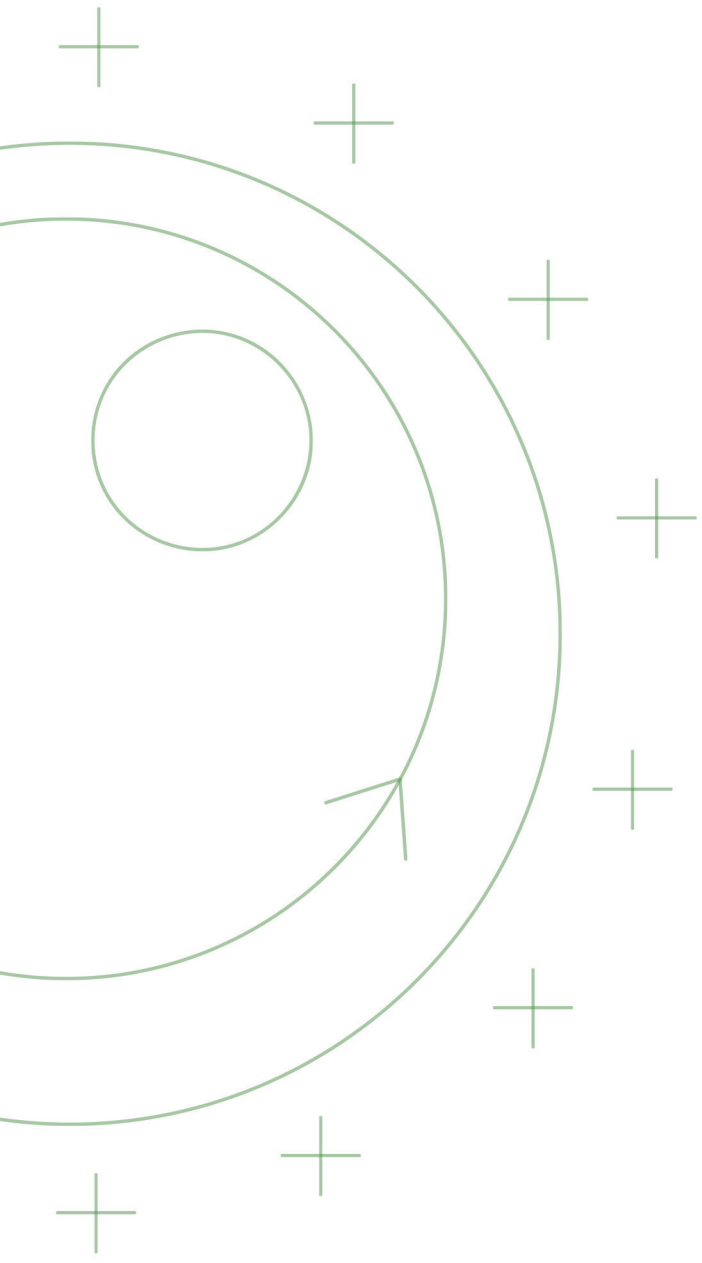
REGENERATIVE & ORTHO CATALOGUE



BPB medica

INDEX:

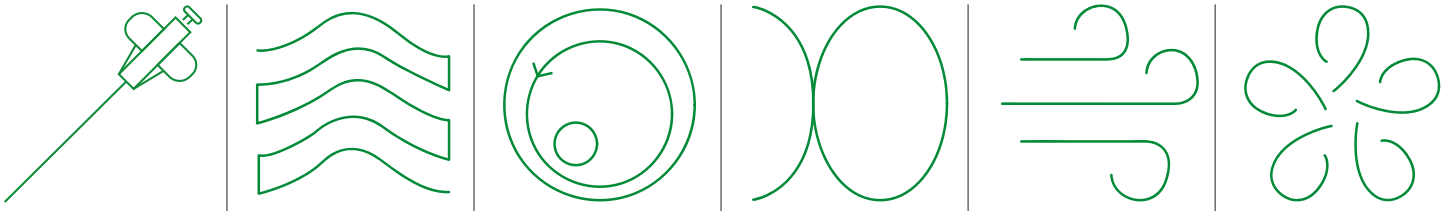
BPB MEDICA™

BPB MEDICA™ is a leading Italian-based healthcare manufacturer, known for its fully integrated, in-house production of innovative medical and surgical devices.

With every stage managed internally, we guarantee **exceptional quality**, **customisation** and **reliability**, making BPB MEDICA™ a preferred partner for healthcare professionals worldwide.

At BPB MEDICA™, we advance in line with the needs of patients, doctors, and hospital staff by leveraging our technical expertise, state-of-the-art technology, and commitment to excellence.

Key Product Lines:



BIOPSY | **SPINE** | **ORTHO-BIOLOGICS & REGENERATIVE MEDICINE** | **ASSISTED REPRODUCTION** | **INTENSIVE CARE** | **AESTHETIC**

Through a commitment to **quality, product distinction**, and **advanced production technologies** across each category, BPB MEDICA™ has established itself as a comprehensive solutions provider in healthcare.

Research & Development:

Continuous Innovation: Our commitment to continuous innovation drives our R&D Department to develop solutions that meet emerging clinical needs, support better patient outcomes, and adhere to industry-leading standards.

Our R&D Department focuses on refining production standards and developing new products, performing ongoing functional testing in collaboration with Quality Control, and ensuring our products meet rigorous standards, even under extreme conditions.

Client-Centric Development: Every product we create is inspired by a commitment to address specific clinical needs, improve patient outcomes, and offer healthcare providers tools that enhance safety and precision.

In-House Manufacturing Advantage

End-to-End Production Process: every step, from conceptual design to final packaging, is completed under one roof, ensuring consistent quality and rapid response to client needs.

Technological Sophistication:

+ **ISO 8 Cleanroom Facility:** Vital for maintaining sterility and ensuring high-quality assembly and packaging.
+ **Metal Refinishing and Moulding Departments:** specialised equipment that allows for advanced processes such as echogenic marking and precise moulding, which make BPB MEDICA™'s products unique.
+ **OEM & Private Label Services:** clients can access à la carte production services, customizing products with their branding, colours, and unique specifications.
+ **Computerized warehouse with reliable permanent stock:** availability for top-selling items, with 24-hour shipment options.

Dedicated Customer Support:

The Regulatory and Quality Departments offer comprehensive support covering:

+ Quality Systems.
+ Regulatory Affairs.
+ Technical Documentation.
+ Clinical Experimentation.
+ Vigilance and Training.
+ Marketing Support: video tutorials, case studies, training sessions and ongoing participation in major medical congresses.

Continuous Commitment to Quality and Compliance

BPB MEDICA™ continuously performs rigorous quality checks:

+ **Incoming Controls:** Dimensional, visual, documental, and functional checks.
+ **In-Process Controls:** Visual and functional controls with sampling or 100% control.
+ **Finished Product Controls:** 100% packaging checks, including post-sterilization inspection.

This thorough quality process ensures that every BPB MEDICA™ product delivered meets the highest standards for safety and performance.

Certifications

Commitment to Compliance: BPB MEDICA™'s dedication to quality has earned certifications such as CE and ISO 13485, ensuring safety, reliability and market access worldwide

FDA Establishment Registration marks BPB MEDICA™ as a trusted provider for the U.S. market

ISO 13485

BUREAU VERITAS
Certification

FDA Establishment
Registration number: 9617616
FEI Number*: 300327275

Biopsybell is registered with **EUDAMED** under SRN IT-MF-000011601, as required by MDR Regulation (EU) 2017/745

Milestones and Growth:

1999: Foundation with the BIOPSY product line

2014: Launch of SPINE line of products

2018: Launch of ASSISTED REPRODUCTION line of products

2019: Launch of ORTHO-BIOLOGICS line of products

2020: Launch of AESTHETIC line of products

2022: Acquisition by BPunto3/Wallaby Group in 2022, further supporting global growth

Why BPB MEDICA™?

» **Full in-house production** and quality control.

» **Comprehensive product range** and **customization.**

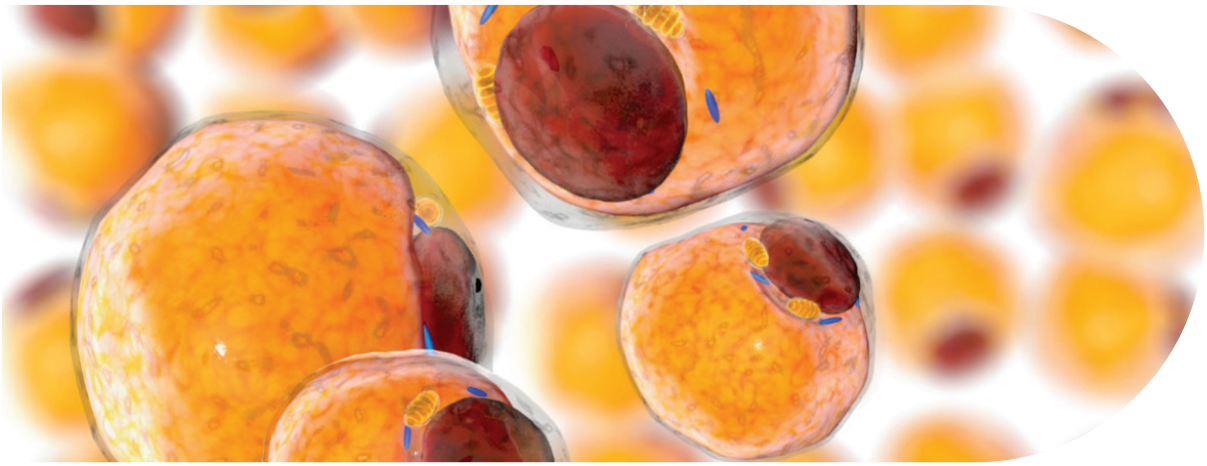
» **Global presence** with a proven track record.

» **Strong customer support** and regulatory guidance.

JOIN US in advancing healthcare with products that prioritize **safety, precision,** and **efficacy**!

ORTHOBIOLOGICS AND REGENERATIVE MEDICINE

Regenerative medicine leverages the body's innate capacity for repair by employing cell-based therapies that restore tissue structure and function. At the forefront of these strategies are mesenchymal stromal cells (MSCs)—multipotent cells with the ability to differentiate into various mesodermal lineages, including bone, cartilage, muscle, and adipose tissue. Among the most clinically relevant sources of MSCs are adipose tissue (AD-MSCs) and bone marrow (BMMSCs).



Both exhibit high therapeutic potential, though they differ in biological behavior, accessibility, and clinical application.

· **BM-MSCs (Bone Marrow-Derived Mesenchymal Stromal Cells)** are considered the gold standard in regenerative orthopedics due to their superior osteogenic potential. Their role in bone healing is welldocumented, especially in applications such as spinal fusions, fracture repair, osteochondral lesions, and subchondral bone regeneration. BM-MSCs secrete bioactive molecules that support angiogenesis, immunomodulation, and the recruitment of endogenous progenitor cells.

· **AD-MSCs (Adipose-Derived Mesenchymal Stromal Cells)** are abundant, easily accessible, and exhibit a high proliferative rate. They possess remarkable anti-inflammatory and immunomodulatory properties, making them ideal for treating chronic musculoskeletal conditions, such as osteoarthritis and tendon disorders.
While BM-MSCs are preferred in bone-related regeneration, AD-MSCs are often used where inflammation modulation and soft tissue repair are key.
The choice between sources is dictated by clinical goals, anatomical site, and procedural context.

THE SMART ALTERNATIVE TO CENTRIFUGATION

Avoiding centrifugation isn't just about simplifying workflow, it's a strategic clinical advantage.

Our proprietary technologies preserve the biological integrity of mesenchymal stem cells (MSCs), deliver higher cell yields, reduce the risk of contamination, and streamline procedures.

+ **BONE MARROW: The MARROW-STEM™ Advantage Centrifugation** can reduce MSC viability and colony-forming units (CFUs) by up to 40% due to g-force stress, impair cell performance, require manipulation outside the sterile field, and fall under complex pharmaceutical regulations.

Traditional needles often have open distal tips that allow peripheral blood contamination, damage the bone channel, and necessitate centrifugation to isolate viable cells. MARROW-STEM™ overcomes these limitations with a patented, innovative sampling technique that minimizes patient discomfort and reduces time and complexity in the operating room.

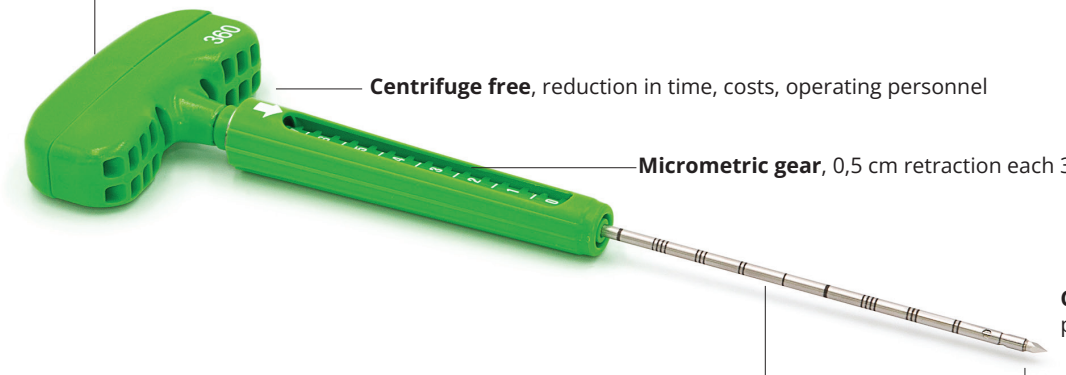
+ **ADIPOSE TISSUE: The LIPO-STEM™ Advantage Instead** of subjecting tissue to high-speed centrifugation, our devices gently wash it with continuous saline flow in a closed circuit.This preserves the structure and function of the stromal vascular niche, yielding adipose tissue with a high concentration of MSCs per milliliter, enhanced vitality, and greater regenerative potential.

MARROW-STEM™

BONE MARROW MESENCHYMAL STEM CELLS ASPIRATION KIT

MARROW-STEM™ is a disposable device for the selective aspiration of mesenchymal cells from the bone marrow. With its innovative features, MARROW-STEM™ optimizes the cellular yield and minimizes the contamination of peripheral blood, thanks to a micrometric system for lateral aspiration and the closed distal tip of the device.

Single step device, faster and easier procedure



Centrifuge free, reduction in time, costs, operating personnel

Micrometric gear, 0,5 cm retraction each 360° rotation

Closed & sealed distal tip, no peripheral blood contamination

Lateral aspiration, high cellular yield related to a reduced volume of marrow aspirate

INNOVATIVE

+ Closed & sealed distal tip: guarantees a high cellular yield.
+ 100% lateral aspiration with level-by-level sampling: no peripheral blood contamination
+ Micrometric gear: 0,5 cm cannula retraction every 360° rotation.

EASY TO USE

+ Single-step device: faster and easier procedure.
+ Point of care therapy: minimally invasive procedure.
+ Residual retraction control thanks to the numbers printed on the gear window.

CONVENIENT

+ Centrifuge-free: saving on time, personnel and tools.
+ No processing time: ready-to-use bone marrow MSC concentrate.
+ Minimizes staff training, or preparation and clean-up.

FIELDS OF APPLICATION

The bone marrow aspirated with MARROW-STEM can be injected to accelerate the natural healing process, or can be combined with other kinds of bone substitutes to create an enhanced bone graft.

BONE MARROW MSC CONCENTRATE

INDICATIONS:

+ bone cysts
+ intraarticular infiltration
+ tendinopathy
+ pain reduction (facet joints)

BONE MARROW ASPIRATE + ANY KIND OF BONE SUBSTITUTE

INDICATIONS:

+ spinal fusions
+ bone marrow lesions
+ foot & ankle fusions

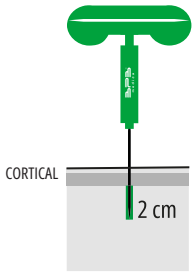
BONE MARROW ASPIRATE + AUTOLOGOUS BONE DOWEL

INDICATIONS:

+ avascular necrosis
+ bone marrow lesions
+ bone regeneration
+ trauma procedures & fractures

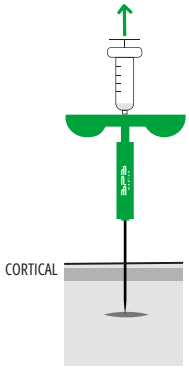
Surgical technique:

1



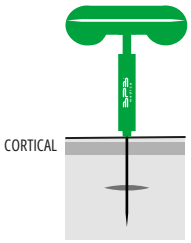
Insert and advance the MARROW-STEM™ just beyond the edge of the cortical bone, keeping the stylet attached.

2



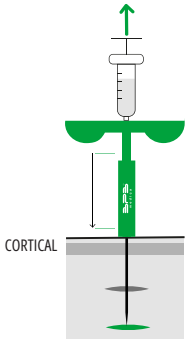
Remove the stylet, connect the VacLok syringe and aspirate 1 mL of bone marrow.

3



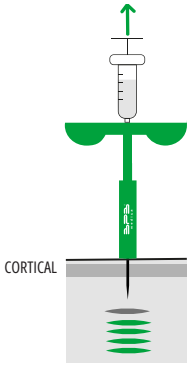
Reinsert the stylet, and advance the device to the deepest desired depth.

4



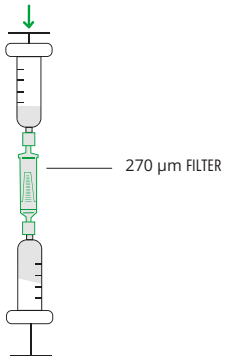
Adjust the gear so that it makes contact with the skin. Remove the stylet again, reconnect the VacLok syringe and aspirate a second mL of bone marrow.

5



Retract the MARROW-STEM™ to the next aspiration target (positioned approximately 1 cm above the previous point) by rotating the handle 360° counterclockwise twice. Keep the gear steady while retracting. Aspirate 1 mL of bone marrow per cm of retraction, repeating this retraction/aspiration process for additional collection points. Refer to the residual excursion (in cm) marked on the gear.

6



Upon completing the aspirations, remove the MARROW-STEM™. If necessary, use the provided 270 µm filtering system to remove bone debris or clots (not available in the U.S).

ORDER GUIDE - MARROW-STEM™

CODES:

MWS1110C-01 (worldwide distribution, except in the U.S.)

MWS11100C-US (distribution only in the U.S.)

STANDARD KIT COMPOSITION

1x MARROW-STEM™ MSCs aspiration device
1x 270 µm filtering system
1x VacLok AT syringe 20 mL
1x Injection syringe 10 mL
1x 270 µm filtering system (not available in the U.S.)

MARROW-STEM™
MSCs aspiration device

VacLok aspiration syringe

Filtering system
(not available in the U.S.)

Injection syringe

Backed by science: MARROW-STEM™ validation test

INTRODUCTION:

Mesenchymal stem cells (MSCs) are a class of adult progenitor cells that can differentiate into various mesenchymal lineages. They are normally isolated from bone marrow (BM) tissue. MSCs can help repair and regenerate a variety of mesenchymal tissues such as bone, cartilage, muscle, and bone marrow stroma. These cells produce growth factors and cytokines that can help repair human tissues [1]. Preclinical and clinical studies show that the main mechanism underlying the therapeutic benefits is related to paracrine effects such as the facilitation of angiogenesis, the prevention of apoptosis, the suppression of inflammation and the modulation of extracellular matrix dynamics. When tissues or cells have been damaged, the MSCs activate or suppress the immune system to control the entire tissue regeneration process. This is because mesenchymal cells can regulate IS components such as macrophages and neutrophils [2].

Friedenstein et al. [3] were the first to isolate MSCs from bone marrow. Friedenstein's method is currently a standard protocol for the isolation of BM-MSCs. The highest concentration of MSCs obtained from bone marrow aspirate is found in the posterior iliac crest [5]. Sampling more than 1 mL of bone marrow from a single site reduces the quality of the aspirate: to increase the proportion of MSCs, many studies concentrate on the bone marrow aspirate (BMA) by centrifugation, thus forming bone marrow concentrate (BMC) [4].

The main disadvantages of using a centrifuge are:

+ A total processing time, including suction, of about 20 minutes
+ Centrifugation is carried out outside the sterile field
+ Substantial aspiration of peripheral blood, resulting in a significant reduction in connective tissue, progenitor cell counts [6][7]
+ Separation by density gradient centrifugation cannot distinguish between nucleated cells in the peripheral blood (which contain very few stem/progenitor cells) and progenitor cells in the bone marrow [6].
+ Centrifugation involves additional handling steps and increases the possibility of contamination [8]
+ Up to 40% of mesenchymal stem cells may die because of the spinning
+ Requires significantly more aspirate (around 10 times more compared to the MARROW-STEM™ device).

Another important aspect concerns the device used to harvest the bone marrow: conventional trocars aspirate from the distal tip of the device, and have several disadvantages:

+ Involve the sampling of a greater volume from a single site, or sampling from multiple angles, which increases patient morbidity
+ Cause excess peripheral blood contamination
+ Diminish cellular yield
+ Require additional manipulation steps (centrifugation required)
+ The cannula retraction causes spongious bone channels breakage
+ Only a limited number of cells MSCs stay in the spongious marrow trabeculae
+ Trocar with both open distal tip and side holes are not efficient since peripheral blood has got a significantly lower viscosity than bone marrow and syringe pressure doesn't help the marrow collection from side holes

METHODS:

The device was qualified by proceeding in accordance with (EU) REGULATION 2017/745 OF THE EUROPEAN PARLIAMENT AND THE COUNCIL of 5 April 2017 concerning medical devices, which amends Directive 2001/83/ EC, (EC) Regulation No. 178/2002 and (EC) Regulation No. 1223/2009, which repeals Council Directives 90/385/ EEC and 93/42/EEC, Legislative Decree 219/05 and the Ministerial Decree of 2 November 2015 on the subject of device qualification and process validation.
Myeloaspirate samples were analysed using a flow cytometric method, and the expression of the MSC markers (see table and FACS image) was specifically quantified. The bone marrow blood was processed as follows:
500ul blood was treated with ACK (Ammonium-Chloride-Potassium) to lysate the red blood cells. After two washes with PBS, the cell pellet was incubated for 15 min at room temperature with the following mix of antibodies: CD45 PB, CD3 Pe Cy7, CD90 APC, CD73 PE, CD105 FITC. The combination of these antibodies enables the detection of the stromal component (CD73+, CD90+, CD105+) in the non-hematopoietic portion (CD45-, CD34-) of the marrow blood. 200ul blood was instead used as an unstained control. After 2 washes in PBS + 2% FBS, the samples were fixed in PBS + 2% PFA and a reading was taken on a flow cytometer (BO Facs Canto) calibrated according to the standard criteria of the OSR Facs facility (Fractal).

RESULTS:

Post-superior iliac crest myeloaspiration procedures were performed on non-haemopathic orthopaedic patients with preserved blood composition. The volume of each sample was 2 mL. From an operational point of view, the device is undoubtedly user-friendly, easy and practical to use and safe for the operator, with minimal trauma to the patient.
The vital and measurable cellularity was >95% of the total, of which ~ 85% were hematopoietic (CD45+). The cytofluorimeter analysis showed that the mesenchymal component constitutes ~0.1% of the cells analysed (see table).

SAMPLE	
Live cells (SSC-A-FSC-A)	98.00%
CD45neg	13,80%
CD73+CD90	0,68%
MSCs (CD90+CD73+CD105)	0,093%

DISCUSSION:

It should be considered that MSCs constitute a very rare population in the marrow, approximately 0.001-0.1% of mononuclear cells (Li H et al. isolation and characterization of primary bone marrow mesenchymal stromal cells. Ann N Y Acad Sci. 2016). Therefore, the results observed were extremely satisfactory:
MSCs = 0,093% of live cells.

Furthermore, a comparative study shows that the use of selective aspiration devices yields more than twice as many fibroblast colony-forming units (CFU-f) per ml than bone marrow concentrate obtained by centrifugation. The selective aspiration devices also resulted in a significantly lower peripheral blood contamination than the sample obtained by centrifuge and required considerably less preparation time and less aspirate.

The results confirm:

1. The device's capability to selectively harvest MSCs with a high percentage of cell viability
2. The possibility offered by the arrangement of suction holes, which provides high cellularity with minimum volumes of myeloaspirate, thereby minimising trauma, a definite advantage in both orthopaedics and haematology (e.g. bone marrow explants)
3. The safety and ease of use for the operator.

The results obtained suggest that new fenestrated trocars such as the MARROW-STEM™ device may be more effective replacements for conventional bone marrow aspiration devices that rely on centrifuge-based systems.
Conventional technologies typically result in the disposal of 35-65% of the cells and growth factors when reduced in centrifuge-based systems during separation from the supernatant [9]. These cells and growth factors are not removed by the MARROW-STEM™ device: the biological material produced by the device does not require handling steps outside the sterile field, and the entire sample can be used. Centrifuge-based systems require the bone marrow aspirate to be removed from the sterile field for centrifugation. The final product then re-enters the sterile field following centrifugation and
withdrawal of the product. The option of keeping the product in a sterile field reduces the risk of infection for the patient undergoing the procedure.

From an operational point of view, the device was found to be intuitive, easy and practical to use, safe for the practitioner and minimally traumatic for the patient [10]. The design automatically repositions the suction cannula and aspirates from the side ports over a wider geography of the bone marrow space, such that consecutive 1mL aspirations can be performed.

This innovative device also minimises peripheral blood contamination. This also suggests that the MARROW-STEM™ device could provide even better results than BMAC alternatives as healthcare practitioners gradually become more familiar with and proficient in using the device.

References:

1. Pfitzinger, Mark F. "Mesenchymal stem cells from adult bone marrow." Mesenchymal Stem Cells. Humana Press, 2008. 27-44.
2. Jiang, Wei, and Jianyong Xu. "Immune modulation by mesenchymal stem cells." Cell proliferation 53.1 (2020): e12712.
3. Friedenstein, Alexander J., J. F. Gorskaja, and NN976387 Kulagina. "Fibroblast precursors in normal and irradiated mouse hematopoietic organs." Experimental haematology 4.5 (1976): 267.
4. Wells, Kristina, et al. "Cellular and clinical analyses of autologous bone marrow aspirate injectate for knee osteoarthritis: a pilot study." PM&R (2020).
5. Hyer, Christopher F., et al. "Quantitative assessment of the yield of osteoblastic connective tissue progenitors in bone marrow aspirate from the iliac crest, tibia, and calcaneus." JBJS 95.14 (2013): 1312-1316.
6. Scarpone, Michael, et al. "Isolation of clinically relevant concentrations of bone marrow mesenchymal stem cells without centrifugation." Journal of Translational Medicine 17.1 (2019): 10.
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8. Varady, Nathan H., et al. "Positive early clinical outcomes of bone marrow aspirate concentrate for osteoarthritis using a novel fenestrated trocar." The Knee 27.5 (2020): 1627-1634.
9. Harrell, David B., O. F. Brt, and Joseph R. Purita. "Novel Technology to Increase Concentrations of Stem and Progenitor Cells in Marrow Aspiration."
10. Hongzhe Li,Stefan Scheding "Isolation and characterization of primary bone marrow mesenchymal stromal cells. Ann N.Y. Acad. Sci ISSN 0077-8923

LIPO-STEM DUO™

MICROFRAGMENTATION, PURIFICATION AND PROCESSING KIT FOR ADIPOSE TISSUE MSCs

LIPO-STEM DUO™ is a closed-circuit single-use kit for adipose tissue microfragmentation and purification without any centrifuge and with minimal manipulation. **The filtering system microfragments the adipose tissue while maintaining its biological properties and maximizing the regenerative potential.** The entire processing phase of the liposuctioned tissue occurs inside the device thanks to continuous saline solution washing. This allows reducing the cellular stress eliminating any traumatic action that may damage the extracellular matrix and its essential trophic and anti-inflammatory function.

The collection and processing bag is equipped with two filters:

+ **The first filter microfragments the adipose tissue** while retaining the eventual fibrotic tissue;
+ **The second filter with a denser mesh retains the microfragmented adipose tissue** that is washed with saline solution, eliminating all the oily and blood residues which might cause inflammation of the treated tissues.

The **final micro-fragmented and purified product is an autologous adipose tissue that keeps the biological properties of the original tissue intact** and can easily be injected even through very thin needles.

TIME EFFICIENT

+ Processes up to 400 mL of adipose tissue in 10 minutes.
+ Centrifuge free: saving on time, personnel and tools.
+ All-in-one system that processes, purifies and microfragments a high-quality adipose tissue rich in mesenchymal cells.

MINIMAL MANIPULATION

+ Preservation of the biological properties of the cells.
+ Complete preservation of tissue architecture and stromal niche components.
+ Continuous saline solution washing eliminates any traumatic action that may damage the extracellular matrix.

EASY TO USE

+ No centrifugation is required.
+ Simple and reproducible technique in a single surgical time.
+ Compared to centrifugation, minimizes staff training, or preparation and clean-up.
+ Only 1 operator is required.

LIPO-STEM™

PURIFICATION AND PROCESSING KIT FOR ADIPOSE TISSUE MSCs

LIPO-STEM™ is a closed-circuit single-use kit for adipose tissue purification without any centrifuge and with a minimal manipulation.

The entire processing phase of the liposuctioned tissue occurs inside the device thanks to continuous saline solution washing. This allows reducing the cellular stress eliminating any traumatic action that may damage the extracellular matrix and its essential trophic and anti-inflammatory function. The sophisticated filtering and washing system preserves the entire vascular stromal niche architecture and the volume of the lipoaspirate and improves the cells' capacity to respond to regenerative stimuli.

The final purified product is a viscous fluid that keeps the biological properties and volume of the original tissue intact.

TIME EFFICIENT

+ Processes up to 400 mL of adipose tissue in 10 minutes.
+ Centrifuge free: saving on time, personnel and tools.
+ All-in-one system that processes, purifies and microfragments a high-quality adipose tissue rich in mesenchymal cells.

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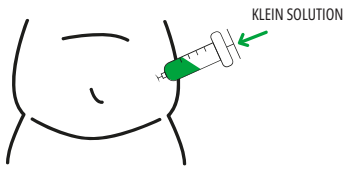
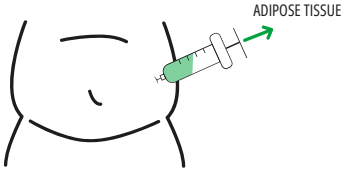
Surgical technique:

1



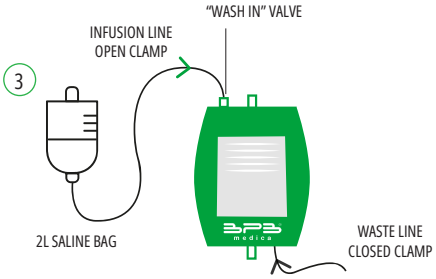
Infiltrate the Klein solution.

2



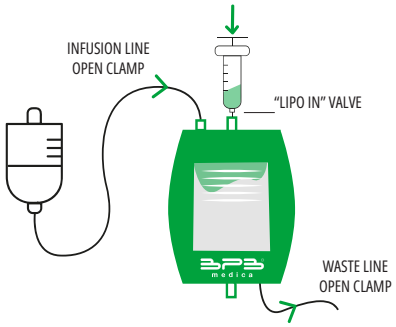
Harvest the adipose tissue using the VacLok syringe. We recommend to generate a soft negative pressure by blocking the VacLok in increments of 10 cc.

3



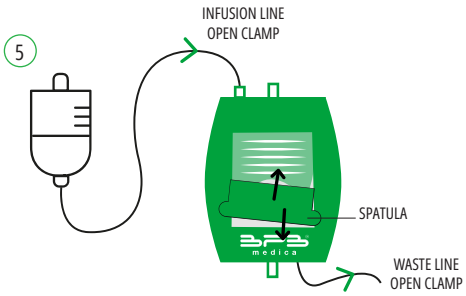
Close the waste line clamp bag tube. Connect a saline bag to the device's "WASH IN" valve and fill the bag with around 150 mL of saline solution.

4



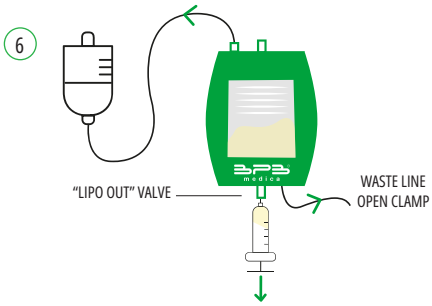
Insert the harvested adipose tissue in the device's "LIPO IN" valve and open the waste line clamp to eliminate residues.

5



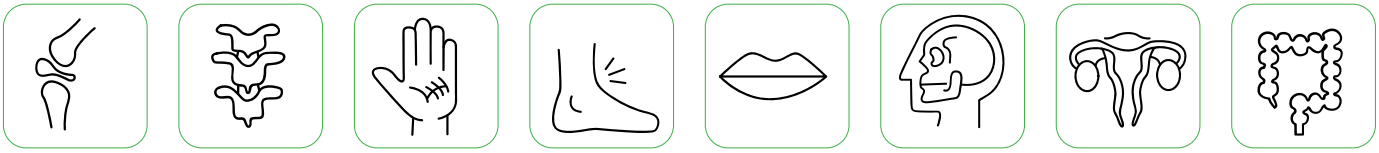
Gently move the spatula up and down until the fat tissue turns pale yellow and the waste liquid becomes transparent.

6



Close the infusion line clamp and use the spatula one more time to remove the remaining contents. Retrieve the adipose tissue from the LIPO-OUT valve.

Applications:



ORTHOPAEDICS & SPORT MEDICINE | SPINAL SURGERY | PAIN THERAPY & WOUND HEALING | VULNOTHERAPY | RECONSTRUCTIVE AND PLASTIC SURGERY | MAXILLOFACIAL SURGERY | UROGYNAECOLOGICAL SURGERY | COLOPROCTOLOGY

ORDER GUIDE - LIPO-STEM™/ LIPO-STEM DUO™

CODES:

LIPO-STEM™: LPKIT-001

LIPO-STEM DUO™: LPKIT-002

STANDARD KIT COMPOSITION

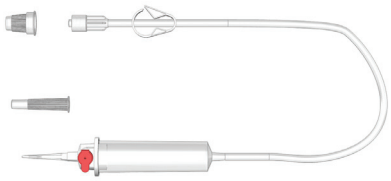
1× LIPO-STEM™ or LIPO-STEM DUO™ processing bag and waste bag.
1x Processing spatula
2x 60 mL syringes for Klein's solution
2x 60 mL Vaclok syringes for liposuction
1x 16G cannula for injection of Klein's solution
1x 13G cannula for liposuction
1x 16G (LIPO-STEM™) or 20G (LIPO-STEM DUO™) infusion needle
2x 10 mL syringes for infusion
2x 3 mL syringes for infusion
2x Combi caps LLF/LLM
2x Male Luer Cap, Non vented, Red
1x Infusion line with air inlet
1x Open side clamp

ACCESSORIES INCLUDED IN THE KIT

LIPO-STEM DUO™ processing bag and waste bag.

Processing spatula

LIPO-STEM™ processing bag and waste bag.



Infusion line with air inlet

Open side clamp

16G cannula for injection of Klein's solution

13G cannula for liposuction

60 mL syringe for Klein's solution

20G infusion needle (LIPO-STEM DUO™)

60 mL syringe for liposuction

16G infusion needle (LIPO-STEM™)

10 mL syringe for infusion

Male Luer Cap, non vented, red

3mL syringe for infusion

Combi caps LLF/LLM

Backed by science: LIPO-STEM DUO™ in University Research Morphology, MSCs viability and proliferation comparison of adipose tissue processed by different devices.

Preliminary Data from an International Public University Study

The abundance of MSCs in adipose tissue along with easy accessibility makes it an attractive source of MSCs for many clinical uses. Autologous microfragmented adipose tissue is a promising option due to its ability to release exosomes and promote tissue regeneration and is increasingly used in orthopaedic, plastic, and reconstructive surgeries. The ability to accurately and efficiently preserve cell health is crucial to determine their regenerative potential. Viability and proliferation are two distinct characteristics of cells: viability measures the number of living cells in a population, whereas proliferation measures cell division. Both contribute to determining the regenerative potential of the autologous implant. These preliminary data compare adipose tissue processed with different devices and show the impact of different methods on cell prosperity and health.

Methodology:

Adipose tissue enzymatic digestion

The remaining portion of adipose tissue has been digested according to the standard laboratory protocol using collagenase type I. The fat digestion has been done under agitation at 37°C for 45 min, and subsequently, the enzymatic action has been blocked with a complete culture medium (DMEM supplemented with 10% FBS (Foetal Bovine Serum), 1% 1:1 P/S (Penicillin/Streptomycin) and 0.6% Amphotericin B) followed by centrifugation at 7000 rpm for 5 min. The formed pellet has been resuspended in 1X lysis buffer for 10 min, filtered and re-centrifuged to obtain the stem cell pellet. The cells will be seeded in a T25 flask for subsequent analysis.

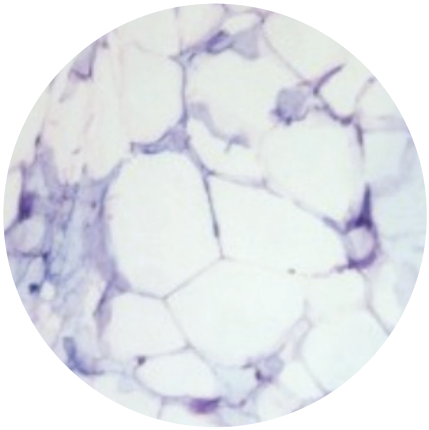
Cellular yield

The extracted cells have been counted for cellular yield calculation considering the number of extracted free cells divided by the processed volume of fat. The number of living cells has been calculated using the Trypan Blue exclusion assay in a CytoSMART counter (Automated Image-Based Cell Counter, version 1.5.0.16380, CytoSMART Technologies B.V., Eindhoven, Netherlands).

Proliferation capacity

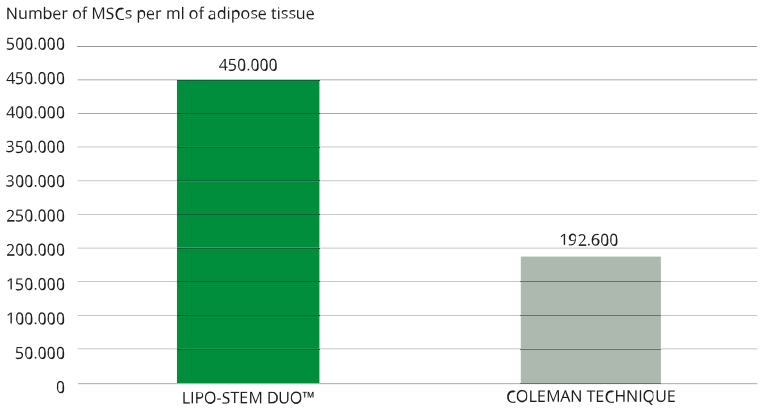
The extracted cells have been seeded on a 25 cm2 T-flask with a complete culture medium and incubated in a humidified atmosphere at 37°C with 5% CO2. The first medium change has been performed after 72 h from the enzymatic digestion and the subsequent changes every 48 h. The proliferation capacity is determined considering the required days to reach 80% confluence.

Remark: reported preliminary data already show trends but they are not statistical yet.



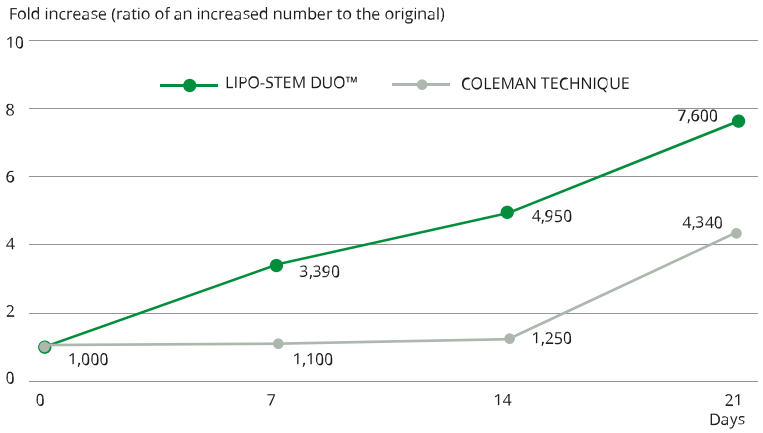
Optical microscopy analysis: a portion of the adipose sample of LIPO-STEM DUO™.

All samples have been evaluated at a morphological level by using the whole-mount assay.
The emulsion has been swiped in a histological glass and stained with Toluidine Blue (Sigma-Aldrich, Milan, Italy).
All slides have been examined under an Olympus BX-51 microscope (Olympus, Tokyo, Japan) equipped with a digital camera (DKY-F58 CCD JVC, Yokohama, Japan).



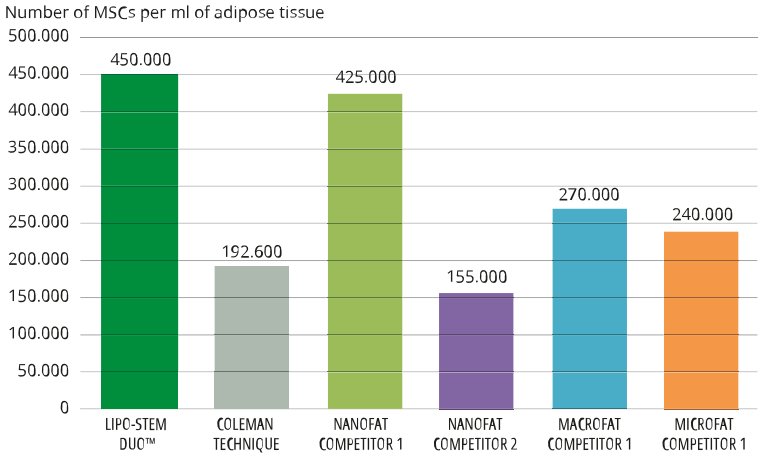
Cell viability after harvest - gentle washing vs centrifugation

The graphic shows a focused comparison between the gentle washing method of LIPO-STEM DUO™ and the Coleman Technique (centrifugation). It is clearly visible how the number of harvested MSCs per mL of adipose tissue with gentle washing outperforms the centrifugation method of more than 2 times.



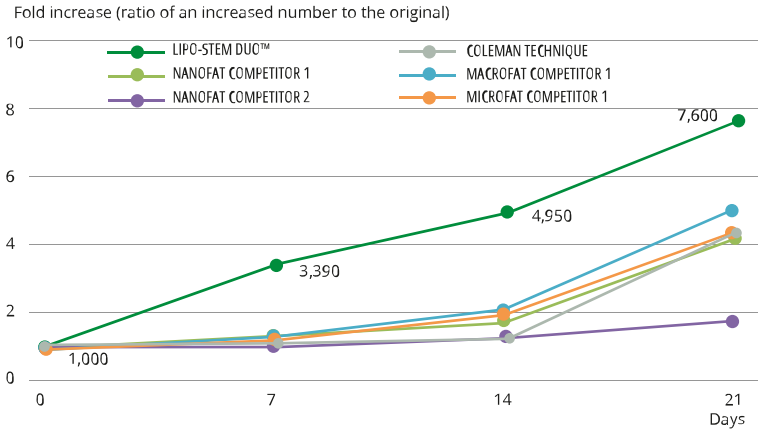
Cell proliferation in vitro after 21 days:

In vitro, MSCs cells of LIPO-STEM DUO™ proliferate growing more than 7 times in 21 days, while MSCs harvested with the Coleman Technique (centrifugation) grew only 4 times. The graphic witnesses the exceptional vitality and health status of cells processed with the gentle washing method.as opposed to the centrifugation method.



Cell viability after harvest - comparison of all samples

The harvesting method has a great impact on cell survival, safeguarding or discouraging MSCs' survival. The count of cellular yield and the comparison among different devices shows how LIPO-STEM DUO™ outperforms all other methods. The second best result was found with NANOFAT COMPETITOR 1 (but later the sample did not show an equally good proliferation). The worst result has been found with NANOFAT COMPETITOR 2. Harvesting methods affect the number of live cells and determine the regenerative potential of the adipose tissue.



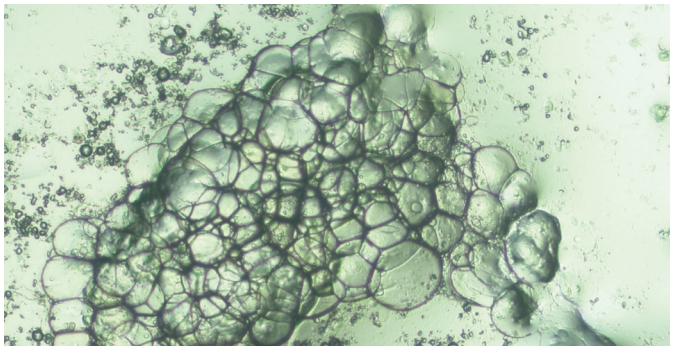
Cell proliferation in 21 days - comparison of all samples

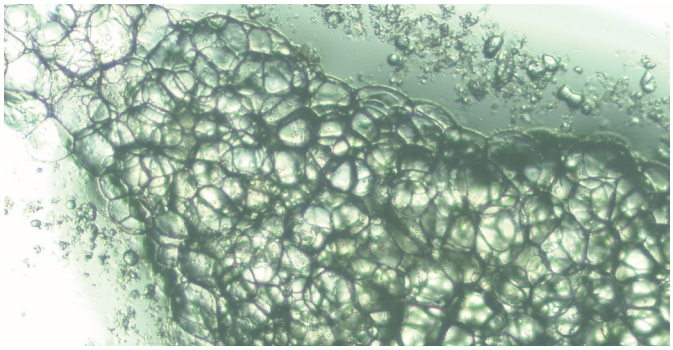
The harvesting method definitely has an impact also on the successive proliferation of cells. Shocked or traumatized cells reveal a significantly lower capacity for proliferation, affecting their successive capacity for tissue regeneration. The graphic shows how the gentle washing method of LIPO-STEM DUO™ outdoes all the others almost doubling all of them. The worst performance of proliferation is given by NANOFAT COMPETITOR 2, which was also the method that returned the worst result of harvesting.

MICROSCOPIC EVIDENCE

LIPO-STEM DUO™

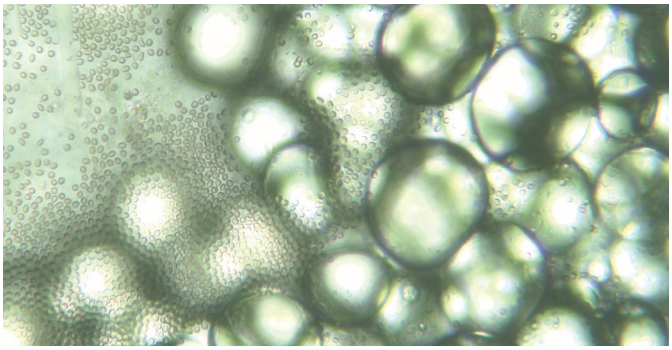
+ Clean, uniform tissue
+ Preserved extracellular matrix

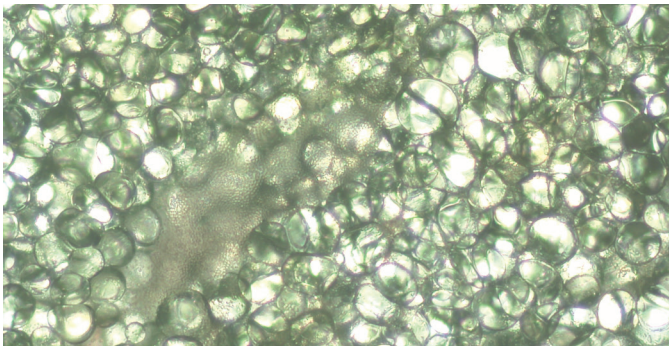




COLEMAN TECHNIQUE

+ Red blood cell contamination visible
+ Damaged structure





CELL-ASSISTED BONE REGENERATION THROUGH CREEPING SUBSTITUTION

Creeping substitution is a physiological process through which bone grafts are gradually resorbed and replaced by new, living bone tissue via orchestrated vascular ingrowth, osteoclastic activity, and osteoblastic bone formation.

This process plays a pivotal role in the integration of both autologous and homologous bone grafts, where the scaffold not only provides osteoconductivity but is also actively involved in biological remodeling and osteointegration.

BPB MEDICA™ enhances this natural mechanism through a cell-assisted bone regeneration strategy, combining:

+ Autologous cancellous bone grafts harvested using the UNLUX SYSTEM™, naturally rich in osteoconductive, osteoinductive, and osteogenic properties
+ Concentrated aspirate of mesenchymal stromal cells (MSCs) obtained through MARROW-STEM™.

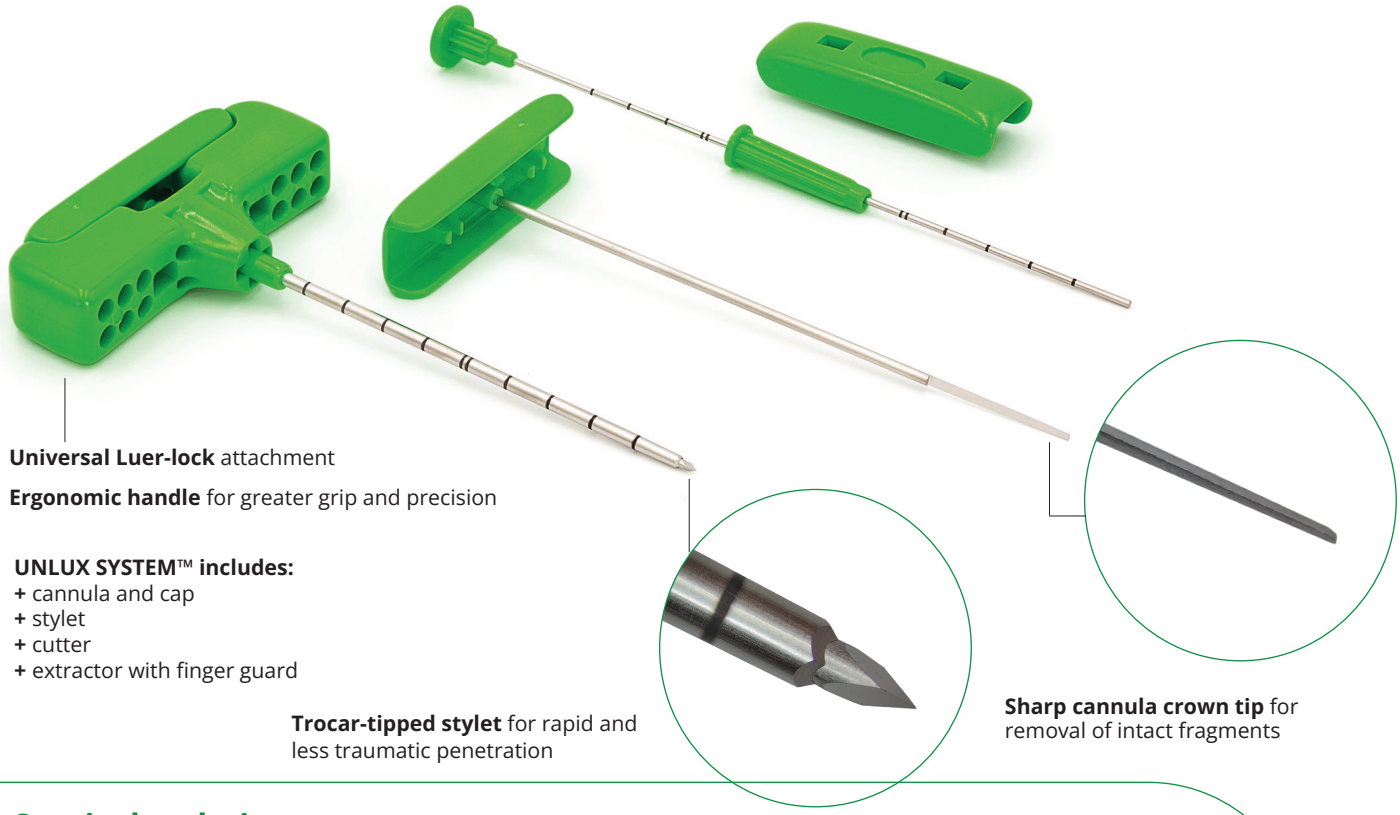
This synergistic approach amplifies biological activity at the defect site, promoting accelerated vascularization, cellular recruitment, and matrix remodeling, ultimately resulting in a dense, high-quality graft with regenerative performance comparable to that of a vascularized autograft.

UNLUX SYSTEM™

CREEPING SUBSTITUTION

UNLUX SYSTEM™ allows the removal of an osteomedullary core sample from subchondral bone with a low risk of infection and low invasiveness for the patient, obtaining an autologous bone graft with osteoconductive, osteoinductive and osteogenetic properties.

This procedure may be further enhanced in combination with MARROW-STEM™: by mixing the selective aspirate of mesenchymal stromal cells with autologous bone dowels, in addition to any other bone substitute of animal, homologous or synthetic origin, the creeping substitution ofthe process shall be accelerated. The result will therefore be an extremely strong graft, like a vascularized graft, capable of achieving a very fast regeneration rate and being of high quality with an extremely high density.



Universal Luer-lock attachment

Ergonomic handle for greater grip and precision

UNLUX SYSTEM™ includes:
+ cannula and cap
+ stylet
+ cutter
+ extractor with finger guard

Trocar-tipped stylet for rapid and less traumatic penetration

Sharp cannula crown tip for removal of intact fragments

Surgical technique:

+ **Harvest a concentrated aspirate of mesenchymal stromal and progenitor cells** using the MARROW-STEM™ technique.
+ **Extract an autologous spongy bone graft from the same access point** using the UNLUX SYSTEM™.
+ **Combine the mesenchymal cell concentrate with the chosen bone substitute** (animal-derived, homologous, or synthetic) and coat the autologous bone dowels with this mixture.
+ **Implant the enhanced graft at the defect site** to initiate and accelerate the creeping substitution process.

ORDER GUIDE - UNLUX SYSTEM™

GAUGE	DIAMETER (mm)	PRODUCT CODE	NEEDLE SIZE	PIECES PER BOX
8G	4,00	ULSEC0810C ULSEC0815C	8G x 10cm 8G x 15cm	10
11G	3,00	ULSEC1110C ULSEC1115C	11G x 10cm 11G x 15cm	10

SUBCHONDRAL BONE PLASTY

Subchondral Bone Plasty is an image-guided, minimally invasive procedure designed to treat Bone Marrow Lesions (BMLs): structural defects of the subchondral bone often associated with early-stage osteoarthritis, subchondral insufficiency fractures (SIFK), or spontaneous osteonecrosis (SONK).

Although frequently undetectable via standard radiography, BMLs are identifiable through MRI and are now recognized as a significant source of joint pain and functional limitation, even in the absence of advanced degenerative changes. Left untreated, these lesions can progress to joint collapse and accelerate the need for joint replacement. The procedure involves the percutaneous injection of a biologic or synthetic bone substitute, optionally enriched with mesenchymal stromal cells (MSCs) directly into the affected subchondral zone underfluoroscopic and/or arthroscopic guidance.

Biological and Mechanical Rationale:

+ Reinforces subchondral bone integrity, improving load distribution across the articular surface.
+ Reduces pain by stabilizing microfractures and decompressing the lesion.
+ Supports endogenous bone remodeling through osteoconduction and, when combined with MSCs, osteogenic stimulation.

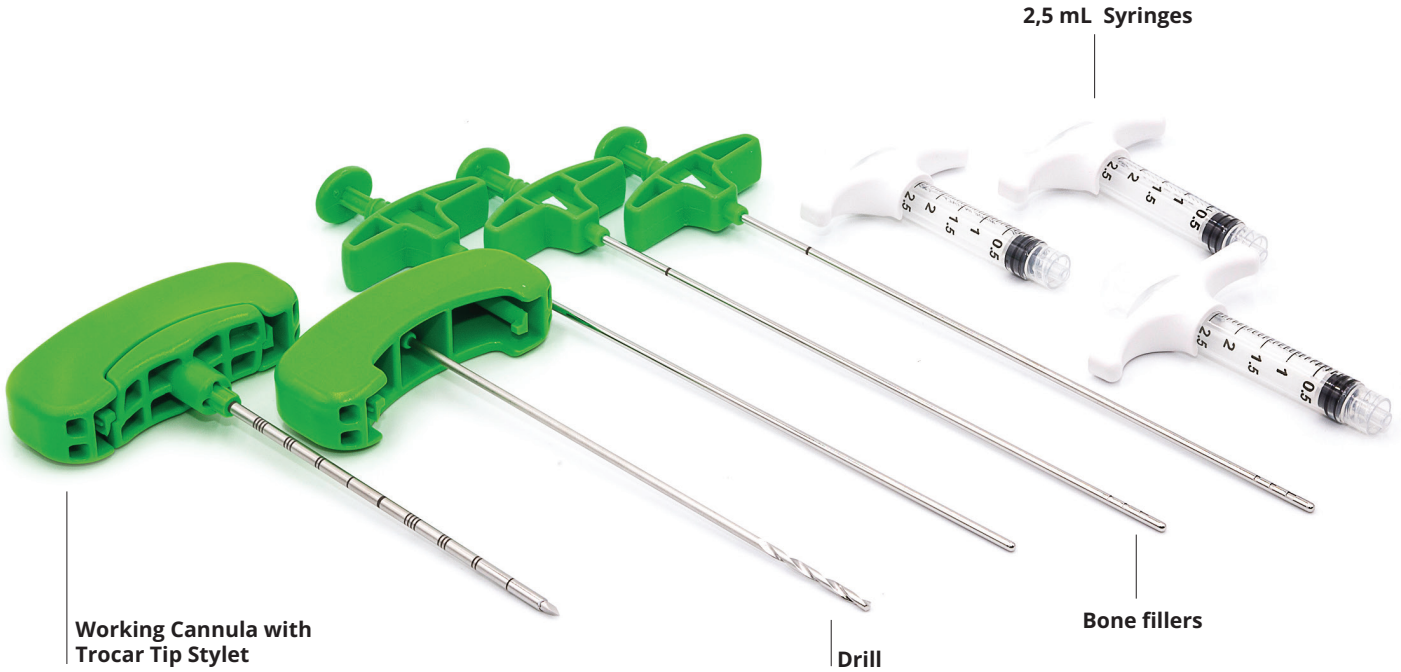
Clinical Highlights

+ Inspired by the principles of vertebroplasty, adapted for periarticular bone.
+ Combines the benefits of biologic regeneration and mechanical support.
+ Minimally invasive: reduced risk of infection, fast recovery time, and potential to delay or avoid joint replacement.

ORTHOPLASTY™

SUBCHONDRAL BONE PLASTY

Subchondral bone plasty is a minimally invasive, fluoroscopically-assisted procedure that identifies and repairs subchondral bone defects, also known as Bone Marrow Lesions (BML). Potential intra-articular leakages of the biological cement can be prevented and monitored by combining the procedure with arthroscopy.



Biological Cement
OPTIONAL

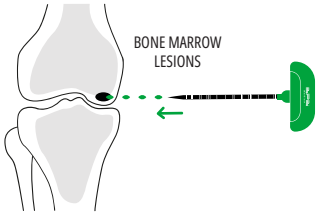
+ Safe and precise MIS Approach.
+ Reduces risk of infections.

Biological cement (OPTIONAL)**:**

+ Ready-to-use bone substitute, no preparation needed
+ Hardens in a wet environment only: no time pressure during application.
+ Truly biologic: composed of a micro-crystalline, calcium- deficient hydroxyapatite, the primary component of bone.
+ Supports load-sharing properties (up to 45 MPa).
+ Radiopaque paste: visible under fluoroscopy and X-rays.
+ Fast recovery after treatment.
+ Bioresorbable during bone remodelling.

Surgical technique:

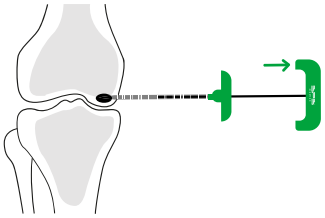
1



IDENTIFY THE LESION AND PLAN THE ACCESS

Preoperatively identify the bone marrow lesion (BML) via MRI, which is crucial as the lesion is not visible under fluoroscopy. Use imaging to plan the optimal trajectory and access point.

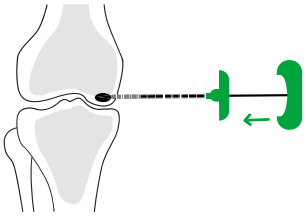
2



ESTABLISH BONE ACCESS

Insert the access trocar from the kit following the pre-planned trajectory. Once the target is reached, remove the internal stylet and leave the outer cannula in place to serve as a working channel.

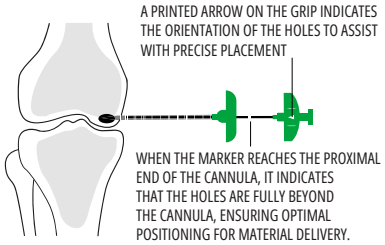
3



CREATE THE DELIVERY CANAL

Insert the provided drill through the working cannula. Rotate the cannula and drill together to create a canal in the bone, facilitating subsequent bone graft infusion. Then remove the drill.

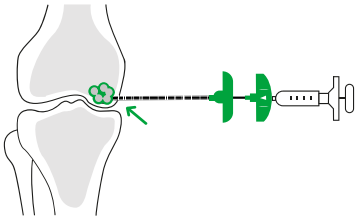
4



PREPARE THE BONE GRAFT DELIVERY

Insert the bone filler pre-filled with hardening bone graft into the working cannula. Alternatively, if using a dispensing system, connect it directly to the cannula.

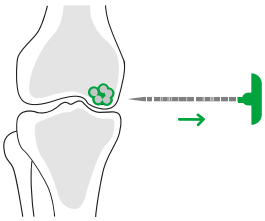
5



INFUSE THE BONE GRAFT

Slowly inject the bone graft through the cannula into the prepared subchondral site, ensuring even distribution within the lesion area. Monitor infusion pressure and volume.

6



COMPLETE THE PROCEDURE

After the bone graft has been successfully delivered, remove the working cannula from the patient, completing the treatment of the BML.

STANDARD KIT COMPOSITION

1x Working Cannula + Trocar Tip Stylet
1x drill
3x Directable Bone Filler + 3 Syringes (2,5 mL)
1x Biological Cement (OPTIONAL)

ORDER GUIDE - ORTHOPLASTY™ kit order codes:

SUB1110C - includes 1 trocar working cannula, 1 drill, 3 directable bone fillers, and 3 syringes (2,5 mL).

SUB1110C-01 - includes 1 trocar working cannula, 1 drill, 3 directable bone fillers, 3 syringes (2,5 mL), and biological cement.

METAPHYSEAL BALLOON AUGMENTATION

Metaphyseal balloon augmentation is a minimally invasive technique designed to restore the anatomical alignment and load-bearing integrity of articular surfaces in cases of metaphyseal bone depression and collapse.

It is particularly indicated in traumatic intra-articular fractures where subchondral bone has been impacted—most frequently involving the **tibial plateau, calcaneus, proximal humerus and distal radius.**

The procedure utilizes a percutaneously inserted **balloon catheter,** which is carefully navigated into the metaphyseal region under fluoroscopic control.
Once correctly positioned beneath the depressed articular fragment, the balloon is inflated in a controlled manner.

This elevation allows for **precise, atraumatic reduction** of the impacted fragment, restoring the native joint surface congruity without requiring extensive open exposure or mechanical levering.

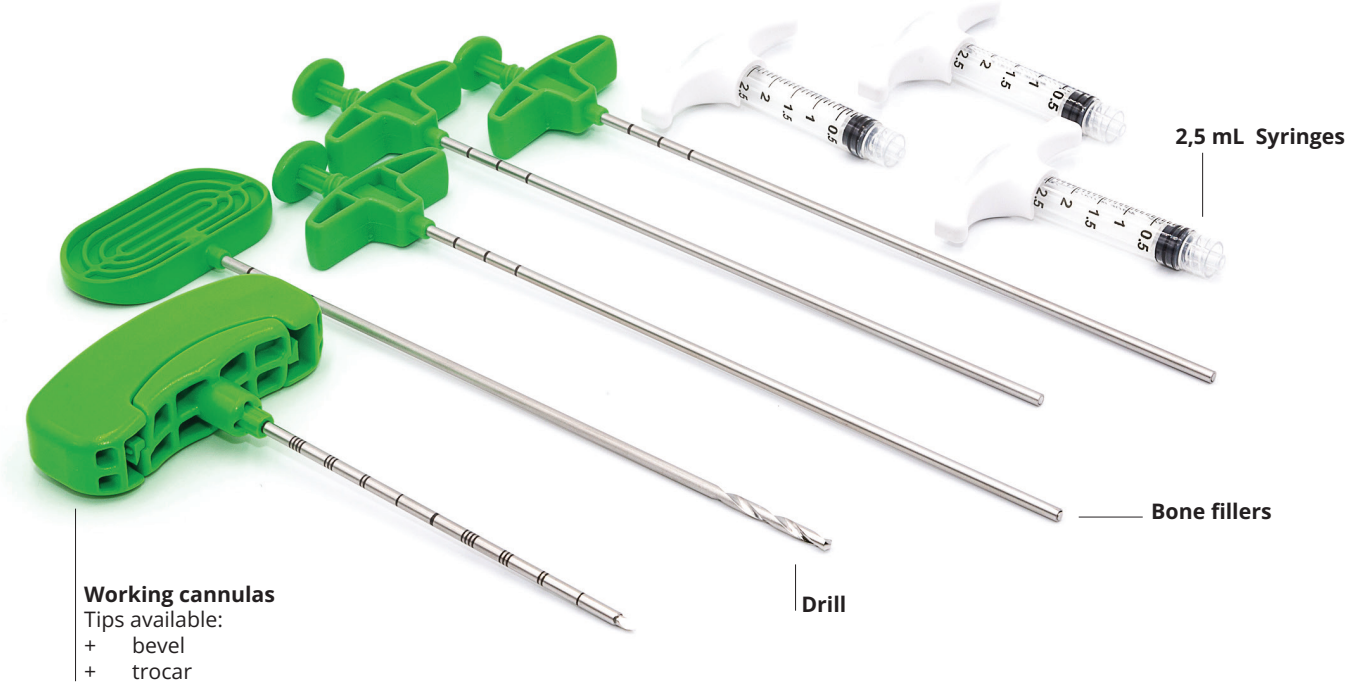
After achieving the desired reduction, the balloon is deflated and removed, leaving behind a well-defined cavity. This void is then **filled with a high-compression-resistance bone substitute** which hardens in situ to support the restored surface and maintain reduction.

The filler acts as a **scaffold for new bone ingrowth,** while also preventing secondary collapse under physiological load.

OSTEOPLASTY™

METAPHYSEAL BALLOON AUGMENTATION

OSTEOPLASTY™ kit is a minimally invasive system for reducing and restoring bone height and alleviating related pain in different types of fracture, such as tibial plateau, calcaneus and distal radius injuries. The kit optionally includes a biologic bone cement capable of restoring the required load-bearing resistance in a short time, while remaining fully bioresorbable through natural bone remodeling.



Biological Cement

Digital inflation device

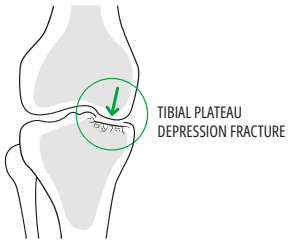
Analog inflation device

Balloon

- \+ Minimally invasive solution.
- \+ Useful for bone height restoration.
- \+ Without plating techniques: applicable for non-load bearing defects.
- \+ With plating techniques: applicable for load-bearing defects.
- \+ Reduced risk of infection.
- \+ Ready-to-use bone substitute, no preparation needed.
- \+ Hardening in a wet environment only: no time pressure during application.
- \+ Truly biologic: composed of micro-crystalline, calcium- deficient hydroxyapatite, the primary component of bone.
- \+ Supports load-sharing properties (up to 45 MPa).
- \+ Radiopaque paste: visible under fluoroscopy and X-rays.
- \+ Fast recovery after treatment.
- \+ Bioresorbable during bone remodelling.

Surgical technique:

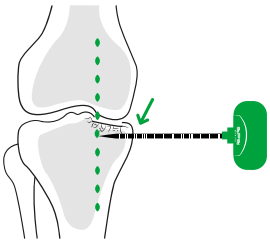
1



PLAN THE APPROACH

Identify the metaphyseal depression using X-rays or C-arm.

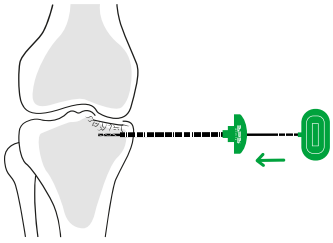
2



ACCESS THE BONE

Use the kit's access trocar to reach the lesion. Once in position, remove the inner stylet and leave the cannula as the working channel.

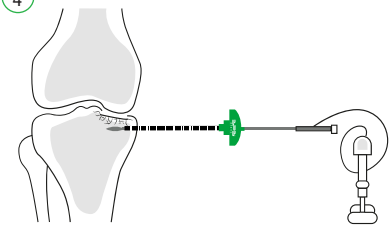
3



CREATE THE WORKING CANAL

Insert the drill into the working cannula and rotate to create a canal for the balloon and hardening bone graft. Remove the drill afterward.

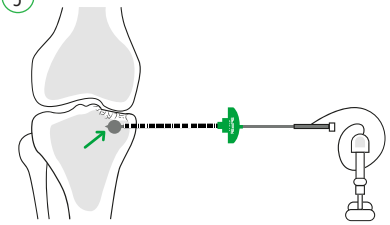
4



INSERT AND POSITION THE BALLOON

Advance the balloon catheter through the canal to the fracture site. Follow the dedicated balloon instructions for optimal placement.

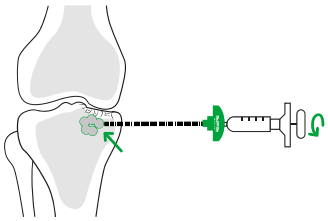
5



PERFORM BALLOON INFLATION

Connect the inflation device and carefully inflate/deflate the balloon to restore bone height and create a cavity for bone graft placement.

6



DELIVER THE BONE GRAFT

Insert the bone filler pre-filled with bone graft and infuse it into the cavity using either the plunger stylet or a connected delivery system. Remove the cannula to complete the procedure.

STANDARD KIT COMPOSITION

1x Working Cannula + Trocar Tip Stylet
1x drill
3x Directable Bone Filler + 3 Syringes (2,5 mL)
1x Balloon Catheter (10 mm or 15 mm or 20 mm)
1x Digital or analog Inflation Device
1x Biological Cement (OPTIONAL)

ORDER GUIDE - OSTEOPLASTY™

	TROCAR CANNULA	DRILL	3 BONE FILLERS	3 SYRINGES (2,5 mL)	INFLATION DEVICE	BALLOON LENGTH	BIOLOGICAL CEMENT
TBP1112J10A	✓	✓	✓	✓	Analog	10 mm	-
TBP1112J15A	✓	✓	✓	✓	Analog	15 mm	-
TBP1112J20A	✓	✓	✓	✓	Analog	20 mm	-
TBP1112J10K	✓	✓	✓	✓	Digital	10 mm	-
TBP1112J15K	✓	✓	✓	✓	Digital	15 mm	-
TBP1112J20K	✓	✓	✓	✓	Digital	20 mm	-
TBP1112J10A-001	✓	✓	✓	✓	Analog	10 mm	✓
TBP1112J15A-001	✓	✓	✓	✓	Analog	15 mm	✓
TBP1112J20A-001	✓	✓	✓	✓	Analog	20 mm	✓
TBP1112J10K-001	✓	✓	✓	✓	Digital	10 mm	✓
TBP1112J10K-001	✓	✓	✓	✓	Digital	15 mm	✓
TBP1112J20K-001	✓	✓	✓	✓	Digital	20 mm	✓

WEBSITE

LINKEDIN

YOUTUBE

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Società soggetta ad attività di direzione e
coordinamento da parte della società Bpunto3 S.r.l.

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