

## The products

BRS-1610 Inion OTPS BioRestore™ Morsels 4.5 cc

BRS-1611 Inion OTPS BioRestore™ Morsels 1.5 cc

BRS-5430 Inion BioRestore™ Morsels 1.5 cc

BRS-5431 Inion BioRestore™ Morsels 4.5 cc



Inion BioRestore™ Morsels

### Clinical indications for use:

The Inion BioRestore™ implants are bone graft substitutes indicated for bony voids or gaps that are not intrinsic to the stability of the bony structure. Inion BioRestore™ is indicated to be gently packed into bony voids or gaps of the skeletal system (i.e., the extremities, spine, pelvis, oral and craniomaxillofacial defects\*). These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. The product provides a bone void filler that resorbs and is replaced with bone during the healing process.

\*For country and item specific indications, please refer to the instructions for use.

Inion BioRestore™ cannot be used for load bearing indications without simultaneous use of traditional rigid fixation.

Inion BioRestore™ is indicated for bony voids or gaps that are not intrinsic to the stability of the bony structure.

Inion BioRestore™ is not intended to withstand the stress of immediate load bearing prior to soft and hard tissue ingrowth without appropriate additional fixation.

In cases of fracture fixation or load bearing applications, standard internal or external stabilisation techniques must be followed to obtain rigid stabilisation in all planes.

The Inion BioRestore™ implants are not intended for use in and are contraindicated for:

- Active or potential infection.
- Patient conditions including:
  1. Use of medication known to affect the skeleton (e.g., chronic glucocorticoid usage >10mg/day for the previous 3 months). Estrogen replacement therapy is allowed.
  2. Need for chronic anticoagulant therapy (e.g., heparin). Prophylactic use of Coumadin or aspirin postoperatively is allowed.
  3. A systemic metabolic disorder known to adversely affect bone healing and mineralisation (e.g., poorly controlled insulin-dependent diabetes, renal osteodystrophy, Paget's disease), other than primary osteoporosis.
  4. Any existing condition or disease that will interfere with good soft tissue and bone healing.
  5. Defects requiring graft material to exceed the volume of 30 cm<sup>3</sup>.
  6. Limited blood supply.
  7. When patient cooperation cannot be guaranteed (e.g. alcoholism, drug abuse).



## Inion BioRestore™ - Bridging the Gap



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### Inion BioRestore™ Bone Graft Substitute

- Biodegradable bioactive glass which is replaced by bone
- Provides scaffold for new bone growth
- Osteoconductive and osteostimulative
- Easy to use



# Inion BioRestore™

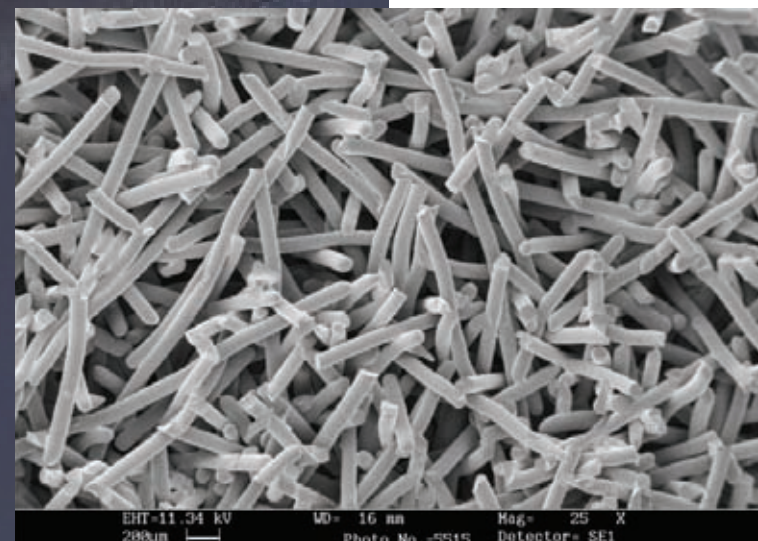
## Introduction

Inion BioRestore™ is a synthetic bone graft substitute, which remodels into bone and is easy to use. Inion BioRestore™ is made from degradable bioactive glass which once in contact with the natural body fluids forms a silica gel and calcium phosphate layer which provides scaffolding for new bone tissue to be formed.

Its synthetic origin and biocompatibility makes it safe to use within the body. The properties of the degradable bioactive glass used in Inion BioRestore™ ensure an excellent in vivo behaviour. The Inion BioRestore™ scaffold provides ideal osteoconductivity and osteostimulativity. Inion BioRestore™ undergoes a time-dependent, kinetic modification of the surface that occurs when implanted in living tissue. Specifically, the surface reaction results in the formation of a calcium phosphate layer that is substantially equivalent in composition and structure to the hydroxyapatite found in bone mineral.

This apatite layer provides scaffolding onto which the patient's new bone will grow allowing repair of the defect. Inion BioRestore™ is gradually resorbed and replaced by new bone during the healing process, this process is estimated to take 6 months *in vivo* (based on preclinical testing). An important point to note is that the Inion BioRestore™ degrades significantly faster than products made of hydroxyapatite. Inion BioRestore™ can be used for orthopaedic trauma and spine surgery for filling bony voids or gaps that are not intrinsic to the stability of the bony structure.

The use of Inion BioRestore™ is an advantageous alternative to harvesting of autograft bone and use of allograft bone. It shortens operative time, overcomes the limitations in quantity and quality of available bone graft, avoids donor site morbidity and risk of disease transmission.



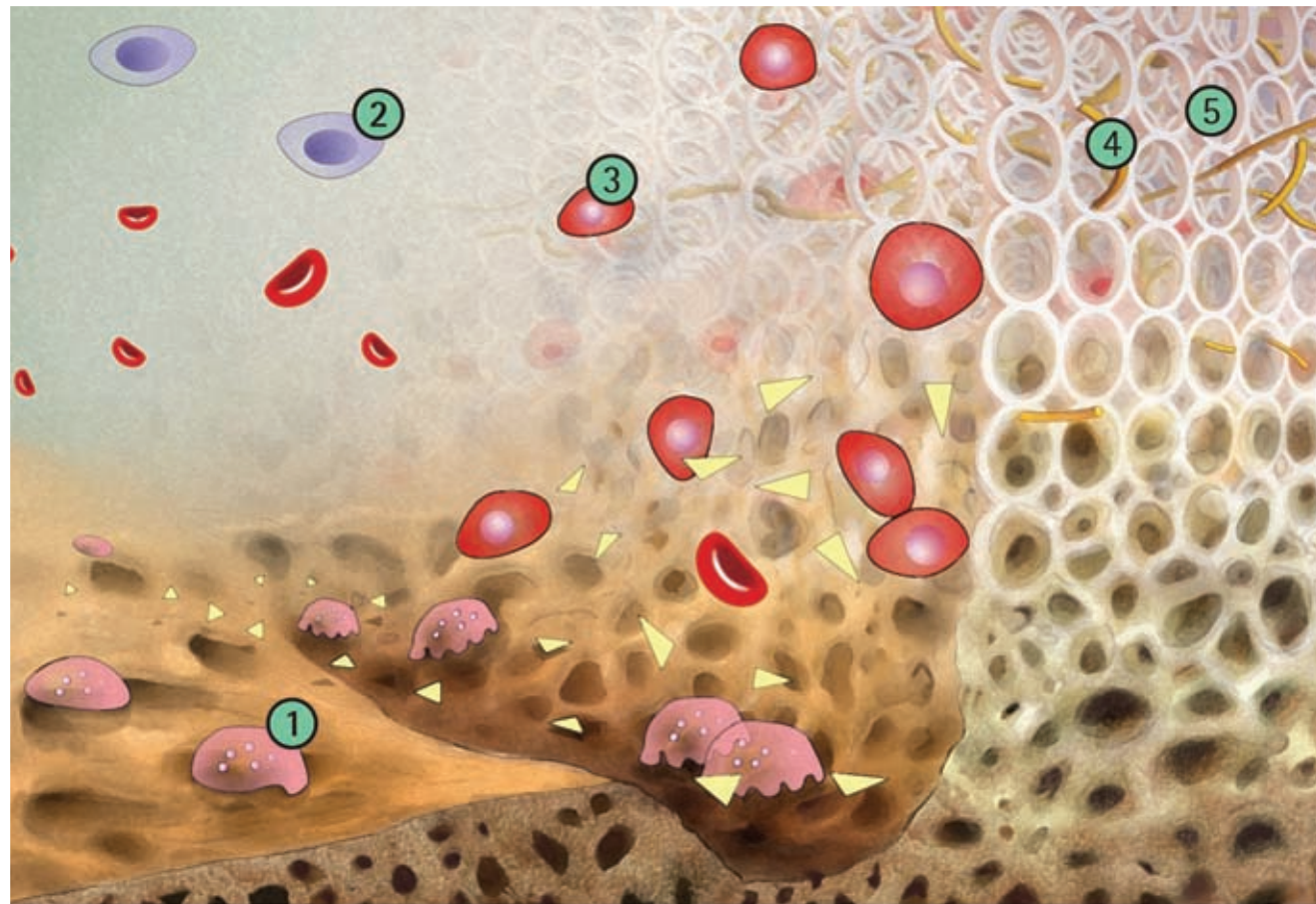
Inion BioRestore™ provides a scaffold or temporary framework used to support new bone formation and remodelling where a bone defect has occurred, for example traumatic injury.

# How Inion BioRestore™ works

Inion BioRestore™ works by osteostimulation which is defined as the active stimulation of osteoblast proliferation and differentiation.\* As shown during *in vitro* studies by increased levels of alkaline phosphatase, Inion BioRestore™ supports higher osteoblast activity and expression and acts as a scaffold around and through which new bone forms.

Scaffolds are composed of fibres which are welded together to form an interconnected, fully open three dimensional structure that allows for the bone cells to weave between the scaffold and lay down a solid matrix of new bone tissue.

\*For a detailed definition please refer to the instructions for use.

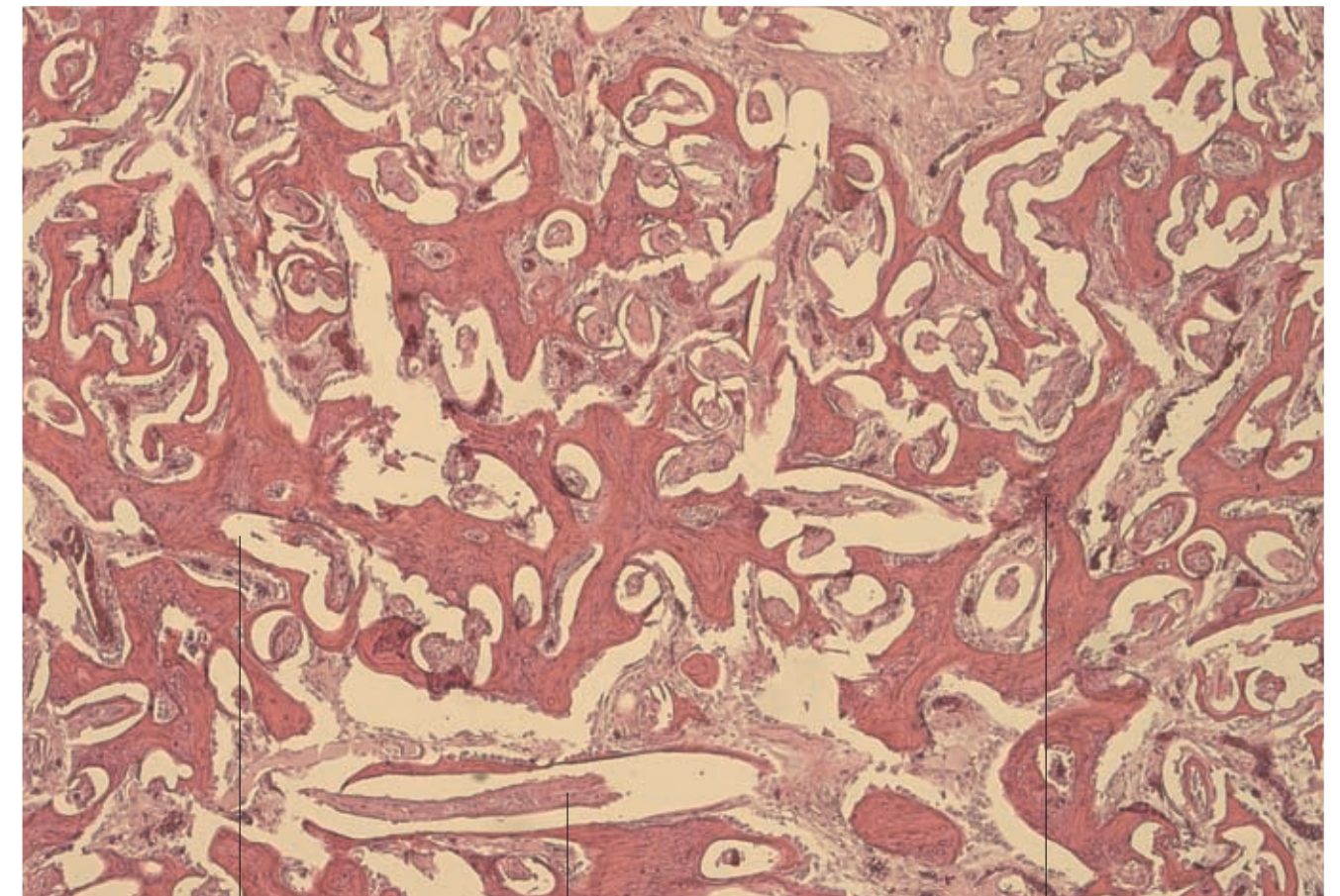


1. Osteoclast
2. Mesenchymal stem cell
3. Osteoblast
4. Protein
5. Inion BioRestore™ scaffold

- Increased level of osteoblast activity and differentiation have been shown by increased levels of alkaline phosphatase
- Bone grows not only from the outside of the defect towards its insides (osteoconductivity), but also throughout the defect (osteostimulativity)

The modified surface of the Inion BioRestore™ immediately begins to interact with the body's own proteins, cells and growth factors for tissue regeneration.

In a continuing chemical reaction occurring over the next few days, a temporary scaffold of hydroxyapatite crystals forms on the surface of the Inion BioRestore™ fibres which traps and bonds these building blocks to create a bed for new tissue growth.



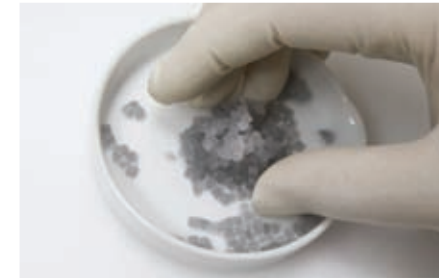
Scaffold material

Bony tissue formation inside a degraded fibre

Bony tissue formation inside the 3D structure

# Advantages of Inion BioRestore™

- Inion BioRestore™ is osteostimulative as it actively stimulates bone cells whilst providing a temporary scaffold to support the new bone formation process.
- The highly porous and fully open structure of the Inion BioRestore™ scaffold enables better flow of fluid, cells and nutrients.
- The ability of Inion BioRestore™ to develop a calcium phosphate layer during degradation provides an extremely high surface area and enhances osteointegration and bone tissue incorporation.
- Inion BioRestore™ scaffolds degrade significantly faster than the commercially available products made from HA and are degraded in a controlled manner.
- The use of Inion BioRestore™ is an advantageous alternative to harvesting autograft bone and use of allograft bone in a variety of surgical procedures. Its synthetic origin excludes risks of disease transmission and overcomes the limitations in quantity and quality of available bone graft. Donor site morbidity is avoided as no autograft needs to be taken or in case autograft is used through filling the donor site defect with Inion BioRestore™.



- Preoperative radiographic evaluation of the defect site is essential to accurately assess the extent of the defect and to aid in the selection and placement of the graft material. Care should be taken not to over compress morsels into defect. Inion BioRestore™ should be gently packed into the bone void so to guarantee that the Inion BioRestore™ morsels retain their three dimensional structure and optimal pore size.
- The Inion BioRestore™ should be wet with patient's blood or marrow, or sterile saline or water before application. While the Inion BioRestore™ can be moistened with either sterile saline or water, osseous regeneration may occur more rapidly by using the patient's osteogenic blood or marrow obtained by scoring the surface or drilling into the cortical bone at the surgical site. Place the desired fluid in a sterile basin or other suitable container. Place the material in contact with the desired fluid to soak up the fluid. The porous structure of the material will allow the fluid to immediately permeate into the implant.

## Comparison of synthetic HA, TCP and Inion BioRestore™ as bone graft substitutes\*

	HA	TCP	Bioactive Glass
Physical Form	Porous / bulk blocks and granules.	Porous blocks, morsels and granules.	Bulk blocks, granules and porous morsels.
Basic Mechanism	Serves as osteoconductive surface.	Serves as osteoconductive surface.	Forms chemical bonding with ongrowing new bone. Osteostimulative in addition to osteoconductive.
Molecular Mechanism of Action In Vivo	Not defined.	Not defined.	Induce high local bone turnover.
Regulation of Bioactivity	Material dependent.	Material dependent.	Tailored by varying composition.
Degradation Rate	Slowly / very slowly degraded (years / decades).	Fast degraded (months).	Fast degraded (months).
Mechanism of Degradation	Chemical dissolution and osteoclastic degradation.	Chemical dissolution and osteoclastic degradation.	Chemical dissolution.

\*Chart has been created using references from various comparison charts published in scientific reviews.