SmartPREP 2

MULTI-BIOLOGIC CONCENTRATE PLATFORM

APC+™
Autologous Platelet Concentrate

BMAC™
Bone Marrow Aspirate Concentrate
**Healing Cascade**

The body’s response to injury is a very specific and well-documented series of steps collectively referred to as the “Healing Cascade”. This cascade is comprised of several distinct phases. The natural healing process requires a systems approach that combines the use of Growth Factors and Stem Cells integrated into a Matrix to optimize bone/tissue repair and regeneration. (Fig. 1)

The use of these bioactive cells to augment and accelerate the natural healing process is considered by many to be a “new frontier” of clinical treatment.

Autologous Platelet Concentrate (**APC⁺**™) is a specific concentration of platelets and plasma that can be directly delivered to any surgical wound to create the conditions to accelerate healing. (Fig. 2)

**Growth Factors**

The early stages of the healing cascade are primarily mediated by platelets and the release of cellular growth factors. (Fig. 3)

**Platelet-Derived Growth Factor (PDGF):**
- Initiates connective tissue healing
- Increases mitogenesis, angiogenesis, and macrophage activation

**Vascular Endothelial Growth Factor (VEGF):**
- Possess potent angiogenic, mitogenic, and vascular permeability enhancing activities

**Transforming Growth Factor-β (TGF-β):**
- Increases chemotaxis and mitogenesis
- Stimulates deposition of collagen

**Epidermal Growth Factor (EGF):**
- Induces epithelial development
- Promotes angiogenesis

**Chemomigration**

As the wound continues to mature, healing progresses by attracting stem cells from the periphery into the affected area.

Autologous Platelet Concentrate (**APC⁺**™) contains high concentrations of growth factors within alpha-granule releasate. This initiates a cascade that results in chemoattraction of circulating stem cells promoting differentiation (proliferation), to develop into mature tissues.
PROCESS STEPS & PERFORMANCE APC+™

1. Draw Venous Blood
2. Fill Process Disposable (PD)
3. Process

<table>
<thead>
<tr>
<th>Blood Volume (ml)</th>
<th>Platelet Concentrate Volume (ml)</th>
<th>Platelet Count/μl</th>
<th>Increase Above Baseline</th>
<th>Growth Factors Derived from APC+™ Increase Above Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>3</td>
<td>1.191.000</td>
<td>4,4x</td>
<td>PDGF-AB 4,4x, TGF-β1 4,4x, VEGF 4,4x, EGF 4,4x</td>
</tr>
<tr>
<td>60</td>
<td>7</td>
<td>1.758.000</td>
<td>6,6x</td>
<td>PDGF-AB 6,6x, TGF-β1 6,6x, VEGF 6,6x, EGF 6,6x</td>
</tr>
<tr>
<td>60</td>
<td>10</td>
<td>1.151.000</td>
<td>4,3x</td>
<td>PDGF-AB 4,3x, TGF-β1 4,3x, VEGF 4,3x, EGF 4,3x</td>
</tr>
</tbody>
</table>

Data on file

4. Withdraw Platelet Poor Plasma
5. Resuspend & Withdraw APC+™
6. Load SmartJet™ Applicator
**Antimicrobial Protection**

“Platelet concentrate appears to have potent antimicrobial capacity against staphylococcus aureus. Platelet concentrate might represent a useful strategy against post operative infections.”
Moojen: University Medical Center Utrecht, Dept. of Orthopaedics, Utrecht, NL

“Platelets can exert a variety of biological functions, one of which is to combat invading microorganisms.”
Zaat: CINIMA (Center of Infection and Immunity Amsterdam), Academic Medical Center, Amsterdam, NL

**Oral Surgery: Sinus Lift Bone Grafting**

“Bone grafts with growth factors from PRP demonstrated greater trabecular bone density than bone grafts without PRP (74% vs. 55%).”

**Cosmetic Surgery: Abdominalplasty**

“The use of PRP in abdominoplasty procedures resulted in fewer seromas wounds healed more rapidly and with a more esthetic result.”
Jackson: Amer Jour Cos Surg Vol.20, No.4, 2003

**Cosmetic Surgery: Face Lift**

“The use of autologous fibrin glue and platelet gel resulted in shorter operating times, elimination of drains, compressive dressings reductions, reduction of pain and post-op swelling and improved wound healing with resultant shorter recovery time.”
Man: Aesth Plast Surg, June 2000

**Cardiac: Sternal Closure**

“The incidence of superficial infection was significantly lower in the PRP group compared with control. There was a similar relationship found when comparing deep sternal wound infections.”
Towbridge: JECT 2005;37:381-386

**Sports Medicine: Lateral Epicondylitis/Tennis Elbow**

“PRP therapy is as effective as surgery, with sustained and significant improvement over time, no side effects, and high patient acceptance.”

**Podiatry: Plantar Fasciitis**

“Injecting APC+™ into recalcitrant, symptomatic plantar fascia may cause a reparative effect leading to a resolution of symptoms.”

**Sports Medicine: ACL Repair**

“Knees that received (platelet) gel showed greater defect filling and increased mechanical strength compared to untreated knees.”

**Chronic Wound: Diabetic Foot Syndrome**

“More patients treated with PRP achieved complete wound healing (55% vs. 24%) than in the control group (p<0,05). The rate of healing was faster in the PRP group (9,2 vs. 12,2 weeks). The frequency and severity of adverse events (infection and vascular complications) was significantly higher in the control group (9 vs. 2, p=0,02).”
Fries: 5th Int´l symposium on the diabetic foot, Noordwijkhout, NL 2007
Human stem cells have the capability to self-replicate or differentiate into the cell types that make up all tissues and organs of the human body. Under normal conditions, the human body has sufficient stem cells to support natural tissue maintenance and healing, but often lacks the quantity of stem cells necessary to successfully regenerate severely damaged tissues.

Harvest’s stem cell development strategy seeks to overcome this shortage of stem and regenerative cells by concentrating “hidden” populations of the patient’s own stem cells in a point-of-care setting for treatments to promote tissue repair and regeneration. (Fig. 4)

**Stem Cell Sources**

There are numerous sources of human stem cells. Adult stem cells are the least controversial and may be collected from the bone marrow, blood or other tissues.

The BMAC™ System utilizes only bone marrow-derived stem cells obtained from the Ileum in a minimally invasive process. The cells are not chemically manipulated or cultured risking cell viability or their ability to regenerate damaged tissue.

**Autologous Regenerative Cells (ARC’s)**

ARC’s are harvested from a specific patient and returned to the same patient in a point-of-care procedure. As patients receive their own cells, there is no concern of rejection or need for immunosuppressive drugs.

ARC’s integrate effectively and interact with the surrounding tissue to promote healing.

The Harvest System provides significantly higher cellular yields and the treatment effect is greater compared to Ficoll. ARC’s are not removed from their natural plasma environment which sustain functionality and may support paracrine mechanisms that regulate cell homing, transmigration, and differentiation. (Fig. 5)

**ARC’s as Therapeutics**

Adult stem cells have a long history of human use as therapeutics beginning with bone marrow transplantation, and continuing with cell-based clinical trials focused on tissue repair.

Harvest seeks to leverage the history and therapeutic potential of bone marrow stem cells by producing a mixed population of stem and early stage progenitor cells that are capable of differentiating into a variety of tissues.

The key advantage of Harvest’s ARC’s is that the number of multi-potent stem, progenitor, and other regenerative cells are significantly concentrated in the patient’s own physiological plasma in a point-of-care procedure within 1.5 minutes.
**BMAC™ PROCESS STEPS & PERFORMANCE**

1. Aspirate Bone Marrow
2. Fill Process Disposable (PD)
3. Process
4. Remove Excess Plasma
5. Resuspend & Remove BMAC™
6. Transfer BMAC™ to Sterile Field

<table>
<thead>
<tr>
<th>Total Nucleated Cells (x10^6/ml)</th>
<th>Bone Marrow Aspirate Baseline (60ml)</th>
<th>Bone Marrow Aspirate Concentrate BMAC™ Post Processing (10ml)</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>23,1 ± 5</td>
<td>23,1 ± 5</td>
<td>89,1 ± 8</td>
<td>64,3</td>
</tr>
<tr>
<td>4,51 ± 0,9</td>
<td>4,51 ± 0,9</td>
<td>18,80 ± 3,41</td>
<td>69,0</td>
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<tr>
<td>0,183 ± 0,060</td>
<td>0,183 ± 0,060</td>
<td>0,800 ± 0,180</td>
<td>75,3</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>3040</td>
<td>-</td>
</tr>
<tr>
<td>103,3</td>
<td>103,3</td>
<td>752</td>
<td>7,3 over baseline</td>
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**Oral Maxillofacial Surgery: Bone Regeneration**

“Cells separated with the Harvest System are more viable than those derived via chemical density gradient separation technique. The method is extremely well tolerated reducing complications associated with autologous graft harvesting, allowing faster and more consistent ossification.”

Sauerbier, Schmelzeisen: University of Freiburg, Department of Oral Maxillofacial Surgery 2007

**Cardiac Surgery**

“Cardiac surgery combined with stem cell therapy may enhance angiogenesis in difficult to treat patients with diffuse coronary artery disease that have no conventional revascularization options.”

Allen: World Cardiothoracic Society, Indonesia, March 2008

**Orthopedic Surgery: Spinal Surgery**

“Autologous adult stem cells employed to facilitate spinal fusion instead of using bone harvested from a patient’s pelvis, may alleviate two potential problems: (1) graft site morbidity (including bleeding, infection, and chronic pain at the donor site); and (2) failure to fuse.”

Johnson: Neurosurgical Assoc., San Antonio TX, USA 2007

**Orthopedic Surgery: Non-Union**

“Percutaneous bone marrow grafting is safe and effective for treating atrophic tibial diaphyseal non-union efficacy appears to be related to the number of progenitors delivered.”

Hernigou: JBJS 87:1430-1437, 2005

**Orthopedic Surgery: Avascular Necrosis Femor/Knee**

“Implantation of autologous bone marrow cells appears to be a safe and effective treatment for early stages of osteonecrosis of the femoral head.”


**Orthopedic Surgery: Trauma**

“The future lies in the regenerative medicine with the prospect of generating new tissues in order to replace destroyed or impaired ones by using concentrated autologous stem cells. Application of concentrated bone marrow is a safe and efficient method in treatment of non-union fractures.”

Beldekos: 6th Orthopedic Dept., KAT Trauma Hospital of Athens, Greece 2007

**Orthopedic Surgery: Cartilage Regeneration**

“One step arthroscopic procedure with use of stem cells, demonstrated to regenerate hyaline cartilage, with advantages of reduced surgical time, lower cost, and lower morbidity.”

Giannini: ICRS Meeting Warsaw, Oct 2007

**Sports Medicine: Infiltration Therapy**

“Bioactive cells and proteins encourage in-growth of collagen and the remodeling of previously injured tissue at the pain initiating site”

Crane: Crane Clinic for Sports Medicine, 2007

**Peripheral Arterial Disease (PAD): Critical Limb Ischemia**

“Angiogenesis induced by autologous bone marrow transplantation is a feasible, secure and with Harvest Tech separation, also a simple therapy. Preliminary results, autologous BMt in CLI can help avoid amputations.”

SMARTPREP 2 SYSTEM

Technology
- Dedicated microprocessor controlled centrifuge
- Patented floating shelf technology optimally separates biological cellular components

Quality
- Complete automation ensures high degree of efficiency & reproducibility
- Reduces incidence of operator inconsistency associated with manual techniques

Simplicity
- Point-of-care processing
- Easily transportable
- Does not require dedicated trained personnel

Efficiency
- High degree of process efficiency allows the system to concentrate a clinically viable number of cells
- Titrate final volume as desired

Safety
- Completely autologous system
- Designed to be used point-of-care reducing contamination risks
- High degree of sterility (closed process system)

Rapidity
- Process time for biologic concentrates is less than 15 minutes
- Can be used intraoperatively (point-of-care setting)

PRODUCT CODES

<table>
<thead>
<tr>
<th>SmartPREP 2 System</th>
<th>Autologous Platelet Concentrate (APC⁺⁺) Sterile Disposable Products</th>
<th>Bone Marrow Aspirate Concentrate (BMA⁺⁺) Sterile Disposable Products</th>
<th>Sterile Accessory Products</th>
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<tbody>
<tr>
<td>SMP-2i</td>
<td>APC⁺⁺ Process Kit 20ml (produces 3ml APC⁺⁺ from 20ml blood)</td>
<td>BMAC 60 Bone Marrow Aspirate Concentrate Kit 60ml (produces 7-10ml BMA⁺⁺ from 60ml Marrow)</td>
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<tr>
<td>WS-2</td>
<td>APC⁺⁺ Process Kit 60ml (produces 7-10ml APC⁺⁺ from 60ml blood)</td>
<td>BMAC 120 Bone Marrow Aspirate Concentrate Kit 120ml (produces 14-20ml BMA⁺⁺ from 120ml Marrow)</td>
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<td>HAT Kit</td>
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<td>Harvest Autologous Thrombin Kit</td>
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<td>GDP-10i</td>
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