of healed tissue through pre-clinical testing of TheriLok™ vs. Orthovita's Vitoss™ (data – Therics, Inc.)

THERICS Products: Comparison vs. OSTEOSET™

	Therics Synthetic Bone Fillers	OsteoSet™ (Wright Medical)
Product Form	Granules, interlocking shapes, wedges, struts, channeled cylinders and disks	Pellets
Indications	FDA cleared for use as bone void filler	FDA cleared for use as bone void filler
Composition	β-Tricalcium phosphate	Calcium Sulfate
Porosity	53-70%	Unknown
Pore Size range	7 – 900 μm	Unknown
Resorption	6 – 12 months	30 – 60 days*
Surgeon Utility	Excellent – many shapes and sizes	Limited
Comparative Cost	<i>Lower</i>	<i>Higher</i>

*From Osteoset™ technical monograph located at www.wmt.com

Points to discuss with users of OsteoSet™

Material Composition

- Osteoset™ is made from calcium sulfate.
- Therics products are made from β-tricalcium phosphate. Emphasize to the surgeon that β-tricalcium phosphate is more related to natural mineral bone than calcium sulfate.

Resorption

- Osteoset™ is made from calcium sulfate that can resorb through chemical dissolution. The graft breaks down very quickly, possibly leaving inadequate structure for complete bone healing to occur.
- Therics products are approximately 60% porous and are designed for controlled resorption (over a 12 month period). This feature is designed to lead to higher quality bone formation (i.e., it is stronger)**. Emphasize to the surgeon that bone needs a structure on which to heal and remodel.

Porosity

- Osteoset™ has no defined porosity since it is molded into a dense pellet.
- Therics products are approximately 60% porous with a controlled interconnected pore structure to facilitate tissue ingrowth. Emphasize to the surgeon that natural bone has a similar porosity and pore structure to allow normal function.

**Stronger - defined as mechanical properties of healed tissue through pre-clinical testing of TheriLok™ vs. Orthovita's Vitoss™ (data – Therics, Inc.)

Product Forms/handling

- Osteoset™ is very dense and is only available in pellet form.
- Therics products handle very well and are designed to be stable during packing into the surgical site. TheriLok™ crosses are designed to interlock and help keep the material in its intended location, with minimal migration. Have the surgeon handle the material to demonstrate superior handling characteristics.
- Therics products also come in multiple shapes and sizes, thereby providing the surgeon maximum utility. For example, tell the surgeon how wedges can be used for backfilling of the iliac crest or realignment in foot surgery. Explain how TheriLok™ can be mixed with blood, bone marrow, or other bone growth promoters and placed, for example, (depending on the preferences of the surgeon) within the area of the spinous process in standard fashion for the indicated fusion.

Wicking Characteristics (for blood and bone marrow)

- Wicking capability of Osteoset™ is undefined.
- Therics products have excellent wicking ability since the porosity, pore size and architecture are precisely controlled to promote rapid blood and bone marrow wicking. Emphasize to the surgeons that the channels designed into Therics implants may improve nutrient delivery.

Price

- Osteoset™ is more expensive than Therics products for all available sizes.

Summary

Key Points to emphasize on every call:

- **Resorption:** Therics` ability to precisely control the architecture and porosity make it the only manufacturer in the industry to control resorption. This feature leads to higher quality bone formation (i.e., it is stronger*).
- **Porosity:** Therics` products are manufactured with porosity similar to human bone. This design allows natural bone growth and excellent wickability. Osteoset™ has no defined porosity.
- **Product Range of Shapes and Applications:** The wide variety of shapes and sizes of the Therics product line allows the surgeon unique flexibility of choice and can reduce surgical time. Osteoset™ is available only in a dense pellet form, thus limiting the surgeon's options for use.

*Stronger - defined as mechanical properties of healed tissue through pre-clinical testing of TheriLok™ vs. Orthovita's Vitoss™ (data – Therics, Inc.)

THERICS Products: Comparison vs. ProOsteon®

	Therics Synthetic Bone Fillers	ProOsteon 200R® (Interpore-Biomet)
Product Form	Granules, interlocking shapes, wedges, struts, channeled cylinders and disks	Blocks, Granules
Indications	FDA cleared for use as bone void filler	FDA cleared for use as bone void filler
Composition	β -Tricalcium phosphate	Calcium phosphate and calcium carbonate
Porosity	53-70%	~57%
Pore Size range	7 – 900 μ m	190-230 microns
Resorption	6 – 12 months	6 – 12 months*
Surgeon Utility	Excellent – many shapes and sizes	Limited
Comparative Cost	<i>Lower</i>	<i>Higher</i>

* From the ProOsteon literature

Points to discuss with users of ProOsteon®

Material Composition

- ProOsteon® resorbable forms are made from calcium phosphate and calcium carbonate.
- Therics products are made from β -tricalcium phosphate. Emphasize to the surgeon that β -tricalcium phosphate is more closely related to mineral bone composition than calcium carbonate.

Resorption

- ProOsteon® resorbs in the 6 – 12 month timeframe.
- Therics products are approximately 60% porous and are designed for controlled resorption (over a 12 month period). This feature is designed to lead to higher quality bone formation (i.e., it is stronger)**. Emphasize to the surgeon that bone needs a structure on which to heal and remodel.

Porosity

- ProOsteon® has a porosity of approximately 57%. Porosity and pore size cannot be readily controlled.
- Therics products are approximately 60% porous with a controlled interconnected pore structure to facilitate tissue ingrowth. Emphasize to the surgeon that natural bone has porosity and pore structure to allow normal function.

**Stronger - defined as mechanical properties of healed tissue through in vivo testing comparing TheriLok™ to Orthovita's Vitoss™ (data source – Therics, Inc.)

Product Forms/handling

- ProOsteon® is available in granules and blocks.
- Therics products handle very well and are designed to be stable during packing into a surgical site. TheriLok™ crosses are designed to interlock and help keep the material in its intended location, with minimal migration. Have the surgeon handle the material to demonstrate superior handling characteristics.
- Therics products also come in multiple shapes and sizes, thereby providing the surgeon maximum utility. For example, tell the surgeon how wedges can be used for backfilling of the iliac crest or realignment in foot surgery. Explain how TheriLok™ can be mixed with blood, bone marrow, or other bone growth promoters and placed, for example, (depending on the preferences of the surgeon) within the area of the spinous process in standard fashion for the indicated fusion.

Wicking Characteristics (for blood and bone marrow)

- ProOsteon® products can wick blood and marrow.
- Therics products have excellent wicking ability since the porosity, pore size and architecture are precisely controlled to promote rapid blood and bone marrow wicking. Emphasize to the surgeons that the channels designed into Therics implants may improve nutrient delivery.

Price

- ProOsteon® is more expensive than Therics products for all available sizes.

Summary

The key points to emphasize on every call:

- **Resorption:** Therics ability to precisely control the architecture and porosity make it the only manufacturer in the industry to control resorption. This feature leads to higher quality bone formation (i.e., it is stronger*).
- **Porosity:** Porosity and pore size at Therics are closely controlled to facilitate tissue ingrowth. ProOsteon® porosity and pore size cannot be controlled.
- **Microarchitecture:** Therics scaffolds are made of Beta-tricalcium phosphate, which is more closely related to mineral bone composition than the materials used in ProOsteon®.
- **Product Range of Shapes and Applications:** The wide variety of shapes and sizes of the Therics product line allows the surgeon unique flexibility of choice and can reduce surgical time.

*Stronger - defined as mechanical properties of healed tissue through in vivo testing comparing TheriLok™ to Orthovita's Vitoss™ (data source – Therics, Inc.)