DELIVER YOUR **ESSENTIAL**

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CONCENTRATED BONE MARROW ASPIRATE SYSTEM

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YOUR PROTOCOL HAS CHANGED

Targeted for use in a variety of clinical settings, the **CellPoint™ Concentrated Bone Marrow Aspirate System** rapidly provides clinicians with concentrated marrow-derived cells via a simple, automated process. With no operator intervention required, the closed-loop system dispenses concentrated bone marrow aspirate (cBMA) directly into a final collection vial, delivering consistent performance to meet your needs.

MUCH MORE THAN A SIMPLE SYSTEM

On the surface, you'll see a smart touchscreen interface and simple pre-loaded protocols that allow for rapid cBMA preparation with minimal set-up. Optical sensors and a vertical elutriation mechanism are employed by the system to precisely separate cells, while a universal cell separation kit offers simplicity and value. But the benefits extend beyond technology.

Designed to improve how you operate, CellPoint enables clinicians to recover a high density of marrow-derived cells at the point-of-care. Think of it as efficiency, evolved. **Think of it as your new protocol.**

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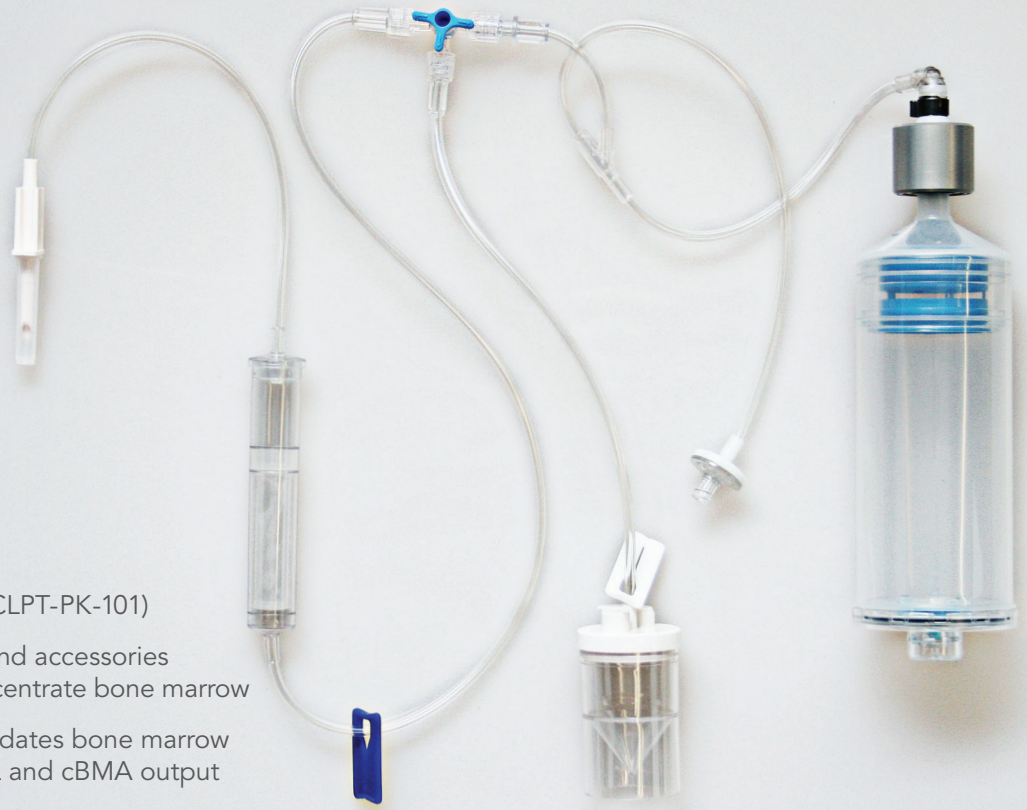
CONCENTRATED BONE MARROW ASPIRATE SYSTEM

Fully automated system	→	Enables consistent, repeatable performance
Specifically designed to concentrate BMA	→	Delivers a high concentration of marrow-derived progenitor cells
Minimal set-up and rapid prep times < 20 minutes	→	Allows for quick and easy cBMA recovery
Universal cell separation kit for all processing volumes	→	Offers flexibility and cost-savings
Vertical elutriation mechanism precisely separates cells	→	Extracts cBMA while maintaining high cell recovery and cell viability



PRODUCT INFORMATION

CellPoint™ Procedure Pack (CLPT-PK-101)

- Includes cell separation kit and accessories required to aspirate and concentrate bone marrow
- Cell separation kit accommodates bone marrow input volumes of 30–220 mL and cBMA output volumes of 7–20 mL

SEPAX 2 RM INTENDED USE

The Sepax 2 RM system is a cell processing system intended for the separation of nucleated cells from various cellular products (e.g., bone marrow, aphaeresis, peripheral blood, diluted components of the same). The Sepax 2 RM is manufactured by Biosafe and is available through ISTO Technologies, Inc. for the CellPoint™ Concentrated Bone Marrow Aspirate System.

The cellular product to be processed (separated) is collected for medical use; the Sepax 2 RM system is not connected to the patient. Following collection, the cellular product is either processed bed-side, point-of-care, or transported to a processing laboratory. The Sepax 2 RM system is not intended for use in transfusion applications where blood circulates directly between a patient and the Sepax 2 RM system. There is no claim of therapeutic benefit in the labeling. Safety and effectiveness of this device for *in vivo* indications has not been established.

The Sepax RM is a Class I device. The Sepax RM is registered with the FDA and is listed as follows:

Listing Number — D079348
Product Code — JQC

Biosafe is the FDA registered manufacturer of the Sepax 2 RM and associated products.
Biosafe America is the FDA registered distribution arm of Biosafe in the U.S. FDA registrations are shown below.

Biosafe FDA Registration Number — 3004728017
Biosafe America FDA Registration Number — 3007508533

Biosafe is ISO 13485 certified. Biosafe certificate number — TUV SUD S 951 06 3563

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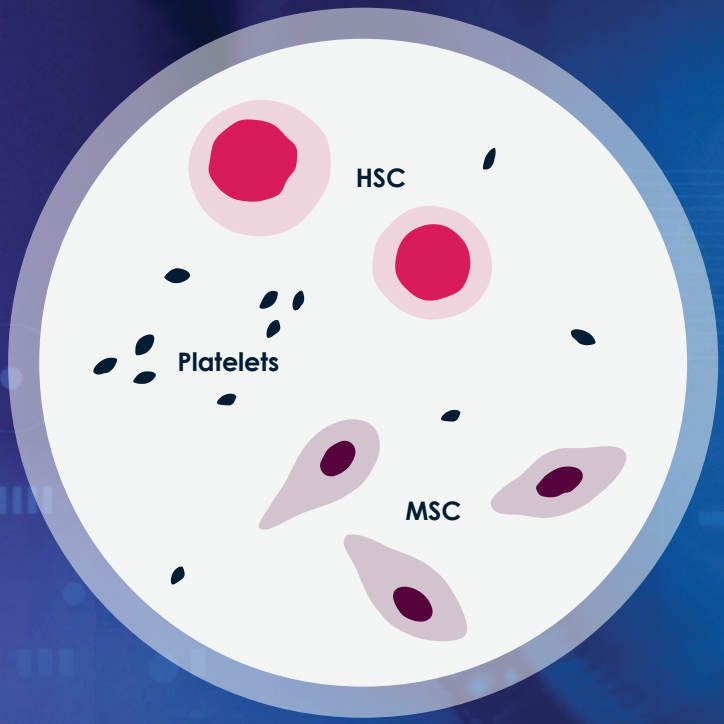
POWERED BY cBMA

Bone marrow aspirate provides a rich source of viable progenitor cells and other soluble factors, but the relative abundance of these elements within human bone marrow is low. CellPoint's precise cell separation process isolates these elements while removing the red blood cells and platelet poor plasma. cBMA contains high concentrations of total nucleated cells and growth factors, including:

- Multi-potent mesenchymal stromal cells (MSCs), which have the potential to differentiate into osteoblasts and chondrocytes[1]
- CD34+ hematopoietic stem cells (HSCs), which give rise to endothelial progenitor cells[2]
- Platelets, which provide a rich source of essential growth and differentiation factors, such as PDGF, VEGF, TGF-b1 and EGF[3]



References

1. Pittinger MF, MacKay AM, Beck SC, et al. **Multilineage Potential of Adult Human Mesenchymal Stem Cells.** *Science.* 284: 143–147. 1999.
2. Lu J, Pompili VJ, Das H. **Neovascularization and Hematopoietic Stem Cells.** *Cell Biochem Biophys.* 67(2): 235–45. 2013.
3. Lubrowska A, Dolegowska B, Banfi G. **Growth Factor Content in PRP and Their Applicability to Medicine.** *J Biol Regul Homeost Agents.* 26 (2 Suppl 1): 3S–22S. 2012.

ONLY THE **ESSENTIAL**

The CellPoint system enables clinicians to quickly recover concentrated, patient-derived nucleated cells, platelets, and other soluble factors in the form of cBMA. The relative concentration of nucleated cells in cBMA is dependent on many factors, including the input BMA volume and the desired cBMA output volume, which are both defined by the user for the CellPoint system. By providing reliable volume reduction, the CellPoint system achieves typical total nucleated cell (TNC) concentration factors that are 3–6 times the baseline TNC concentration in BMA.

CELLPOINT CONCENTRATED BONE MARROW ASPIRATE SYSTEM PERFORMANCE*

VOLUME REDUCTION FACTOR	TNC COUNT PER mL BMA	TNC COUNT PER mL cBMA	TNC CONCENTRATED FACTOR	CD34 + CELL RECOVERY
6.3	2.1×10^7	8.2×10^7	4.5	92.6%

* ISTO internal analysis of CellPoint System Performance in 263 clinical procedures

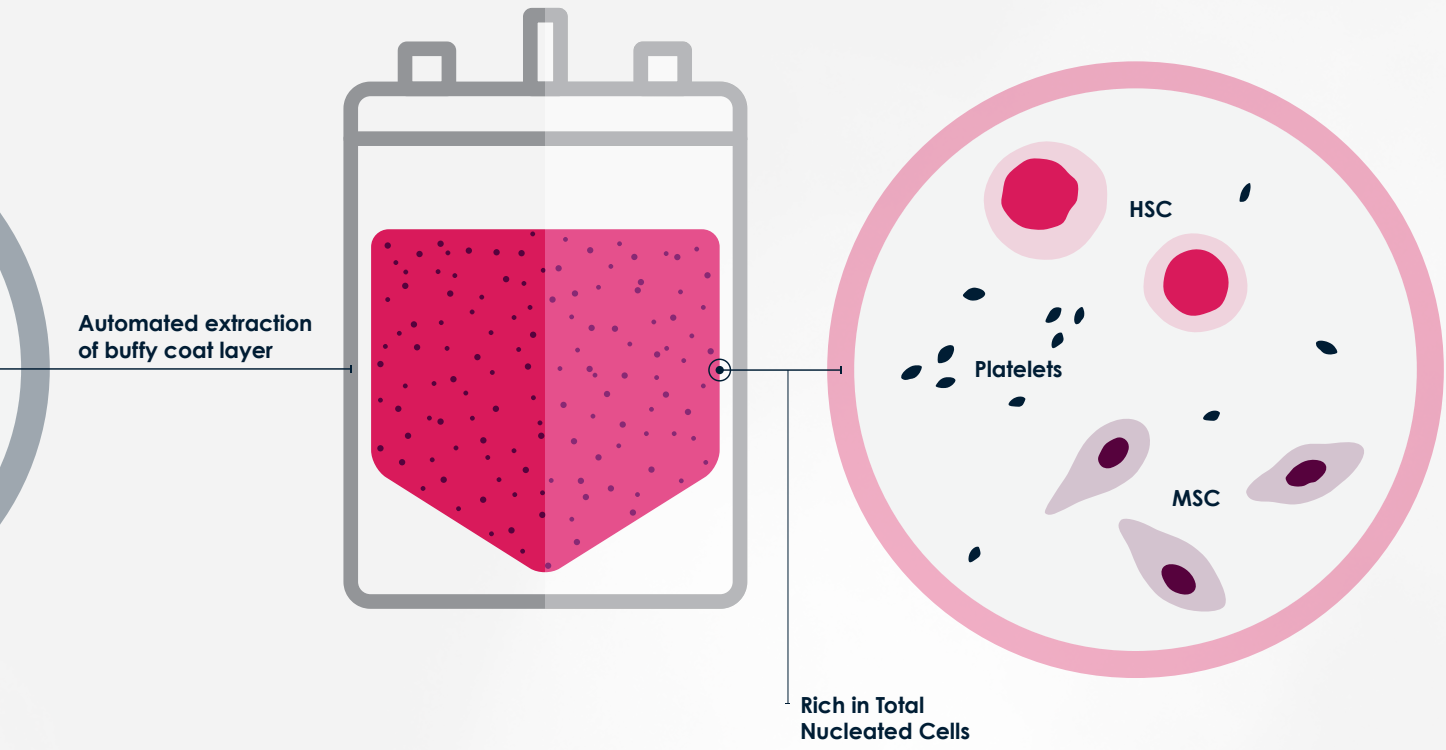
BONE MARROW ASPIRATE → **CELL SEPARATION**

SEPAX 2 RM
SOPHISTICATED DESIGN FOR EASY PREPARATION

CellPoint utilizes the most cutting-edge technology available, the **Sepax 2 RM,** along with a disposable cell separation kit, to create a fully automated closed-loop system for separating nucleated cells from bone marrow. An advanced optical sensor detects the cell fractions and eliminates the need for operator intervention to separate the nucleated cell layer. Platelet-poor plasma and hematocrit are extracted, and volume-reduced cBMA is delivered into a sterile final collection vial. With the addition of pre-loaded protocols and minimal set-up, CellPoint makes cBMA preparation easy.

- Smart touchscreen interface is easy to use
- Pre-loaded protocols for rapid cBMA preparation with minimal set-up
- Selectable range of BMA input and cBMA output volumes allows users to customize the volume reduction factor achieved
- Universal cell separation kit is used for all processing volumes, providing flexibility and cost-savings
- Vertical elutriation mechanism precisely separates cells while maintaining high cell recovery and viability
- User-defined cBMA volume is output into closed final collection vial

CONCENTRATED BONE MARROW ASPIRATE (cBMA)



cellpoint™ CONCENTRATED BONE MARROW ASPIRATE SYSTEM

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Through our Medical Liaison Program, ISTO Technologies is committed to being your partner in providing scientific and clinical research information in the field of regenerative medicine. In response to your request, below is a list of scientific references. Please indicate which topic areas or specific references you would like to receive from our Medical Liaison by circling them below. Alternatively, you may request a full packet containing abstracts of the references listed.

BONE MARROW-DERIVED CELLS

- Ambikaipalan A, Wong JM, and Khan WS. **Preclinical and Clinical Studies on the Use of Stem Cells for Bone Repair: A Systematic Review.** *Current Stem Cell Research & Therapy.* 8: 210–216. 2013.
- Arthur A, Zannettino A, Gronthos S. **The Therapeutic Applications of Multipotential Mesenchymal/Stromal Stem Cells in Skeletal Tissue Repair.** *J Cell Physiol.* 218: 237–45. 2009.
- Kasten P, et al. **Instant Stem Cell Therapy: Characterization and Concentration of Human Mesenchymal Stem Cells *In Vitro*.** *European Cells and Materials.* 16: 47–55. 2008.

CELL SEPARATION TECHNOLOGY

- Guven S, et al. **Validation of an Automated Procedure to Isolate Human Adipose Tissue-Derived Cells by Using the Sepax® Technology.** *TISSUE ENGINEERING: Part C.* 18(8). 2012.
- Zinno F, et al. **Processing of Hematopoietic Stem Cells from Peripheral Blood before Cryopreservation: Use of a Closed Automated System.** *Transfusion.* 51(12): 2656–2663. 2011.

CRITICAL LIMB ISCHEMIA

- Iafrati MD, et al. **Early Results and Lessons Learned from a Multicenter, Randomized, Double-blind Trial of Bone Marrow Aspirate Concentrate in Critical Limb Ischemia.** *Journal of Vascular Surgery.* 54(6): 1650–1658. 2011.

CARDIOVASCULAR

- References available upon request.

NERVE REPAIR

- References available upon request.

BONE MARROW TRANSPLANTATION FOR CANCER

- References available upon request.

PLATELET-RICH PLASMA (PRP) VS. CONCENTRATED BONE MARROW ASPIRATE (cBMA)

- Betsch M, et al. **Bone Marrow Aspiration Concentrate and Platelet Rich Plasma for Osteochondral Repair in a Porcine Osteochondral Defect Model.** *PLOS One.* 8(8): e71602. 2013.
- Peerbooms JC, et al. **No Positive Bone Healing after Using Platelet Rich Plasma in a Skeletal Defect. An Observational Prospective Cohort Study.** *International Orthopaedics.* 36: 2113–2119. 2012.

SPINAL FUSION

- Gan Y, et al. **The Clinical Use of Enriched Bone Marrow Stem Cells Combined with Porous Beta-Tricalcium Phosphate in Posterior Spinal Fusion.** *Biomaterials.* (29): 3973–3982. 2008.
- Johnson, RG. **Bone Marrow Concentrate With Allograft Equivalent to Autograft in Lumbar Fusions.** *Spine.* 39(9): 695–700. 2014.
- Vadala G, et al. **Use of Autologous Bone Cells Concentrate Enriched with Platelet-rich Fibrin on Corticocancellous Bone Allograft for Posterolateral Multilevel Cervical Fusion.** *J Tiss Eng Regen Med.* 2: 515–520. 2008.

GENERAL ORTHOPEDICS

- Connolly J, et al. **Autologous Marrow Injection as a Substitute for Operative Grafting of Tibial Nonunions.** *Clinical Orthopaedics and Related Research.* 263: 259–270. 1991.
- Ganji V, et al. **Treatment of Osteonecrosis of the Femoral Head with Implantation of Autologous Bone-Marrow Cells: A Pilot Study.** *Journal of Bone and Joint Surgery.* 1153–1160. 2004.
- Hendrich C, et al. **Safety of Autologous Bone Marrow Concentrate Transplantation: Initial Experiences in 101 Patients.** *Orthop Rev.* 1: e32. 2009.
- Hernigou P, et al. **Cancer Risk Is Not Increased in Patients Treated for Orthopaedic Diseases with Autologous Bone Marrow Cell Concentrate.** *J Bone Joint Surg Am.* 95(24): 2215–2221. 2013.
- Hernigou P, Poignard A, Beaujean F, and Rouard H. **Percutaneous Autologous Bone Marrow Grafting for Nonunions. Influence of the Number and Concentration of Progenitor Cells.** *J Bone Joint Surg Am.* 87: 1430–1437. 2005.

CONTACT INFORMATION

(Please print. Complete form and return directly to ISTO Medical Science Liaison by fax: 314.475.3150 or email: medinfo@istotech.com)

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PHYSICIAN SIGNATURE

*** Isto Biologics has compiled this list of scientific resources as an aid in your research activities. Isto Biologics is not promoting any specific application for the CellPoint Technology.**