

TERUMO Corporation  
Business Strategy Conference



Gary Tureski  
President & CEO  
Harvest Technologies Corporation  
December 5, 2011

# A Cell Therapy Company

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## ■ BUSINESS STRATEGY

- To design and market devices that concentrate **autologous cells** and proteins at **point of care** for bone and soft tissue regeneration.

## ■ AUTOLOGOUS CELLS

- Patient's own cells - naturally required for tissue regeneration.

## ■ POINT OF CARE:

- Prepared at the time of and in the place of treatment

## ■ UNIQUE CENTRIFUGAL TECHNOLOGY

(Patented)

- Decanting function
- Floating shelf

# Technologies & Products



SmartPReP 2  
Platform



Platelet Rich Plasma (PRP)  
BMAC (Stem Cells)



fFat  
Bioactive Scaffold

Approvals	USA	EU	India
PRP	Yes	Yes	Yes
fFat	Pending	Pending	N/A
BMAC	Ortho	Ortho	Ortho/Vasc.

# Cellular End Products

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- **PRP** – Platelets, Progenitor Cells, Signal Proteins & Plasma  
– from *Blood*
  - Growth Factors and Messenger Cells – 5X Native
  - 1MM per mL
- **BMAC** – Stem Cells, Progenitor Cells, Platelets Signal Proteins & Plasma – from *Bone Marrow*
  - 1 Billion Total Nuclear Cells
- **fFAT** – Concentrated Fat with tumescent fluid removed – from *abdominal fat*
  - Bio-active Scaffold with Stem Cells

# Cell Therapy

Introducing new cells into a tissue to cure a disease

## ■ Acute Condition

- Brief and severe medical condition

**PRP & fFat**

## ■ Chronic Condition

- Long term and progressive medical condition

**BMAC/Stem Cells**

## How stem cells work

### ■ Autocrine Effect

- Cells secrete a chemical messenger that binds to receptors and changes the cell

### ■ Paracrine Effect

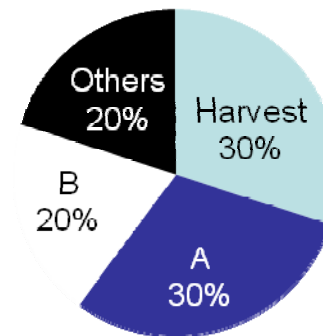
- Form of cell signaling where the signal cell is near the target cell

# Current Markets

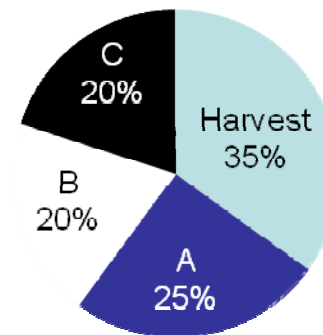
## ■ PRP – US \$300 to \$600 Million Potential, \$50 Million Current

- Injection Therapy
  - Sports Medicine
  - Pain Management
- Cardiovascular
- Cosmetic
- Oral Surgery

**PRP Market Share**



**BMAC Market Share**



## ■ BMAC

- Orthopedic

\*Estimated by Terumo

# PRP Injections: Famous Golfer Achilles



# Fat Transfer and PRP injection

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# **BMAC: Autologous, Point of Care Stem Cells**

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- **Chronic End-Stage Diseases**

- Few or no treatment options

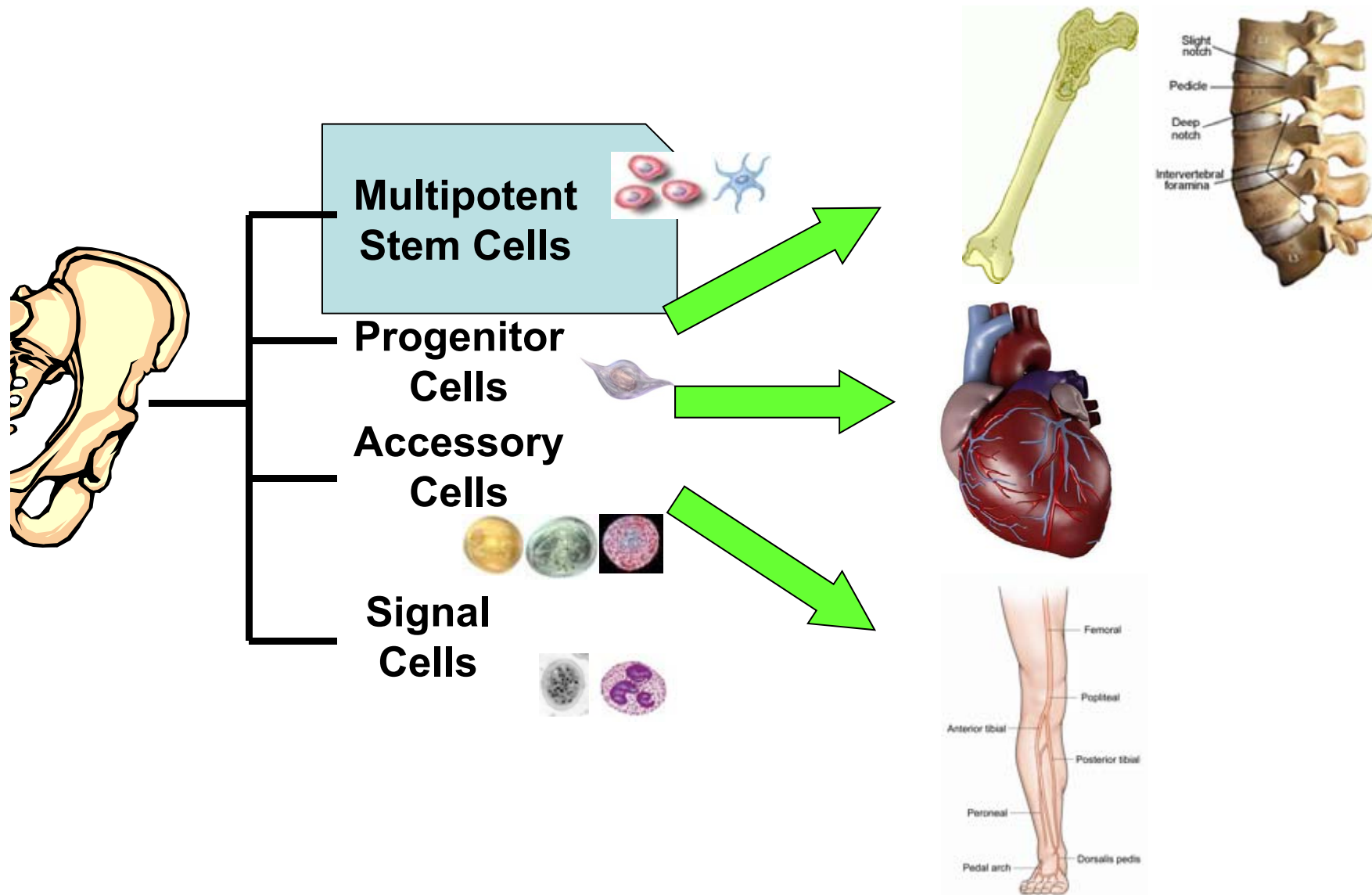
- **Safe**

- Product stays with the patient
- Autologous (from the patient)

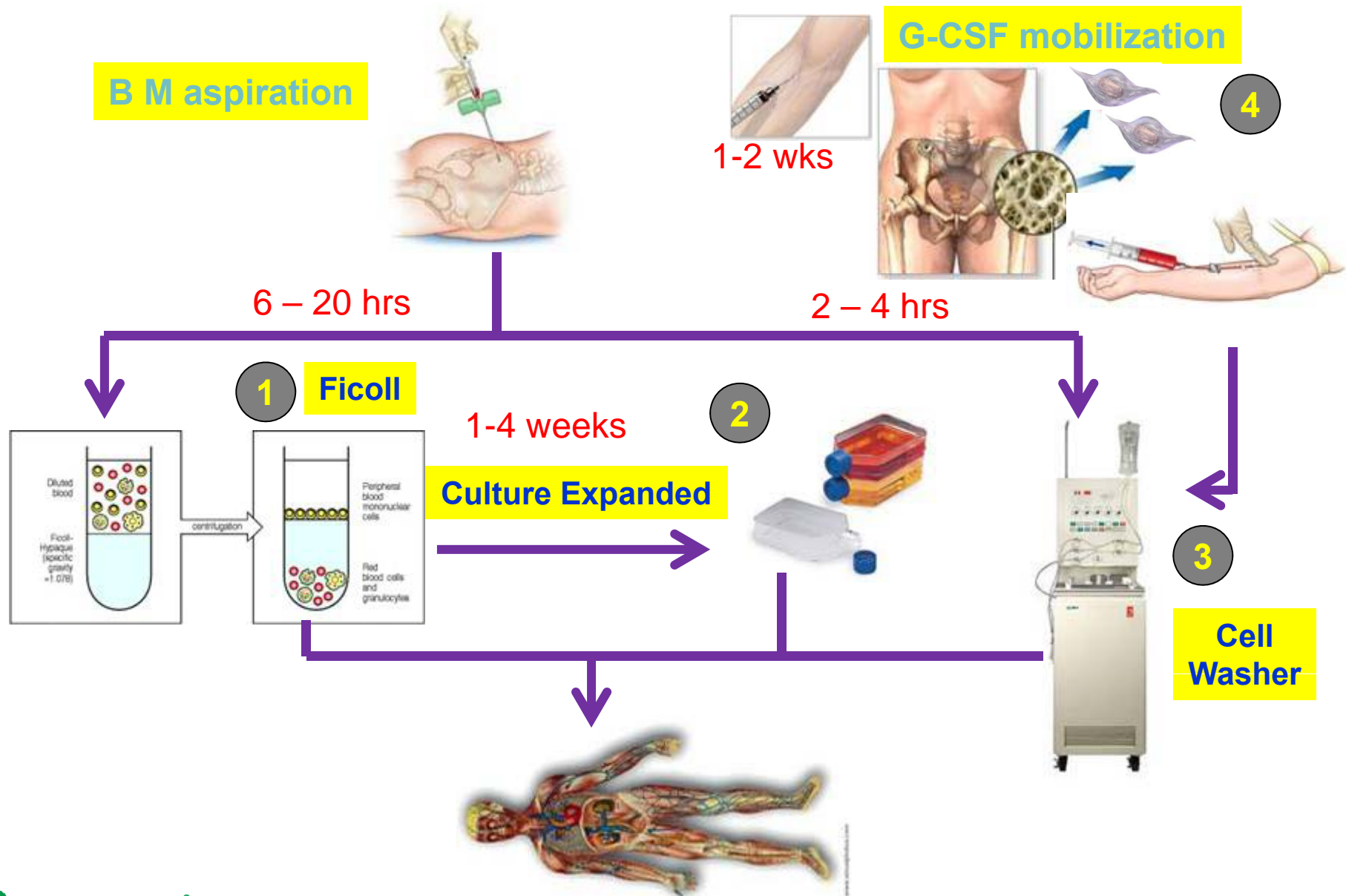
- **Extremely cost effective**

- Outpatient treatment

# BMAC In Cell Therapies

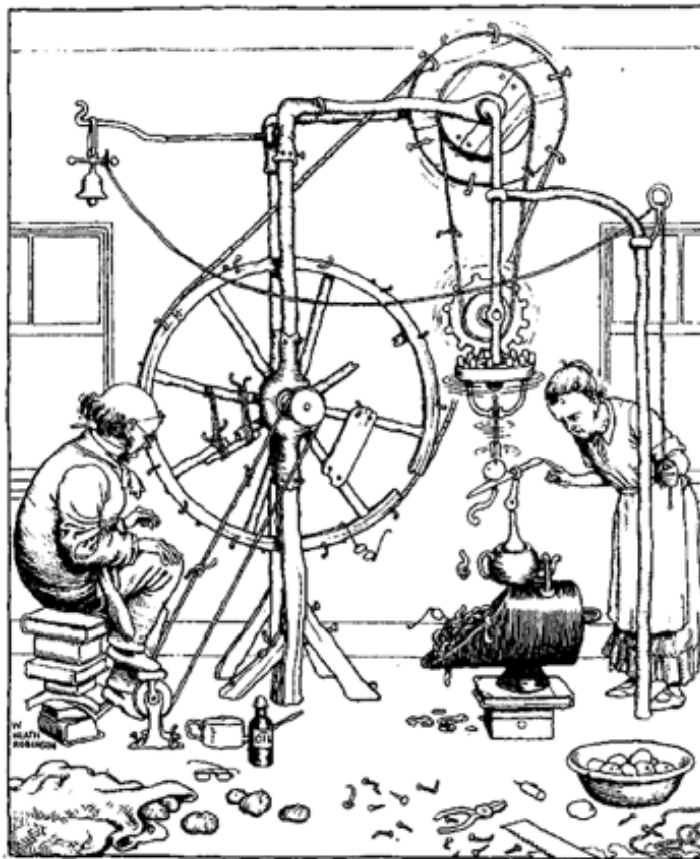


# Published Research Methods to OBTAIN BM CELLS

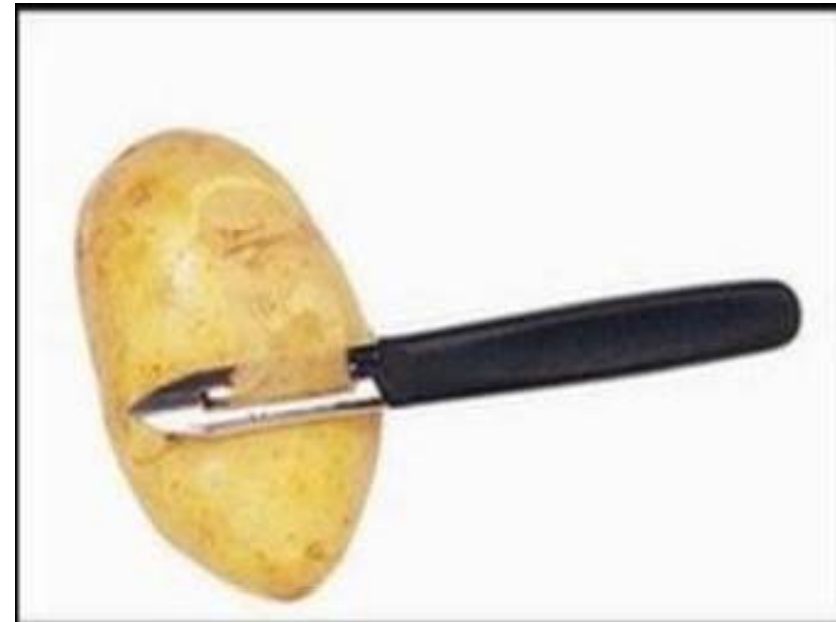


# To Achieve the Same Result Simpler is *Always* Better

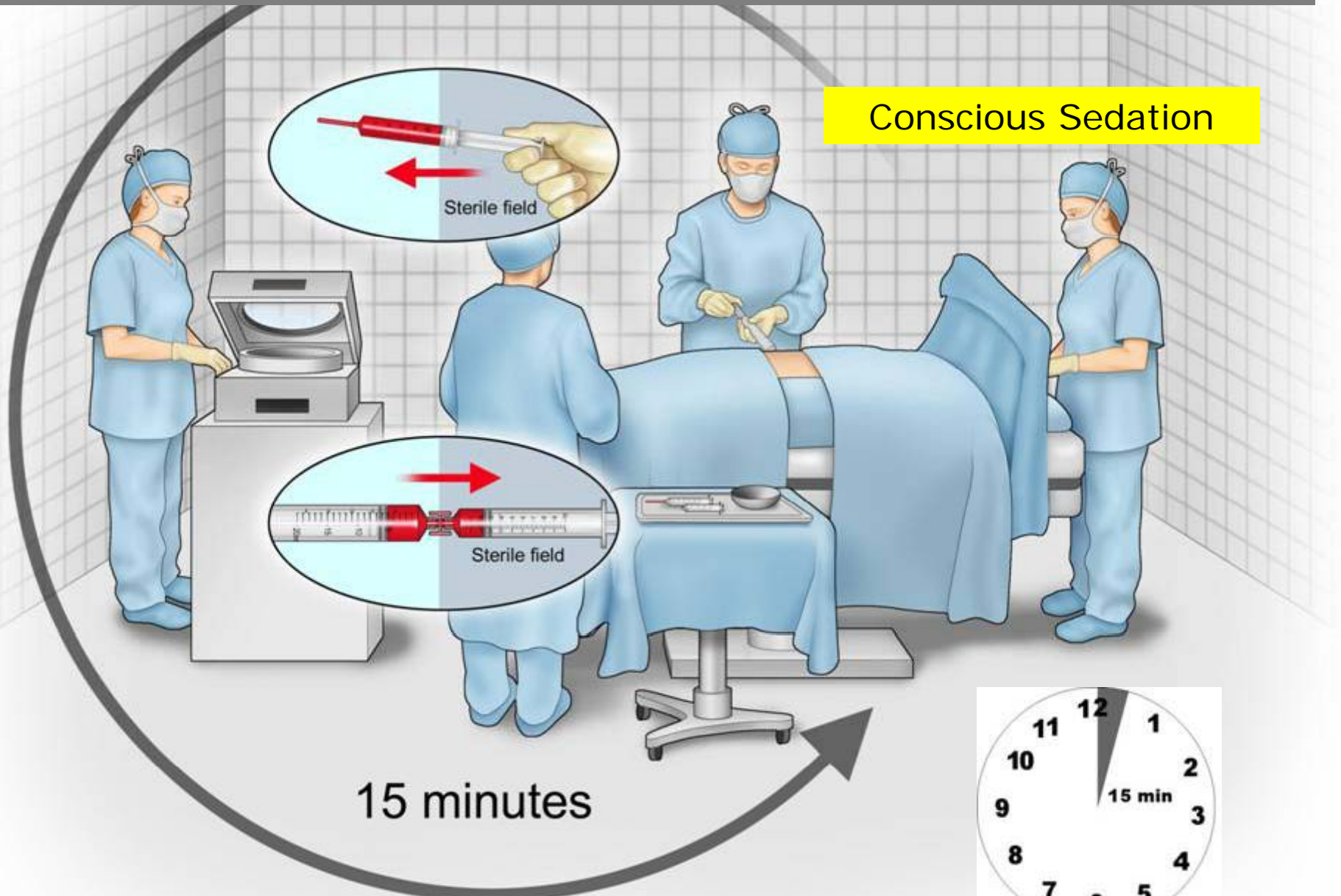
## Potato peeler



The Professor's invention for peeling potatoes.



# HARVEST BMAC System: Facilitates Autologous Bone Marrow Therapy



# What we have learned from treating over 60,000 Patients!

- BMAC Cells are extremely effective at stimulating the growth of vasculature and bone cells.
- A full cellular composition is better than a limited composition **Paracrine**
- The more severe the disease state the better the cells work **Effect**
  - EF of <40 better effect than >40%
- The more cells the better the outcomes
- BMAC the number 1 worldwide stem cell approach

# BMAC Strategy

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- Vascular, Cardiac & Cardiovascular
  - End-stage disease states
  - No other viable treatment alternatives
  - Large Markets
  - Easiest to implement, lowest cost technology
  - First to market opportunity

# Initiative 1: No Option CLI

**PAD  
Disease**

**Critical  
Limb  
Ischemia**

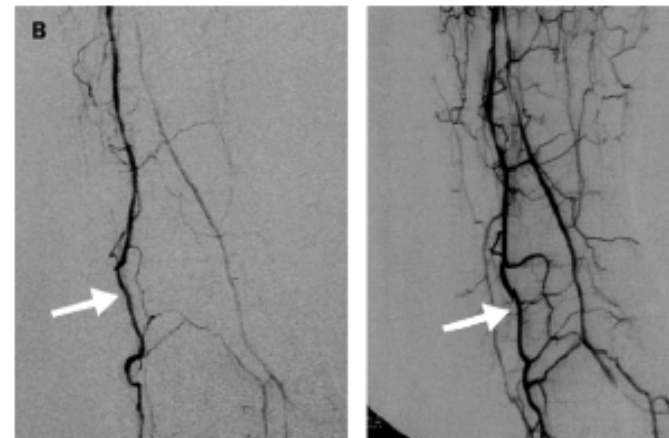
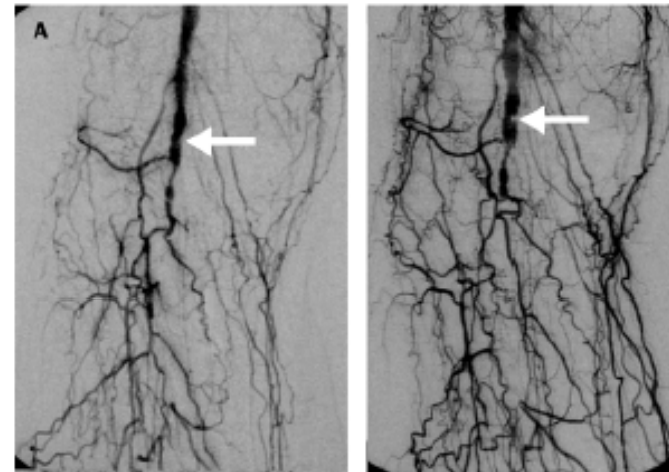
**No  
Option**

**PAD : Peripheral Arterial Disease  
CLI : Critical Limb Ischemia**

<b>Market</b>	<b>Estimate</b>
<b>United States</b>	<b>300,000</b>
<b>European Union</b>	<b>870,000</b>
<b>India</b>	<b>200,000</b>
<b>TOTAL</b>	<b>1.37 million</b>

# Critical Limb Ischemia FDA Study

FDA 210 Pivotal IDE Study Treating No-option  
Critical Limb Ischemia with BMAC injections



# Harvest Clinical Trials

## w/ No Option Critical Limb Ischemia Patients

Study	Population Number Subjects	Study Type
India N = 60	TAO: 91% Avg age: 46 (30-66)	Randomized to delivery
Czech Repub N = 96 (42/54)	DM: 94% Avg Age: 65 (+/- 10.6)	RCT unblinded best med treatment;
BONMOT-1 CLI: Germany N = 51	DM: 55% Avg age: 65 ((+/- 12)	Non-Random open label
BONMOT-2 CLI Germany N = 47 (26/21)	DM: 64% Avg Age: 74 (+/- 12)	RCT blinded (1:1 BMAC to placebo)
BMAC IDE trial N = 48 (34/14)	DM: 50% Avg Age: 69.7 (+/- 12.4)	RCT blinded (2:1 BMAC to placebo)
Total 302 subjects (213 BMAC)		

w/ No O

Study

India  
N = 60

Czech Repub  
N = 96 (42/54)

BONMOT-1 CLI:  
N = 51

BONMOT-2 CLI  
N = 47 (26/21)

BMAC IDE trial  
N = 48 (34/14)

Total 302 subjects

Patients

Study Type

Randomized to delivery

Controlled treatment;

Open label

Blinded to placebo)

Blinded to placebo)

Early results and lessons learned from a multicenter, randomized, double-blind trial of bone marrow aspirate concentrate in critical limb ischemia

Mark D. Irfani, MD,<sup>1</sup> John V. Halperin, MD,<sup>2</sup> George Gills, MD,<sup>3</sup> Gregory Peck, MD,<sup>4</sup> John Lomstedt, MD,<sup>5</sup> Eric Pelech, MD,<sup>6</sup> Dennis Rudysk, MD,<sup>7</sup> K. S. Vijayaraghavan, MD,<sup>8</sup> R. Radhakrishnan, MD,<sup>9</sup> Basim Anwar, MD,<sup>10</sup> Axel Hingorani, MD,<sup>11</sup> and Sean Roddy, MD,<sup>12</sup> Basim Anwar, MD,<sup>13</sup> Dallas and Houston, Tex; Tampa, Fla; Chennai, India; and Houston and Dallas, TX

Autologous Bone Marrow Cell Transplantation Increases Leg Perfusion and Reduces Amputations in Patients With Advanced Critical Limb Ischemia Due to Peripheral Artery Disease

Berthold Amann,<sup>1</sup> Claus Lindemann,<sup>2</sup> Richard Bazzi,<sup>3</sup> and J. Anselm Schneider-Lucke<sup>4</sup>

<sup>1</sup>Department of Medicine, Franziskuskrankenhaus, Berlin-Verlinden Campus, Berlin, Germany; <sup>2</sup>ICH Market Laboratory, HELIOS Klinikum Berlin-Buch, Berlin, Germany

Intraoperative Adjunctive Stem Cell Treatment in Patients with Critical Limb Ischemia Using a Novel Point-of-Care Device

R. Koberbach,<sup>1</sup> Carla Brinija,<sup>2</sup> Catherine Capomoni,<sup>3</sup> Rene Ahr,<sup>4,5</sup> and Eva Schmalz,<sup>6</sup> Dillenburg, Germany

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www.lippincott.com

Cell Therapy, a New Standard in Management of Chronic Critical Limb Ischemia and Foot Ulcer

V. Pucháček,<sup>1</sup> I. Čermáček,<sup>2</sup> F. Jirák,<sup>3</sup> D. Salovejová,<sup>4</sup> T. Jirák,<sup>5</sup> D. Čermáček,<sup>6</sup> J. Kráča,<sup>7</sup> E. Uvárov,<sup>8</sup> P. Klement,<sup>9</sup> J. Martinek,<sup>10</sup> and G.L. Klement<sup>11</sup>

<sup>1</sup>Radiooncology Institute, University Hospital Olomouc, Olomouc, Czech Republic; <sup>2</sup>Human-Cellological Center, University Hospital Olomouc, Olomouc, Czech Republic; <sup>3</sup>Biogeny Clinic and Anesthesiology Department, University Hospital Olomouc, Olomouc, Czech Republic; <sup>4</sup>Department of Mathematical Methods in Economics, VSB-Technical University Ostrava, Ostrava, Czech Republic; <sup>5</sup>Microbiology Research Center, Masaryk Memorial Cancer Institute, Prague, Czech Republic; <sup>6</sup>Clinical Laboratory, I.G. Mendel College of Health Sciences, Brno, Czech Republic; <sup>7</sup>Children's Hospital, Dana Faber Cancer Institute, Harvard Medical University, Boston, MA, USA

The role of amputation as an outcome measure in cellular therapy for critical limb ischemia: implications for clinical trial design

De Benedictis, Thomas F. O'Donnell, J., Mark D. Irfani,<sup>1</sup> Ericka Adler,<sup>2</sup> Dennis J. Banda,<sup>3</sup> John V. Halperin,<sup>4</sup> Man R. Lomstedt,<sup>5</sup> Gregory J. Peck,<sup>6</sup> Sean F. Roddy,<sup>7</sup> Vishwanath Vijayaraghavan,<sup>8</sup> and Arnd H. Fiebert<sup>9</sup>

Concentration of Bone Marrow Total Nucleated Cells by a Point-of-Care Device Provides a High Yield and Preserves Their Functional Activity

Fatima C. Hermann,<sup>1</sup> Stephan L. Haber,<sup>2</sup> Tanja Fentler,<sup>3</sup> Christoph von Heyder,<sup>4</sup> Joachim Andriav, Sherwin V. Ravy,<sup>5</sup> Mai N. Jacobson,<sup>6</sup> and Christopher Hirscher<sup>7</sup>

<sup>1</sup>Department of Surgery, Ludwig Maximilian University, 81337 Munich, Germany; <sup>2</sup>ICB System for Biomedical Research, Boston, MA 02115, USA

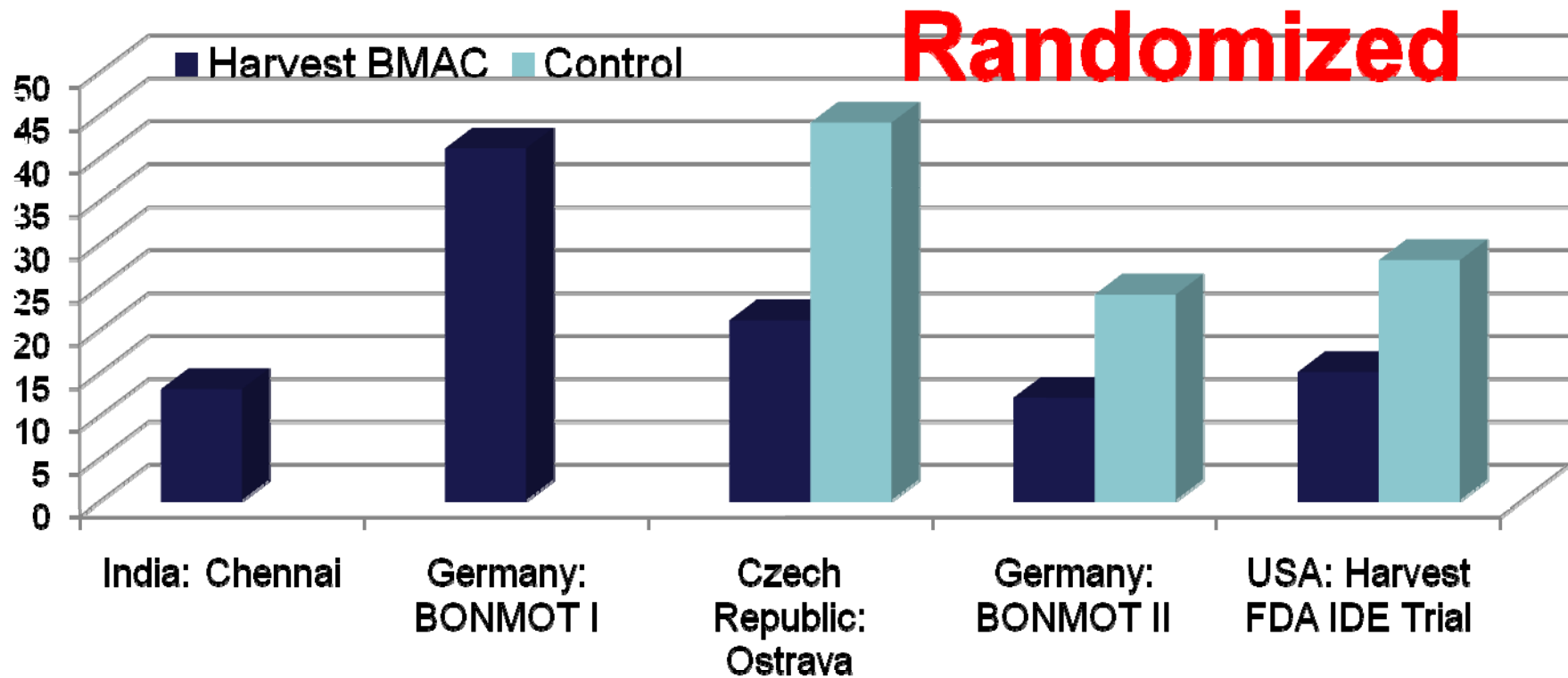
Abstract and introduction text from the article 'Concentration of Bone Marrow Total Nucleated Cells by a Point-of-Care Device Provides a High Yield and Preserves Their Functional Activity'.

Key words: Bone marrow; Point of care; Transcatheter; Ischemia; Cell therapy

# Bone Marrow Aspirate Concentrate [BMAC] Trials

## Amputation Rates

No Option Critical Limb Ischemia (CLI) Patient Population



# Wound Closure as Result of Treatment

Oxygen Pressure  
0 mmHg



3 mon. Oxygen Pressure  
52mmHg



# Wound Closure as Result of Treatment

2 Surgeries; Oxygen Pressure 5 MMHg

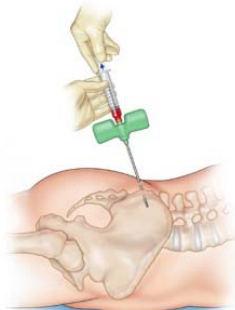


4 mon: Oxygen Pressure 37 MMHg



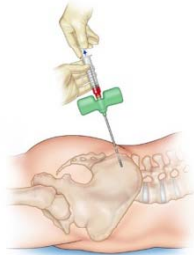
# FDA Pivotal: Randomized (2:1) double blind

**SALINE**



**ASPIRATE**

**PLACEBO**



210 Patient  
25 Center Study

**INVESTIGATOR BLINDED  
TO INJECTATE**



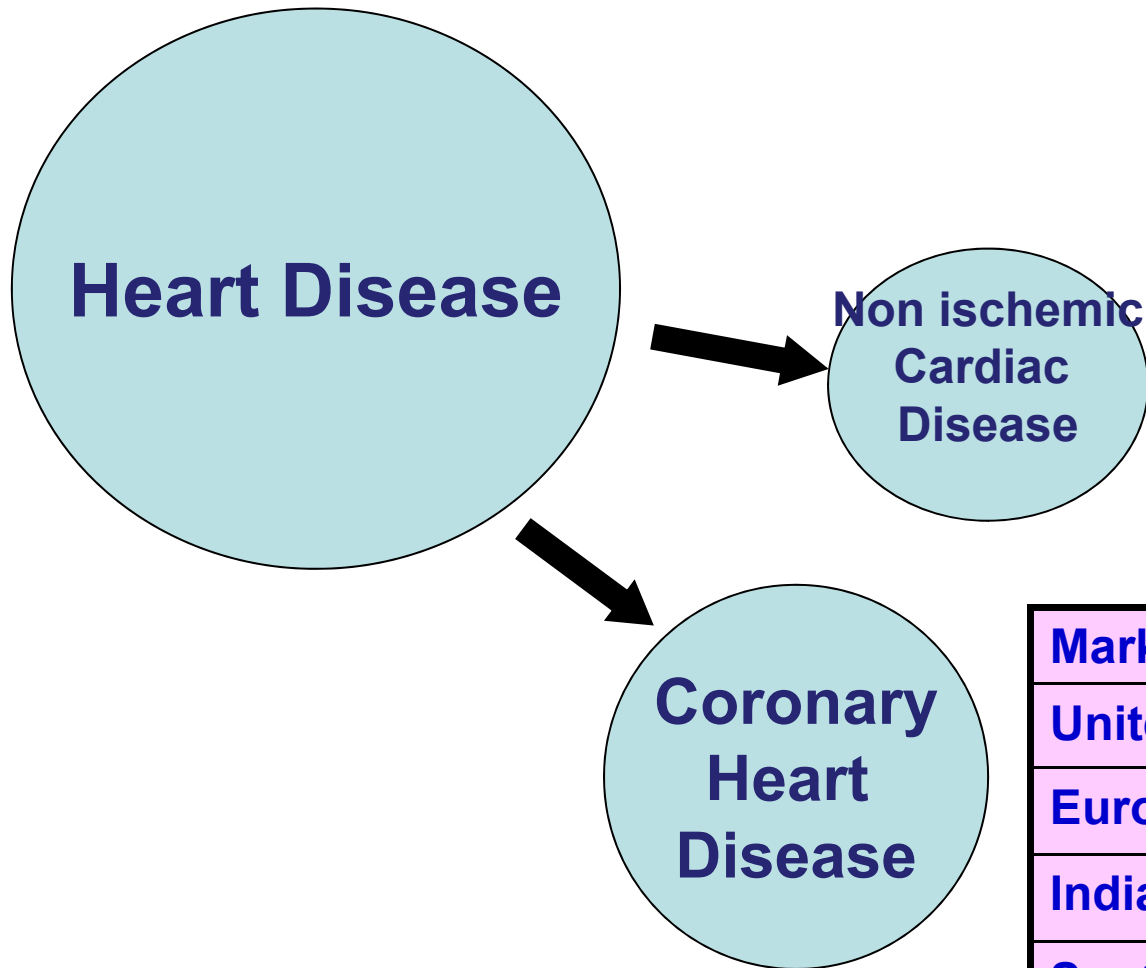
- 40 injections
- 1 mL per injection

3 year study  
Started 6/11

Expecting CE: FY 2011

# Initiative 2: Heart Failure

## Ischemic & Non-ischemic

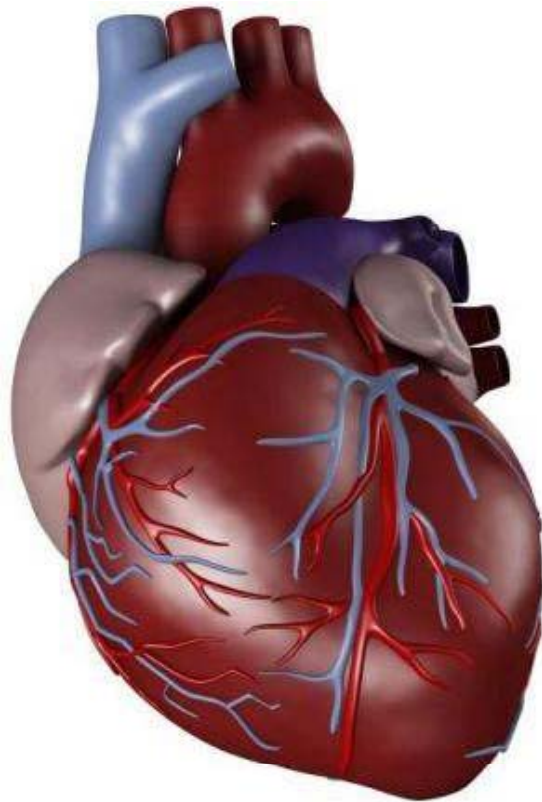


Market	Estimate
United States	5.8 million
European Union	6.8 million
India	3.1 million
South America	4.3 million
<b>TOTAL</b>	<b>20.0 million</b>

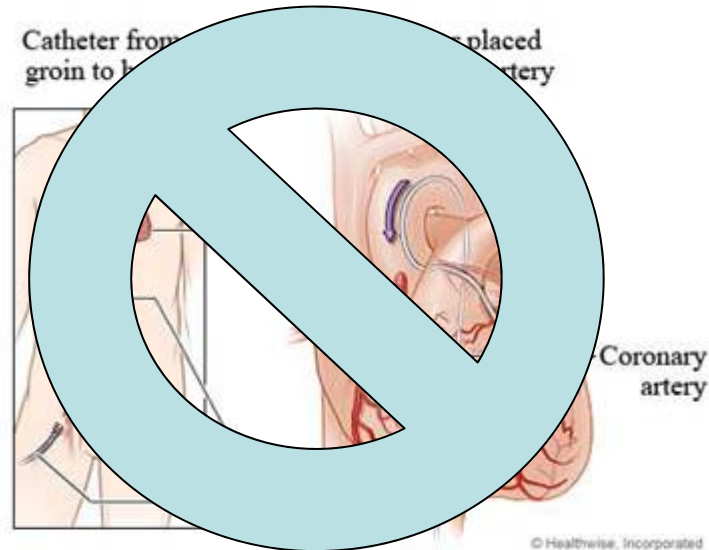
# Heart Failure Feasibility Study

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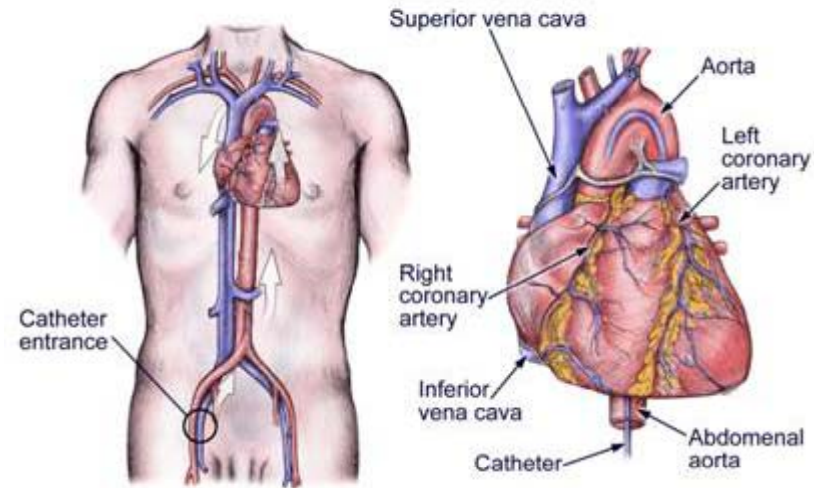
## Treating Congestive Heart Failure with BMAC infusion



# Unique Delivery Approach



**Antegrade Delivery**



**Retrograde Delivery**

## Retrograde Delivery

7 to 10 times more cells

Easier and safer approach

Cells longer contact with heart

Delivery into healthy versus unhealthy vessels

# Published Clinical Study

Trial of 40 patients with Heart Failure (ischemic and non-ischemic) with EF  $\leq$  25%. Treatment: bone marrow cells delivered by retrograde technique.

## Patient data with 1 year follow up: (Results sustained @ 4 years)

	IHF (n=20)	nIHF (n=19)
$\Delta$ LVEF (median, %)	10.0 (p<0,001)	20.1 (p<0,001)
$\Delta$ EDV (median, ml)	25.0 (p=0,10)	36.0 (p=0,23)
$\Delta$ ESV (median, ml)	43.0 (p=0,004)	42.0 (p=0,02)

**Conclusions:** Infusion of ABMMC into the coronary sinus is safe and feasible in terminal HF. It is associated with significant improvement in symptoms and functional capacity benefit in heart transplant list patients.

**TCT meeting Sep 2010**

# Heart Failure Retrograde Study

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## ■ 60 Patient Randomized Controlled Safety and Feasibility Study

- 60 Patients enrolled within FY2011
- Patient follow-up 6 months

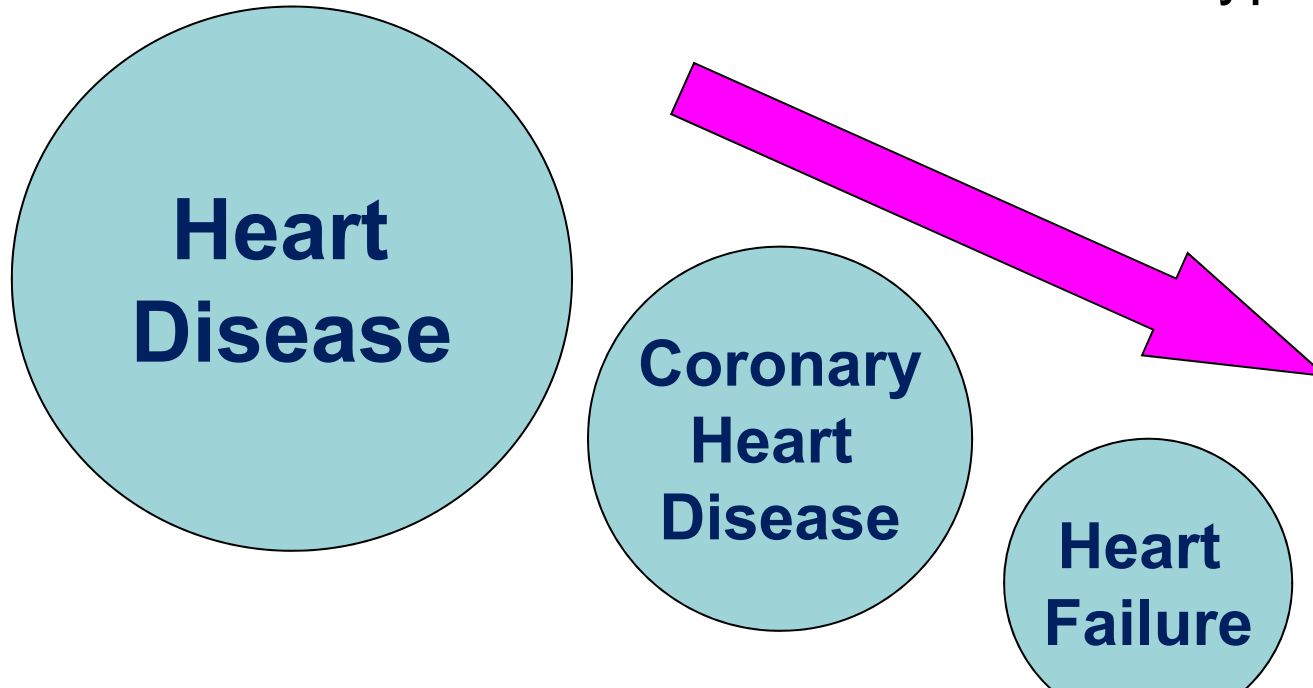
## ■ Study Objectives

- Provide safety and efficacy data for EU and US Trial
- EU & US Trial Starts – 2012
- 3 year trial US, approx 250 patients
- 2 year trial EU, 150 patients.

**Estimates**

# Initiative 3: Ischemic Heart Disease

Patients able to be treated with bypass surgery



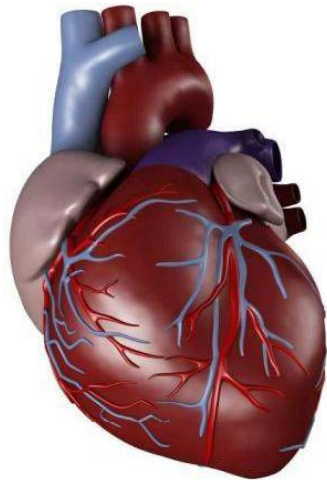
Market 2008	Estimate
United States	480000
European Union	400,000
India	120,000
<b>TOTAL</b>	<b>1,000,000</b>

# Enhanced CABG Study

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**Bypass Surgery and BMAC injections**

**BMAC Enhanced CABG (B.E.C.) Study**



# Off Pump Coronary Artery Bypass Grafting with STEM Cells

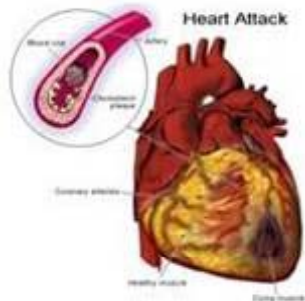
## Surgical treatment for congestive heart failure with autologous adult stem cell transplantation: A prospective randomized study



Amit N. Patel, MD, MS,<sup>a,b,c</sup> Luis Geffner, MD,<sup>b</sup> Roberto F. Vina, MD,<sup>b</sup> Jorge Saslavsky, MD,<sup>b</sup> Harold C. Urschel, Jr, MD,<sup>c</sup> Robert Kormos, MD,<sup>a</sup> and Federico Benetti, MD<sup>b</sup>

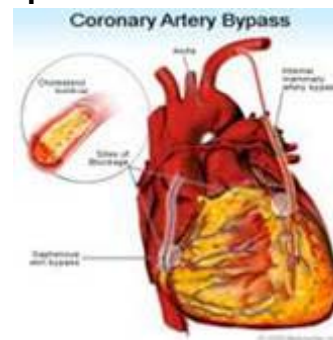
$p < .001$	OPCAB	OPCAB + stem cell therapy
N	10	10
Mean EF (%)		
Preoperative	30.7 ± 2.5	29.4 ± 3.6
1 mo	36.4 ± 2.6	42.1 ± 3.5*
3 mo	36.5 ± 3.0	45.5 ± 2.2*
6 mo	37.2 ± 3.4	46.1 ± 1.9*

Total Δ in EF: **6,5%**                      **16,7%**



$p < .001$	OPCAB	OPCAB + Stem Cells
NYHA Class Pre	3,4	3,5
NYHA Class Post	2,7	0,7

Classification Δ **,7**                      **2,8**



# **BMAC Enhanced CABG (B.E.C.) Study**

## **FDA Safety Study**

### ■ 40 Patient R/C Trial

- 5ml of BMAC
- 3 Clinical Sites
- 6 patient review by DSMB
  - 5/6 Patients Enrolled

### ■ 20 Patient Dose R/C Study

- 5 at 10ml; 5 at 15ml; 5 at 20ml; 5 control
- 20/20 patients enrolled
- Data complete Q1

Next steps: 1. Start EU study to expand approvals  
2. Consult with FDA

# *IR Contact*

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## **TERUMO Corporation**

**Corporate Communication (IR) Dept.**

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**The market share information in this presentation is partly derived from our own independent research.**