# Comparison of Arthrex Angel® System and Celling℠ Biosciences ART PRP and BMC Systems – Cellular Concentration

Arthrex Research and Development

## Objective

This study analyzed the outputs of the Arthrex Angel cPRP system and the Celling Biosciences ART systems. Angel PRP was compared to the Celling ART PRP system; and Angel PRP concentrate from bone marrow aspirate ($cPRP_{BMA}$) was compared to the Celling ART BMC system. The differences in cellular concentration and fold change between the systems were evaluated.

## Materials and Methods

*Blood Collection:* Anticoagulant citrate dextrose, solution-A (ACD-A) was used as the anticoagulant per each manufacturer's recommended ratio (13.3% vol/vol for the Angel system, 10% vol/vol for the Celling systems). From each of 6 (N = 6) blood donors, a total of 120 mL anticoagulated blood was drawn into 2 syringes preloaded with the correct volume of ACD-A via a standard arm venipuncture. From each donor, a small aliquot of anticoagulated whole blood (WBA) from each syringe was reserved for baseline analysis. The WBA was then processed in both systems based on each manufacturer's instructions.

*Bone Marrow:* Heparinized fresh human bone marrow aspirate (BMA) from the ilium of 6 (N = 6) donors was ordered from commercial vendors (AllCells or StemExpress) with volume received totaling 92 mL-110 mL. Samples were received and used within 24 hours of harvest. A small aliquot of BMA was reserved for baseline analysis. The BMA was split evenly between the systems and was processed according to each manufacturer's instructions.

*Processing Times:* For both blood and bone marrow, the Angel system's automated centrifugation settings were determined by the input volume (between 16.5- and 17-minute total processing time, including PRP collection). Hematocrit settings of 7% and 15% were used for blood and bone marrow, respectively. For the Celling, the device was set to centrifuge for 15 minutes at 3200 rpm and products were collected by manipulating the collection window to the appropriate locations relative to the buffy coat per manufacturer's standard operating procedure (SOP) (shown in **Figure 1**).

*Sample Analysis:* Baseline, PRPs, Angel $cPRP_{BMA}$, and ART BMC products were analyzed for specific cell concentrations using a hematology analyzer (Sysmex XE-5000™). Concentrations of white blood cells (WBCs), red blood cells (RBCs), platelets (PLTs), neutrophils (NE), lymphocytes (LYMPH), monocytes (MONO), and hematopoietic progenitor cells (HPCs [BMA samples only]) were analyzed. Additionally, to estimate mesenchymal stem cell levels for all BMA samples, 1 million total nucleated cells were cultured in triplicate for 10 days and fibroblast colony-forming units (CFU-Fs >50 cells) were counted poststaining in crystal violet via standard methods.[1,2] Statistical differences between devices were determined using a paired *t*-test, $\alpha = .05$.

**Figure 1**: Process by which ART PRP (top) and ART BMC (bottom) are extracted from the Celling devices.

Step 1: Inject WBA

Step 2: Centrifuge Device

Step 3: Extract PPP

Step 4: Extract PRP

Step 1: Inject BMA

Step 2: Centrifuge Device

Step 3: Extract PPP

Step 4: Extract BMC

## Results

For PRP preparation, average input volume to both devices was 58.7 ± 1.6 mL WBA. The Celling and Angel devices produced true volume (TV) averages of 3.7 ± 0.4 mL and 2.9 ± 0.9 mL of PRP, respectively. This difference was not statistically significant (P = .13). A matched volume (MV) calculation of the cellular components was also done for each PRP device by matching all individual donor volumes to the highest volume obtained (4.2 mL) using PPP.

For Angel $cPRP_{BMA}$ and ART BMC, the average input volume for both devices was 49.9 ± 3.5 mL BMA. The Celling device produced a TV average of 5.3 ± 1.5 mL ART BMC and the Angel system produced a $cPRP_{BMA}$ volume of 2.6 ± 0.7 mL (P = .014). A MV calculation was also done by matching all individual donor ART BMC or $cPRP_{BMA}$ volumes to the highest volume obtained (6.8 mL) using PPP.

The matched volume calculation is described as the following:

$$[\text{PRP or cPRP}_{\text{BMA MV}}] = \text{TV} \cdot \frac{[\text{PRP or cPRP}_{\text{BMA TV}}] + (\text{MV} - \text{TV}) \bullet [\text{PPP}]}{\text{MV}}$$

Replaced $cPRP_{BMA}$ with ART BMC for the Celling calculations.

**Tables 1** and **2** and **Figure 2** depict the cellular fold changes of the true and matched PRP and $cPRP_{BMA}$ products when compared to WBA and BMA inputs on a donor-by-donor basis as described by: fold change = [PRP or $cPRP_{BMA}$]/[WBA or BMA].

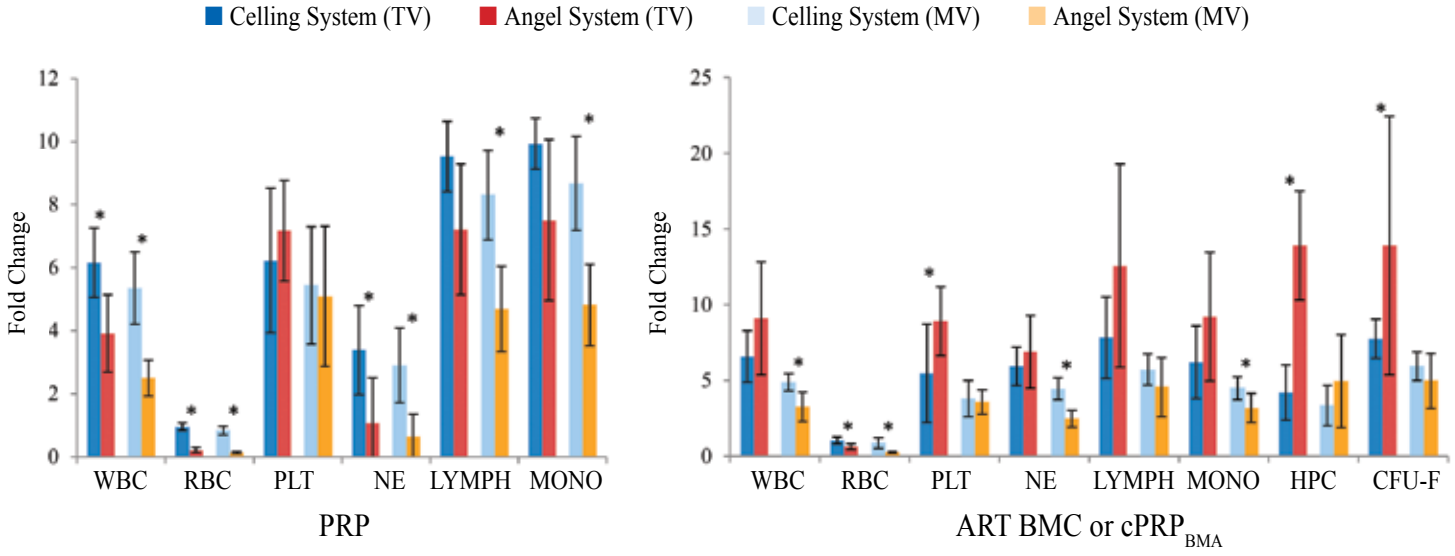
**Table 1**: Cellular fold changes of PRP compared to baseline WBA (mean ± SD).

| | | WBC | RBC | PLT | NE | LYMPH | MONO |
|---|---|---|---|---|---|---|---|
| True Volume | Celling PRP | 6.2 ± 1.1 | 1.0 ± 0.1 | 6.2 ± 2.3 | 3.4 ± 1.4 | 9.5 ± 1.1 | 9.9 ± 0.8 |
| | Angel PRP | 3.9 ± 1.2 | 0.2 ± 0.1 | 7.2 ± 1.6 | 1.1 ± 1.5 | 7.2 ± 2.1 | 7.5 ± 2.6 |
| Matched Volume | Celling PRP | 5.4 ± 1.1 | 0.8 ± 0.1 | 5.4 ± 1.9 | 2.9 ± 1.2 | 8.3 ± 1.4 | 8.7 ± 1.5 |
| | Angel PRP | 2.5 ± 0.6 | 0.1 ± 0.03 | 5.1 ± 2.2 | 0.6 ± 0.7 | 4.7 ± 1.3 | 4.8 ± 1.3 |

**Table 2**: Cellular fold changes of Celling ART BMC and Arthrex Angel $cPRP_{BMA}$ compared to baseline BMA (mean ± SD).

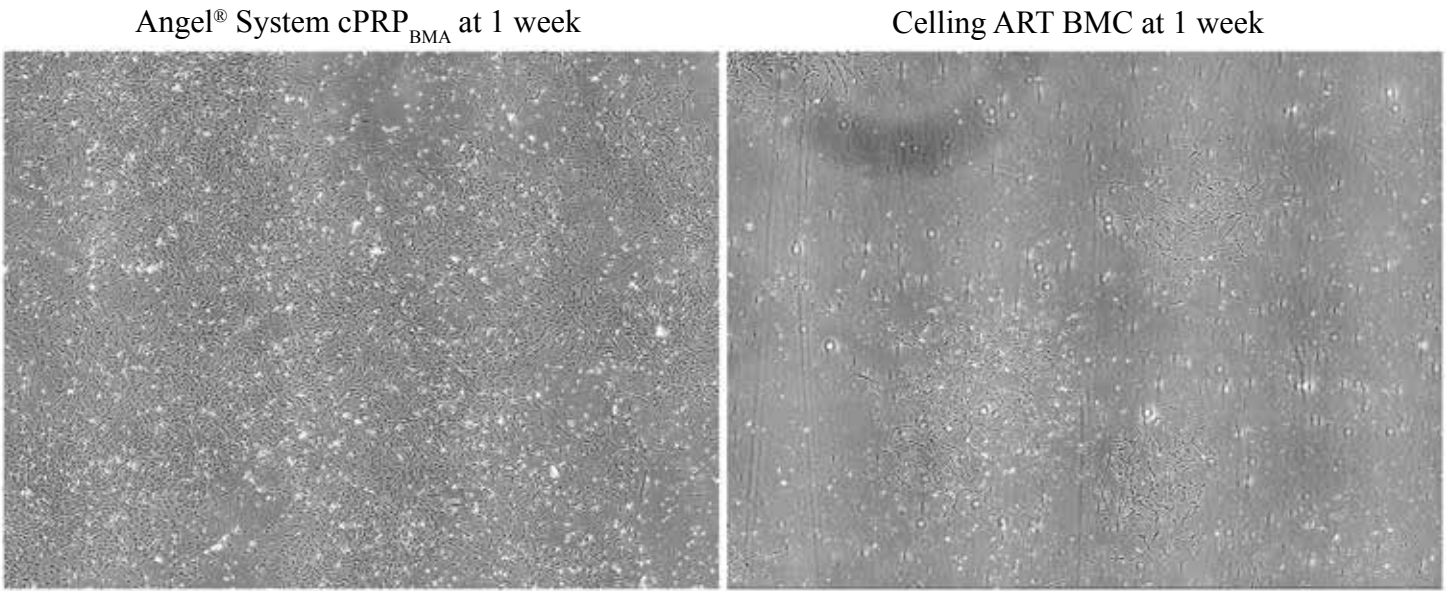
| | | WBC | RBC | PLT | NE | LYMPH | MONO | HPC | CFU-F |
|---|---|---|---|---|---|---|---|---|---|
| True Volume | Celling ART BMC | 6.6 ± 1.7 | 1.0 ± 0.2 | 5.4 ± 3.2 | 5.9 ± 1.3 | 7.8 ± 2.7 | 6.2 ± 2.4 | 4.2 ± 1.3 | 7.8 ± 2.7 |
| | Angel $cPRP_{BMA}$ | 9.1 ± 3.7 | 0.6 ± 0.2 | 8.9 ± 2.3 | 6.9 ± 2.4 | 12.6 ± 6.7 | 9.2 ± 4.3 | 13.9 ± 8.5 | 13.9 ± 6.3 |
| Matched Volume | Celling ART BMC | 4.9 ± 0.6 | 0.9 ± 0.4 | 3.8 ± 1.2 | 4.4 ± 0.7 | 5.7 ± 1.0 | 4.5 ± 0.7 | 3.3 ± 1.3 | 5.9 ± 0.9 |
| | Angel $cPRP_{BMA}$ | 3.2 ± 1.0 | 0.2 ± 0.05 | 3.6 ± 0.8 | 2.5 ± 0.5 | 4.5 ± 2.0 | 3.2 ± 1.0 | 4.9 ± 3.1 | 5.0 ± 1.8 |

**Figure 2**: Cellular fold changes of each system.




*Indicates a statistically significant difference between the devices.

**Figure 3**: Relative mesenchymal stem cell (MSC) density after 1 week of culture when an equal volume of Angel $cPRP_{BMA}$ and Celling ART BMC were cultured.




**Discussion**

Both systems require approximately the same processing time. The Celling devices require manual manipulation to collect the end product. In contrast, the Arthrex Angel system is fully automated, which contributes to the ease of processing samples in clinical environments. Variability in end product volume produced by the Angel system is based on a combination of cells present in the sample that are detected by the sensor and the chosen hematocrit setting. Relative to the Celling devices, the Angel system produced a more concentrated products. The highly concentrated output of the Angel system allows the clinician to deliver a concentrated end product or to expand the treatment volume with PPP. This feature is beneficial when the treatment sites present volume limitations.

The PRP produced by the Angel system had a 7.2x increase in platelet concentration as compared to 6.2x with the Celling devices. The Angel system PRP had significantly lower RBC, WBC, and NE fold changes than the Celling PRP system, both with true and matched volume. Matching the volume further reduces WBC concentration in the Angel system PRP. This is significant because increased levels of WBCs (specifically NEs) and RBCs have the potential to decrease healing potential.[3]

The $cPRP_{BMA}$ prepared by the Angel system contained significantly higher concentrations of PLTs, HPCs, and CFU-Fs compared to the Celling ART BMC system (**Figure 3**). The Angel system also had significantly lower RBCs in the final $cPRP_{BMA}$ end product compared to Celling system. The MV Angel system $cPRP_{BMA}$ showed significantly decreased WBCs (specifically NE and MONO) compared to the Celling ART BMC. MSCs were also enriched to a higher degree as demonstrated by the CFU-F frequency among total nucleated cells count ($0.005 \pm 0.002\%$ vs $0.004 \pm 0.002\%$, $P = .008$) with the Angel system. This is because the Celling device captures all WBCs, including heavier granulocytes and neutrophils, whereas the Angel system minimizes collection of these cells. An ideal $cPRP_{BMA}$ system would both concentrate and enrich the progenitor cells in the product (MSCs or HPCs).[1] The Angel system was found to be superior to the Celling systems in the concentration and enrichment of whole blood and BMA samples.

**References**

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3. Martin P, Leibovich SJ. Inflammatory cells during wound repair: the good, the bad and the ugly. *Trends Cell Biol*. 2005;15(11):599-607. doi:10.1016/j.tcb.2005.09.002.