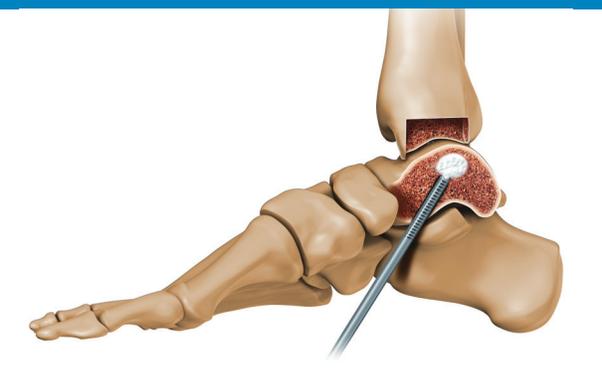
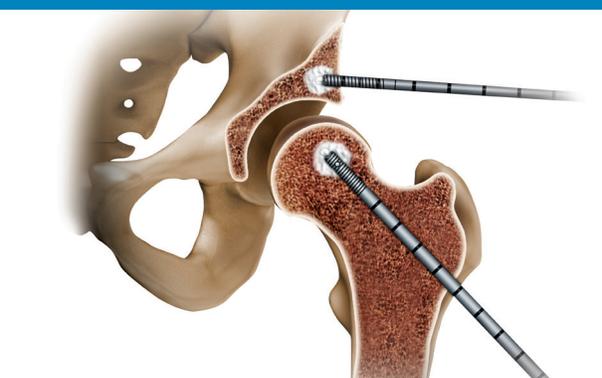
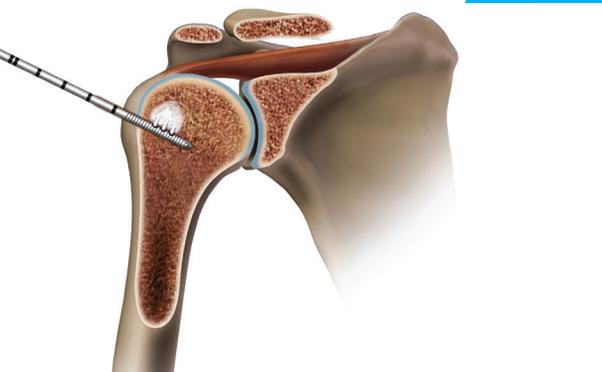


AccuFill® Bone Substitute Material (BSM)

The Subchondroplasty® Procedure



ZIMMER BIOMET

Your progress. Our promise.®

AccuFill BSM

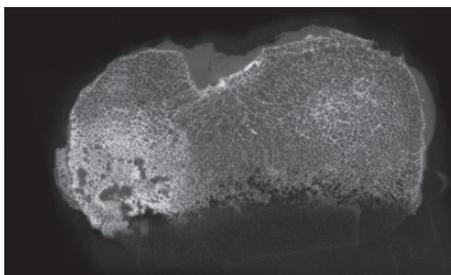


BML Bone Defect on T2 MRI

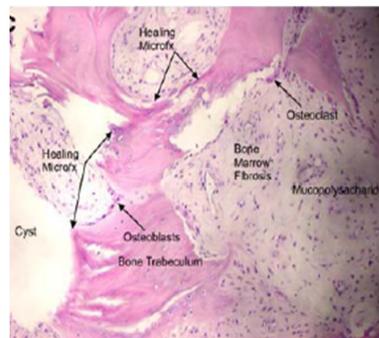
The Subchondroplasty Procedure is a minimally-invasive fluoroscopically-assisted procedure that targets and fills subchondral bone defects not intrinsic to the bony structure. These defects can be associated with bone marrow lesions (BML), insufficiency or microtrabecular fractures, repetitive stress injuries to the cancellous bone, or cysts. Successfully filling osseous defects of the trabecular bone requires an injectable BSM with very specific characteristics.

An optimal material for the Subchondroplasty Procedure:

1. Flows readily into closed trabecular bone¹
2. Sets hard upon implantation, with properties comparable to healthy cancellous bone²
3. Undergoes cell-mediated remodeling as the bone heals²



Micro CT from patient with bone marrow lesion.



Histologic section of patient with bone marrow lesion, showing evidence of microfracture non-union of the subchondral bone.³



AccuFill BSM: Performance Characteristics

AccuFill BSM is an engineered calcium phosphate compound. It flows readily to fill subchondral bone defects, then crystallizes and sets in an isothermic reaction at 37°C to form a nanocrystalline*, macroporous scaffold in the bone. Inclusion of a binding agent (CMC [carboxymethylcellulose]) allows the material to remain bound in a paste form, and interdigitate into closed cancellous bone.

- Passes through delivery devices as small as 15 ga without phase separation of hydrant from powder
- Flowable into trabecular network
- Isothermic hard setting - no thermal damage to surrounding tissue



Standard Injectable BSM



AccuFill BSM

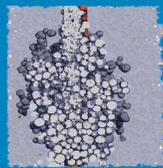


AccuFill BSM Injection Study¹

Results and images from a BSM injection study in the setting of closed cancellous bone model show that AccuFill BSM flows readily and reproducibly, under light digital pressure, to fill a larger volume than other evaluated materials.

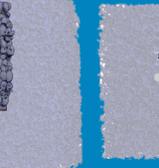
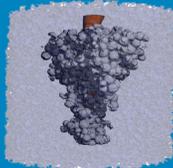


AccuFill BSM



Other BSM 1:

Tri-Calcium Phosphate Apatite



Other BSM 2:

Calcium Sulfate/Hydroxyapatite

Important Safety Information: The use of AccuFill BSM is not intended to be intrinsic to the stability of the bony structure. Radiographic studies should be used to confirm that the adjacent cortical bone is intact. AccuFill BSM is not intended for use in vertebroplasty or similar load-bearing indications. AccuFill BSM is not intended for the treatment of cartilage defects or injury. AccuFill BSM is not intended to support articular cartilage or cortical bone.

* The grain size of the hydroxyapatite (HA) crystals that form as part of the amorphous and crystalline mixture of calcium phosphate sets are on the nanometer scale. The size of the crystalline structures were measured by x-ray diffraction to be less than 100 nanometers.

AccuFill BSM: Performance Characteristics

Intraoperative Images of AccuFill BSM Interdigitation



Proximal Femur

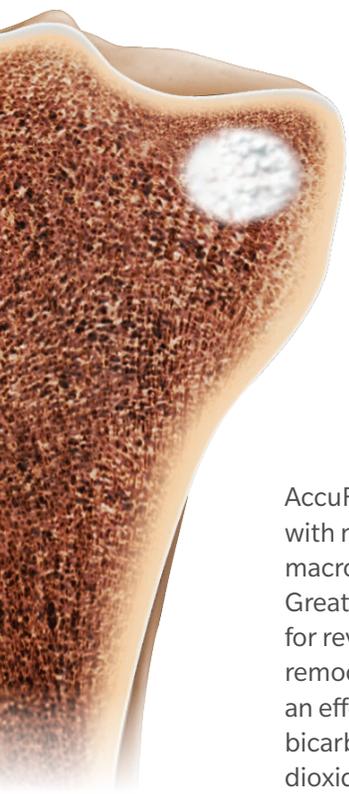


Distal Tibia

AccuFill BSM: Properties²

- Mimics chemical composition and crystalline structure of natural human bone mineral
- Incorporation of metal ions (M) keeps the crystal domain of AccuFill BSM to a size similar to those formed by bone apatite
- Reactive material, undergoes cell-mediated remodeling

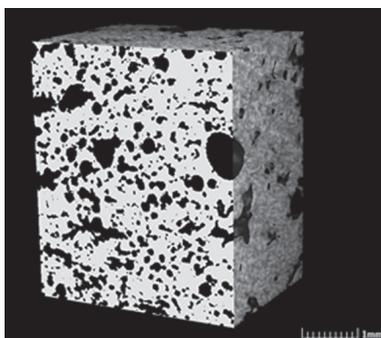
AccuFill BSM is composed of two distinct forms of calcium phosphate - amorphous calcium phosphate (ACP) and dicalcium phosphate dihydrate (DCPD). Due to rapid hydrolysis of the ACP into apatite, the final product is a calcium deficient, nanocrystalline* material which has the crystal structure and chemical formulation to undergo cell-mediated remodeling.



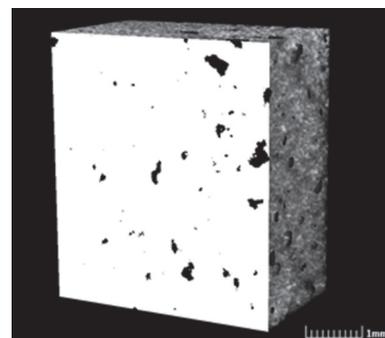
Chemical Formula/Crystalline Structure

Material	Chemical Composition	Average Nano Crystal			Total Volume (nm ³)
		Length (nm)	Width (nm)	Height (nm)	
Human Bone Mineral	$\text{Ca}_{10-x}(\text{M})_x(\text{PO}_4)_{6-x}(\text{HPO}_4, \text{CO}_3)_x(\text{OH})_{2-x}$	23-32	6.7-8.0	6.7-8.0	1,485
AccuFill BSM	$\text{Ca}_{10-x}(\text{M})_x(\text{PO}_4)_{6-x}(\text{HPO}_4, \text{CO}_3)_x(\text{OH})_{2-x}$	26	8	8	1,664
Standard Calcium Phosphate	$\text{Ca}_{10-x}(\text{PO}_4)_{6-x}(\text{HPO}_4, \text{CO}_3)_x(\text{OH})_{2-x}$	22	26	26	14,872

AccuFill BSM is 55% porous, with micropores and macropores up to 300µm. Greater surface area allows for revascularization and remodeling.^{5,6} The inclusion of an effervescent agent (sodium bicarbonate) releases carbon dioxide during the setting process and forms pores within the material.



AccuFill BSM Porosity⁴



Standard CaP Porosity⁴

* The grain size of the hydroxyapatite (HA) crystals that form as part of the amorphous and crystalline mixture of calcium phosphate sets are on the nanometer scale. The size of the crystalline structures were measured by X-ray diffraction to be less than 100 nanometers.

AccuFill BSM: Handling Properties

- May be mixed with saline or whole blood
- 15 minute working time - easy, closed syringe mixing
- Inject with 1cc syringes - digital injection pressure



AccuFill BSM: Summary

Criteria	Feature	Benefit
Performance	Truly injectable and flowable through cancellous bone. Remains Cohesive. Isothermally sets in 10 minutes at 37° C.	Interdigitates easily into trabecular network – no need to create a void. No phase separation from injection pressure. Sets hard, no thermal necrosis.
Properties	Proprietary engineered apatite, similar to apatite of bone. Osteoconductive. Nanocrystalline* structure, macroporous scaffold. 55% total porosity; 1-300µm pore size. ~7-9 MPa compressive strength. ²	Undergoes cell-mediated remodeling into natural bone. Porosity and pore size give it greater surface area for cellular activity. ⁷ Physical properties comparable to cancellous bone.
Handling	15 minutes of working time. May be mixed with saline or whole blood. Injectable under digital pressure.	Long window for implantation; intraoperative flexibility. Tactile feedback during injection.

AccuFill Bone Substitute Material is an injectable, self-setting, macroporous, osteoconductive, calcium phosphate bone graft substitute material that is intended for use to fill bony voids or gaps of the skeletal system of the extremities, spine (i.e., posterolateral spine), and the pelvis that are not intrinsic to the stability of the bony structure. These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. AccuFill Bone Substitute Material is a bone graft substitute that resorbs and is replaced with new bone during the healing process.

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Animal data is not necessarily indicative of clinical outcomes.

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MANUFACTURED BY:**
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55 Messina Drive
Braintree, MA 02184

**AccuFill BSM
DISTRIBUTED BY:**
Zimmer Knee Creations, Inc.
841 Springdale Dr.
Exton, PA 19341

AccuFill BSM: Properties

AccuFill BSM in a Femoral Condyle Preclinical Canine Model⁸

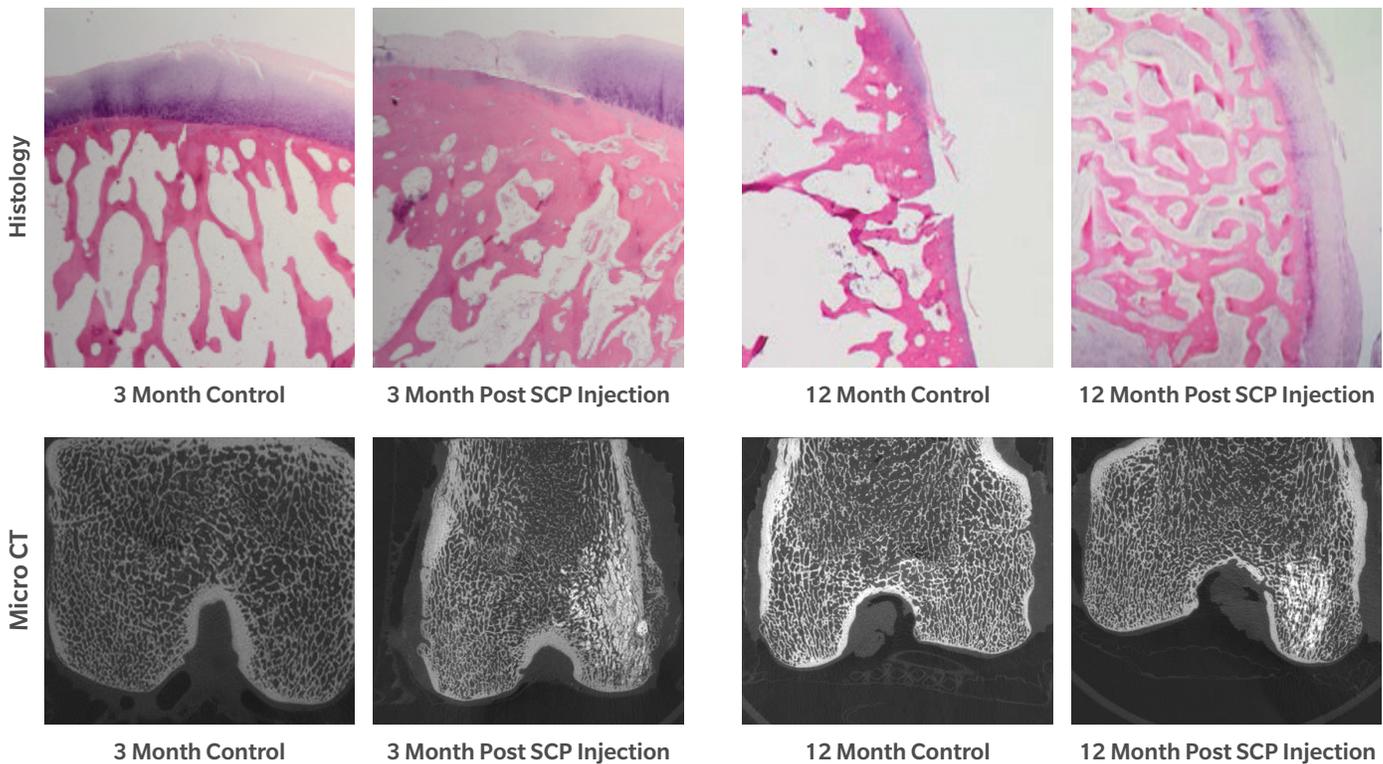
Subchondroplasty Canine Impact Model Study 1 year report

James L. Cook, DVM, PhD

Comparative Orthopaedic Laboratory

Missouri Orthopaedic Institute

Study tested canine subjects' healing response to an artificially created bone defect treated with SCP, vs control group with no treatment. The bone defects were created using a validated impact model, replicating the pathology of a chronic BML.⁹



Note the incorporation of the AccuFill BSM in the SCP samples vs. the loss of trabeculae and unresolved subchondral insufficiency fractures in the control samples.

Canine models may not be predictive of human clinical results.

MRI Evidence of AccuFill BSM Undergoing Cell-Mediated Remodeling



AccuFill BSM 1 Month Post-Operative

Postoperative MRI evaluation following SCP Procedure shows gradual remodeling of AccuFill BSM into natural cancellous bone.



AccuFill BSM 14 Months Post-Operative