nanOss® Bioactive
nanOss® Bioactive Loaded
nanOss® Bioactive 3D
Bone Void Fillers
Overview
nanOss Bioactive, nanOss Bioactive Loaded and nanOss Bioactive 3D Bone Void Fillers

nanOss Bioactive, nanOss Bioactive Loaded and nanOss Bioactive 3D are bone void fillers that combine osteoconductive nano-structured hydroxyapatite (HA) and an engineered extracellular matrix bioscaffold (carrier) to provide a natural bone growth solution.¹

Large Surface Area

nanOss Bioactive, nanOss Bioactive Loaded and nanOss Bioactive 3D are composed of nano-structured HA that has a large surface area. The nano-structured HA in these advanced bone graft substitutes has approximately 100X more surface area than competitive synthetic based* products.²,¹² Large surface area allows increased potential for cell attachment.

Similar to Bone

Nano-structured HA is similar to bone, which increases its potential to remodel into new bone. Nano-structured HA is a similar size as bone, similar composition as bone and similar shape as bone.

Supports Bone Repair

The engineered extracellular matrix bioscaffold (carrier) in nanOss Bioactive and nanOss Bioactive Loaded supports bone repair.⁶ Thus, the entire product is helping to remodel bone.

Peer Reviewed Evidence

nanOss Bioactive and nanOss Bioactive Loaded are among the few synthetic based bone grafts with peer-reviewed evidence of posterolateral fusion. 93% of the total individual sites treated exhibited posterolateral bridging bone in a retrospective, multi-center study of 46 patients at approximately 12 months postoperatively. CT scans were analyzed by an independent radiologist for the presence of bridging bone. The study included a small cohort of smokers.¹⁰

* A product that is manufactured from synthetic material, but may also include carrier materials derived from non-human materials.
NANO-STRUCTURED HA HAS LARGE SURFACE AREA SIMILAR TO BONE

• Approximately 100X more surface area than competitive synthetic based products

<table>
<thead>
<tr>
<th>SURFACE AREA</th>
<th>Bone</th>
<th>Nano-structured HA(^2)</th>
<th>Competitive Synthetic Based Products(^{12})</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 m(^2)/g</td>
<td>70 m(^2)/g</td>
<td>Less than 0.70 m(^2)/g</td>
<td></td>
</tr>
</tbody>
</table>

• Large surface area provides increased potential for cell attachment

• Osteoblasts readily attach to nano-structured HA

Nano-structured HA at 100,000X magnification shows nano-crystalline size, interconnected porosity and a large surface area

Osteoblasts attached to nano-structured HA shows cells readily attach to the nanostructured HA of nanOss Bioactive, nanOss Bioactive Loaded and nanOss Bioactive 3D\(^{2}\)
### SIMILAR SIZE AND SHAPE AS BONE

<table>
<thead>
<tr>
<th>Nano-structured HA&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Bone&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal size: 15-100nm</td>
<td>Crystal size: 5-50nm</td>
</tr>
</tbody>
</table>

Note the similarity in size and shape. Pertaining to mineral phase.

- Traditional calcium phosphate<sup>2</sup>  
  Crystal size: 1,000-10,000nm

### Comparative Images

<table>
<thead>
<tr>
<th>Nano-structured HA&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Bone&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Actifuse&lt;sup&gt;2,4&lt;/sup&gt;</th>
<th>Vitoss&lt;sup&gt;2,5&lt;/sup&gt;</th>
<th>Chronos&lt;sup&gt;2,11&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,200X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7,000X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40,000X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note the similarity in size and shape of the nano-structured HA to bone, especially when compared to other synthetic based bone grafts.
**ENGINEERED CARRIERS ARE DESIGNED FOR CELLS**

<table>
<thead>
<tr>
<th>nanOss Bioactive &amp; nanOss Bioactive Loaded</th>
<th>nanOss Bioactive 3D</th>
</tr>
</thead>
<tbody>
<tr>
<td>A proprietary manufacturing process unwinds the collagen, producing an open scaffold.</td>
<td>A proprietary manufacturing process creates a stable foam matrix comprised of an engineered collagen and embedded nano-structured HA granules.</td>
</tr>
</tbody>
</table>

Most collagen carriers have closed triple helix structures.

nanOss Bioactive & nanOss Bioactive Loaded engineered collagen carrier

- The engineered carriers provide the physical structure for cell infiltration and attachment, providing an ideal environment for bone formation.
- The carriers are synthesized of a highly purified derivative of porcine collagen.

**BOTH SCAFFOLDS:**

- Present an ideal pathway for cell infiltration and attachment.²
- Provide the healing environment necessary for bone formation.⁷,⁹
- Support the bone healing process.⁷,⁹
NANOSS BIOACTIVE: CLINICALLY PROVEN FUSION.\textsuperscript{10}

93\% of the total individual sites treated exhibited posterolateral bridging bone\textsuperscript{10} in a retrospective, multi-center study of 46 patients approximately 12 months postoperatively. CT scans were analyzed by an independent radiologist. The study included a small cohort of smokers.

NANOOSE BIOACTIVE 3D

3D reconstruction of CT scans of nanOss Bioactive 3D used in posterolateral spine in conjunction with BMA and autograft at approximately 1 year.

Radiographic images not taken as part of a study.
**Comparison study of nanOss Bioactive to Actifuse and Autograft in a rabbit posterolateral fusion model.**

Histology of posterolateral fusion mass with nanOss Bioactive + BMA + autograft. Note the fusion masses between the Transverse Processes (TP). With nanOss Bioactive, bone fills the entire space between TPs and integrates with the HA. Results showed 2.5 times more new bone formation than the Actifuse group (Actifuse + BMA + autograft) and statistically stronger fusions (peak load and stiffness) than the Actifuse group.

Histology of posterolateral fusion mass with Actifuse + BMA + autograft. Note the lack of bone in the center of the fusion mass.

**Comparison study of nanOss Bioactive 3D to Vitoss BA and Autograft in a rabbit posterolateral fusion model.**

nanOss Bioactive 3D + BMA + autograft: Three dimensional reconstruction of μCT image of rabbit posterolateral spinal fusion study at 26 weeks.

Vitoss BA + BMA: Three dimensional reconstruction of μCT image of rabbit posterolateral spinal fusion study at 26 weeks.

nanOss Bioactive 3D + BMA + autograft: H&E paraffin histology panel taken from the middle of the fusion mass at 12 weeks.

Vitoss BA + BMA: H&E paraffin histology panel taken from the middle of the fusion mass at 12 weeks.
For more information or to place a spine order, call RTI Surgical directly or call your local representative.

**NANOSS® BIOACTIVE**  
Bone void filler composed of nano-structured HA granules and an open structured engineered collagen carrier.

<table>
<thead>
<tr>
<th>CATALOG NUMBER</th>
<th>UNIT SIZE</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-100-02E</td>
<td>2cc</td>
</tr>
<tr>
<td>90-100-05E</td>
<td>5cc</td>
</tr>
<tr>
<td>90-100-10E</td>
<td>10cc</td>
</tr>
</tbody>
</table>

*Store the product in a clean, dry environment at room temperature.*

**NANOSS® BIOACTIVE LOADED**  
Pre-filled mixing syringe is a closed system for consistency, sterility, compression, and easy delivery of nanOss Bioactive. Quickly connecting the bone graft delivery syringe allows for nanOss Bioactive placement during MIS graft placement.

<table>
<thead>
<tr>
<th>CATALOG NUMBER</th>
<th>UNIT SIZE</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-200-05KE</td>
<td>5cc Syringe</td>
</tr>
<tr>
<td>90-200-10KE</td>
<td>10cc Syringe</td>
</tr>
</tbody>
</table>

*Store the product in a clean, dry environment at room temperature.*

**NANOSS® BIOACTIVE 3D**  
Advanced bone graft composed of nano-structured HA granules suspended in a porous gelatin-based foam matrix.

<table>
<thead>
<tr>
<th>CATALOG NUMBER</th>
<th>UNIT SIZE (W x L x H) &amp; VOLUME</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-300-25504E</td>
<td>25 x 50 x 4mm, 5cc</td>
</tr>
<tr>
<td>90-300-251004E</td>
<td>25 x 100 x 4mm, 10cc</td>
</tr>
<tr>
<td>90-300-25508E</td>
<td>25 x 50 x 8mm, 10cc</td>
</tr>
<tr>
<td>90-300-251008E</td>
<td>25 x 100 x 8mm, 20cc</td>
</tr>
</tbody>
</table>

*Store the product in a clean, dry environment at room temperature.*
NANOS BIOSACTIVE BONE VOID FILLERS

STERILE IMPLANTS

CAUTION:
Federal law restricts this device to sale and use by or on the order of a licensed physician.

DESCRIPTION:
nanOss Bioactive is a resorbable porous calcium phosphate bone void filler for use as a bone graft substitute or bone void filler. It is an osteoconductive implant with a multidimensional porosity similar to human cancellous bone and acts as a scaffold for the ingrowth of new bone. nanOss Bioactive is composed of porous hydroxyapatite granules and a porcine gelatin based carrier (highly purified derivative of porcine collagen). The product forms a cohesive and adhesive dough with a putty-like consistency upon rehydration, allowing the shape of the implant to conform to the defect maximizing direct contact with viable host bone.

nanOss Bioactive is provided sterile by prior exposure to gamma irradiation and is intended for single use only.

INDICATIONS:
nanOss Bioactive is intended for bony voids or gaps that are not intrinsic to the stability of bony structure. The product is indicated to be gently packed into bony voids or gaps in the spine in conjunction with bone marrow aspirate or bone marrow aspirate and autograft bone. These defects may be surgically created osseous defects or defects created from traumatic injury to the bone. The product provides a bone void filler that resorbs and is replaced by the growth of new bone during the healing process.

CONTRAINDICATIONS:
Use of nanOss Bioactive is contraindicated in the presence of one or more of the following clinical situations:

- fractures of the epiphyseal plate
- metabolic or systemic bone disorders that affect bone or wound healing
- fractures for which stabilization of the fracture is not possible
- significant vascular impairment proximal to the graft site
- infected or contaminated wounds, or fractures for which intraoperative soft tissue coverage is not planned or possible
- acute and chronic infections in the surgical area (soft tissue infections; inflammatory, bacterial bone disorders, osteomyelitis)
- impaired calcium metabolism
- treatment with steroids and other drugs affecting calcium metabolism
- immunosuppressant therapy
- use in the area of the open epiphyseal growth plate
- patients allergic to porcine collagen products

WARNING:
One of the potential risks identified with any surgical procedure is death. Other potential risks which may require additional surgery, include:

- inflammation
- infection
- neurological injury
- vascular or visceral injury
- implant migration
- non-union or delayed union

nanOss Bioactive does not possess sufficient mechanical strength to support the reduction of a fracture site prior to soft and hard tissue ingrowth or to support a load. Standard internal fixation techniques such as the use of plates and/or screws must be followed to obtain rigid stabilization. External stabilization alone is not sufficient to achieve the rigidity necessary for bony ingrowth of the nanOss Bioactive material. nanOss Bioactive must not be used to gain screw purchase or to stabilize screw placement. Screws used with nanOss Bioactive and fixation devices must attain rigid fixation into the host bone.

Complete postoperative wound closure is essential. nanOss Bioactive must not be used to repair metaphyseal defects where complete soft tissue coverage cannot be achieved. Avoid application of nanOss Bioactive beyond intended treatment site; this may result in product migration and/or damage surrounding tissues.

This system has not been evaluated for safety and compatibility in the MR environment. This system has not been tested for heating or migration in the MR environment.

PRECAUTIONS:

- This product is intended for use only by surgeons familiar with bone grafting and rigid fixation techniques. Postoperative patient management should follow the same regimen as similar cases utilizing autogenous bone grafting. Standard postoperative practices should be followed, particularly as applicable to defect repairs involving the use of fixation devices.
- nanOss Bioactive granules are radiopaque and the radiopacity may mask underlying pathological conditions.
- nanOss Bioactive is intended for single use only.
- Do not resterilize nanOss Bioactive.
- Discard any un-used nanOss Bioactive.
- Do not expose to temperature extremes such as freezing or excessive heat.
- Do not apply nanOss Bioactive dry to the defect.
- nanOss Bioactive has no weight bearing function.
- Always follow recommended mixing instructions when rehydrating nanOss Bioactive.
- The use of non-steroidal anti-inflammatory drugs or other immune modulators should be avoided as they may inhibit bone fusion.
- For best results, product should fill the defect and contact viable bone as much as possible. Over-filling the defect site should be avoided.

See insert for complete labeling limitations related to this device.
NANOSS BIOACTIVE LOADED BONE VOID FILLER

STERILE IMPLANTS AND STERILE INSTRUMENTS

CAUTION:
Federal law restricts this device to sale and use by or on the order of a licensed physician.

DESCRIPTION:
nanOss Bioactive Loaded consists of a mixing chamber pre-filled with nanOss Bioactive Bone Void Filler (nanOss Bioactive) granules and packaged with a hydration syringe, graft applicator adapter and graft applicator in a double sterile barrier system. The package is contained in a tamper evident box with a package insert. The product is offered in 5cc and 10cc sizes. nanOss Bioactive Loaded is sterilized using irradiation and intended for single use only.

nanOss Bioactive is a resorbable porous calcium phosphate bone void filler for use as a bone graft substitute or bone void filler. It is an osteoconductive implant with a multidimensional porosity similar to human cancellous bone and acts as a scaffold for the in-growth of new bone. nanOss Bioactive is composed of porous hydroxyapatite granules and a porcine gelatin based carrier (highly purified derivative of porcine collagen). The product forms a cohesive and adhesive dough with a putty-like consistency upon rehydration, allowing the shape of the implant to conform to the defect maximizing direct contact with viable host bone.

INDICATIONS:
nanOss Bioactive is intended for bony voids or gaps that are not intrinsic to the stability of bony structure. The product is indicated to be gently packed into bony voids or gaps in the spine in conjunction with bone marrow aspirate or bone marrow aspirate and autograft bone. These defects may be surgically created osseous defects or defects created from traumatic injury to the bone. The product provides a bone void filler that resorbs and is replaced by the growth of new bone during the healing process.

CONTRAINDICATIONS:
Use of nanOss Bioactive is contraindicated in the presence of one or more of the following clinical situations:

• fractures of the epiphyseal plate
• metabolic or systemic bone disorders that affect bone or wound healing
• fractures for which stabilization of the fracture is not possible
• significant vascular impairment proximal to the graft site
• infected or contaminated wounds, or fractures for which intraoperative soft tissue coverage is not planned or possible
• acute and chronic infections in the surgical area (soft tissue infections; inflammatory, bacterial bone disorders, osteomyelitis)
• impaired calcium metabolism
• treatment with steroids and other drugs affecting calcium metabolism
• immunosuppressant therapy
• use in the area of the open epiphyseal growth plate
• patients allergic to porcine collagen products

WARNINGS:
One of the potential risks identified with any surgical procedure is death. Other potential risks which may require additional surgery, include:

• inflammation
• infection
• neurological injury
• vascular or visceral injury
• implant migration
• non-union or delayed union

nanOss Bioactive does not possess sufficient mechanical strength to support the reduction of a fracture site prior to soft and hard tissue in-growth or to support a load. Standard internal fixation techniques such as the use of plates and/or screws must be followed to obtain rigid stabilization. External stabilization alone is not sufficient to achieve the rigidity necessary for bony in-growth of the nanOss Bioactive material. nanOss Bioactive must not be used to gain screw purchase or to stabilize screw placement. Screws used with nanOss Bioactive and fixation devices must attain rigid fixation into the host bone.

Complete postoperative wound closure is essential. nanOss Bioactive must not be used to repair metaphyseal defects where complete soft tissue coverage cannot be achieved. Avoid application of nanOss Bioactive beyond intended treatment site; this may result in product migration and/or damage surrounding tissues.

The following additional warnings apply when using nanOss Bioactive Loaded:

• Never introduce nanOss Bioactive into closed cavities under pressure, as this may lead to fat embolization or embolization of device into the blood stream.
• Avoid over-pressurizing the device because this may lead to extrusion of the device beyond the site of its intended application and damage to the surrounding tissues.
• When mixing nanOss Bioactive with autograft for use in posterolateral spine and using the graft applicator, morseize autograft particles to smaller than two (2) millimeters to prevent risk of clogging. Use of a bone mill to morseize autograft prior to addition to nanOss Bioactive is recommended for best results.

This system has not been evaluated for safety and compatibility in the MR environment. This system has not been tested for heating or migration in the MR environment.

PRECAUTIONS:
• This product is intended for use only by surgeons familiar with bone grafting and rigid fixation techniques. Postoperative patient management should follow the same regimen as similar cases utilizing autogenous bone grafting. Standard postoperative practices should be followed, particularly as applicable to defect repairs involving the use of fixation devices.
• nanOss Bioactive granules are radiopaque and the radiopacity may mask underlying pathological conditions.
• Components of this product are intended for single use only.
• Do not resterilize any component of this product.
• Discard any un-used product.
• Do not expose to temperature extremes such as freezing or excessive heat.
• Do not apply nanOss Bioactive dry to the defect.
• nanOss Bioactive has no weight bearing function.
• Always follow recommended mixing instructions when rehydrating nanOss Bioactive.
• The use of non-steroidal anti-inflammatory drugs or other immune modulators should be avoided as they may inhibit bone fusion.
• For best results, product should fill the defect and contact viable bone as much as possible. Over-filling the void should be avoided.

See insert for complete labeling limitations related to this device.
NANOSS BIOACTIVE 3D BONE VOID FILLER
STERILE IMPLANT

CAUTION:
Federal law restricts this device to sale and use by or on the order of a licensed physician.

DESCRIPTION:
nanOss Bioactive 3D is a resorbable porous calcium phosphate bone void filler that provides a scaffold for the in-growth of new bone. nanOss Bioactive 3D is an osteoconductive implant with an interconnected porosity similar to human cancellous bone. nanOss Bioactive 3D is a semi-rigid three dimensional construct that consists of porous hydroxyapatite granules suspended within porous porcine gelatin-based foam matrix (highly purified derivative of porcine collagen). It is provided in the form of strips that can be further cut as required at the time of surgery.

When hydrated at the point of use, nanOss Bioactive 3D becomes a compressible and elastic sponge that allows the shape of the implant to conform to the defect maximizing direct contact with viable host bone. nanOss Bioactive 3D is provided sterile by prior exposure to gamma irradiation and intended for single use only.

INDICATIONS:
nanOss Bioactive 3D is intended for bony voids or gaps that are not intrinsic to the stability of bony structure. The product is indicated to be gently packed into bony voids or gaps in the spine in conjunction with viable host bone. nanOss Bioactive 3D is provided as a semi-rigid three dimensional construct that consists of porous hydroxyapatite granules suspended within porous porcine gelatin-based foam matrix (highly purified derivative of porcine collagen). It is provided in the form of strips that can be further cut as required at the time of surgery.

When hydrated at the point of use, nanOss Bioactive 3D becomes a compressible and elastic sponge that allows the shape of the implant to conform to the defect maximizing direct contact with viable host bone. nanOss Bioactive 3D is provided sterile by prior exposure to gamma irradiation and intended for single use only.

INDICATIONS:
nanOss Bioactive 3D is intended for bony voids or gaps that are not intrinsic to the stability of bony structure. The product is indicated to be gently packed into bony voids or gaps in the spine in conjunction with viable host bone. nanOss Bioactive 3D is provided as a semi-rigid three dimensional construct that consists of porous hydroxyapatite granules suspended within porous porcine gelatin-based foam matrix (highly purified derivative of porcine collagen). It is provided in the form of strips that can be further cut as required at the time of surgery.

CONTRAINDICATIONS:
Use of nanOss Bioactive 3D is contraindicated in the presence of one or more of the following clinical situations:

- metabolic or systemic bone disorders that affect bone or wound healing
- fractures for which stabilization of the fracture is not possible
- significant vascular impairment proximal to the graft site
- infected or contaminated wounds, or fractures for which intraoperative soft tissue coverage is not planned or possible
- acute and chronic infections in the surgical area (soft tissue infections; inflammatory, bacterial bone disorders, osteomyelitis)
- impaired calcium metabolism
- treatment with steroids and other drugs affecting calcium metabolism
- immunosuppressant therapy
- patients allergic to porcine collagen products

WARNINGS:
One of the potential risks identified with any surgical procedure is death. Other potential risks which may require additional surgery, include:

- inflammation
- infection
- neurological injury
- vascular or visceral injury
- implant migration
- non-union or delayed union

nanOss Bioactive 3D does not possess sufficient mechanical strength to support the reduction of a fracture site prior to soft and hard tissue in-growth or to support a load. Standard internal fixation techniques such as the use of plates and/or screws must be followed to obtain rigid stabilization. External stabilization alone is not sufficient to achieve the rigidity necessary for bony in-growth of the nanOss Bioactive 3D material. nanOss Bioactive 3D must not be used to gain screw purchase or to stabilize screw placement. Screws used with nanOss Bioactive 3D and fixation devices must attain rigid fixation into the host bone.

Do not use nanOss Bioactive 3D where complete soft tissue coverage cannot be achieved.

This system has not been evaluated for safety and compatibility in the MR environment. This system has not been tested for heating or migration in the MR environment.

PRECAUTIONS:

- nanOss Bioactive 3D is intended for use only by surgeons familiar with bone grafting and rigid fixation techniques.
- nanOss Bioactive 3D is radiopaque and the radiopacity may mask underlying pathological conditions.
- nanOss Bioactive 3D is intended for single use only.
- Always follow recommended mixing instructions when rehydrating nanOss Bioactive 3D.
- Do not apply nanOss Bioactive 3D dry to the defect.
- Do not resterilize nanOss Bioactive 3D.
- Discard any un-used nanOss Bioactive 3D.
- Do not expose nanOss Bioactive 3D to temperature extremes such as freezing or excessive heat.
- nanOss Bioactive 3D has no weight bearing function.
- The use of non-steroidal, anti-inflammatory drugs or other immune modulators should be avoided as they may inhibit bone fusion.
- For best results, product should fill the defect and contact viable bone as much as possible. Over-filling the defect site should be avoided.
- Postoperative patient management should follow the same regimen as similar cases utilizing autogenous bone grafting. Standard postoperative practices should be followed, particularly as applicable to defect repairs involving the use of fixation devices.

See insert for complete labeling limitations related to this device.
REFERENCES


2. Data on file at RTI Surgical.


4. K082575.

5. K032409.

6. Data on file at RTI Surgical, Inc.


12. MacMillan et al. Similar healthy osteoclast and osteoblast activity on nanocrystalline hydroxyapatite and nanoparticles of tri-calcium phosphate compared to natural bone. *International Journal of Nanomedicine. Volume 2014:9(1). 5627-5637. The authors would like to thank RTI Surgical for funding the proposed study.