Medtronic

Sygnacel™ cellular bone matrix (CBM)

Signal-driven. Surgery **simplified.**

Compatible with AiBLE™

Innovative and efficient allograft signals cells to action

With its vibrant signal, SygnaCel™ CBM influences uncommitted cells to form bone. Designed for surgeon's and OR staff's convenience, it ensures rapid thawing and no decanting, with no need to replace the cryoprotectant and no rinsing required for hassle-free preparation.

Seamlessly integrating with Accelerate™ graft delivery system in both minimally invasive surgeries (MIS) and open surgeries, SygnaCel™ CBM delivers high osteoinductive capabilities and viable cells. SygnaCel™ CBM's broad potential applications, backed by Grafton™ DBM fiber technology and proprietary D-MIN™ and Xpel™ processes, makes it a versatile and reliable choice for surgeons.

SygnaCel™ CBM snapshot

Vibrant signal

- 1.8 OI score†,[1]
- 325,000 viable cells/cc[2]
- 99% cell viability at 1 hour[3]

Hassle-free prep

- Rapid thaw: 3-6 minutes[4]
- No decanting or rinsing of cryoprotectant[4]
- User-friendly packaging[5]

Surgical versatility

- Accelerate™ graft delivery system compatible[6]
- Proprietary fiber technology[6]
- Robotic-guided delivery[7]

Tissue safety

- 35+ years of tissue processing experience
- American Association of Tissue Banks (AATB)
- Incorporates proprietary Xpel™ broad-spectrum antibiotic/anti-mycotic treatment

†Animal testing is not necessarily indicative of human clinical outcomes

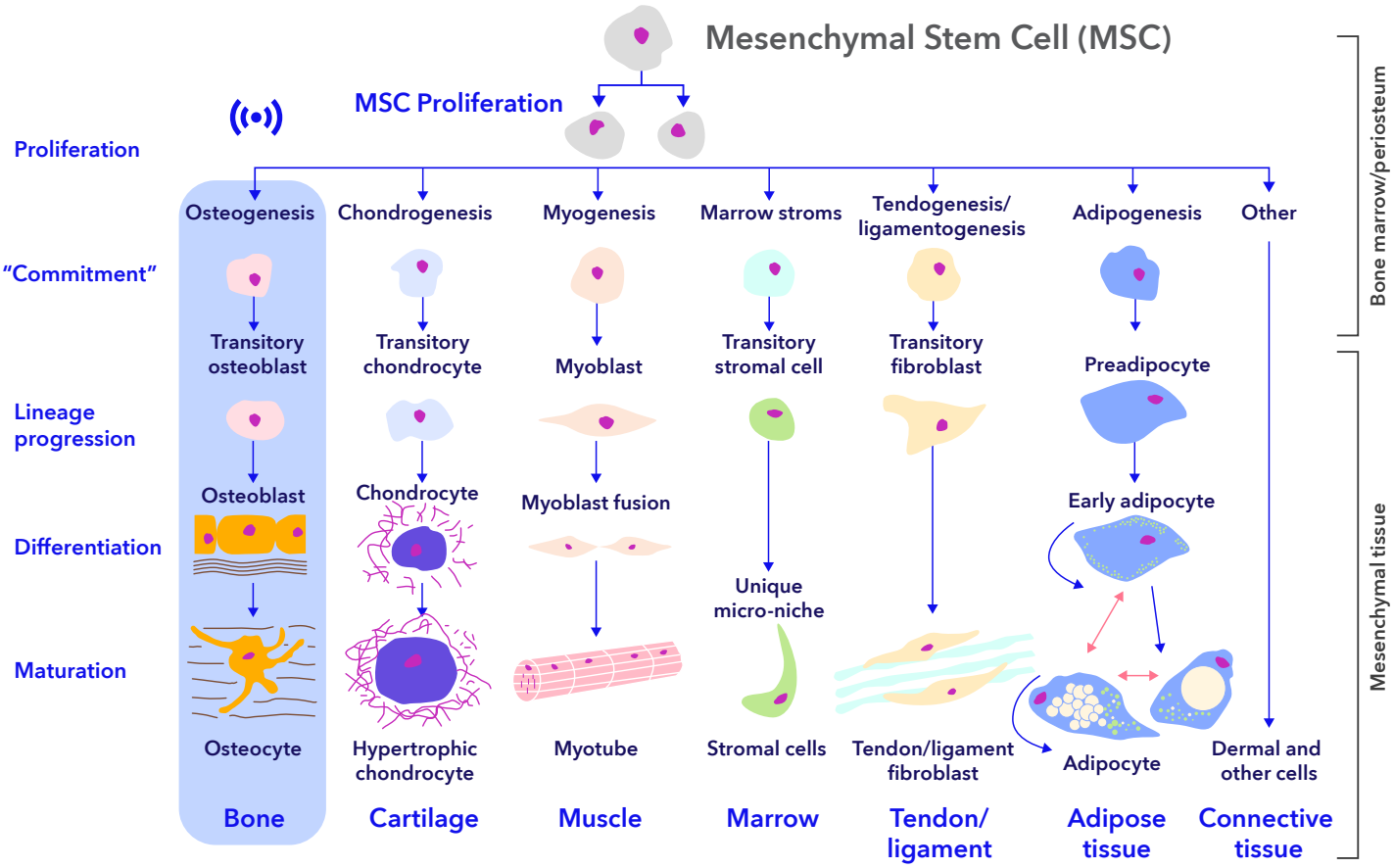
Vibrant signal – why it is important

Mesenchymal stem cells (MSCs) are undifferentiated cells found predominantly in bone marrow. They are not only precursors to bone cells, but also to other cells such as cartilage, muscle, fat, and ligament. To transform into bone cells, MSCs require the presence of the appropriate vibrant signal, which prompts them to differentiate along the desired pathway[8] (see figure below).

What is the Signal?

The signal to induce bone formation comes from the growth factor proteins such as Bone Morphogenetic Proteins (BMPs), such as BMP-2 and BMP-7 that are unmasked in the demineralized bone component of SygnaCel™ CBM. These signaling proteins stimulate the migration (chemotaxis) of MSCs and prompt their differentiation into osteoblasts, which is crucial for bone formation.[9]

Mesenchymal Stem Cells (MSCs) differentiation pathway[8]



How SygnaCel™ CBM's vibrant signal and viable cells work

SygnaCel™ CBM's formulation is comprised of two components:

1. Cryopreserved viable cells embedded within a cortical cancellous bone matrix
2. Demineralized cortical bone fibers that is the source of the vibrant signal.

The cells in SygnaCel™ CBM encompasses osteoblasts, osteoprogenitor cells, and mesenchymal stem cells (MSCs). The procurement and processing of SygnaCel™ CBM involves:

1. Stringent donor age criteria that surpasses AATB recommendations
2. Short timeframe – retrieval through cryopreservation
3. A non-DMSO cryoprotectant that minimizes cellular trauma during thawing.

The cortical bone fibers in SygnaCel™ CBM are demineralized using the proprietary D-MIN™ process that has been shown to preserve the functionality of the unmasked growth factor proteins.[10] It is important to recognize that many process variables including, acid type, temperature, demineralization time, presence of harsh chemicals such as peroxides, and terminal sterilization can affect the activity of osteoinductive proteins. The D-MIN™ process has optimized each aspect of the demineralization treatment through a validated process that has been proven to maintain a high osteoinductivity score for 15+ years.

While osteoprogenitor cells within SygnaCel™ CBM are inherently predisposed to differentiate into bone cells, MSCs require the presence of specific signals for this transformation. The growth factor proteins such as BMP-2 and BMP-7 present in cortical fibers that are unmasked by the D-MIN™ process provide the necessary signals that are needed for MSCs to transform into osteoblasts. The cortical fibers also provide an interconnected pathway for cells to migrate providing a better osteoconductive scaffold than particles.[11]

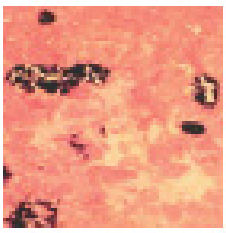
SygnaCel™ CBM's mechanism of action includes:

- Vibrant Signal that directs MSCs to differentiate into osteoblasts‡
- Viable osteoprogenitor cells that are naturally predisposed to develop into bone cells
- Osteoconductive Matrix of fibers and chips that provide a scaffold for bone growth

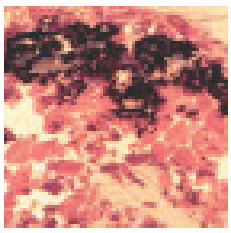
Medtronic uses athymic rat assay† to determine the signal strength/osteoinductivity of SygnaCel™ CBM

†Animal testing is not necessarily indicative of human clinical outcomes

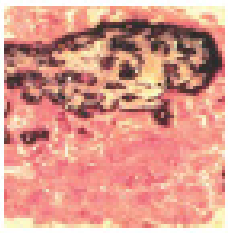
OI = 1
(<25% bone formation)



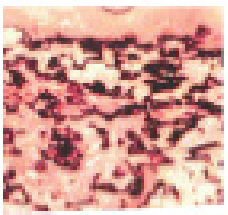
OI = 2
(26-50% bone formation)



OI = 3
(51-75% bone formation)



OI = 4
(>75% bone formation)



Vibrant Signal – Key for MSC to bone cell differentiation

MSCs are precursors not only to bone cells but also to cartilage, muscle, and fat cells. A proper vibrant signal is crucial to guide MSCs into becoming bone cells.

1.8 OI score‡,[1]

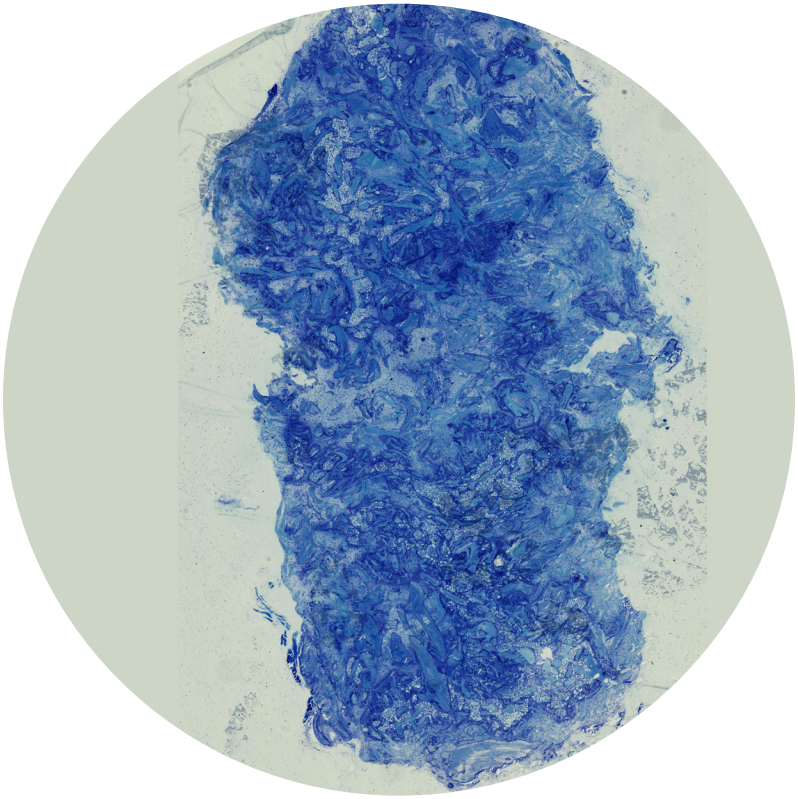
High osteoinductivity demonstrated through bone formation in an athymic rat muscle pouch.

325,000 viable cells/cc[2]

Measured live cells naturally present in bone such as MSCs, osteoprogenitors, and osteoblasts with Trypan blue in digested samples.

99% cell viability at 1 hr[3]

Long-use window post-thaw is demonstrated by 80% cell viability at 5 hours.



Representative histologic section stained with Toluidine Blue showing new bone formation in athymic rat muscle pouch after SygnaCel™ implantation.‡

‡Animal testing is not necessarily indicative of human clinical outcomes

Hassle-free prep – prioritizing OR efficiency

Products designed for orthopedic or reconstructive bone grafting procedures should not only enhance performance but also simplify the workflow for surgeons and OR staff, streamlining the process for efficient surgical preparation.

Rapid thaw: 3-6 min[4]

Reduces ice crystal formation to enhance cell viability[12] and ensures quick availability for immediate use.

No decanting or rinsing of cryoprotectant[4]

DMSO-free biocompatible cell-friendly cryoprotectant provides high cell viability.

User-friendly packaging[5]

Pouch packaging allows easy access to graft and minimizes the product footprint in the freezer.

Surgical versatilitiy – a single solution for MIS and open surgeries

Spinal surgeries are evolving, with a rise in minimally invasive and robot-assisted procedures. SygnaCel™ CBM is MIS and open surgery-enabled, with a broad intended use tailored to meet the diverse grafting needs of surgeons in both spine and orthopedics.

Accelerate™ graft delivery system compatible[6]

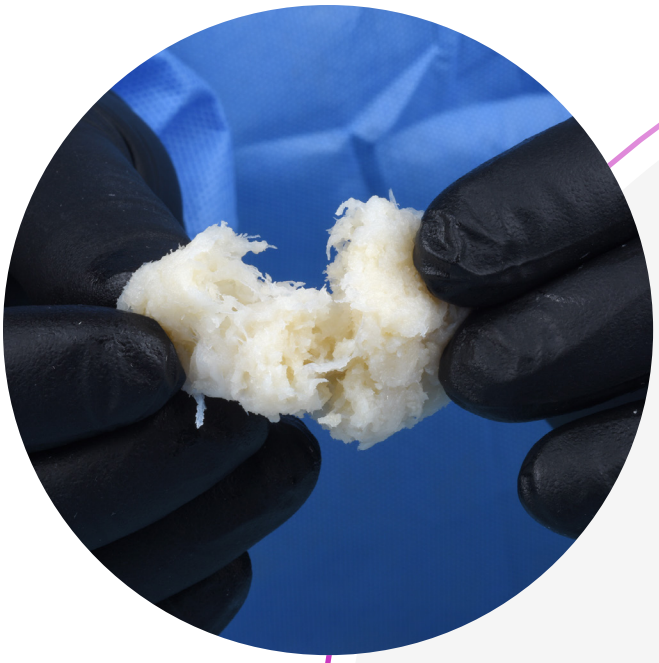
Allows for delivery of SygnaCel™ CBM with local bone for faster, uninterrupted and precise placement of bone graft while providing real-time tactile feedback.

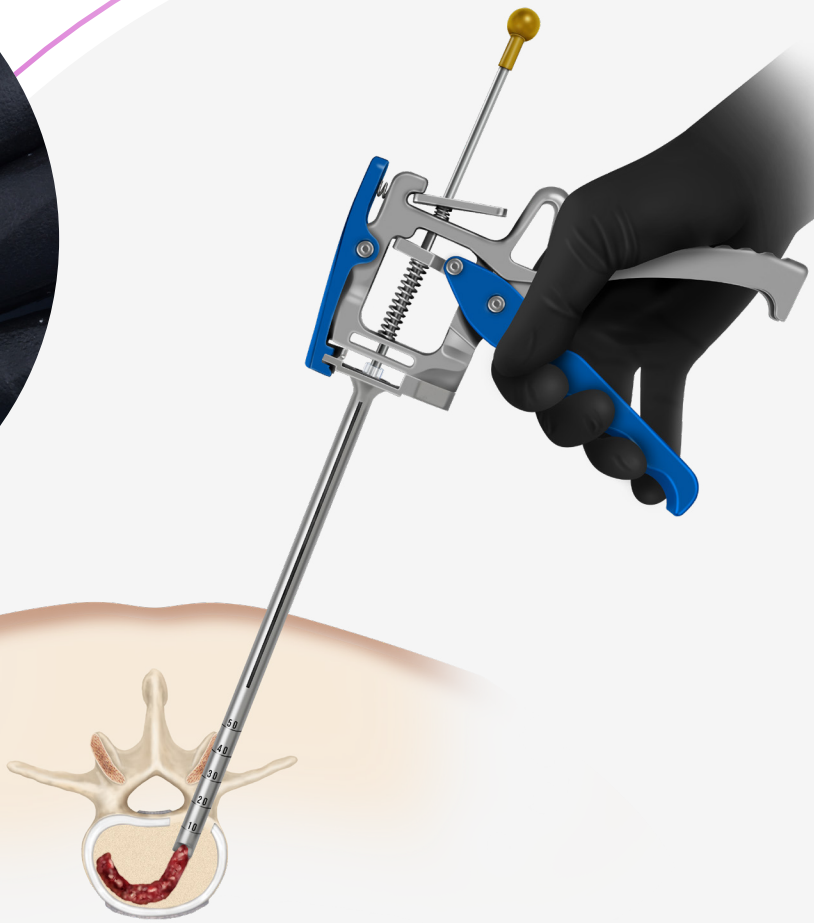
Proprietary fiber technology[6]

Enhances cohesivity and minimizes shedding when mixed with autograft, enabling surgeons to mold and pack the product effectively for fusion.

Robotic guided delivery[7]

Can be delivered with the Mazor™ 5.1 robotic guidance system for facet fusion.

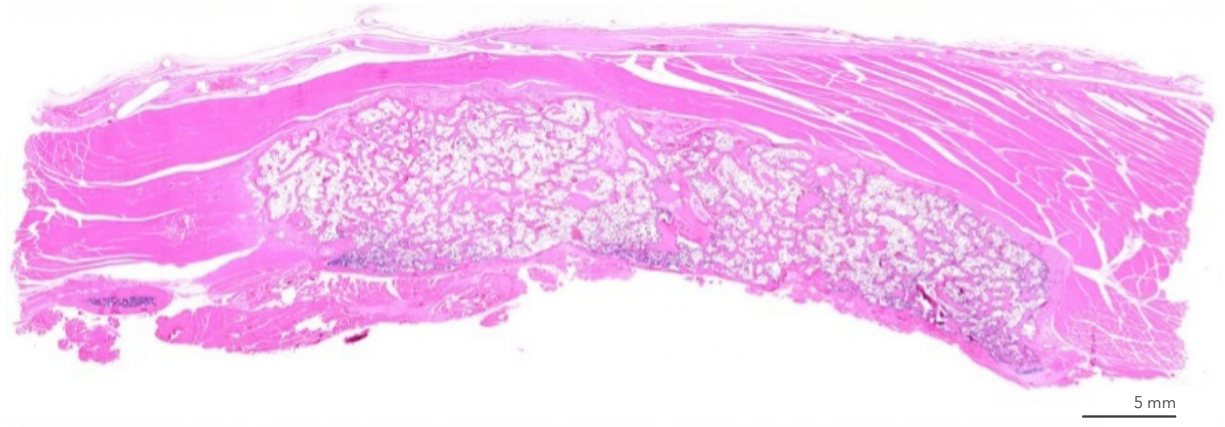




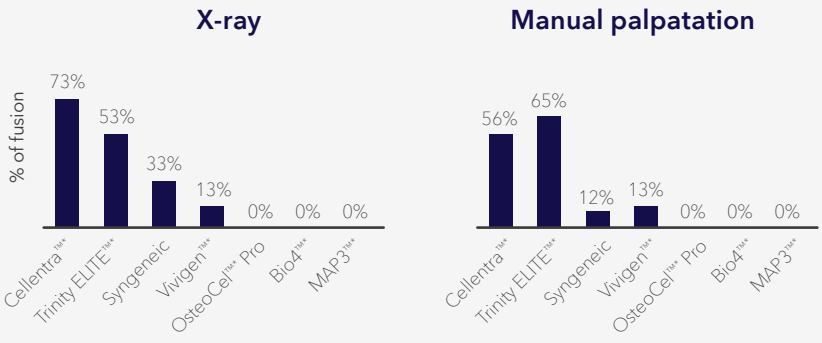
Rat PLF results – high fusion rates

Challenging 2-level Rat PLF[12,‡]

- SygnaCel™ CBM placed in rats for 8 weeks
- 100% fusion by manual palpation and X-rays
- Histology confirmed extensive formation of new bridging bone

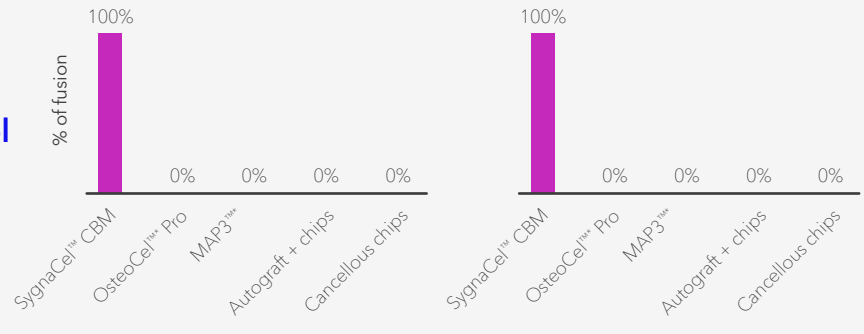


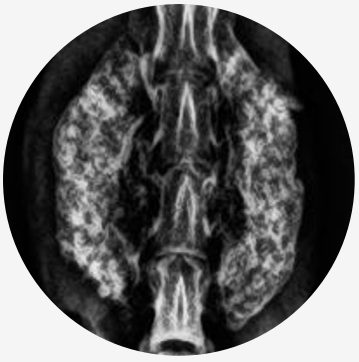
1 and 2-level Rat PLF fusion results[‡,12,13]



METHODS PAPER

Comparing cellular bone matrices for posterolateral spinal fusion in a rat model





‡ Animal testing is not necessarily indicative of human clinical outcomes.

SygnaCel™ CBM preparation instructions

Open box

Step 1a

Remove the SygnaCel™ CBM from the freezer. Tear open the frost cover pouch using the notch. Pull out and examine the SygnaCel™ CBM carton. Do not use if there is evidence that the integrity of the carton or the tamper-seal has been compromised.

Figure 1

Pulling out tissue pouch from 1 cc SygnaCel™ CBM carton

Step 1b

Open the SygnaCel™ CBM carton and pull out the double pouch containing the tissue product **(Figure 1, 2)**. Inspect the outer pouch to ensure the integrity has not been compromised.

Note

For the 2.5 cc, 5 cc, 10 cc, and 15 cc sizes, the SygnaCel™ CBM carton also encloses another smaller carton containing cannulas for optional use with the Accelerate™ graft delivery system.

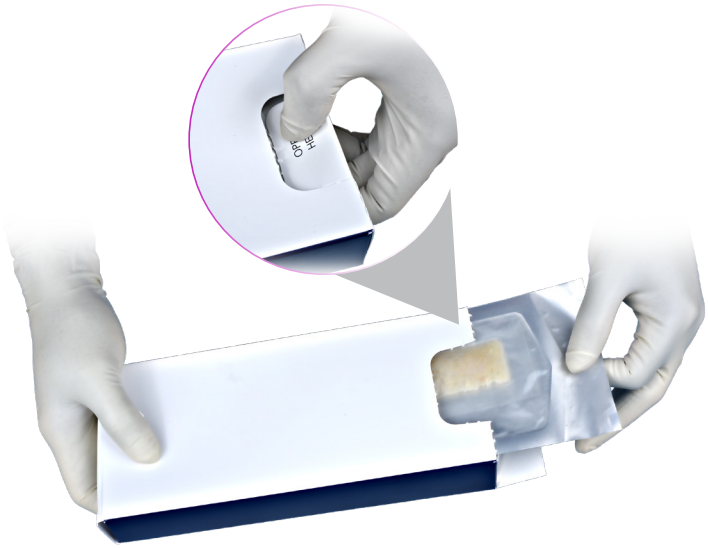


Figure 2

Pulling out tissue pouch from 2.5 cc -15 cc SygnaCel™ CBM carton

Transfer aseptically

Step 2

Using proper sterile technique, peel open the outer pouch. Confirm that the integrity of the inner pouch has not been compromised. Aseptically transfer the sterile inner nylon pouch containing SygnaCel™ CBM bone graft to the sterile field **(Figure 3)**.

Figure 3

Thaw contents

Step 3a

In the sterile field, pour warm sterile isotonic solution into a sterile basin. The starting temperature of the solution should be 37°C ± 2°C.

Step 3b

Submerge the nylon pouch containing frozen tissue into the sterile isotonic solution in the sterile basin **(Figure 4)**. Thaw until contents of the pouch flow freely (approximately 3-6 minutes, depending on product size).

Figure 4

Step 3c

Massage the nylon pouch to ensure the product has thawed and is pliable **(Figure 5)**. If the tissue product is still frozen, warm by holding in sterile gloved hands.

SygnaCel™ CBM should be transplanted within five hours of thawing and all unused product must be discarded. SygnaCel™ CBM is intended for single use, single patient, and the product should not be refrozen or sterilized.

Figure 5

Note
Thawed tissue is malleable and flows freely.

Cut pouch

Step 4

Remove pouch from basin. Using sterile scissors, cut open one end of the nylon pouch **(Figure 6)**.

Figure 6

Squeeze contents

Step 5

Squeeze out the tissue product into a sterile surgical basin **(Figure 7)**. Alternatively, the tissue product can also be scooped out of the pouch.

Note
Inspect the tissue to confirm it is free of foreign materials. SygnaCel™ CBM should not be allowed to dry out before implantation.

When using with Accelerate™ graft deliery instrument, avoid removing too much graft fluid to reduce clogging risk.

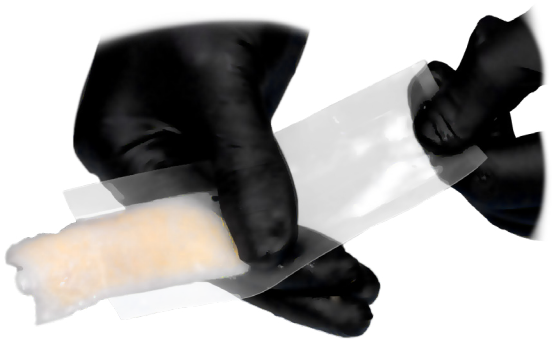
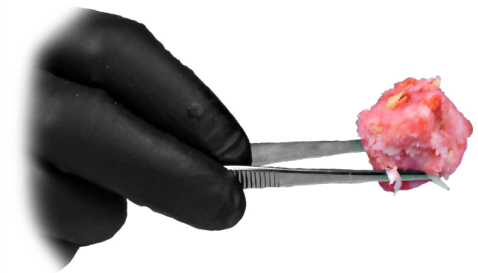


Figure 7

Step 6

Mix SygnaCel™ CBM with local autograft and/or bone marrow aspirate (BMA) prior to implantation.

SygnaCel™ CBM and autograft



SygnaCel™ CBM mixed with autograft

Optional use with Accelerate™ graft delivery system *(available only for 2.5 cc, 5 cc, 10 cc, and 15 cc sizes)*

Bone graft material preparation

Once SygnaCel™ CBM and local autograft and/or BMA are mixed together, the bone graft material is ready for loading into the cannulas.

Note
When using Accelerate™ graft delivery system, mill the autograft to less than 3.2 mm in size and use less than 50% autograft. This helps prevent the cannulas from getting clogged.

Accelerate steps

Step 1

From the non-sterile field, remove the cannula carton from the SygnaCel™ CBM box and pull out the cannula tray **(Figure 8)**.

Figure 8

Step 2

Peel open the shrink wrap **(Figure 9)**.

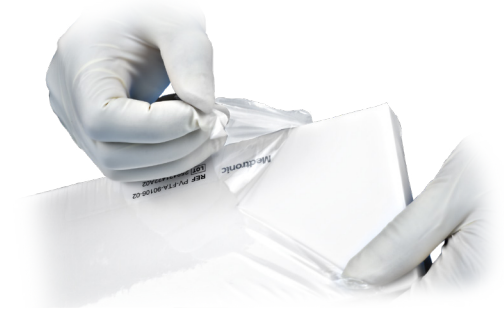


Figure 9

Step 3

Remove the cannula tray from the carton **(Figure 10)**. Inspect the tray to ensure the packaging integrity has not been compromised.

Figure 10

Step 4

Using proper sterile technique, transfer the die card containing the cannulas into the sterile field **(Figure 11)**.

Figure 11

Step 5

Remove the cannulas from the die card **(Figure 12)**.

Figure 12

Note
Cannulas will be stacked on each other and must be separated before use.

Step 6

Close and open the cannulas once or twice to make the closing of the cannula easier once it has been loaded with bone graft material.

Place the cannula into the grooves on the Accelerate™ graft delivery system loading platform concave up **(Figure 13)**. Up to two cannulas may be placed simultaneously on the loading platform.

Figure 13

Figure 14

Step 7

Spread the bone graft material uniformly in the cannula ensuring the bone graft material stays within the top of the cannula curvature **(Figure 14)**. After the cannula is filled, close the cannula **(Figure 15)**.

Figure 15

Note
If the cannula won't completely close, redistribute or remove small amounts of bone grafting material until the cannula completely closes.

Overfilling of cannula increases the likelihood of clogging.

Step 8

To load the cannula into the Accelerate™ funnel, insert the filled cannula into the proximal end of the Accelerate™ funnel **(Figure 16)**.

When properly inserted, the cannula will protrude approximately 5 mm from the proximal end of the Accelerate™ funnel **(Figure 17)**. An internal ledge prevents the cannula from sliding out of the distal end of the Accelerate™ funnel.

Note
Do not force the cannula into the Accelerate™ funnel. If you experience resistance loading the cannula into the Accelerate™ funnel, redistribute or remove small amounts of bone grafting material.

Note
The Accelerate™ instrument set contains two Accelerate™ funnels for simultaneous preloading of bone graft material.

Figure 16

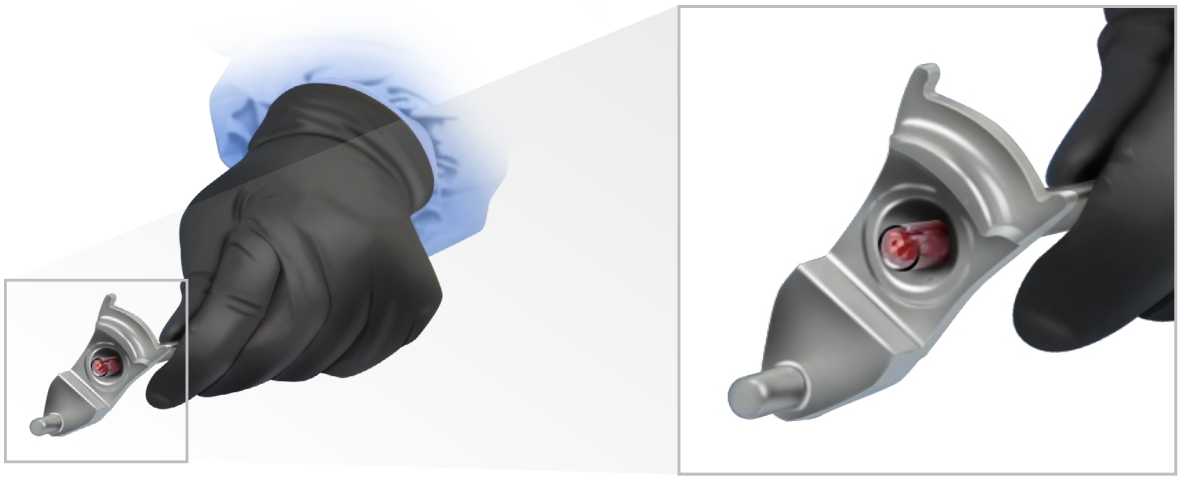


Figure 17

Cannula protrudes 5 mm

Step 9

Attach the Accelerate™ funnel to the Accelerate™ body by sliding the funnel pin into the body socket at a perpendicular angle **(Figure 18)**.

While depressing the clasp on the body **(Figure 19)**, rotate the Accelerate™ funnel into alignment with the Accelerate™ body **(Figure 20)**. Once the Accelerate™ funnel and body are aligned, release the clasp and ensure the Accelerate™ funnel is securely attached to the body.

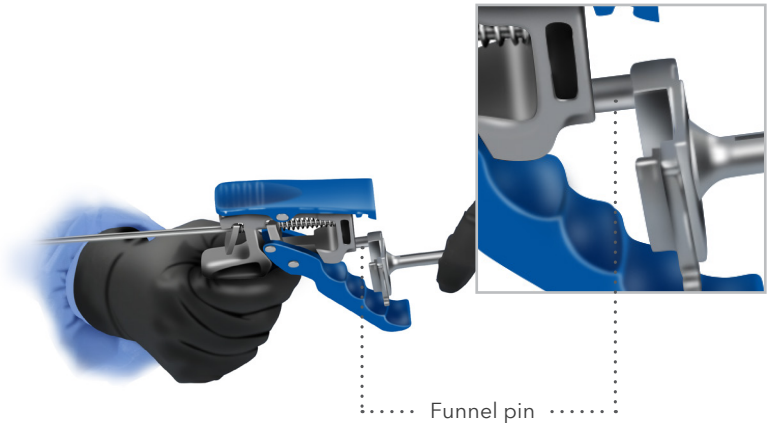


Figure 18

Note
If the cannula (inside of the Accelerate™ funnel) is hitting the body and preventing the Accelerate™ funnel from properly engaging, ensure the cannula is fully seated **(Figure 17)**.

Note
The proximal tip of the cannula should be aligned with the plunger.

Advance the plunger into the Accelerate™ funnel by squeezing the trigger (approximately 2-3 times). The positive engagement of the plunger into the cannula will improve the overall stability of the instrument.

Figure 19

Figure 20

Step 10

To deliver the bone graft material to the surgical site squeeze the trigger. The plunger will advance the bone graft material with each trigger squeeze until the cannula is empty **(Figure 21)**.

Note

It may take several trigger squeezes prior to delivery of the bone graft material. Typically, the bone graft material in the cannula first compresses, and then begins to flow through the distal end of the Accelerate™ funnel.

The bone graft material should flow easily with each trigger squeeze.

Note

If there is increasing resistance/difficulty in squeezing the trigger, remove the Accelerate™ graft delivery instrument from the surgical site and disassemble it in accordance with the instructions in the reloading and disassembly section of this user guide.

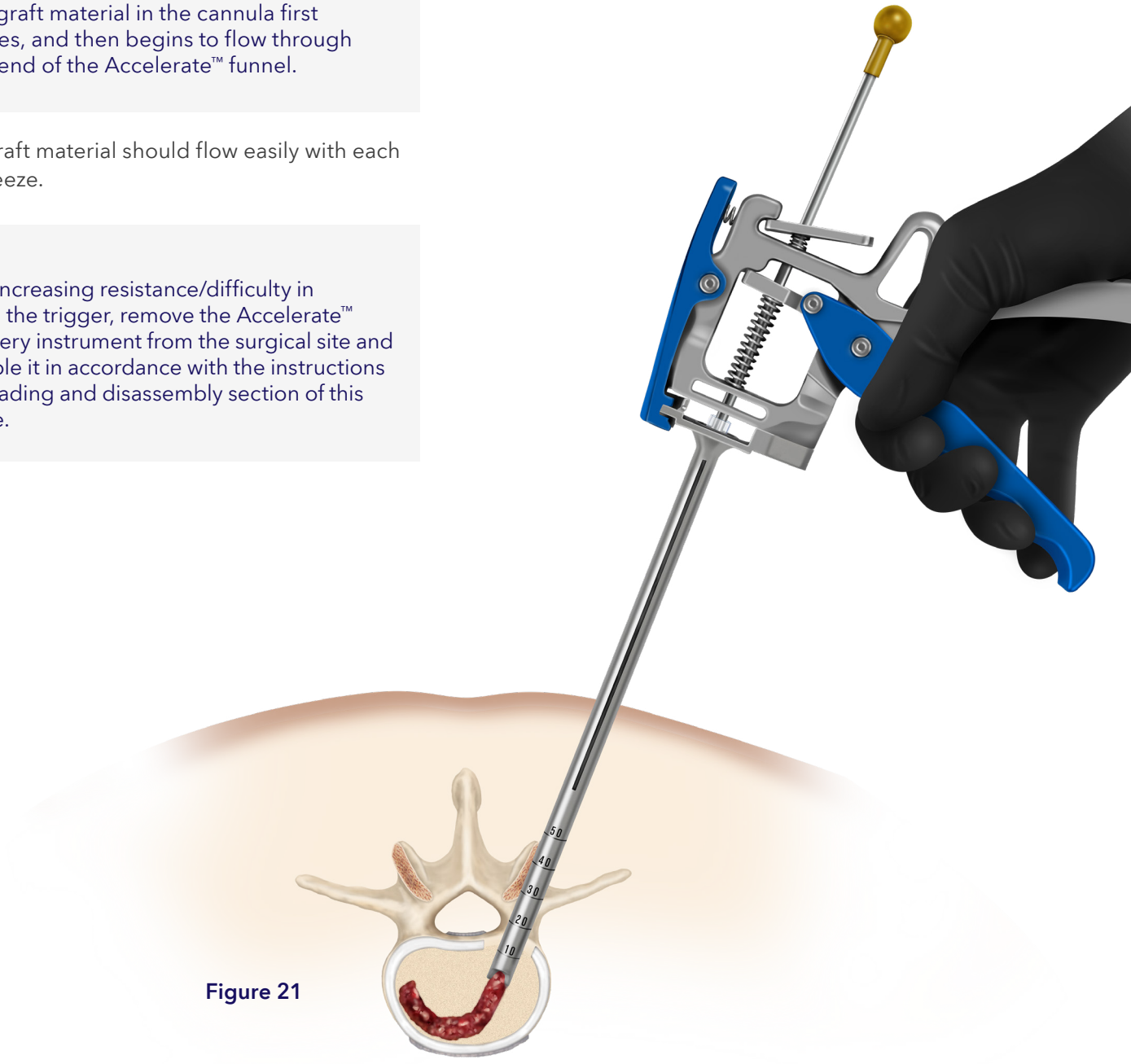


Figure 21

Step 11

To reload and disassemble the Accelerate™ graft delivery instrument, remove the plunger from the Accelerate™ funnel, simultaneously grasp the back handle (do not squeeze the trigger) and depress the grey plunger release tab with one hand. While depressing the release tab, completely pull the plunger out of the Accelerate™ funnel with the other hand **(Figure 22)**.

Next, remove the Accelerate™ funnel by depressing the clasp with one hand, and rotating it perpendicular to the body with the other hand **(Figure 23)**.

Disengage the Accelerate™ funnel from the body, then remove the cannula from the Accelerate™ funnel and discard the cannula **(Figure 24)**.

Note

- If the plunger is hard to pull back, confirm that the trigger has been fully reset and sits flush with the Accelerate™ body.
- The cannula is intended for SINGLE USE ONLY. If additional bone graft is needed, repeat the loading process with a new cannula until the desired amount of bone graft material is delivered.
- If the cannula is difficult to remove, simultaneously twist the Accelerate™ funnel while pulling out the cannula.
- For rapid bone graft delivery, it is recommended that the spare Accelerate™ funnel is prepped and loaded with a cannula to allow for rapid Accelerate™ funnel exchange.
- Be sure to remove the cannula after use (and prior to sterilization).

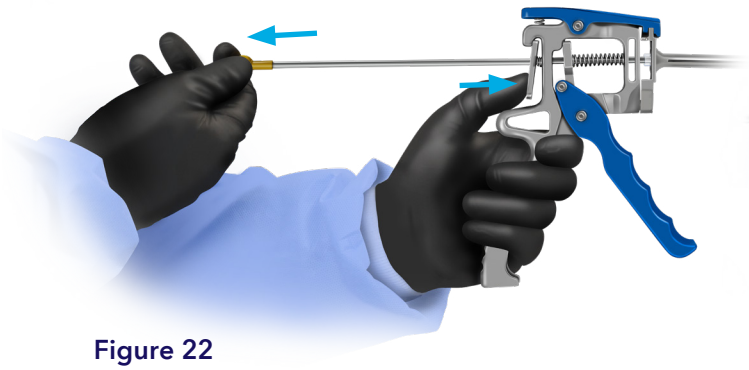


Figure 22

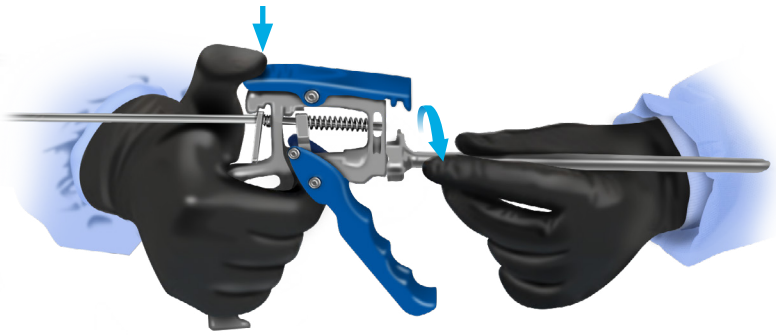


Figure 23

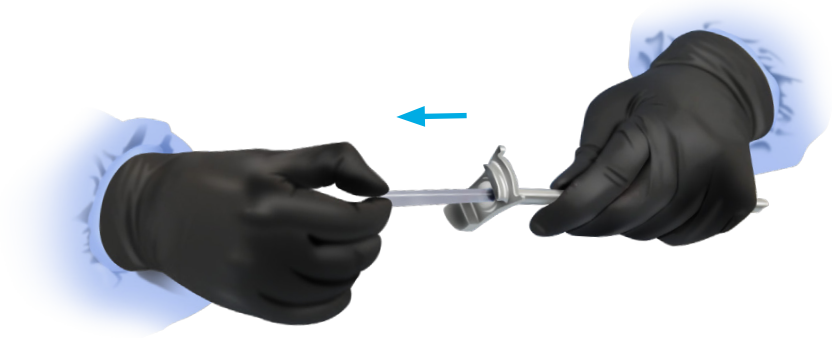


Figure 24

Step 12

If a jam occurs, there are provisions to recover the clogged bone graft. First, remove the Accelerate™ graft delivery instrument from the surgical site. Follow the disassembly instructions as outlined in step 11 to remove the Accelerate™ funnel from the body.

Attach the proximal end of the Accelerate™ funnel to the top of the graft recovery platform **(Figure 25)**. Then, insert the graft recovery tool into the distal tip of the Accelerate™ funnel **(Figure 26)**.

To push the cannula out of the Accelerate™ funnel, gently mallet the graft recovery tool into the Accelerate™ funnel **(Figure 27)**. The cannula may bend and/or collapse as it is malleted from the Accelerate™ funnel **(Figure 28)**. Recover bone graft material by gently opening the cannula.

The recovered bone graft material may be delivered with the standard bone funnel included in the set. The graft recovery tool will act as the bone tamp for this backup graft delivery method **(Figure 29)**.

Figure 25

Figure 26

Figure 27

Figure 28

Figure 29

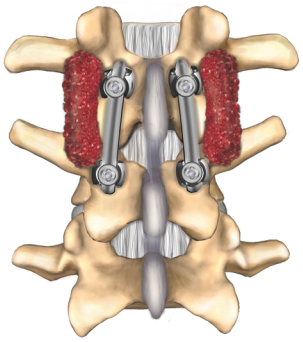
Potential uses

Spine

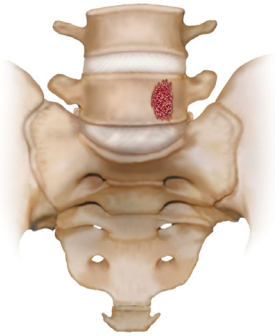
Ortho

Oral maxillofacial

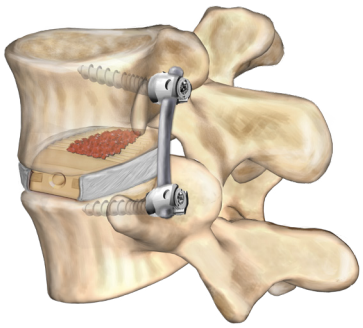
Trauma



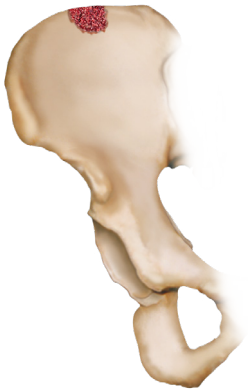
Posterolateral Procedures



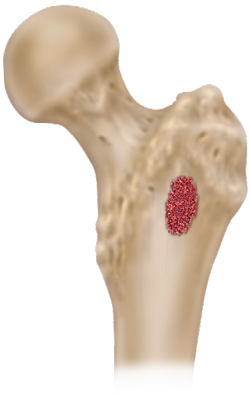
Spinal Defect



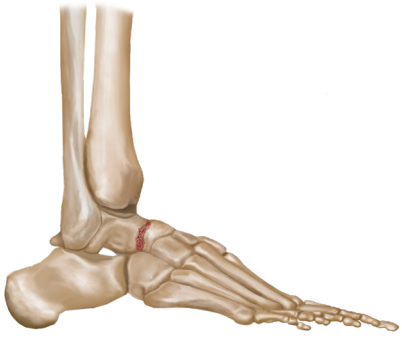
Certain Medtronic Interbody Cages when used with BMA



Pelvis



Extremities



Foot and Ankle

Product ordering information

SygnaCel™ CBM

Part number	Description	Number of cannulas
T90101	CBM T90101 SygnaCel™ 1 cc	0
T90102	CBM T90102 SygnaCel™ 2.5 cc	2
T90105	CBM T90105 SygnaCel™ 5 cc	4
T90110	CBM T90110 SygnaCel™ 10 cc	4
T90115	CBM T90115 SygnaCel™ 15 cc	6

Accelerate™ graft delivery instrument set SPS02688

Part number	Description	User guide description
6061006	Graft delivery funnel	Accelerate™ funnel (qty 2)
6061007	Graft gun	Accelerate™ body
6061020	Graft loading platform	Accelerate™ graft delivery loading platform
6061023	Graft recovery tool	Accelerate™ graft recovery tool
6061024	Recovery platform	Accelerate™ recovery platform
2940171	Bone funnel	Standard bone funnel

Midas Rex™ bone mill

Part number	SAP description
BM110	Midas Rex™ bone mill base
BM120	Midas Rex™ bone mill console
BM130	Midas Rex™ bone mill instrument
BM210	Midas Rex™ dual blade disposable
EA600	Power cord, US

Important Product Information

SygnaCel™ Cellular Bone Matrix

READ BEFORE USE

This graft is derived from human tissue which was generously donated so others may benefit. Each unit is intended for single patient, single use only.

Caution: restricted to use by a physician, podiatrist, or dentist. No additional sterilization step is to be performed.

DESCRIPTION

SygnaCel™ Cellular Bone Matrix is a formulation of human cryopreserved viable cortical cancellous bone matrix and demineralized bone fibers. This allograft was prepared from tissue recovered from a cadaveric donor using aseptic surgical techniques and was further processed and packaged under aseptic conditions. The viable cortical cancellous bone matrix component is prepared from milled bone cleaned using purified water and lactated Ringer's solution and treated with antibiotics (gentamicin, vancomycin) and antimycotic (amphotericin B) agents. The demineralized bone fibers are prepared from milled bone cleaned using purified water. These fibers are demineralized using the D-MIN™ proprietary demineralization process resulting in demineralized bone matrix with calcium content level that meets current American Association of Tissue Banks (AATB) standards. The formulated and packaged tissue is soaked and stored in a biocompatible cryoprotectant solution containing glycerol and lactated Ringer's solution to help retain cell viability of the cortical cancellous bone matrix during frozen storage.

- Each SygnaCel™ Cellular Bone Matrix finished product lot is sampled, thawed, and tested to confirm cellular viability.
- SygnaCel™ Cellular Bone Matrix is osteoconductive as well as osteoinductive in an athymic rat assay.
- SygnaCel™ Cellular Bone Matrix is prepared via a proprietary processing method validated to consistently produce DBM that is osteoinductive in an athymic rat assay. Product and process consistency are confirmed by testing each SygnaCel™ Cellular Bone Matrix finished product lot for osteoinductivity in this validated athymic rat assay using a five-point linear scale (0,1,2,3,4) to score bone formation at 28 days post implantation*. Bone forming activity exhibited by SygnaCel™ Cellular Bone Matrix in this athymic rat surrogate assay should not be interpreted as a predictor of clinical performance.
  *Edwards, J.T., PhD, Diegmann, M.H., MS, Scarborough, N.L., PhD.: Osteoinduction of Human Demineralized Bone: Characterization in a Rat Model. Clinical Orthopaedics, December, 1998, Vol 357.

INDICATIONS FOR USE

SygnaCel™ Cellular Bone Matrix can be used as a bone graft in orthopedic or reconstructive procedures. Use SygnaCel™ Cellular Bone Matrix in combination with autologous bone and/or bone marrow aspirate.

STERILITY

SygnaCel™ Cellular Bone Matrix is labeled as "Aseptically Processed, Passes USP Sterility Tests" which means it was aseptically processed and tested for sterility according to procedures in the current US Pharmacopeia. When explanting and/or disposing of a product, be sure to avoid exposure to bodily substances such as blood, tissue, aerosols, etc., as contact could lead to infection or disease. Always wear and use proper protective equipment (PPE), taking special care with sharp objects and needles. Follow your healthcare center's policy regarding both the disposal of devices and any events of exposure.

Note: the cannulas (2.5cc, 5cc, 10cc, and 15cc) were sterilized using gamma radiation.

CONTRAINDICATIONS

The presence of infection at the implantation site is a contraindication for the use of this allograft.

WARNINGS

- **SygnaCel™ CBM is a cellular bone matrix product containing viable cells.**
- **Bone matrix products containing viable cells have been linked to, or associated with, two Mycobacterium tuberculosis outbreak events in the United States.**
- **Some affected by these outbreaks have died.**
- **Current donor screening, processing, and testing cannot fully eliminate the risk of disease transmission from bone matrix products containing viable cells.**
- **For additional information see: STERILITY, POTENTIAL ADVERSE EVENTS, CAUTION, PRECAUTIONS, ANDDONOR SCREENING AND TESTING.**

POTENTIAL ADVERSE EVENTS

Donor screening methods are limited. Therefore, certain diseases and infectious agents may not be detected and/or eliminated during processing. The following complications of tissue transplantation may occur:

- Loss of function or integrity of transplanted tissue due to resorption, fragmentation, or disintegration including associated loss of continuity, or displacement, and/or fracture at treatment site.
- Non-union (or pseudarthrosis), delayed union, and/or mal-union.
- Immune rejection of transplanted grafts or infection.
- Transmission or causation of known diseases as well as diseases of unknown etiology and characteristics.
- Transmission of known infectious agents including HIV, Hepatitis B, Hepatitis C, and bacteria (e.g. syphilis, Mycobacterium tuberculosis).
- Death.

Note: additional surgery may be necessary to correct some of these potential adverse events.

All of the same medical/surgical conditions that may complicate any surgical procedure may occur during or following transplantation of an allograft. Adverse outcomes potentially attributable to SygnaCel™ Cellular Bone Matrix must be promptly reported to Medtronic at (800) 933-2635 or (901) 396-3133.

CAUTION

This allograft may contain trace amounts of processing agents including antibiotics (gentamicin, vancomycin), antimycotic (amphotericin B), acid, and alcohol solutions. Residual cryoprotectant (less than 10% glycerol in lactated Ringer's solution) is present. Caution should be exercised if the patient is allergic to any of these agents or chemicals. This product was designed for single patient use only. Do not reprocess or reuse this product. Reuse or reprocessing may compromise the structural integrity of the product and/or create a risk of contamination of the product, which could result in patient injury, illness, or death.

PRECAUTIONS

Extensive donor blood serum testing, medical and social history screening procedures, and tissue microbiological testing were used to qualify tissue donors. Despite extensive tissue donor selection and qualification processes used in providing this tissue graft (see DONOR SCREENING AND TESTING), transmission of disease (communicable or donor derived) is still possible.

Bacterial or fungal infection at the graft site may also occur.

When administering SygnaCel™ Cellular Bone Matrix into the defect site, precaution should be taken not to:

- Over-pressurize the delivery device, as this may lead to extrusion of the SygnaCel™ Cellular Bone Matrix beyond the site of its intended application and damage to the surrounding tissues.
- Over-pressurize the defect site, as this may lead to fat embolization or embolization of the SygnaCel™ Cellular Bone Matrix material into the bloodstream.

Note: it is important to assess unique surgical factors (e.g. patient comorbidities, graft implantation site challenges, procedural complexities, etc.) for their impact to successful bony healing. With these in mind, it is the responsibility of the treating physician to select an appropriate bone graft and volume necessary to achieve the desired clinical outcome.

! USA Caution: Federal law (USA) restricts these devices to sale by or on the order of a physician, podiatrist, or dentist.

DONOR SCREENING AND TESTING

Prior to donation, the donor's blood, tissues, and medical/social history were screened for medical conditions or disease processes that would contraindicate the donation of tissues in accordance with FDA regulations and standards established by the AATB. The donor's medical/social history was also screened for HIV, Hepatitis, and CJD/vCJD high risk factors in accordance with US Public Health Services recommendations and FDA regulations and guidance documents.

Important Information on the SygnaCel™ Cellular Bone Matrix (CBM)

Testing of donor blood and tissue samples began at the site of recovery and continued into processing. Donor blood samples taken at the time of recovery were tested for communicable disease by a laboratory registered with the FDA to perform donor testing and certified to perform such testing on human specimens under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) (42 U.S.C. 263a) and 42 CFR Part 493 using the following FDA approved, licensed, or cleared tests:

- HBsAg (Hepatitis B Surface Antigen).
- HBc-IgM/IgG (Hepatitis B Total Core Antibody).
- HCV (Hepatitis C Antibody).
- HIV 1/2-Ab (Antibody to Human Immunodeficiency Virus Types 1 and 2).
- RPR/STS or Equivalent (Syphilis Detection).
- HIV 1 NAT (Human Immunodeficiency Virus type 1 nucleic acid amplification testing).
- HCV NAT (Hepatitis C virus nucleic acid amplification testing).
- HTLV I/II (Human T-lymphotrophic virus types I and II).
- HBV NAT (Hepatitis B virus nucleic acid amplification testing).

Results of the communicable disease tests referenced above were negative or non-reactive.

In addition to the tests listed above, other tests may have been performed including WNV NAT (West Nile Virus nucleic acid amplification testing). Laboratory testing with a validated laboratory-developed Mtb NAT (Mycobacterium tuberculosis nucleic acid amplification testing) was conducted with a result of not detected. Culture testing for Mtb was also performed with a result of no growth or culture negative. Note that there are currently no FDA approved tests for Mtb detection in cadaveric tissues.

Negative results do not guarantee the product is free of Mtb organisms. This testing for Mtb may not detect inactive (latent) mycobacteria.

Communicable disease test results, together with the informed consent, medical and social history interview, physical assessment, available medical records (to include previous medical history, laboratory test results, autopsy and coroner reports, if performed), and information obtained from any source or records which may pertain to donor eligibility were evaluated. Based on this evaluation, the donor met donor eligibility criteria current at the time of recovery. Donor eligibility criteria used to screen donors are in compliance with FDA regulations published in 21 CFR Part 1270 and/or Part 1271. All procedures for donor screening meet or exceed current standards established by the American Association of Tissue Banks.

Donor eligibility was determined by the following tissue bank: American Tissue Services Foundation, Glendale, AZ 85303.

Names and addresses of the testing laboratories, the listing and interpretation of all required communicable disease tests, a listing of the documents reviewed as part of the relevant medical records, and the name of the person or establishment determining eligibility of this human tissue are on file at Medtronic, Eatontown, NJ and available upon request.

Final, processed tissue allograft product was released by Medtronic based on initial donor eligibility determination and on a post-processing review and determination the product met all processing requirements and specifications.

This tissue allograft product was released for transplantation.

TISSUE TRACKING

Federal (USA) regulations under 21 CFR 1271 establish requirements for tracking human tissue. In accordance with these regulations, the package label of each tissue unit distributed by Medtronic bears a lot or serial number that serves as a distinct identification code recorded in Medtronic's distribution records to track the tissue to the consignee or user/tissue transplant facility. This lot or serial number should be recorded on the provided tissue tracking record (TTR), in the user/tissue transplant facility's records, and in the tissue recipient's medical record, along with the following:

1. Description of tissue
2. Lot number (donor ID)
3. Product code
4. Expiration date
5. Quantity implanted
6. Antibiotics used
7. Description of procedure
8. Date and time of procedure
9. Surgeon name
10. Other pertinent information

VISUAL INSPECTION

Visually inspect all sterile-barrier packaging before use. If the sterile barrier is damaged or the integrity is compromised, do not use. Contact Medtronic for return information. Visually inspect the product before use. If the product is damaged, do not use. Contact Medtronic for return information.

PACKAGING & FROZEN SHIPMENT RECEIPT

SygnaCel™ Cellular Bone Matrix is supplied sterile. Sterile means it was aseptically processed and tested for sterility according to procedures in the US Pharmacopeia. SygnaCel™ Cellular Bone Matrix is shipped frozen in insulated shippers containing dry ice which have been validated to maintain appropriate product temperatures. The shipping container should be intact upon receipt. Transfer SygnaCel™ Cellular Bone Matrix to long-term freezer storage according to the label requirements prior to the expiration date printed on the exterior of the insulated shipping container. The SygnaCel™ Cellular Bone Matrix package should be intact upon receipt. Once the seal on the sterile SygnaCel™ Cellular Bone Matrix package is broken, the product should not be re-sterilized. Damaged packages or products should not be used and should be returned to Medtronic.

STORAGE

Each SygnaCel™ Cellular Bone Matrix carton is sealed in a frost cover pouch and is contained inside a corrugated sleeve. The corrugated sleeve can be discarded prior to storage. SygnaCel™ Cellular Bone Matrix product carton shall remain in the sealed frost cover pouch and should be stored frozen at -70°C to -80°C. Short term storage of up to -40°C for up to 4 weeks is acceptable. Tissue stored up to -40°C can be returned to the recommended storage environment of -70°C to -80°C at any time during that period. This temporary storage temperature would also allow for any internal temperature fluctuations between -40°C to -69°C that may occur during long-term storage due to cycling of the freezer or opening of freezer doors. It is the responsibility of the transplant facility or clinician to maintain tissue intended for transplantation in the appropriate recommended storage conditions prior to transplant. SygnaCel™ Cellular Bone Matrix which has not been properly stored should be disposed of in accordance with recognized procedures for discarding medical waste material.

RETURNS

For any returns deemed necessary as a result of an error by Medtronic, or a product complaint, a Return Authorization Number is required from Medtronic prior to return. Full credit will be issued. For returns other than an error by Medtronic or a product complaint, refer to Medtronic's Return Policy.

REFERENCES

Standards for Tissue Banking (current version), American Association of Tissue Banks, McLean, VA. Current Policies and Procedures of Medtronic, Eatontown, N.J.

FDA Final Rule for "Eligibility Determination for Donors of Human Cell, Tissue and Cellular and Tissue Based Products", 21 CFR, Parts 210, 211, 820 and 1271.

Federal Register, May 25, 2004 (Volume 69. Number 101) pg. 29785 – 29834.

FDA Final Rule for "Current Good Tissue Practice for Donors of Human Cell, Tissue and Cellular and Tissue-Based Products", 21 CFR Parts 16, 1271, Federal Register, November 24, 2004 (Volume 69, Number 226) pg 68611- 68688.

PHS Guidelines for Preventing Transmission of HIV through Transplantation of Human Tissue and Organs, MMWR 1994:43, 1-17.

PHS Guideline for Screening Donors of Blood, Plasma, Organs, Tissue and Semen for Evidence of Hepatitis B and Hepatitis C, MMWR 1991:40, 1-17.

FDA Recommendations to Blood Establishments for "Deferral of Current and Recent Inmates of Correctional Institutions as Donors of Whole Blood, Blood Components, Source Leukocytes, and Source Plasma," 6/8/95.

FDA Recommendations to Blood Establishments for "Precautionary Measures to Further Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease by Blood and Blood products," 01/31/20.

MRI INFORMATION

MR MR Safe

SygnaCel™ Cellular Bone Matrix is MR Safe.

SygnaCel™ Cellular Bone Matrix is a nonconducting or a nonmagnetic item which poses no known hazards in all MR environments for magnetically induced displacement force and magnetically induced torque. In addition, SygnaCel™ Cellular Bone Matrix is not susceptible to heating due to RF (radio frequency) fields. As such, SygnaCel™ Cellular Bone Matrix can justifiably be labeled as MR- Safe per ASTM F2503.

If SygnaCel™ Cellular Bone Matrix is used in connection with any device which is not MR Conditional, be advised this combination was not tested in the MR environment and, therefore, higher heating and possible injury to the patient may occur.

SygnaCel™ Cellular Bone Matrix (CBM) User Guide

Important Information on the SygnaCel™ Cellular Bone Matrix (CBM)

PRODUCT COMPLAINTS

For product problems, contact Medtronic.

FURTHER INFORMATION

Recommended directions for use of this system (surgical operative techniques) are available at no charge upon request. If further information is required, contact Medtronic.

DISTRIBUTED BY:
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Telephone: 800 933 2635 (USA)
901 396 3133 (Outside USA)

EXPLANATION OF SYMBOLS

- ℞only CAUTION: Federal law (USA) restricts these devices to sale by or on the order of a physician.
- Temperature limit
- Do not re-use Manufacturer
- Date of manufacture
- Catalogue number
- REF Serial Number
- ! USA For US audiences only
- STERILE A Sterilized using aseptic processing techniques
- STERILE R Sterilized using irradiation
- Use-by date
- Consult instructions for use at this website.
- Do not use if package is damaged and consult instructions for use
- Do not resterilize
- MR MR Safe
- *Single sterile barrier system
- Double sterile barrier system
- Single sterile barrier system with protective packaging inside
- Single sterile barrier system with protective packaging outside
  *Single barrier packaging systems may not contain a sterile barrier system symbol. Per ISO 11607-1, a symbol is only required if more than one barrier is present.

For a complete list of indications, safety, and warning, please visit **https://manuals.medtronic.com/manuals/main/en_US/home/index** and search for "SygnaCel" to access the most recent IFU.

For more information visit **Medtronic.com** or call (800) 933-2635.

Accelerate™ Bone Graft Delivery Instrument Set

Intended Use

These orthopedic manual surgical instruments are intended for use in surgical procedures to manipulate tissue, bone, or for use with other devices in orthopedic surgery. An instrument may incorporate a measuring function which has uses as described on the label and the instrument.

DO NOT IMPLANT THE INSTRUMENTS.

MEDTRONIC does not and cannot warrant the use of this instrument nor any of the component parts upon which repairs have been made

or attempted, except as performed by MEDTRONIC or an authorized MEDTRONIC repair representative. Implied warranties of merchantability and fitness for a particular purpose or use are specifically excluded.

Risks

Breakage, slippage, misuse, or mishandling of instruments, such as on sharp edges, may cause injury to the patient or operative personnel. It is important that the surgeon exercise extreme caution when working in close proximity to vital organs, nerves or vessels, and that the forces applied while correcting the position of the instrumentation is not excessive, such that it might cause injury to the patient.

For a complete list of indications, safety, and warnings for Accelerate™ Graft Delivery Instrument Set, please visit **https://manuals.medtronic.com/content/dam/emanuals/spinal/0380035E_MDT_Reusable_Instruments_and_Accessories_eManual_revG.pdf**

For more information visit **Medtronic.com** or call (800) 933-2635.

Midas Rex™ Bone Mill

INDICATIONS

The Midas Rex™ Electric Bone Mill is intended to mill bone, producing bone particles 1 to 5 mm in size. The bone mill is not restricted to a specific patient population.

INTENDED USE

The intended target populations include adult and pediatric patients.

CONTRAINDICATIONS

There are no known contraindications.

For a complete list of indications, safety, and warnings for Midas Rex™ Bone Mill, please visit **https://manuals.medtronic.com/content/dam/emanuals/st/M333083W001DOC1REVAFINAL.pdf**

For more information visit **Medtronic.com** or call (800) 933-2635.

References

1. Animal data on file (2024). Average score based on n=8 lots.
2. Internal benchtop testing data on file (2024). Average based on n=7 lots.
3. Average based on internal benchtop testing data (2024).
4. SygnaCel™ CBM IFU.
5. Data on file based on survey (2024).
6. Internal validation testing data on file.
7. Internal data on file.
8. Caplan AI. *Stem Cells Transl Med*. 2017 Jun;6(6):1445-1451.
9. Martin GJ, Boden SD, Titus L, Scarborough NL. New formulations of demineralized bone matrix as a more effective graft alternative in experimental posterolateral lumbar spine arthrodesis. *Spine*. 1999;24(7):637–645.
10. Internal animal data on file.
11. Linkova DD, Rubtsova YP, Egorikhina MN. Cryostorage of Mesenchymal Stem Cells and Biomedical Cell-Based Products. *Cells*. 2022;11(17):2691.
12. Internal Medtronic animal data on file
13. Lin C, Zhang N, Waldorff EI, et al. Comparing cellular bone matrices for posterolateral spinal fusion in a rat model. JOR Spine. 2020;3(2):e1084

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medtronic.com

Consult instructions for use at this website www.medtronic.com/manuals.

This product may be protected by US Patents listed at medtronic.com/patents

Note: Manuals can be viewed using a current version of any major internet browser. For best results, use Adobe Acrobat™*Reader with the browser.

Please see the package insert for the complete list of indications, warnings, precautions, and other important medical information.

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