OVERCOME LIMITATIONS & MAXIMIZE CELL YIELDS

MARROW CELLUTION™

Autologous Bone Marrow Aspiration & Bone Graft Harvesting

ASPIRATE TO APPLICATION®

ACCELLERATED BIOLOGICS

800-367-0844

www.AcCELLeratedBiologics.com

Ranfac®

www.marrowcellution.com

U.S. & Foreign Patent(s) Pending

Life Sustaining Bone Marrow Stem Cells & Cancellous Bone Graft

Bone Marrow Cells (BMC) reside deep inside bone cavities in the most protected part of the body and are redundant throughout the organism.

Bone marrow is the flexible tissue in the interior of bones. In humans, red blood cells are produced by cores of bone marrow in the heads of long bones in a process known as hematopoiesis.[1]

On average, bone marrow constitutes 4% of the total body mass of humans; in an adult having 65 kilograms of mass, bone marrow typically accounts for approx. 2,6 kilograms.[2]

The hematopoietic component of bone marrow produces approximately 500 billion blood cells per day, which use the bone marrow vasculature as a conduit to the body's systemic circulation.[2]

Bone marrow is also a key component of the lymphatic system, producing the lymphocytes that support the body's immune system.[3]

(1) Birbrair A, et al. Niche heterogeneity in the bone marrow. Ann N Y Acad Sci. 2016 Apr;1370(1):82-96.
(2) Vunjak-Novakovic G, et al. Challenges in Cardiac Tissue Engineering. Tissue Eng Part B Rev. 2010 Apr;16(2):169-87.
(3) The Lymphatic System. allonhealth.com, March 2017.

Marrow Cellution™

MC-RAN-11C Marrow Cellution™ System components:
From left: Introducer Needle with Sharp Stylet, Aspiration Cannula, Blunt Stylet.
Set also includes a 10ml Syringe (not shown).

The Marrow Cellution™ Bone Marrow Aspiration & Cancellous Bone Graft Harvesting System is a novel bone marrow access and retrieval device that incorporates features designed to minimize limitations of traditional trocar needles.

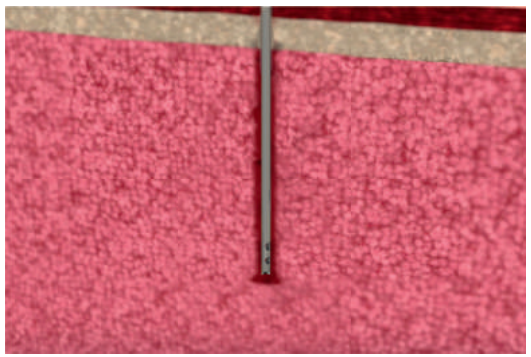
Marrow Cellution™ maximizes stem and progenitor cell recovery while minimizing peripheral blood infiltration. Because fluid under force follows the path of least resistance, trocar needles with side ports aspirate primarily through the distal end of the cannula. This leads to excessive blood collection, requiring additional manipulation, i.e. centrifugation or chemical separation in a laboratory.

Marrow Cellution™ accesses aspirate flow collected exclusively laterally as the tip of the aspiration cannula is closed allowing marrow collection perpendicular to and around the channel created by the device. It incorporates technology to precisely reposition the retrieval cannula within the marrow space after each aspiration. These features achieve a clinicians' desire for a single entry point.

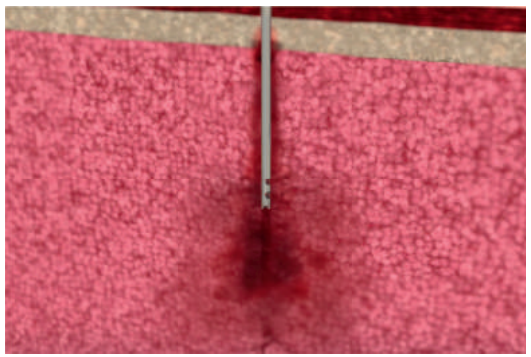
A single puncture with Marrow Cellution™ provides high quality bone marrow aspirate and cancellous bone graft, collected from numerous sites within the marrow geography.

Overcome Aspiration Limitations & Maximize Cell Yield

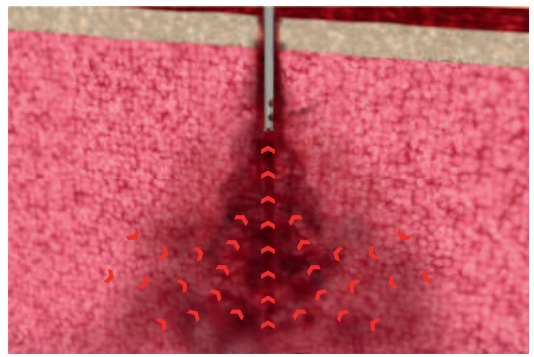
Traditional Aspiration



Traditional open ended (distal) trocars are designed to operate for small biopsy volumes (1-2ml). After aspirating the first 1-2ml of bone marrow, peripheral blood fills the vacated space, limiting the additional harvest of key stem and progenitor cells.



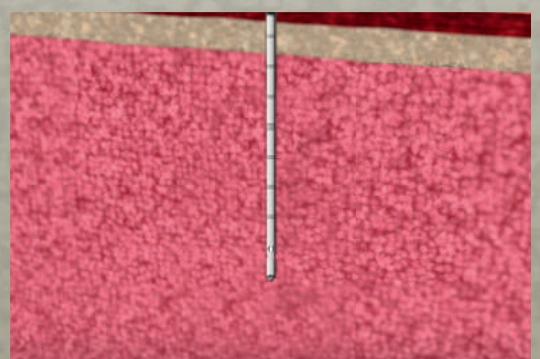
Further aspiration attempts diminish the number of total nucleated cells (TNC). Cells in the aspirate drop dramatically due to the lower viscosity of blood following the path of least resistance through the distal end channel, minimizing efficiency of side channels.



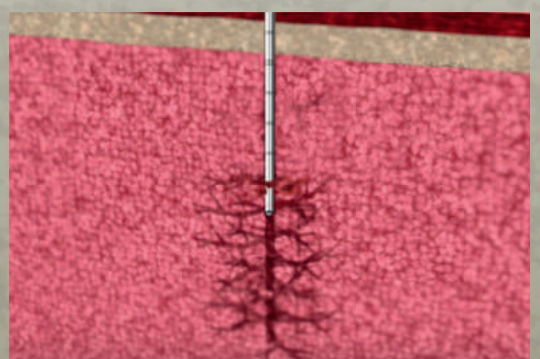
Aspiration of larger quantities of bone marrow, typically required for most clinical indications, necessitates further manipulation and volume reduction processing steps such as, centrifugation or chemical gradient separation in a laboratory.

Requires additional manipulation i.e. centrifugation.

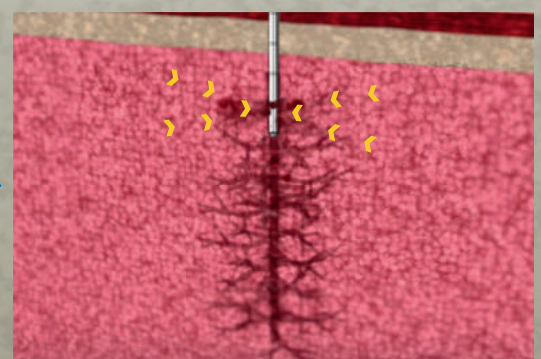
Marrow Cellution™



Marrow Cellution™ allows for easy access through soft tissue and cortical bone. A fenestrated blunt trocar is then introduced to create access for closed end, side port aspiration stylet. The design minimizes trauma to cancellous bone and marrow, thereby mitigating pooling of peripheral blood.



The patent pending design consists of a closed end stylet which forces aspiration of marrow laterally from the marrow space. The manual rotation of the handle allows the fenestrated stylet to be raised to a desired position in a new level of undisturbed marrow for subsequent aspiration aliquots.



From a single stick, Marrow Cellution™ is capable of collecting up to 10ml of high quality bone marrow equivalent or superior to other systems that require additional manipulation steps such as centrifugation or chemical separation in a laboratory.

All components stay in sterile field.

No further manipulation required.

Marrow Cellution™ Bone Marrow Aspiration

The Marrow Cellution™ Bone Marrow Aspiration System is intended for use for aspiration of bone marrow or autologous blood. It allows the user to aspirate in a measured and controlled manner over a large geography within the marrow space.

Marrow Cellution™ is available in 11 Gauge and 13 Gauge diameters and includes an introducer needle, sharp and blunt stylet, aspiration cannula and 10ml syringe.

Marrow Cellution™ also comes in multiple lengths and is designed for use in the Iliac Crest, Pedicle, Calcaneous or Tibia.

Marrow Cellution™ includes two important unique features:

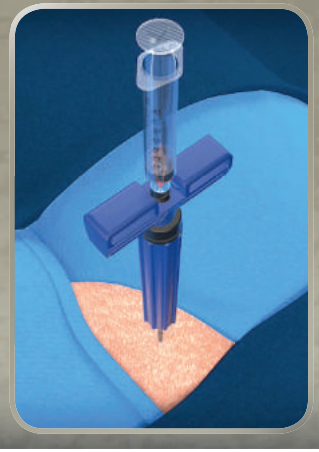
1. A closed-end needle tip to prevent aspiration of excess blood from the entry channel, and

2. A handle with threaded guide for controlled positioning of the aspiration cannula within the marrow space.

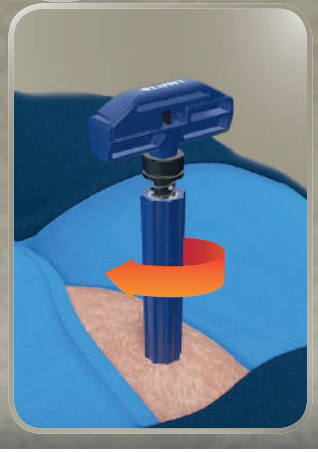
Process Steps for Marrow Aspiration:*

1
- Select & Prep aspiration site
- Insert heparin coated Introducer Needle just past cortex into medullary space

2
- Remove Sharp Stylet
- Attach Syringe
- Aspirate 1ml marrow to ensure proper positioning



3
- Insert Blunt Stylet
- Advance Access Needle to desired depth
- Rotate Guide Grip to skin level



4
- Remove Blunt Stylet
- Insert & secure Aspiration Cannula and Syringe
- Aspirate 1ml marrow

5
- Hold Guide Grip and rotate Handle 360° counter-clockwise
- Aspirate 1ml marrow

6
- Repeat Step 5 as needed
- Reassemble for additional puncture sites (if required)

Marrow Cellution™ Percutaneous Bone Graft Collection

Produces Autologous Cancellous Graft Material with Osteoconductive, Osteoinductive & Osteogenic Properties

Minimally Invasive Cancellous Bone Core Extraction Technique

May Be Combined with Allogeneic, Autologous or Synthetic Bone Chips Hydrated with Marrow Cellution™ Aspirate

Intact Bone Cores vs. Morselized Bone

- Harvesting intact cancelleous bone cores without disrupting the highly-organized living tissue is superior to transplanting pieces of bone. Intact grafts maintain the micro-vascular network within the graft promoting bone callus formation/ remodeling and do not exhibit extensive resorption.[1] [2]
- Intact bone exploits the biology of normal fracture healing rather than through slow creeping substitution associated with the slow incorporation of a non-vascularized graft.[1]
- Research demonstrates the enhanced survival of a bone graft as long as its primary blood supply is preserved. A living bone graft will shorten the time for boney union because the reconstructed bone is comparable to a bone with a double fracture. [1] [2]
- Allogenic or synthetic bone chips hydrated with marrow can be packed around the living bone graft/core to accelerate anastomosis into the graft and minimize morbidity.[1] [2]

Minimally Invasive Bone Grafts

- Vascularized and cancellous autograft shows optimal skeletal incorporation but is limited by morbidity concerns.[3]
- Using the Marrow Cellution™ Graft Delivery Syringe and the Marrow Cellution™ Bone Core Harvest Device, the clinician can create a combination graft of a vascularized intact bone core in the center of the graft surrounded by allogeneic, autologous or synthetic bone chips hydrated with cellular marrow aspirate.
- Higher quality, less quantity, delivered appropriately minimizes host morbidity.

(1) Bleuming SA, et al. Bone morphogenetic protein signaling suppresses tumorigenesis at gastric epithelial transition zones in mice. Cancer Res. 2007 Sep 1;67(17):8149-55.
(2) Ostrup LT, et al. Distant transfer of a free, living bone graft by microvascular anastomoses. An experimental study. Plast Reconstr Surg. 1974 Sep;54(3):274-85.
(3) Taylor GI, et al. The free vascularized bone graft. A clinical extension of microvascular techniques. Plast Reconstr Surg. 1975 May; 55(5):533-544.

Marrow Aspiration & Cancellous Bone Graft

The Marrow Cellution™ Bone Marrow Aspiration- & Autologous Bone Harvesting System allows physicians to combine high quality bone marrow aspirate and percutaneously harvested cancellous bone autograft.

Harvesting intact cancellous bone cores without disrupting highly vascularized and organized tissue is superior to transplanting small pieces of morselized bone.

The highly active cellular composition of Marrow Cellution™ Aspirate combined with percutaneously harvested bone core(s) deliver autograft without the associated morbidity.

- Autologous graft material with Osteoconductive, Osteoinductive and Osteogenic properties.
- Minimally invasive technique – uses an 8 Gauge Trephine Needle for bone core extraction.
- Graft material may be combined with allogenic, autologous or synthetic bone chips hydrated with highly cellularized marrow aspirate.
- Percutaneous harvesting reduces donor site morbidity associated with standard harvesting techniques.

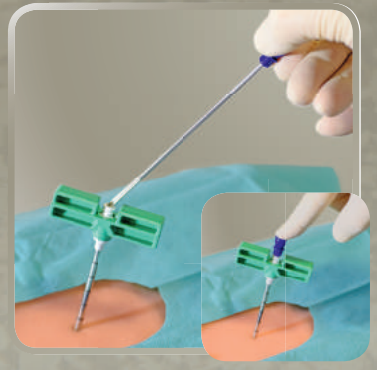
Process Steps for Bone Collection:*

A

- Insert and advance Trephine Needle to desired depth and remove Sharp Stylet
- Insert Marked Measurement Probe to check sample length & remove Probe

B

- Insert Extraction Tool into the Trephine Needle cannula
- Push Extraction Tool to luer connection of the handle



C

- Rotate Trephine Needle and Extraction Tool together(!) to cut bone core
- Remove both tools together

D

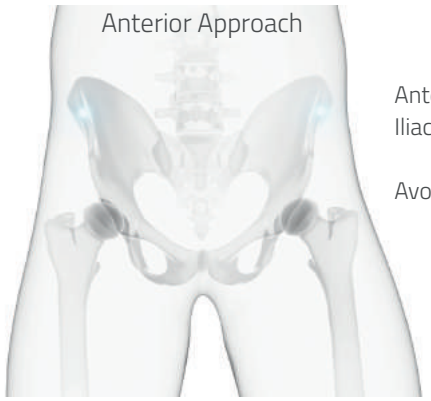
- Remove Extraction Tool from Trephine Needle
- Use Measurement Probe to push out the bone core

* Abbreviated instructions overview. Refer to package insert for detailed instructions for use.

Marrow Cellution™ Tips & Techniques

1 Orientation & Location Selection

Anterior Approach

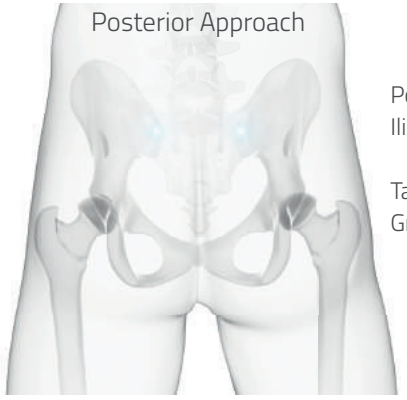


Anterior Superior Iliac Spine (ASIS)

Avoid Inguinal Ligament

or

Posterior Approach



Posterior Superior Iliac Spine (PSIS)

Target Direction: Greater Trochanter

2 Palpate & Mark Target Site

Prior to disinfection, palpate anatomy to select desired entry point and mark with surgical marker.

3 Sedate & Wait

Choose sedation method and allow sufficient period of time for sedation medication to take full effect.

4 Disinfect & Drape Site

Following sterile technique, disinfect aspiration site with appropriate disinfection product and then drape site.

5 Puncture & Aspirate

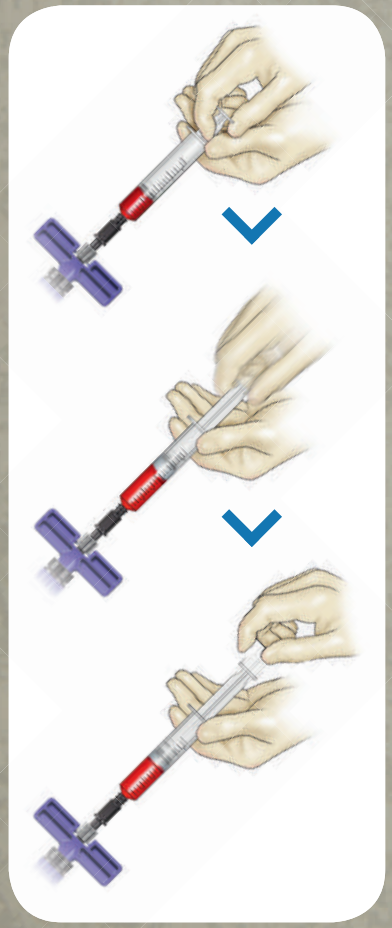
Carefully make stab incision with sharp blade. Palpate Marrow Cellution™ to selected periosteum position. Drive Marrow Cellution™ through periosteum and confirm with 1,0ml aspiration.

"Snap Back" Aspiration

The Marrow Cellution™ Aspiration System provides a 10ml syringe.

Aspirate ~1ml from each aspiration level by retracting the syringe plunger and immediately release it.

Reposition the Marrow Cellution™ Needle and repeat the process.



Suggested Heparin Flush Procedure for Bone Marrow Aspiration

1. Withdraw 2,000 units/mL* of Heparin from sterile bowl into 10mL syringe.
2. Remove Stylets from Introducer Needle and Aspiration Cannula with distal end of needle inside sterile bowl.
3. Connect Heparin-filled syringe to the shorter Introducer needle and inject Heparin until needle is fully rinsed (is flowing through end of needle). Aspirate Heparin back into syringe and disconnect from needle.
4. Repeat step 3 for the longer aspiration needle.
5. Rinse each stylet (3), short introducer sharp (1) and blunt (2), longer aspiration stylet (3).
6. With needle guards in place, rinse the outside of each needle by injecting Heparin into the open end of the guard.

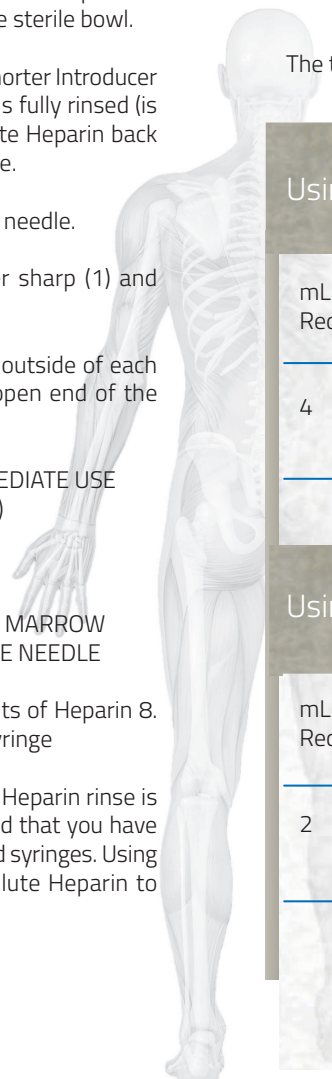
BEGIN ASPIRATION PROCEDURE FOR IMMEDIATE USE
(EX. MIXING WITH BONE GRAFT)

OR

CONTINUE FOLLOWING STEPS FOR BONE MARROW ASPIRATE INJECTION THROUGH 22 GUAGE NEEDLE

7. Rinse 22 Gauge Needle with 2,000 units of Heparin 8. Add 1⁄2 mL of Heparin into collection syringe

*It is important that the strength per mL of the Heparin rinse is at least 1,000/mL but preferably 2,000/mL and that you have adequate volume (10mL) to rinse all needles and syringes. Using a sterile bowl, add sterile Saline or PBS to dilute Heparin to 2,000 units/mL.



The tables below detail the amount of Heparin and Saline or PBS needed to dilute the Heparin to 2,000 units/mL.

Using 5,000/mL Heparin

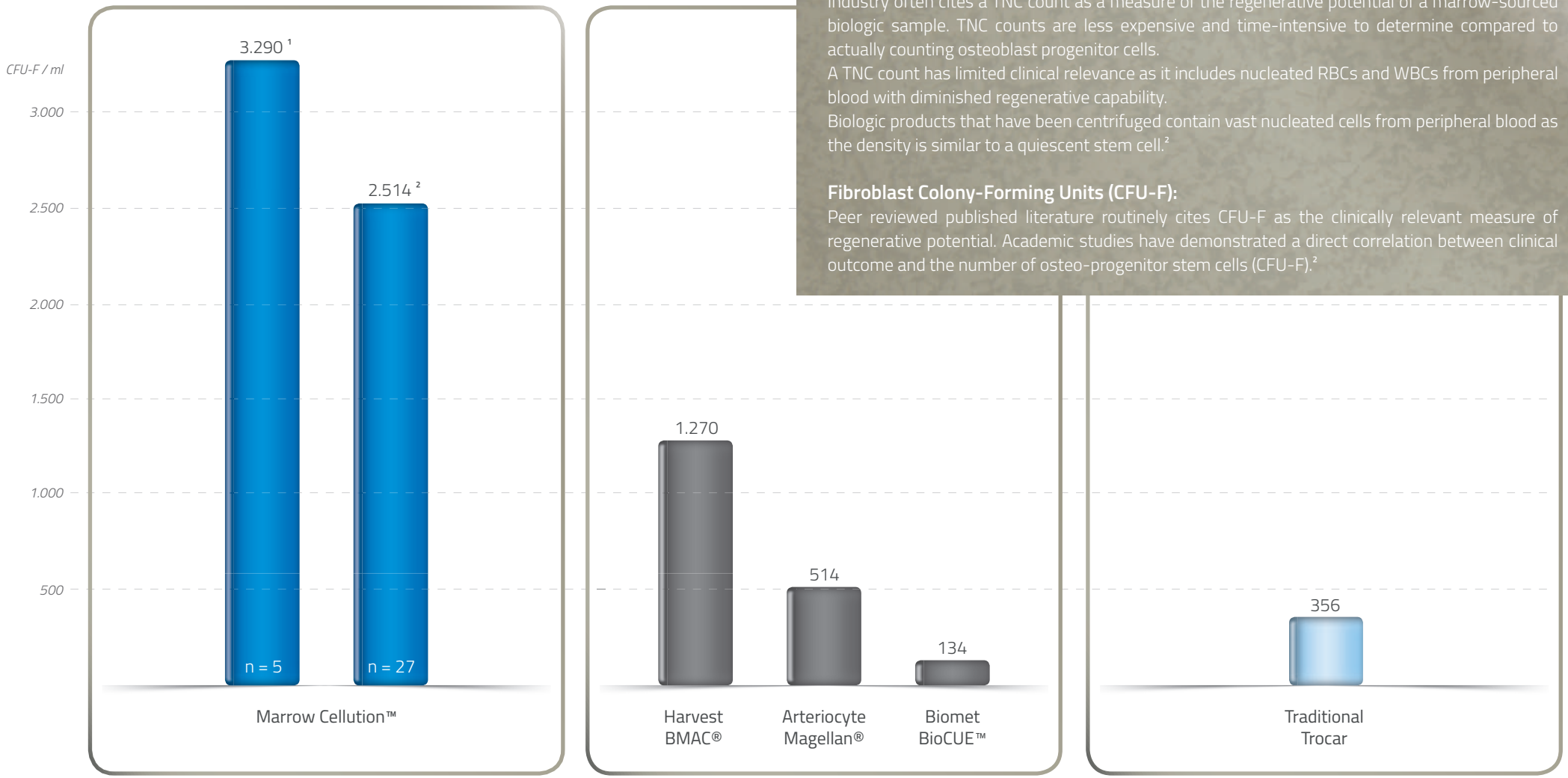
mL of Heparin Required	ml of Saline or PBS	Total Heparin Units	Total mL	Heparin/mL
4	6	20,000	10	2,000

Using 10,000/mL Heparin

mL of Heparin Required	ml of Saline or PBS	Total Heparin Units	Total mL	Heparin/mL
2	8	20,000	10	2,000

Competitive Performance

CFU-F Cell Count Comparison



Total Nucleated Cells (TNC):
Industry often cites a TNC count as a measure of the regenerative potential of a marrow-sourced biologic sample. TNC counts are less expensive and time-intensive to determine compared to actually counting osteoblast progenitor cells.
A TNC count has limited clinical relevance as it includes nucleated RBCs and WBCs from peripheral blood with diminished regenerative capability.
Biologic products that have been centrifuged contain vast nucleated cells from peripheral blood as the density is similar to a quiescent stem cell.[2]

Fibroblast Colony-Forming Units (CFU-F):
Peer reviewed published literature routinely cites CFU-F as the clinically relevant measure of regenerative potential. Academic studies have demonstrated a direct correlation between clinical outcome and the number of osteo-progenitor stem cells (CFU-F).[2]

(1) Scarpone MA, et al. Marrow Cellution Bone Marrow Aspiration System and Related Concentrations of Stem and Progenitor Cells. White Paper 2015.

(2) Harrell DB, Purita JR. Novel Technology to Increase Concentrations of Stem and Progenitor Cells from Marrow Aspiration. White Paper 2016.

Hegde V, et al. A prospective comparison of three approved systems for autologous bone marrow concentration demonstrated non-equivalency in progenitor cell number and concentration. J Orthop Trauma. 2014 Oct;28(10):591-8.

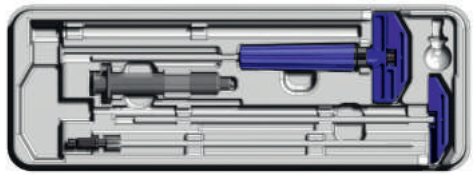
McLain R, et al. Aspiration of osteoprogenitor cells for augmenting spinal fusion: comparison of progenitor cell concentrations from the vertebral body and iliac crest. J Bone Joint Surg Am. 2005 Dec;87(12):2655-61.

Marrow Cellution™ Product Details

Marrow Cellution™ Bone Marrow Aspiration:

Marrow Cellution™ is available in both 11G and 13G diameters and includes an introducer needle, sharp and blunt stylet, aspiration cannula and a 10ml syringe. The technology is available in multiple lengths and is designed for use in the Iliac Crest, Pedicle, Calcaneus or Tibia.

Article code	*Introducer size*
MC-RAN-13FA*	13G x 2" (5cm)
MC-RAN-13C	13G x 3.5" (9cm)
MC-RAN-11C	11G x 3.5" (9cm)
MC-RAN-11CSTS (for obese patients)	11G x 4.5" (11.4cm)

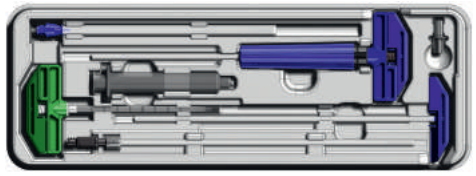


MC-RAN-11C

Marrow Cellution™ Bone Marrow Aspiration & Autologous Bone Graft Harvesting:

Delivering "Gold Standard" autograft in a minimally invasive manner, this version includes an 11 Gauge Marrow Cellution™ Bone Marrow Aspiration System (MC-RAN-11C) with all componentry along with an 8 Gauge Trephine Needle with a specially designed cancellous Bone Extraction Tool to harvest bone cores percutaneously.

MC-RAN-13FAB*	13G x 2" (5cm)
MC-RAN-8C	11G x 3.5" (9cm) with 8G x 4" Trephine Needle
MC-RAN-8CSTS (for obese patients)	11G x 4.5" (11.4cm) with 8G x 6" Trephine Needle

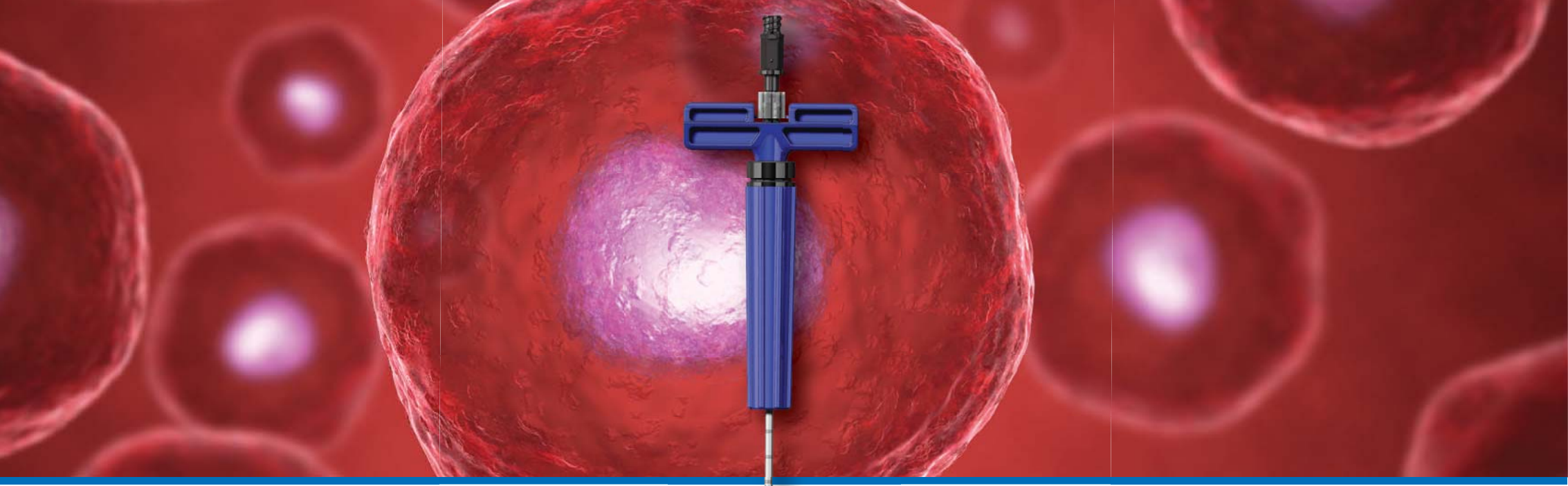


MC-RAN-8C

****MC-RAN-13FA** and **MC-RAN-13FAB** are designed for use in foot and ankle surgery and feature a closed tip, sharp introducer needle. No blunt stylet or aspiration cannula is included.*

Marrow Cellution™ provides substantial savings in time, effort and expense.

It reduces patient trauma, morbidity and risk of infection.



ASPIRATE TO APPLICATION®

Distributed by:

ACCELLERATED BIOLOGICS

800-367-0844

www.AcCELLeratedBiologics.com

Ranfac®

To trial the device or to speak with a representative, please contact:
Ranfac Corp.® | 30 Doherty Ave. | Avon, MA 02322
Domestic: 800.272.6322 | International: 508.588.4400
Email: info@ranfac.com | www.ranfac.com | www.marrowcellution.com

CE 0086

Ranfac Corp. | 30 Doherty Avenue
Avon/MA 02322 | USA

DOC07-04/17