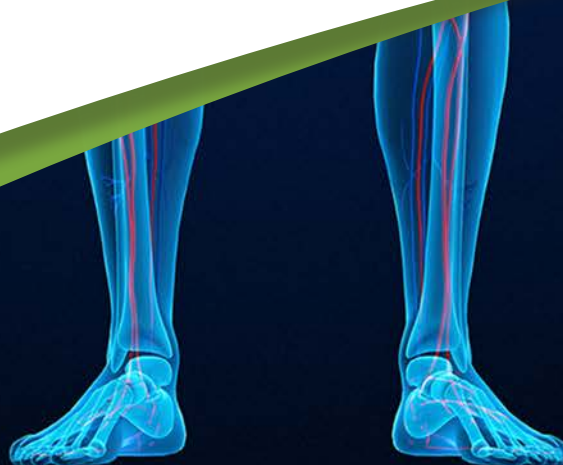




CERAMENT™ | BONE VOID FILLER

Mechanism of Action





How CERAMENT™ Works

This article explains how CERAMENT™|BONE VOID FILLER works to support bone formation and healing.

By filling a bone defect with CERAMENT™|BONE VOID FILLER, which contains 60% calcium sulfate (CaS) and 40 % hydroxyapatite (HA), an optimal balance is achieved between implant resorption rate and bone ingrowth rate. This fulfills three important needs for bone healing:

1. The void is filled and therefore it can not be invaded by fibrous tissue.
2. CERAMENT™ hardens in situ, augments the bone, and gives long term structural support to newly formed bone.
3. CERAMENT™ acts as a scaffold for the ingrowth of bone.

The Composition of CERAMENT

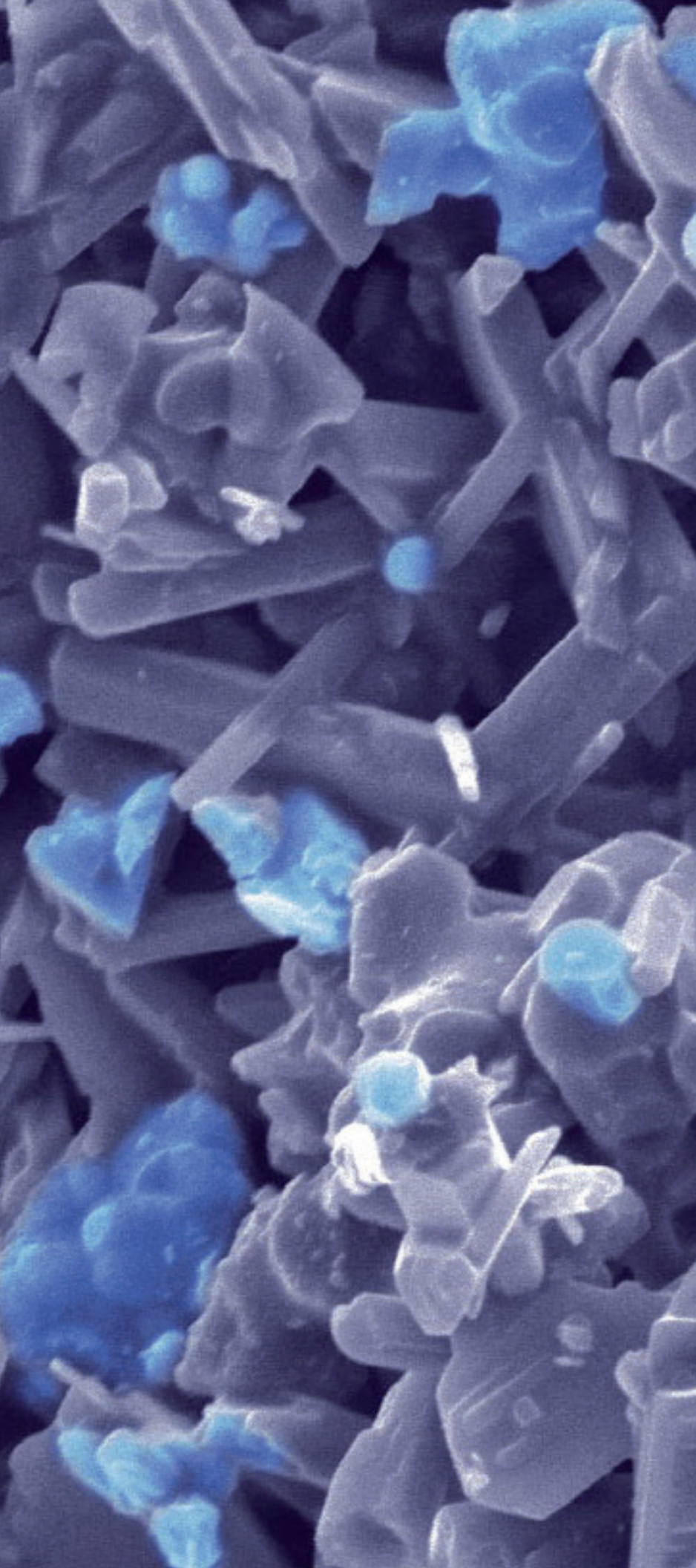
CERAMENT™|BONE VOID FILLER is a biphasic injectable bone graft substitute. It is synthetically made and has one osteoconductive component, hydroxyapatite (HA), and one resorbable component, calcium sulfate (CaS). CERAMENT™|BONE VOID FILLER also includes a radio-opacity enhancing component (iohexol), which makes the material highly visible under fluoroscopy and x-ray.

The Mechanism of Action

To achieve bone formation and healing, a bone substitute must be porous to allow penetration of living cells. Blood capillaries, osteoblasts and osteoclasts have to be able to invade the material to allow bone remodeling. Therefore, the resorption rate of an implant material must correspond to the bone ingrowth rate in order to optimize the healing of the defect:

- Too slow resorption of the implant will obstruct the growth of new bony tissue and will slow down the healing process.
- Too fast resorption of the implant will leave a gap between the implant and the ingrowing bone with a risk of fibrous tissue interpositioning.

With CERAMENT™|BONE VOID FILLER, the controlled resorption of CaS matches the rate of bone ingrowth and allows contact between HA and the bone, which in turn supports new bone growth.



Important Terms

Biphasic - A biphasic system is one which has two phases.

Bioactive - Relating to a substance that has an effect on living tissue.

Biocompatibility - The property of being biologically compatible by not producing a toxic, injurious, or immunological response in living tissue.

Osteoconductivity - Osteoconduction occurs when the bone graft material serves as a scaffold for new bone growth that is perpetuated by the native bone.

Porosity - is a measure of the void (i.e., "empty") spaces in a material.

Vascularization - The formation of blood vessels and capillaries in living tissues.

Osteoblasts - Are mononucleate cells that are responsible for bone formation.

Osteoclasts - Are cells that resorb bone tissue.

CERAMENT™'S 40/60 ratio of HA/CaS provides maximum osteoconductivity while keeping a strength suitable for augmentation of cancellous bone defects.

Step 1: Biphasic

CERAMENT™|BONE VOID FILLER consists of a powder that is mixed with a liquid and becomes an injectable paste which hardens in situ.

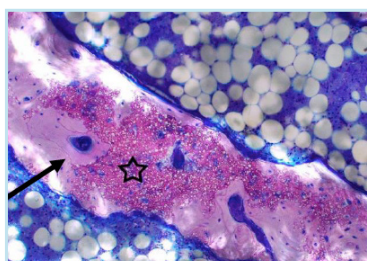
CaS is used for its tissue integration and biocompatibility. CaS makes it possible to create an injectable paste and works as a delivery tool for the HA. The CaS will dissolve and be actively resorbed by osteoclastic activity⁷ within 6-12 months⁹. Dissolution of the CaS creates space for new bone growth.

The HA used in CERAMENT™ is engineered to be stable. It offers high injectability and gives long-term support to the defect. The HA particles form an osteoconductive scaffold, augmenting the CaS to retard its resorption rate.⁸ The HA particles are embedded into newly formed bone.

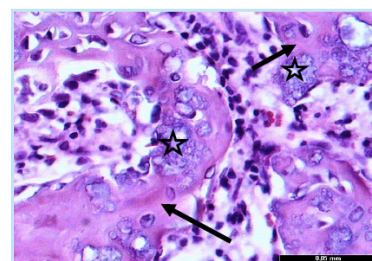
Step 2: Implantation

When mixing the powder component with the liquid component of CERAMENT™|BONE VOID FILLER, a paste is formed which can be injected into cavities or drill holes, or molded and implanted.

The liquid component of CERAMENT™|BONE VOID FILLER is an iohexol solution (CERAMENT™|IC-TRU). Iohexol is an iodine based non-ionic radio opacity enhancing agent.¹² Iohexol does not metabolize and is cleared from the body through renal excretion¹³. Iohexol also increases lubrication of the powder for high injectability through narrow needles and ensures an excellent spread in the trabecular system. Injection of CERAMENT™|BONE VOID FILLER can thus be followed visually under fluoroscopy and x-ray.



Shows CERAMENT™ with transluminescent HA particles (star) inside a newly formed bone trabecula (arrow).



Shows fragments of CERAMENT™ (star) incorporated in new, immature bone tissue (arrow).

Step 3: Bioactivity

CERAMENT™|BONE VOID FILLER is bioactive, which means that a precipitated layer of endogenous hydroxyapatite will spontaneously form on the material surface approximately 1-3 days after implantation. This enhances the direct contact between material and bone because the bone cells recognize the apatite layer as bone mineral.

Step 4: Osteoconductivity

CaS alone is not an osteoconductive material. The calcium sulfate component in CERAMENT™ delivers the osteoconductive HA. By having 40% HA in CaS, CERAMENT™|BONE VOID FILLER provides maximum osteoconductivity while keeping strength suitable for augmentation of cancellous bone defects. The mechanical properties of this unique combination closely match cancellous bone.¹¹

When CERAMENT™|BONE VOID FILLER is implanted and after the CaS has resorbed, new bone will completely surround and embed the HA particles.¹⁶

Step 5: Bone Formation

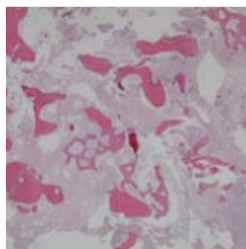
Through initial micro porosity and later macro porosity, early vascularization and invasion of osteoblasts enable multiple site formation of bone throughout the cured CERAMENT™|BONE VOID FILLER implant.

Immature bone tissue is first formed by the osteoblasts but is later mineralized and remodeled into new trabecular bone. The bone remodeling process includes both osteoclasts and osteoblasts and they are both seen at the material bone interface. The new trabeculae will become thicker and denser, which increases the mechanical strength of the newly formed bone.¹⁶

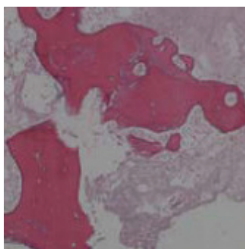
The CaS in CERAMENT will dissolve and be actively resorbed by osteoclastic activity⁷ within 6-12 months⁹.



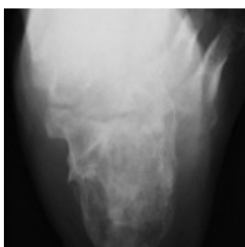
X-ray immediately post surgery.



Histology at 4 months showing new bone growth.

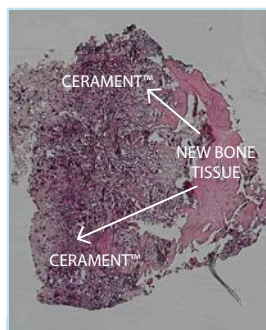


X-ray after removal of the plate.

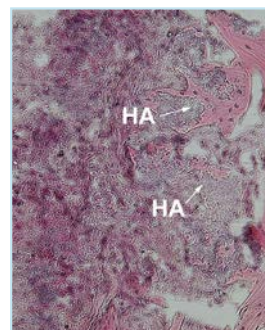


Credit: Damiano Papadia

Reparto di Ortopedia e, Traumatologia Ospedale, Santa Chiara, Trento, Italy



A close contact was found between CERAMENT™ and new bone tissue at 6 weeks post implantation of CERAMENT™. The new bone tissue invaded CERAMENT™ and no sharp bone/implant interface was observed.



Bony tissue completely surrounded and embedded the HA particles.

Conclusion

CERAMENT™|BONE VOID FILLER will facilitate bone ingrowth based on its micro and macro porosity properties, allowing for multiple islets of de novo bone formation throughout the implant.^{2-6, 9}

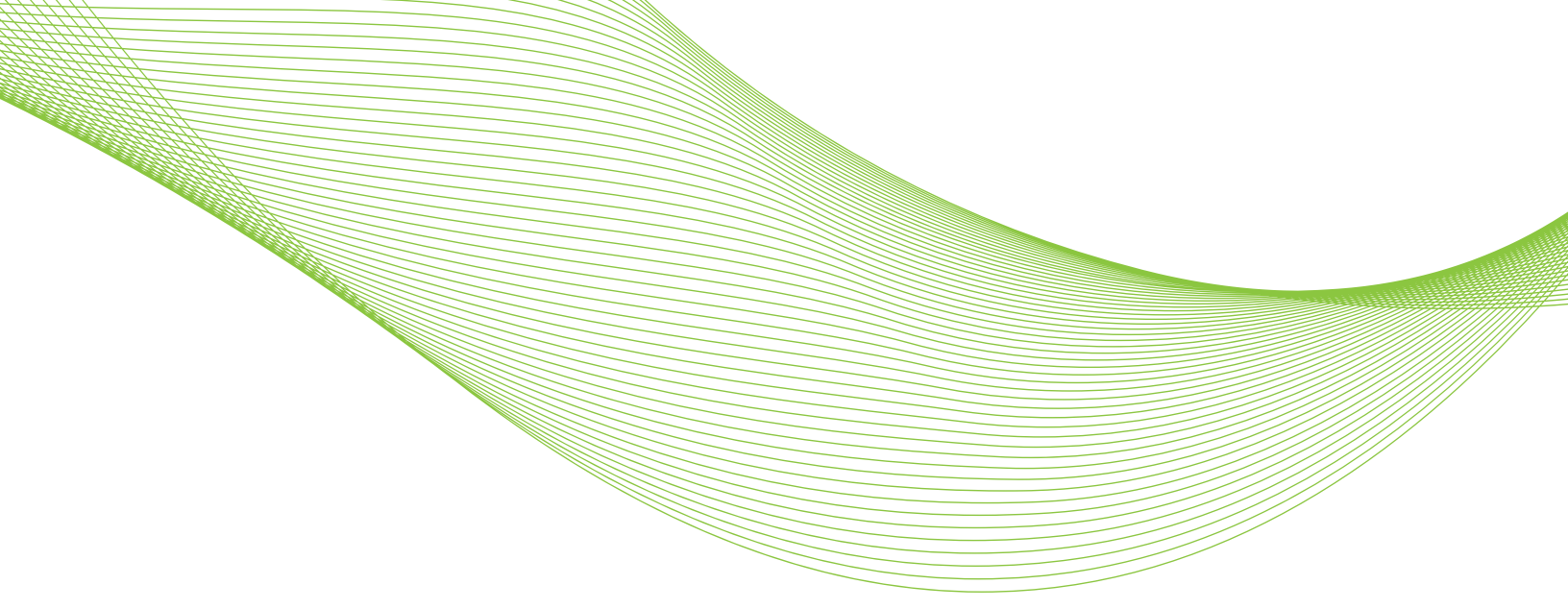
The resorption rate of the material is designed to match the speed of new bone tissue ingrowth. By using CaS as a complement to the osteoconductive HA, the material resorption will be complete and the HA particles ultimately get incorporated into the newly formed bone trabecula.^{8, 9, 15}

The bioactivity of the material initiates a precipitated layer of endogenous HA resulting in a thin layer of apatite on the implant surface¹⁰, which enhances the material-bone cell contact¹⁴ and retards the CaS resorption.¹⁰

New bone has not only been deposited on the outside of the material but the bone generation has occurred at multiple sites throughout the material^{2-6, 9}, which accelerates the transformation of CERAMENT™|BONE VOID FILLER into bone.

When bone-forming cells are in direct contact with CERAMENT™|BONE VOID FILLER, the HA particles get incorporated into the newly formed bone, which increases the bone density. After treatment with CERAMENT™|BONE VOID FILLER, complete bone healing is demonstrated within 6-12 months.¹

The material is easy to mix and handle. It hardens in situ and all in vivo studies have shown good biocompatibility, adequate resorption rate and good bone healing.



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OUR MISSION is to improve the lives of patients suffering from bone disorders that cause bone voids, lead to injury, breakage, pain, and reduced quality of life.

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