PLYMOUTH MEDICAL

EmCyte Corporation
A Biotechnology Company

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Premium Concentration systems for Autologous Cellular Biologics.
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Introduction.

EmCyte Corporation has become a leader in autologous cellular biologics with the new PureBMC® and PurePRP® 544E concentrating systems for advanced blood and bone marrow processing.

These EmCyte processing systems consist of a centrifuge and separate, sterile containers to collect bone marrow and blood to guarantee maximum safety. They provide patients with the best opportunity for the application of autologous cellular biological therapies, and they are developed to meet every clinical requirement, giving the physician a better clinical choice for regenerative therapies.

Purpose.

The purpose of this document is to provide information on the availability and characteristics of different commercially available systems on the market, with emphasis on concentration capability of the systems. Since no generally accepted standardization criteria exist for the preparation of bone marrow concentrate, it is difficult to present a uniform standard, especially on the total volume of the product.

Regenerative adjunctive injection treatments are the next phase in the progression of modern surgical interventions. Biologically augmented regenerative, and autologous, cellular techniques are at the very foreground of modern treatments and have the potential to transform the practice of medicine and surgery significantly in a very short period, the best of patient care. Whereas regenerative knowledge has expanded significantly in volume and across disciplines. Significant outcomes involving biological solutions, like bone marrow concentration injection therapy, has been demonstrated in clinical settings like rotator cuff lesions, ligament tears, discogenic low back pain and disc degeneration, support during articular cartilage surgical repair, and bone and cartilage repair.

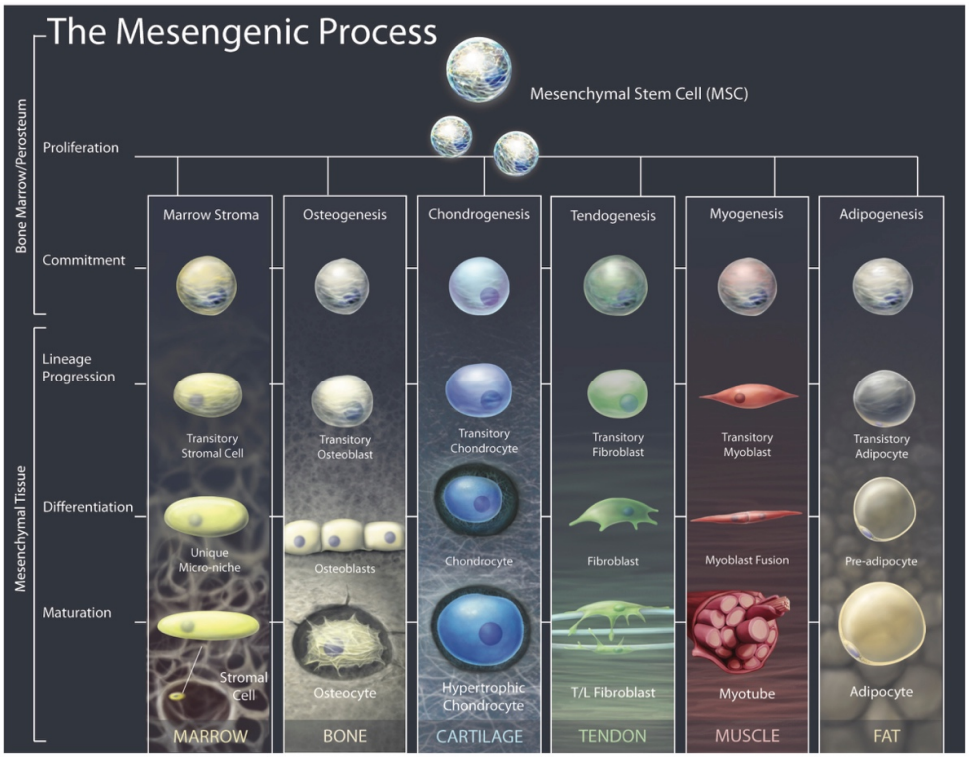
The EmCyte PureBMC® and PurePRP® 544E concentrating systems allow for customization of different autologous cellular products. The physician has the ability to choose from different preparation protocols and starting volumes. By using a specific preparation protocol, a clinician can tailor a specific cellular formulation for individual patients-indication specific formulations.

Specifically, the EmCyte PureBMC® 544E concentrating system are capable of producing a high concentrations of high quality cell types which are found in very small quantities in bone marrow aspirate:

Cell differentiation in PureBMC®

- *Mesenchymal Stem Cells*

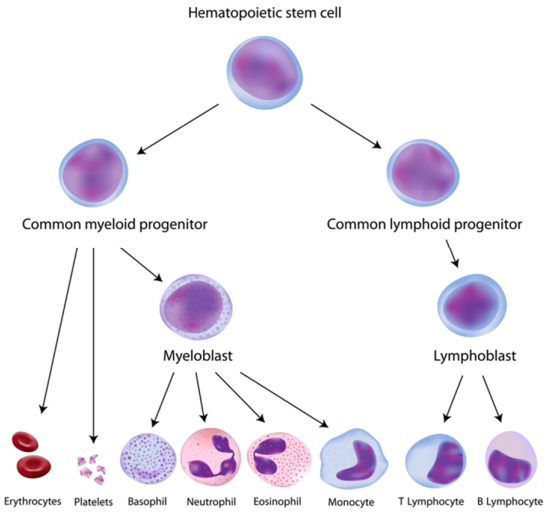
Mesenchymal stem cells (MSC's) are multipotent stromal cells that have the capacity to differentiate into a variety of cell types, including mainly cartilage, bone, tendon, muscle, and adipose cells (Figure 1).
MSCs derived from bone marrow maintains effectiveness, because it has a great capacity for self-renewal.
An accepted biomarker for MSC's present in bone marrow concentrate is the measurement of colony forming units of fibroblast (CFU-F).



Source: https://stemcellgurus.files.wordpress.com

- *Hematopoietic Stem Cells*

Hematopoietic stem cells (HSCs) are blood cells that have the ability to replace all blood cell types (multipotency) and have the ability to self-renew. These cell types are crucial for both, long term and short term regenerative processes required for active tissue repair. These specific cells comprise of monocytes, macrophages, erythrocytes, megakaryocytes, platelets, neutrophils, basophils, eosinophils, dendritic cells and lymphoid lineage cells. These cells are often called CD34+ stem cells, referring to a marker on the cell surface, capable of angiogenesis, upregulation of growth factors, and stem cell release.



Source: https://www.axolbio.com

- *Total Nucleated Cells*

The total nucleated cells (TNC's) present in the PureBMC® product are a gross indicator of the quality of the bone marrow concentrate.
Caution: a total nucleated cell count performed by any method is a count of cells with nuclei. In order to properly represent the TNC cell count, as a performance indicator, a correction calculation that removes nucleated red blood cells (nRBCs) should be performed.

Results.

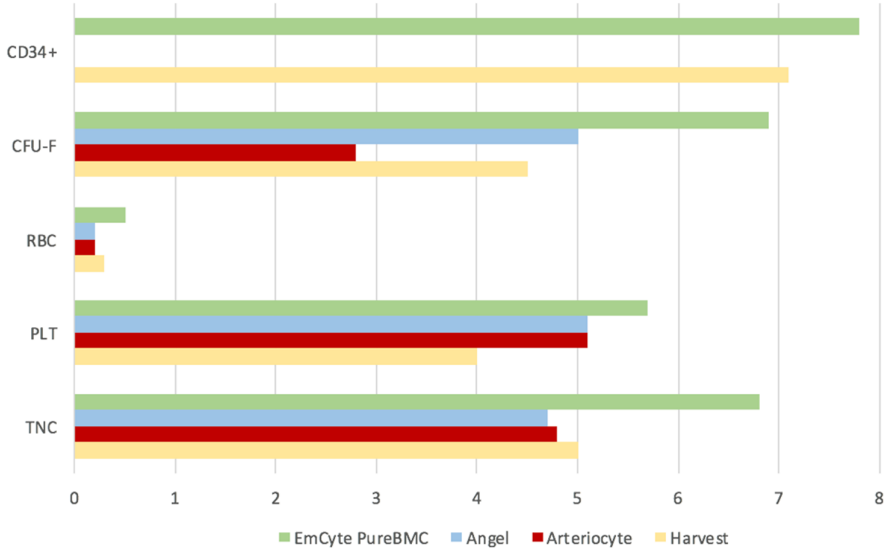
Figures 1 illustrates the differences in the ratio of cellular concentrations in 4 different bone marrow concentrating devices. This figure depicts the cellular ratio's, or fold increase of these systems. Data are collected from available figures presented by companies, and research performed at the BioSciences Research Associates laboratory (BSR) in Cambridge MA.

During laboratory testing at BSR the following equipment was used:

- Total Nucleated Cell Counts (TNC): determined with a Coulter AcT Diff2 hematology analyzer.
- Platelet Counts (PLT): determined with the Coulter analyzer
- CD34+ Cells: measured using an Accuri C6 flow cytometer.

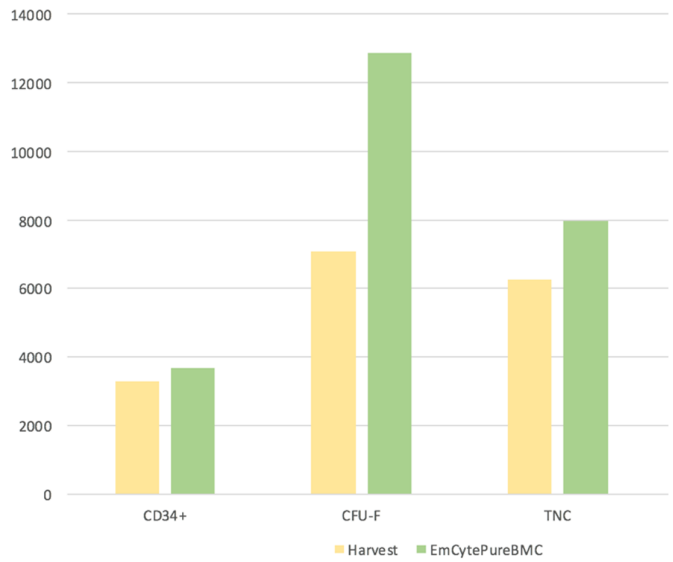
Figure 2 represents the total deliverable amount of cells that can be injected after a bone marrow concentration process has been executed.

Figure 1: Cell ratio's comparison between concentration systems when compared to bone marrow baseline values.



Legend: CD34+: Hematopoietic progenitor cell protein antigen CD34
CFU-F: colony Forming Units Fibroblast
RBC: Red Blood Cells
PLT: Platelet count
TNC: Total nucleated cells

Figure 2: Total deliverable amount of cells for injection after bone marrow concentration with two different systems.



Legend: CD34+: Hematopoietic progenitor cell protein antigen CD34, value x 10^3
CFU-F: colony Forming Units Fibroblast
TNC: Total nucleated cells, value x 10^2

Conclusion:

The advanced technology of the EmCyte PureBMC® system generates the highest number of MSC's, HSC's, and TNC's, when compared to Harvest, Arteriocyte and Angel systems. Furthermore, most of the systems produce only 4 mL specimens for therapy purposes, whereas the EmCyte PureBMC® system on average produces 7 mL of injectate. Once corrected for total volume, the total deliverable cells are clearly higher than with the Harvest system. Elevated levels of TNC 's are a parameter to determine whether a baseline bone marrow aspirate was concentrated by concentrating devices. This is of importance because the EmCyte PureBMC® system has the lowest presence of red blood cells (who have nuclei) in the concentrated product.

Therefore, the TNC count in this system correlates with higher numbers of MSC's and HSC's, since the majority of these cells are stratified within the TNC layer.

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