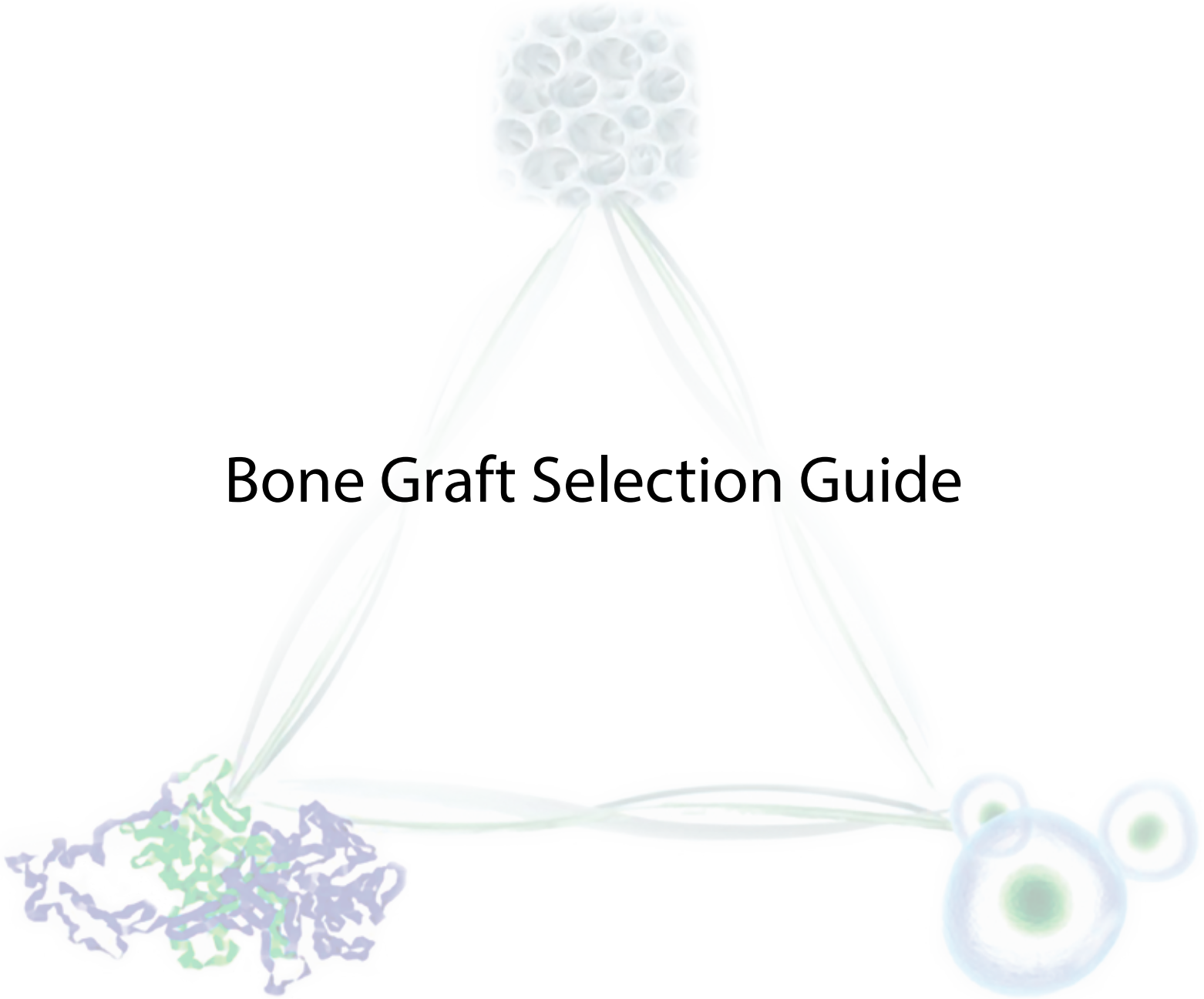
Bone Graft Selection Guide



BIOMET
BIOLOGICS

One Surgeon. One Patient.

Over 1 million times per year, Biomet helps one surgeon provide personalized care to one patient.

The science and art of medical care is to provide the right solution for each individual patient. This requires clinical mastery, a human connection between the surgeon and the patient, and the right tools for each situation.

At Biomet, we strive to view our work through the eyes of one surgeon and one patient. We treat every solution we provide as if it's meant for a family member.

Our approach to innovation creates real solutions that assist each surgeon in the delivery of durable personalized care to each patient, whether that solution requires a minimally invasive surgical technique, advanced biomaterials or a patient-matched implant.

When one surgeon connects with one patient to provide personalized care, the promise of medicine is fulfilled.

Purpose

Sales Representative Education Tool *Provides*

- Guidance on positioning Biomet Biologics bone-grafting products for various orthopaedic applications.
- Examples of clinical applications for various bone-grafting products.
- Definition of Mechanism of Action (MOA) and Handling Characteristics/Delivery Mechanism for the various bone-grafting options.
- Guidance on product combinations (i.e., PRP+DBM, etc.).
- Information on FDA-cleared clinical indications.

Bone Graft Selection Guide

Published Scientific Literature References to MOA Terms

- **Osteoconductive** materials provide the framework or scaffolding within a bone environment for cells to infiltrate and attach. It also offers the porosity for vascular pathways and cell migration. Materials that are generally referred to as osteoconductive include certain calciumphosphate/-sulphate based synthetics and allograft cortical or cancellous chips, sponges, and strips.[1, 2]
- **Osteopromotive*** materials enhance the natural bone-healing process.[3, 4, 5] Osteopromotive materials, such as PRP, are mixed with autograft or allograft materials to impart better graft-handling characteristics.[3, 4, 5]
- **Osteoinductive** materials induce bone-formation in a bony or non-bony environment via the action of growth factors or signaling proteins, such as Bone Morphogenetic Proteins (BMPs). These proteins stimulate the conversion of progenitor cells into bone forming osteoblasts.[2, 4]
- **Osteogenic** materials, such as autograft and/or bone marrow aspirate, contain viable cells, such as mesenchymal stem cells, osteoprogenitor cells, or osteoblasts, which are capable of synthesizing new bone.[2]

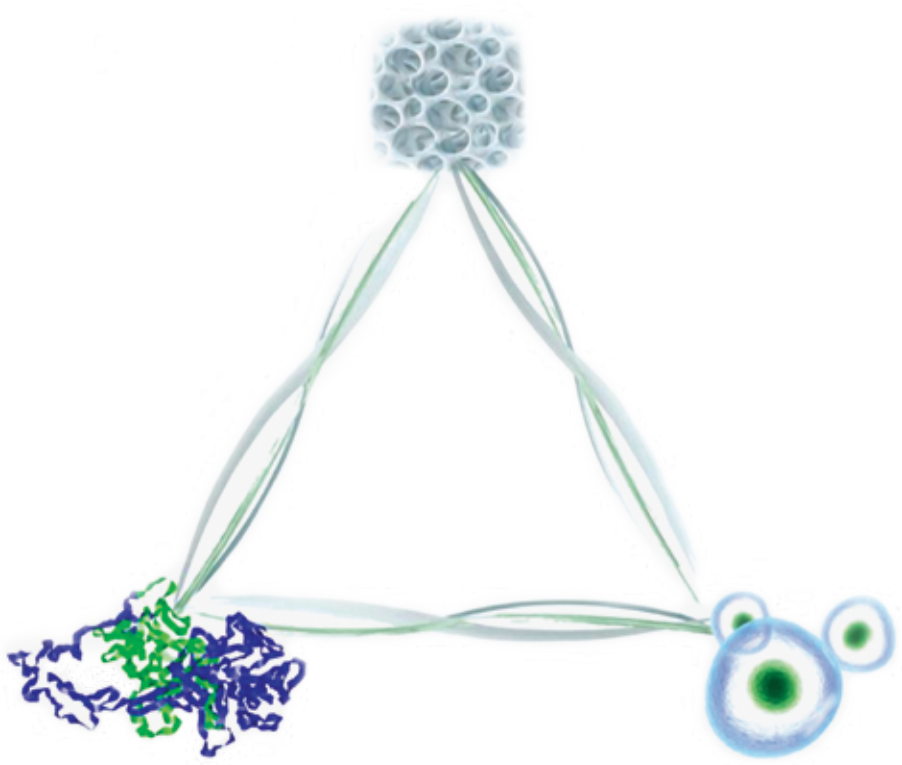
***Products that produce a PRP output do not currently have FDA clearance to be characterized with a specific mechanism of action. PRP, in and of itself (i.e., without the autograft or allograft), is not FDA cleared as "osteopromotive".**

1. Hak, The Use of Osteoconductive Bone Graft Substitutes in Orthopedic Trauma, J Am Acad Orthop Surg 2007; 15:525-36
2. Khan *et al*, The Biology of Bone Grafting, J Am Acad Orthop Surg 2005: 13:77-86.
3. Gandhi *et al*, The Role of Platelet-Rich Plasma in Foot and Ankle Surgery, Foot Ankle Clin N Am, 10 (2005) 621– 637.
4. Lewandrowski *et al*, Advances in Spinal Fusion – Molecular Science, Biomechanics and Clinical Management, p. 384-385, Marcel Dekker, Inc., 2004
5. Watson, Overview of Biologics, J Orthop Trauma, Vol. 19 No 10 Suppl, Nov./Dec. 2005.

Bone Graft Selection Guide

Essentials of Bone Healing

Scaffold / Matrix:
Osteoconductive



Osteoprogenitor Cells:
Osteogenic

Proteins / Growth Factors:
Osteoinductive
Osteopromotive

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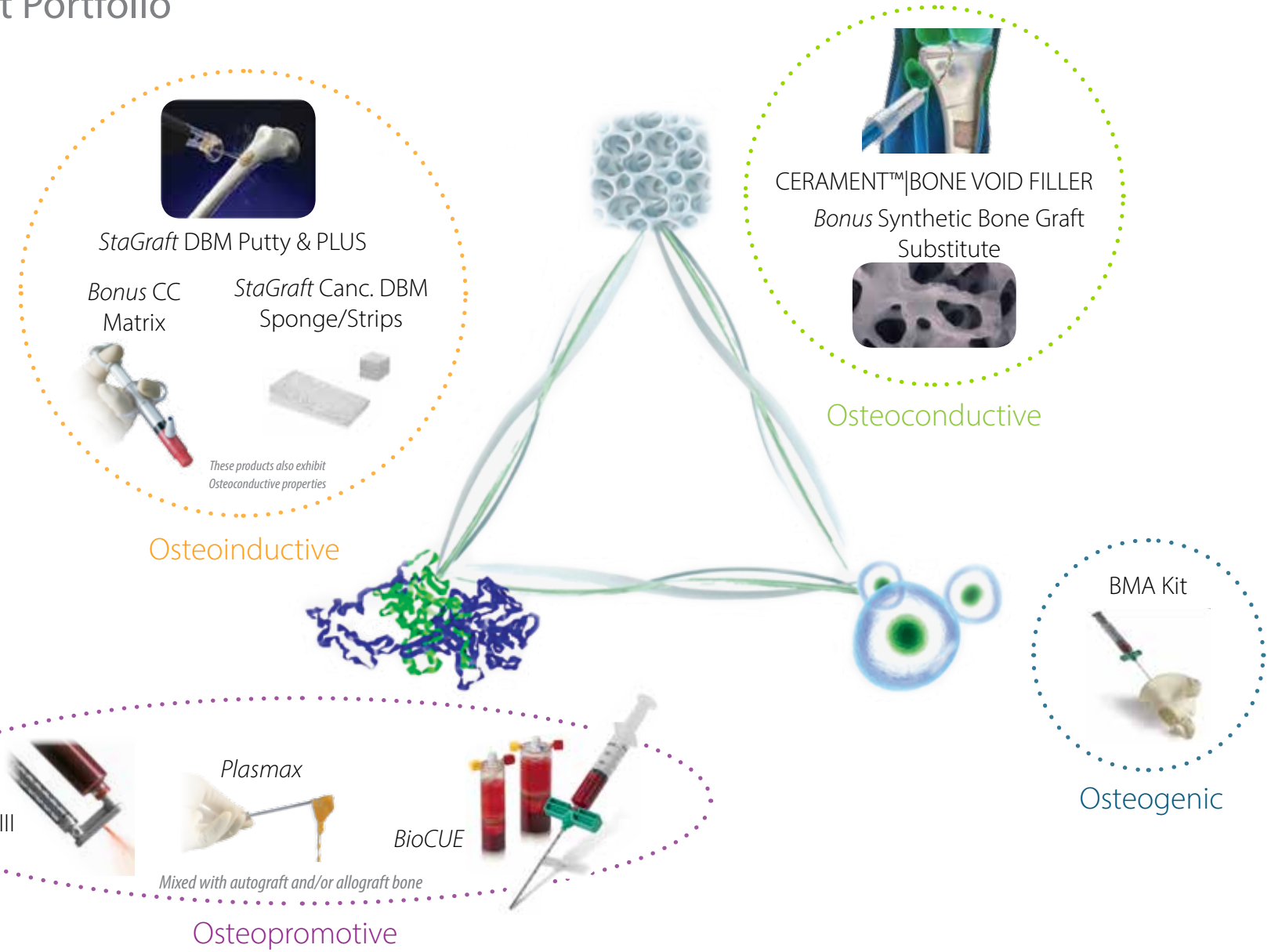
Product Portfolio



Bone Graft Selection Guide

1

Material: Synthetic granules
***Bonus* Synthetic Bone Graft Substitute**
MOA: Osteoconductive
Clinical Demand: Low
Handling: Medium

2

Material: Synthetic self-setting paste
CERAMENT™|BONE VOID FILLER
MOA: Osteoconductive
Clinical Demand: Medium
Handling: Very High

3

Material: DBM putty or DBM putty+Synthetic granules
***StaGraft* Putty/Plus**
MOA: Osteoconductive, Osteoinductive
Clinical Demand: Medium
Handling: Very High

4

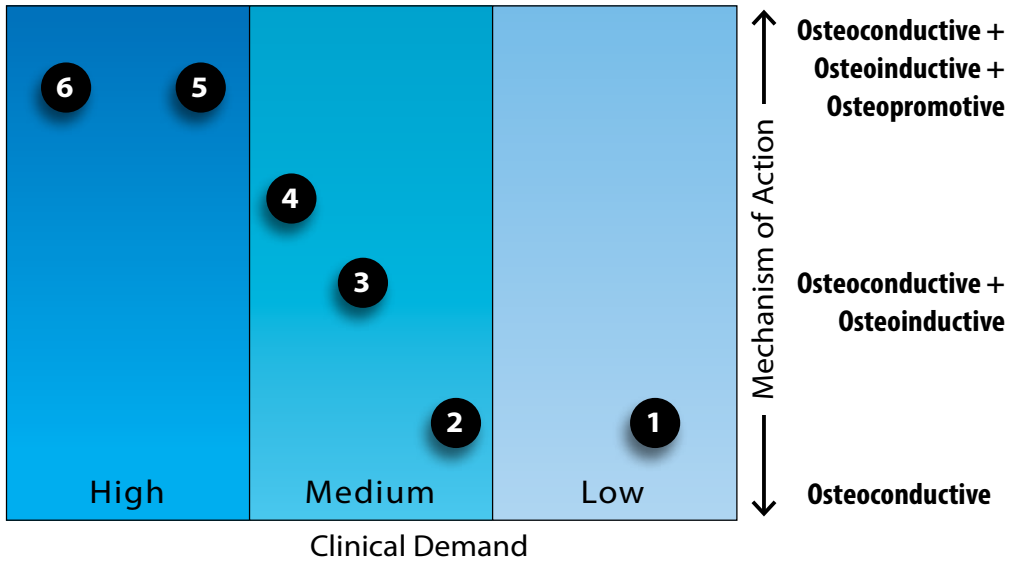
Autologous Input Materials: Whole blood
Graft Material: PPPc + allograft materials
(DBM or DBM + Cancellous Chips)
PPPc: *Plasmax*
Allograft Materials:
***StaGraft* Canc. DBM (or) *Bonus* CC Matrix**
MOA: Osteoconductive, Osteoinductive, Osteopromotive
Clinical Demand: Medium
Handling: Very High

5

Autologous Input Materials: Whole blood
Graft Material: PRP + allograft materials
(DBM or DBM + Cancellous Chips)
PRP: *GPS* III
Allograft Materials: *StaGraft* Cancellous DBM (or) *Bonus* CC Matrix
MOA: Osteoconductive, Osteoinductive, Osteopromotive
Clinical Demand: High
Handling: High

6

Autologous Input Materials: *B*BMA (blood and bone marrow aspirate)
Graft Material: PRP from *B*BMA + allograft materials
(DBM or DBM + Cancellous Chips)
PRP: *BioCUE*
Allograft Materials: *StaGraft* Cancellous DBM (or) *Bonus* CC Matrix
MOA: Osteoconductive, Osteoinductive, Osteopromotive
Clinical Demand: High
Handling: High



Handling Properties*: Low: Extremely low cohesion, sand-like particles. **Medium:** Not cohesive, i.e., loose granules. **High:** Good cohesion and/or molding properties. **Very High:** Excellent cohesion and/or molding properties.

***Data on file at Biomet.**

Bone Graft Selection Guide

Examples of Non-load Bearing Potential Clinical Applications & Graft Delivery

1 Material: Synthetic granules
**Fractures and bone cysts.*
Delivery via finger-packing and push/tamp with curette

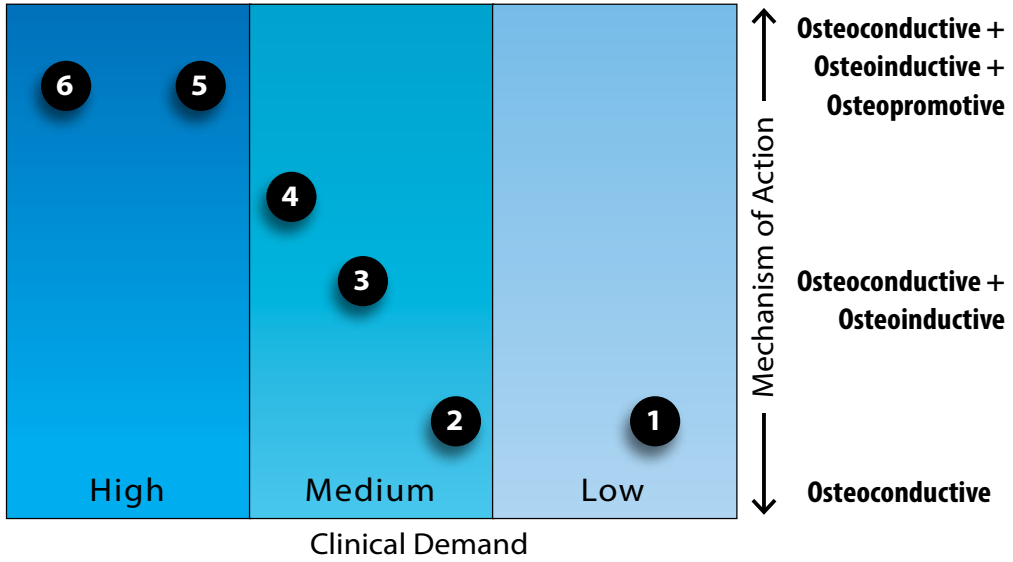
2 Material: Synthetic self-setting paste**
**Proximal and distal tibial, femoral and humeral fractures, forefoot and midfoot fusions, osteotomies, bone voids, osteolytic lesions, distal radial fractures.*
Delivery - inject via 16g or larger needle, or finger-pack and push/tamp with curette

3 Material: DBM putty or DBM putty+Synthetic granules
**Proximal and distal tibial, femoral and humeral fractures, forefoot and midfoot fusions, osteotomies, bone cysts, osteolytic lesions, posterolateral spine fusions.*
Delivery via open bore syringe or finger-packing and push/tamp with curette

4 Autologous Input Materials: Whole blood
Graft Material: PPPc + allograft materials
(DBM or DBM + Canc. Chips)
**Proximal and distal tibial, femoral and humeral fractures, forefoot and midfoot fusions, osteotomies, bone cysts, osteolytic lesions, spine fusions as an autograft extender.*
Create hydrated "log"or hydrated strip/cube. Delivery via finger-packing and push/tamp with curette

5 Autologous Input Materials: Whole blood
Graft Material: PRP + allograft materials
(DBM or DBM + Canc. Chips)
**Proximal and distal tibial, femoral and humeral fractures, forefoot and midfoot fusions, osteotomies, bone cysts, osteolytic lesions, spine fusions as an autograft extender, non-unions.*
Create hydrated "log" or hydrated strip/cube. Delivery via finger-packing and push/tamp with curette

6 Autologous Input Materials: ʙBMA (blood and bone marrow aspirate)
Graft Material: PRP from ʙBMA + allograft materials
(DBM or DBM + Canc. Chips)
**Proximal and distal tibial, femoral and humeral fractures, forefoot and midfoot fusions, osteotomies, bone cysts, osteolytic lesions, spine fusions, non-unions. Charcot foot reconstruction.*
Create hydrated "log" or hydrated strip/cube. Delivery via finger-packing and push/tamp with curette



***The procedures listed above are not specified in Biomet Biologics' individual product clearances. The above procedures are listed solely for sales force education as examples of applications wherein surgeons might select and utilize various biologics products. Unless specifically identified in the product's FDA clearance, sales representative must not target or promote the use of Biomet Biologics products for specific clinical applications.**

****Contraindicated for vertebroplastyand kyphoplasty. ***Data on file at Biomet.**

Handling Properties*: Low:** Extremely low cohesion, sand-like particles. **Medium:** Not cohesive, i.e., loose granules. **High:** Good cohesion and/or molding properties. **Very High:** Excellent cohesion and/or molding properties.

Bone Graft Selection Guide

User Preference-Based Graft Choices

Synthetic User

1 Material: Synthetic granules
***Bonus* Synthetic**
Bone Graft Substitute

2 Material: Synthetic self-setting paste
CERAMENT™|BONE VOID FILLER

Canc. Chip / DBM User

3 Material: DBM putty & DBM putty +Synthetic granules
***StaGraft* Putty/Plus**

4 Graft Material: PPPc + allograft materials (DBM or DBM + Canc. Chips)
PPPc: *Plasmax*
Allograft Materials: *StaGraft* Cancellous DBM (or) *Bonus* CC Matrix

5 Graft Material: PRP + allograft materials (DBM or DBM + Canc. Chips)
PRP: *GPS* III
Allograft Materials: *StaGraft* Cancellous DBM (or) *Bonus* CC Matrix

Autograft User

6 Graft Material: PRP from βBMA + allograft materials (DBM or DBM + Canc. Chips)
PRP: *BioCUE*
Allograft Materials: *StaGraft* Cancellous DBM (or) *Bonus* CC Matrix

Bone Graft Selection Guide

Indications for Use - Please see package inserts for additional device information/labeling.

Device	Clinical Indications
GPS III Platelet Concentrate Separation Kit with ACD-A BK110040	The *GPS* III Platelet Concentrate Separation Kit with ACD-A is designed to be used for the safe and rapid preparation of autologous platelet-rich plasma (PRP) from a small sample of the patient's blood at the point of care. The PRP can be mixed with autograft and allograft bone prior to application to an orthopedic surgical site as deemed necessary by the clinical use requirements.
Plasmax Plasma Concentrator BK070026	The *Plasmax* Plasma Concentrator with *GPS* III Platelet Concentrate Separation Kit with ACD-A is designed to be used for the safe and rapid preparation of concentrated platelet-poor-plasma (PPPc) and autologous platelet-rich-plasma (PRP) from a small sample of blood at the patient's point of care. The PPPc and PRP can be mixed with autograft and allograft bone prior to application to an orthopedic surgical site as deemed necessary by the clinical use requirements.
BioCUE Platelet Concentration System BK100027	The *BioCUE* Platelet Concentration System is designed to be used in the clinical laboratory or intraoperatively at the point of care for the safe and rapid preparation of platelet poor plasma (PPP) and platelet rich plasma (PRP) from a small sample of blood and bone marrow mixture. The plasma and concentrated platelets produced can be used for diagnostic tests. Additionally, the platelet rich plasma (PRP) can be mixed with autograft and/or allograft bone prior to application to an orthopedic site.
CERAMENT™|BONE VOID FILLER K073316	CERAMENT™|BONE VOID FILLER is a ceramic bone void filler intended only for orthopedic applications as a filler for gaps and voids that are not intrinsic to the stability of the bony structure. CERAMENT™|BONE VOID is indicated to be injected into bony voids or gaps in the skeletal system, i.e. extremities, pelvis, and spine (only during open surgery in the spine). These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. CERAMENT™|BONE VOID FILLER provides a bone void filler that resorbs and is replaced by bone during the healing process. CERAMENT™|BONE VOID FILLER is not intended for use in load bearing applications such as vertebroplasty and kyphoplasty.
Bonus Synthetic Bone Graft Substitute Resorbable Bone Graft Substitute K063346	*Bonus* Synthetic Bone Graft Substitute Resorbable Bone Graft Substitute is indicated only for bony voids or gaps that are not intrinsic to the stability of the bony structure. *Bonus* Synthetic Bone Graft Substitute is indicated to be gently packed into bony voids or gaps of the skeletal system (i.e., the extremities, spine and pelvis). These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. *Bonus* Synthetic Bone Graft Substitute can be combined with autogenous bone marrow aspirate, autogenous blood, and/or sterile fluids (saline or Ringer's solution). The product provides a bone void filler that resorbs and is replaced with bone during the healing process.
StaGraft Cancellous Graft *Bonus* CC Matrix 361 HCT/P – Exempt	These allografts meet the definition of a tissue-based product as defined in 21 CFR Part 1271, Human Cells, Tissues and Cellular and Tissue-based products (HCT/Ps) and are solely regulated under Section 361 of the Public Health Services Act. Tissue-based products regulated as 361 HCT/Ps are exempt from premarket requirements.
StaGraft DBM (Putty, Plus) also known as *InterGro* DBM (Putty, Paste, Plus) K082793	*StaGraft* DBM products (Putty, Plus) are to be used for filling bony voids or gaps in the extremities and pelvis that are not intrinsic to the bony stability of the structure, and as an autograft extender in spine. *StaGraft* Plus may also be used as a bone void filler in the spine (posterolateral spine). These defects may be surgically created osseous defects or osseous defects created from traumatic injury to bone. *StaGraft* DBM may also be used for filling craniofacial defects and craniotomies that are no larger than 25 cm^2. The amount of *StaGraft* DBM products to be used should be based on the type of procedure and size of graft site.
BMA Kit	The Bone Marrow Aspiration Needle is intended for use in aspirating bone marrow.

Bone Graft Selection Guide

Questions/Comments

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