



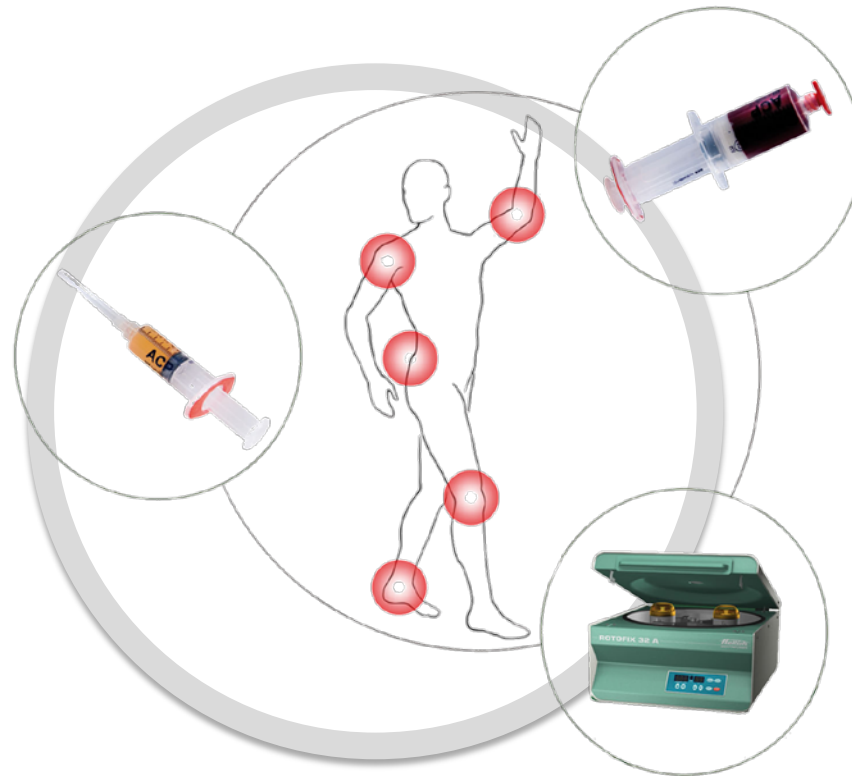
Helping
States
Strengthen
State-together-Art
Institutions
Improve
Performance
Better.



Arthrex[®]



ACP Therapy Basics





John Hunter
Anatomy –Legend
1728 – 1793

„don´t think , try“



Rita Levi-Montalcini

Discovered EGF and NGF
(50´s)
Nobelprice 1986

„The body does what he likes to do.
I´m not the body,
I´m the memory.“



Eduardo Anitua



PRP, PPP, ACP ???

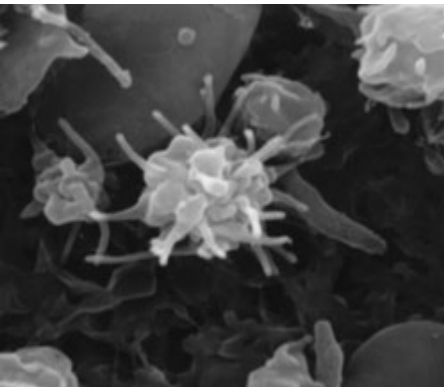
PRP = Platelet-Rich Plasma
describes a plasma product, which is produced using appropriate separation techniques (scientific umbrella term)

PPP = Platelet-poor plasma
plasma w/o thrombocytes / platelets

ACP = **A**utologous **C**onditioned **P**lasma,
tradename of Arthrex
ACP is a PRP



- ✓ Fragments of cytoplasm derived from megakaryocytes in bone marrow that exist between 5-9 days
- ✓ Do not contain a nucleus
- ✓ GF's effect confined to site of delivery
- ✓ Growth factors and other molecules help modulate healing and hemostasis



Alpha granules

■ Growth Factors

- More than 300 GF's in platelets along with other anabolic proteins

Dense Granules

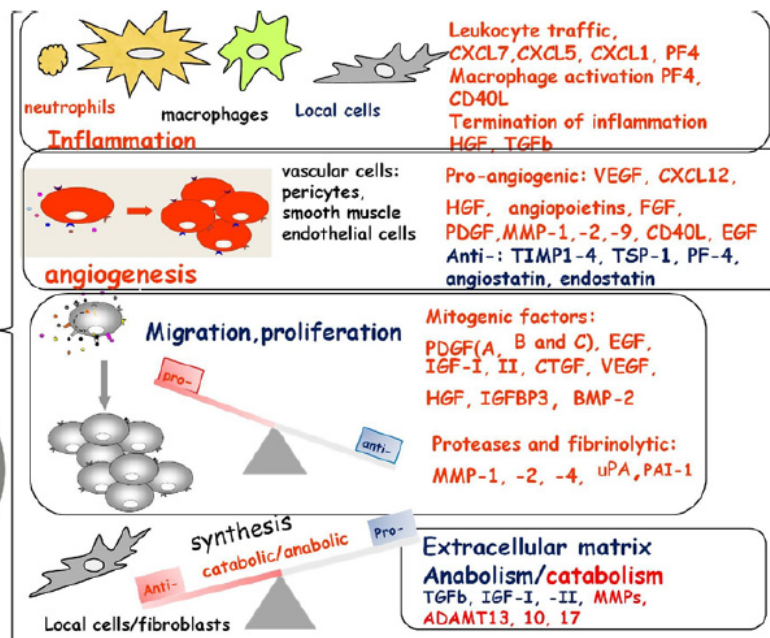
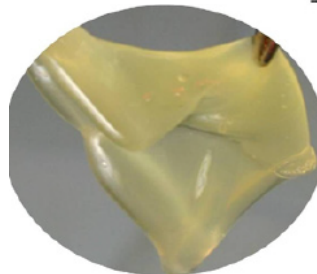
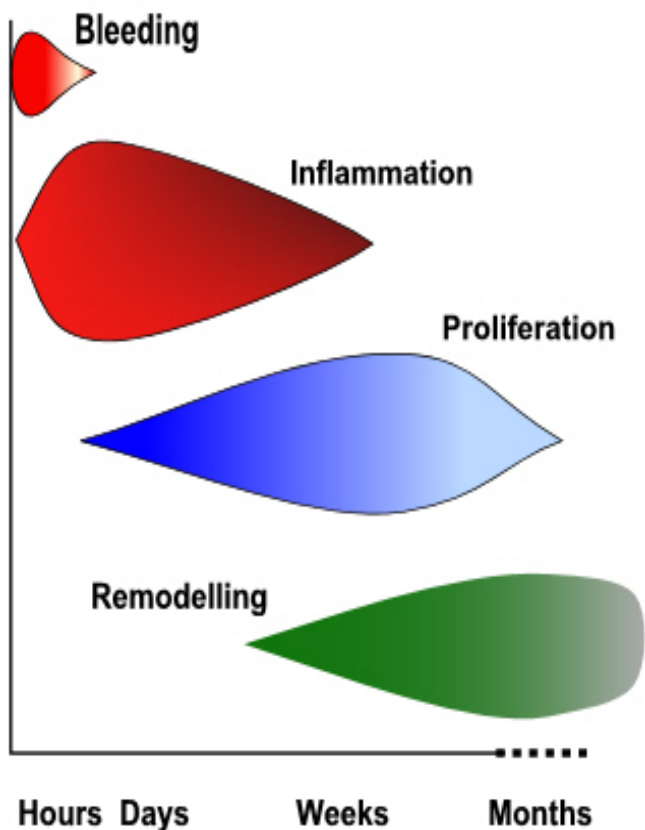
■ Serotonin, Histamine, Adenosine

All of these factors an important role in the three stages of healing:

- Inflammation
- Proliferation
- Remodeling

Stages of the Healing Process

Tissue Repair Phases and Timescale



Isabel Andia et al 2012

Growth Factors contained in Platelets (Gelse 2007)

Platelet derived growth factor (PDGF)

- Mitogenic for mesenchymal stem cells and osteoblasts; stimulates chemotaxis and mitogenesis in fibroblast/glia/smooth muscle cells; regulates collagenase secretion and collagen synthesis; stimulates macrophage and neutrophil chemotaxis.

Vascular endothelial growth factor (VEGF)

- Increases angiogenesis and vessel permeability; stimulates mitogenesis for endothelial cells.

Transforming growth factor-beta (TGF-B1)

- Stimulates undifferentiated mesenchymal cell proliferation, regulates endothelial, fibroblastic and osteoblastic mitogenesis; regulates collagen synthesis and collagenase secretion; regulates inhibits macrophage and lymphocyte proliferation.

Basic fibroblast growth factor (bFGF)

- Promotes growth and differentiation of chondrocytes and osteoblasts; mitogenic for mesenchymal stem cells, chondrocytes, and osteoblasts.

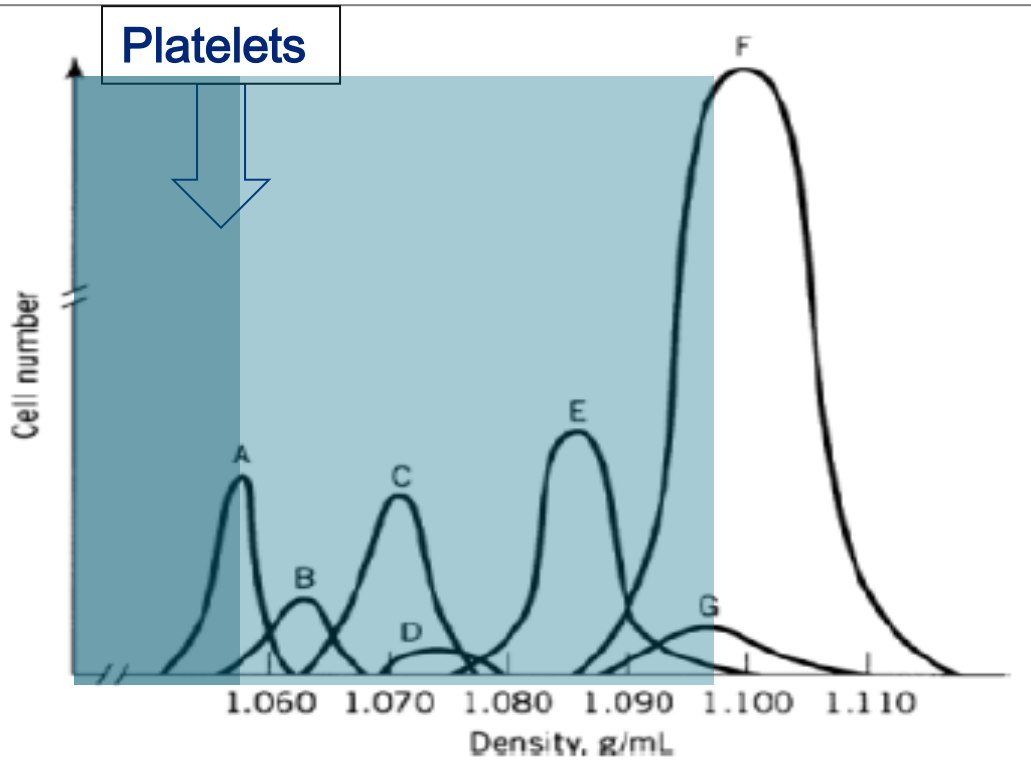
Epidermal growth factor (EGF)

- Stimulates endothelial chemotaxis/angiogenesis; regulates collagenase secretion; stimulates epithelial/mesenchymal mitogenesis.

Hepatocyte growth factor (HGF)

- Secreted by mesenchymal cells and targets and acts primarily upon epithelial cells and endothelial cells, but also acts on haemopoietic progenitor cells; has a role in embryonic organ development, in adult organ regeneration, and in wound healing.

How is it done ?



Mass density distribution of blood components:

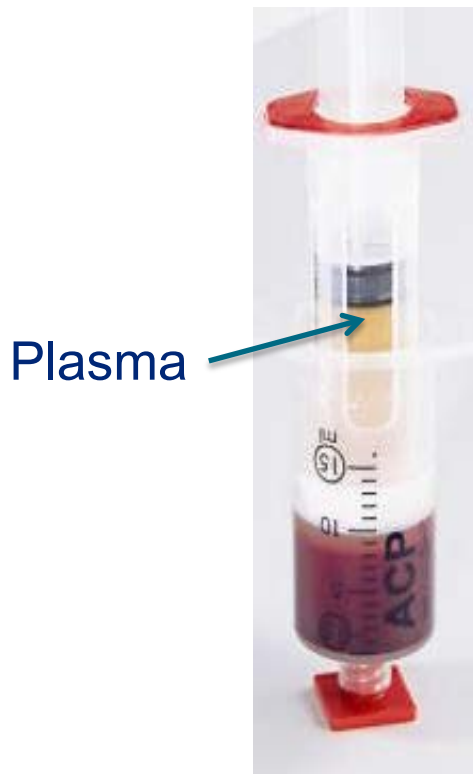
- A – Platelets,
- B – Monocytes,
- C – Lymphocytes,
- D – Basophils,
- E – Neutrophils,
- F – Erythrocytes,
- G – Eosinophils



PRP is obtained by utilizing centrifugation to separate Platelets (A) from other cell types. Due to the overlap and proximity of densities of Platelets and other cell types, specifically white blood cells, the possibility for contamination exists



Plasma versus Buffy Coat



Plasma based systems:
Arthrex ACP, MTF Cascade, PRGF

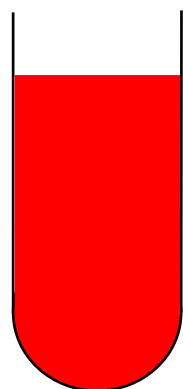


Buffy Coat based systems:
Biomet GPS, Recordati Genesis

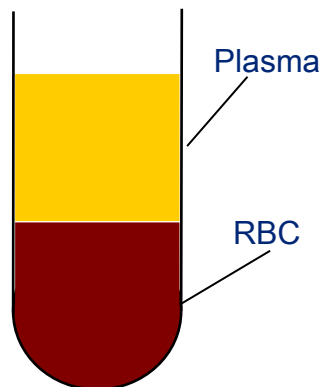
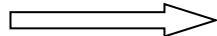
Normally two centrifugation steps with the end product being a Buffy-coat PRP layer

- PRP will contain increased concentration of platelets (4-6X)
- BUT, will also have increased concentration of WBCs (4-6X) and will contain RBCs
- Normally require 60-120cc of blood
- Anticoagulant is always required
- Procedure time (~ 30 minutes)

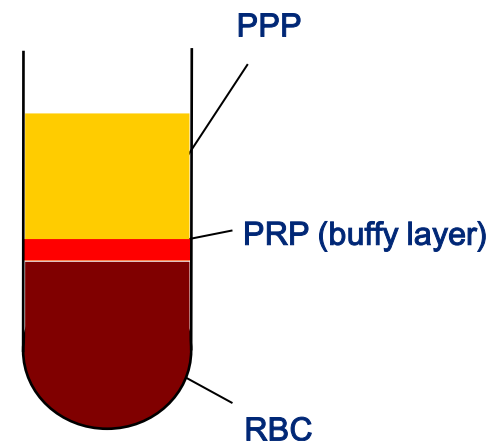
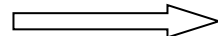
Blood + anticoagulant



1st centrifugation

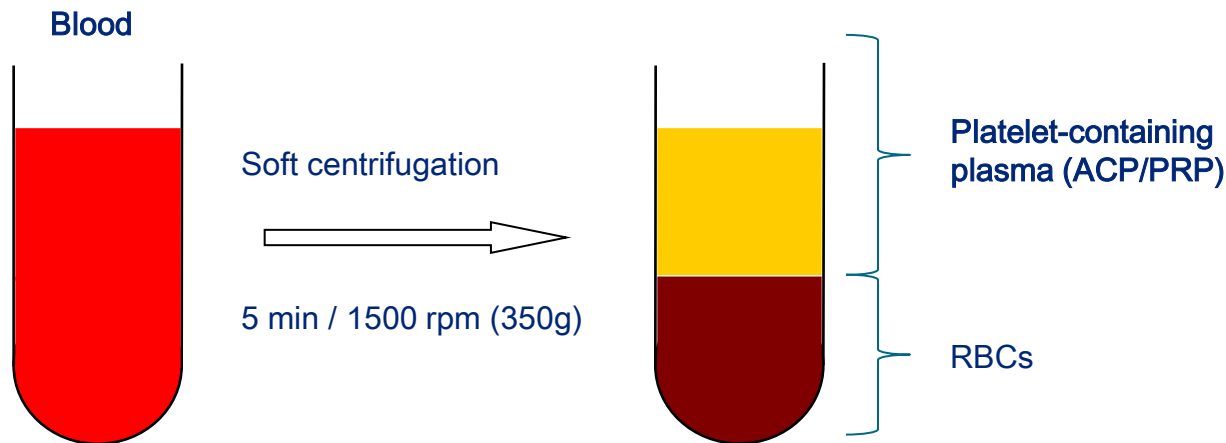


2nd centrifugation



Normally a single centrifugation step with the end product being the plasma containing plasma separated from WBCs and RBCs

- Easy to use system that concentrates platelets and growth factors within a plasma layer
- Separates out the red and white blood cells, minimizing the detrimental affects these cells can cause when concentrated at the injury site
- Growth factors and other molecules within the plasma layer may help modulate healing



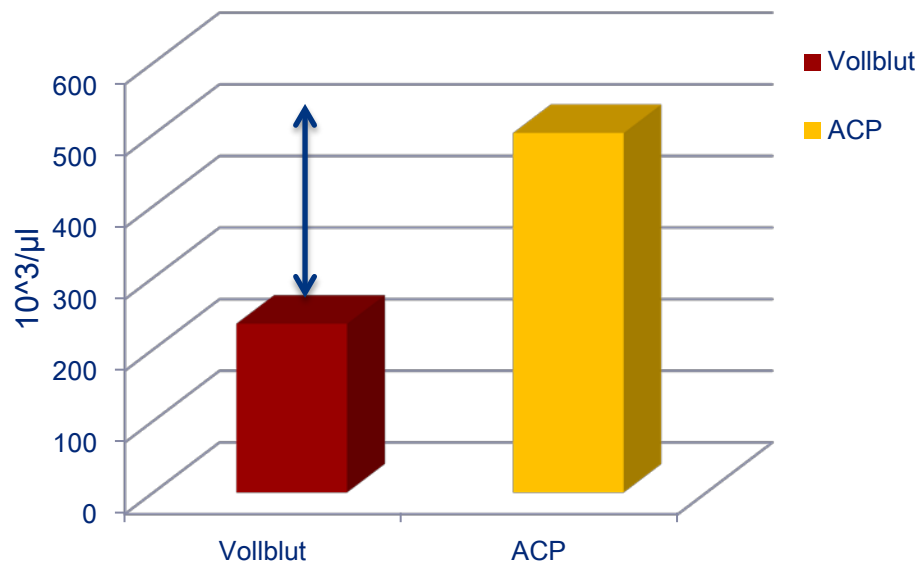
Frequently asked Questions

1. Concentration of Platelets
2. Concentration of WBCs
3. Activation of Platelets



ACP Specific

Platelet concentration 2-3x



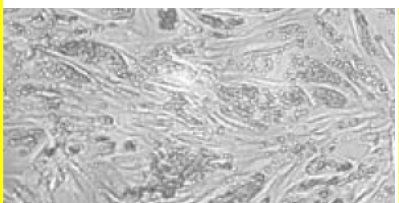
Effective Concentration ?

Tenocyte Proliferation

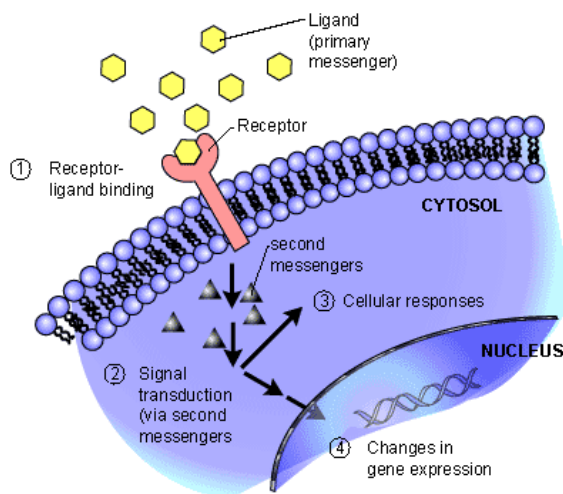


Positive Control

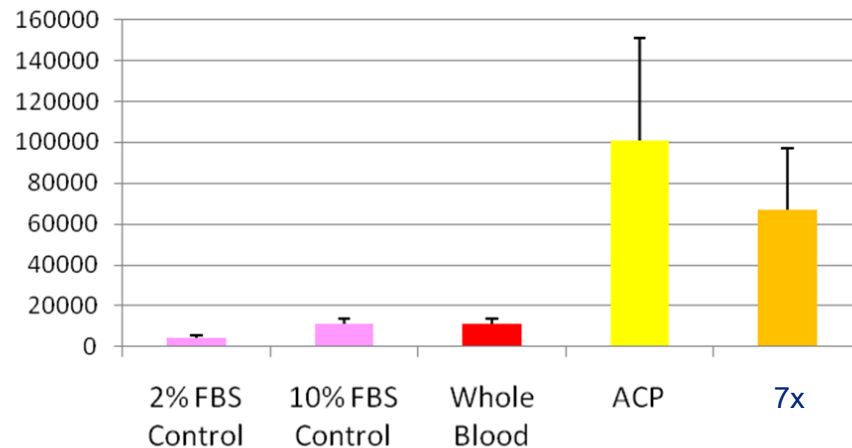
Tenocyte Proliferation



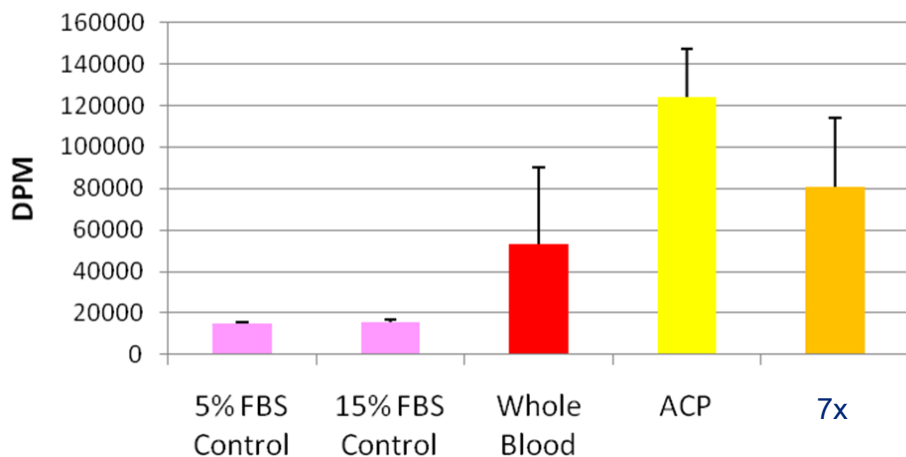
ACP



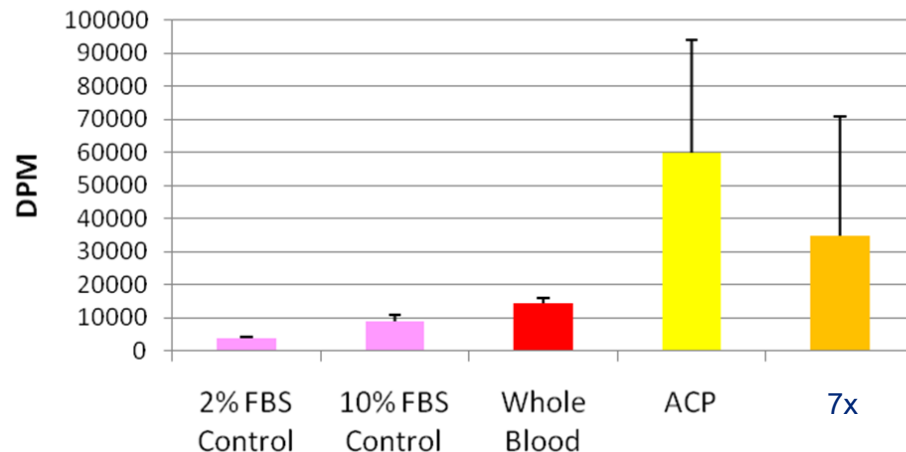
Tenocyte Proliferation



Osteoblast Proliferation

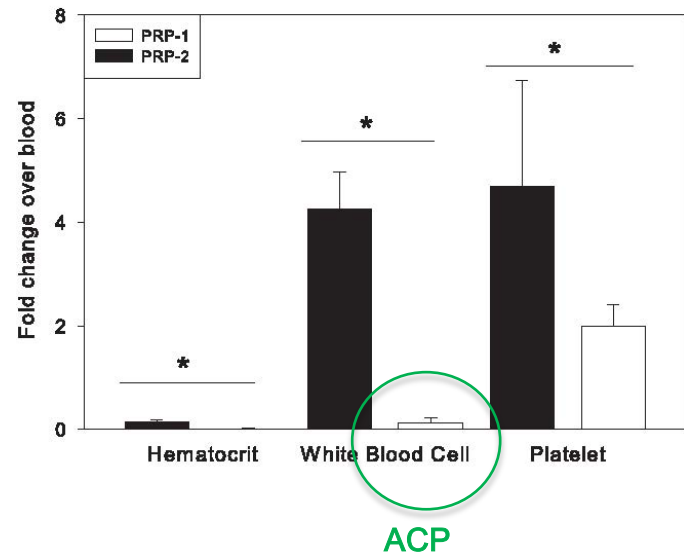
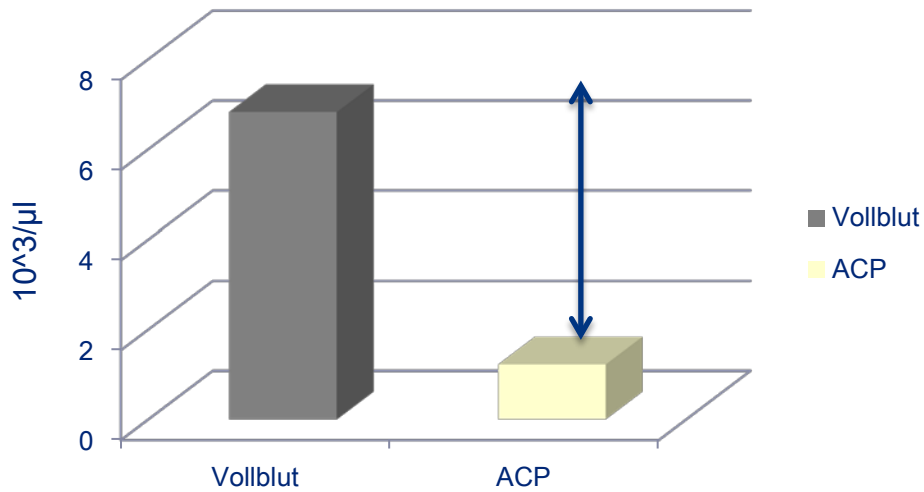


Myocyte Proliferation



ACP Specific

Low Concentration of WBCs



Concentrating WBCs is NOT Beneficial

	WBC Concentration	
	r	p
COL3A1	0.55	<0.01
COL1A1:COL3A1	-0.55	<0.01
COMP	-0.40	<0.01
Decorin	-0.34	0.02
MMP-3	0.65	<0.01
MMP-13	0.45	<0.01

Tendons cultured with plasma, BMA, PRP containing WBCs, and pure lyophilized platelets w/o WBCs

Increase in WBCs cause:

- More scar tissue (COL3)
- Less healthy tissue (COL1:COL3)
- Less matrix synthesis (COMP, Decorin)
- More matrix catabolism (MMP-3, MMP-13)



Activation of Platelets

- Exogen: Thrombin, Calciumchlorid
mech. Stress (centrifugation)

- Endogen: collagen in the tissue



Platelet



Activated Platelet

Update on platelet-rich plasma

JM. DeLonga, K Beitzelb, AD. Mazzoccab, D Shepard,

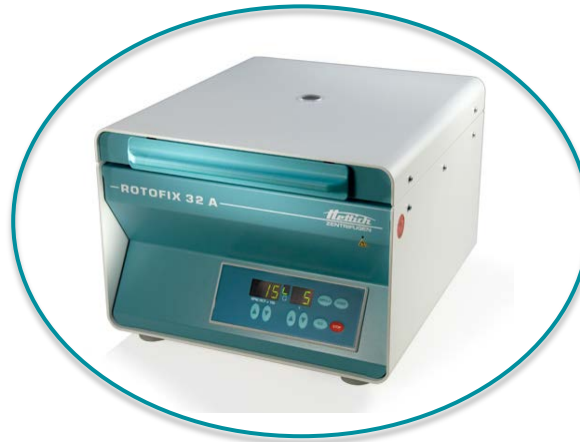
BL. Roller and BT. Hanypsiak, Current Orthopaedic Practice Volume 22 Nr 6, 2011

Products needed

ACP Double Syringe and **Centrifuge**
(Med. Device)



CE





The Idea

“2 Syringes in One”

- Single centrifugation step (slow spin)
 - Supernatant with Platelets
 - Time needed 15min.
-
- **Improved syringe**
 - **2 quick „Checks“**
 - ✓ prime large syringe
 - ✓ fix inner, small syringe

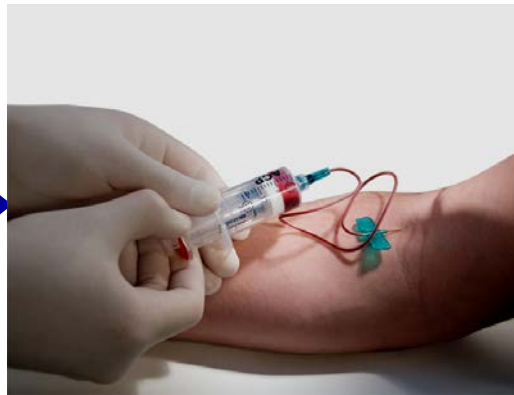


Procedure



Optional:

1,5 ml Anticoagulant
when used within 30 min.
not necessary



Blood withdrawal

15ml venous blood
Seal with red cap



Place double syringe into
the centrifuge
1500 rpm, 5 min

Procedure



To transfer the supernatant (ACP) slowly push down on the outer syringe while slowly pulling up the plunger of the small syringe

Unscrew small syringe and place needle on it
- ACP ready for use

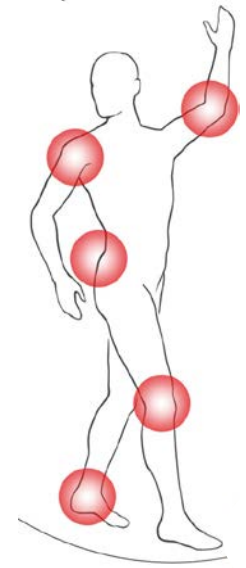


Effects / Impact

- accelerated regeneration time
- pain reduction
- improved function

OA Indication

- Alternative to HA
- > Cerza et al, 2012, Level I Study ACP versus HA
- > Patel et al, 2013, (Placebo)
- > Sanchez et al, 2012 , Level 1 Study



Indications

Acute

- **tendon injuries**
e.g. Achilles Tendon,
Rotator cuff
- **ligament injuries**
ACL, ankle ligaments
- **Muscle tears**
- Intra / Post Op
 - ✓ RC
 - ✓ Pain reduction after AC decomp.
 - ✓ Pain reduction after arthroplasty
 - ✓ MFX (Knee, Talus)
 - ✓ BioMatrix CRD
 - ✓ Meniscus Repair
 - ✓ ACL (partial or complete)



Chronic

- **arthrosis**
- **tendinopathies**
e.g. Patella tendon
Achilles tendon, Elbow
Plantar fasciitis



Usage

■ Number of Injections

Several authors show an improved effect after multiple injections

-> **Recommendation :**

2-5 ACP Injections depending on indication

Organe/Technik	Adjuvanz	Injektion Abstand	Injektion Häufigkeit	Anzahl der Nadeln
Knie i.a.		1/Woche	5x	1
Achillessehne	Bougierung Gleitgewebe mit NaCl	1/Woche	5x	3
Plantarfaszie		1/Woche	5x	1
Epikondylitis		1/Woche	5x	1
Patellaspitze		1/Woche	5x	1
intramuskulär		alle 2-3 Tage	bis zu 5x	5-7

Tab.: Behandlungsschema mit ACP bei unterschiedlichen Indikationen

Klein et al, Jatro July 2012

Mazzocca AD. Biological healing enhancement in shoulder surgery using autologous growth factors. 14th ESSKA Congress 2010, Oslo
DeLong et al., Update on platelet-rich plasma, Current Orthopaedic Practice 2011

■ Combination corticosteroids or local anaesthetics

In vitro positive effect of PRP on cells significantly reduced

Recommendation : -> ACP Injection w/o local anaesthetics

-> time interval to corticosteroid injection



HELPING SURGEONS TREAT THEIR PATIENTS BETTER

WADA Guidelines

Approval for PRP products such as ACP ist

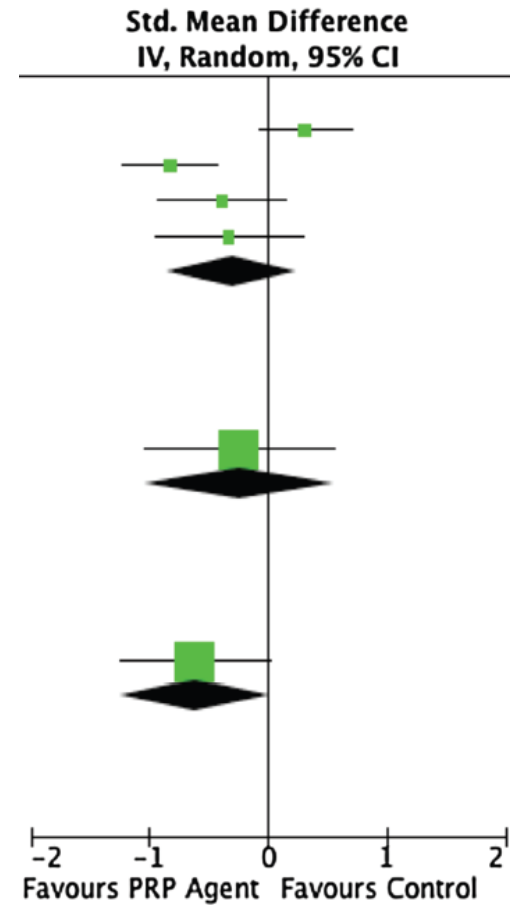
If controlled Athlete has to declare usage



Literature ?

Sheth et al (J of Bone and Joint Surgery, 2012)

MEDLINE , Embase
23 RT, 10 pros. cohort studies





Arguments for ACP

✓ Positive Effect

- ➔ Optimized composition
 - ✓ 2-3 x Platelets concentration
 - ✓ Minimal concentration of WBCs
 - ✓ No exogene Activation

✓ Closed System

- ➔ Single -use
- ➔ Sterile
- ➔ Safe

✓ Ease to use, patient friendly



Thank you very much !



Back Up

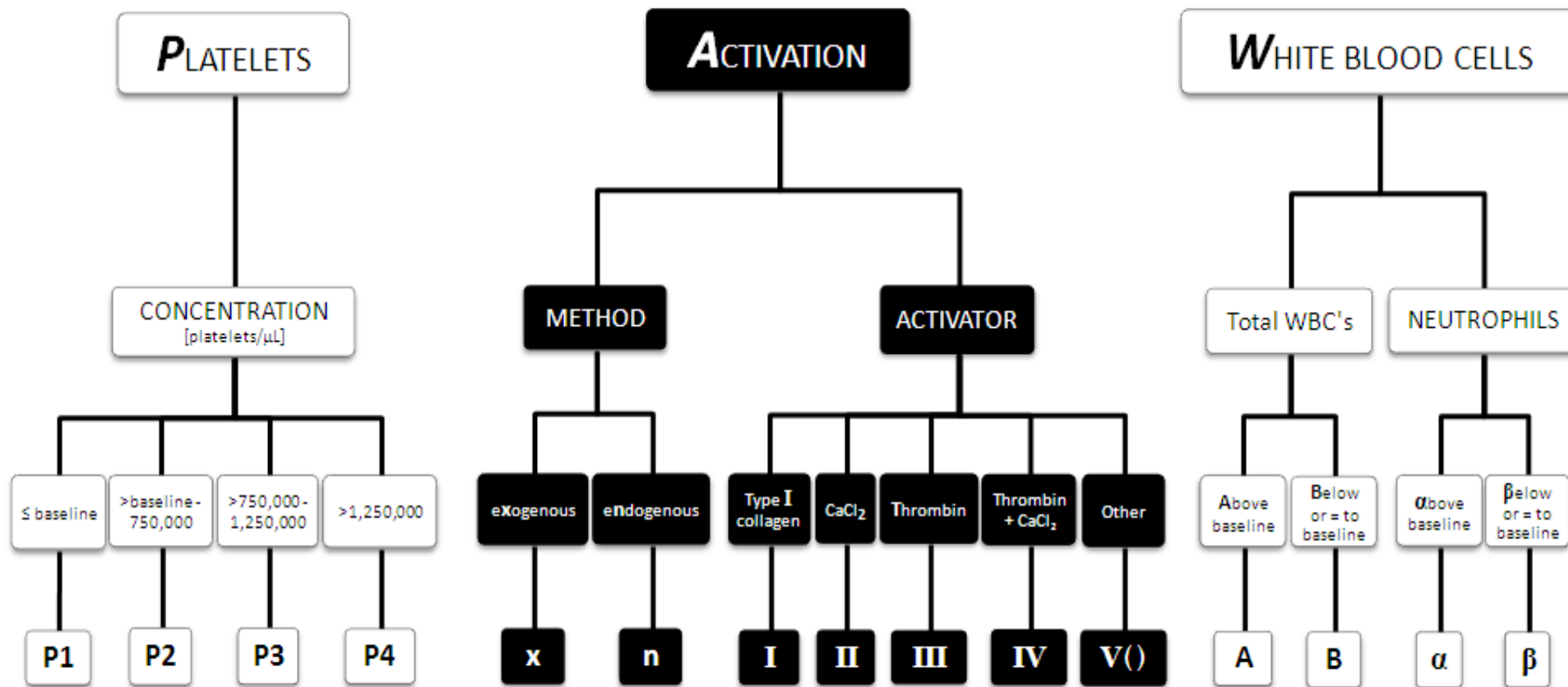
Mishra PRP Classification System

	White Blood Cells	Activation?	Platelet Concentration
Type 1	Increased	No Activation	A: 5x or > B: < 5x
Type 2	Increased	Activated	A: 5x or > B: < 5x
Type 3	Minimal or No WBCs	No Activation	A: 5x or > B: < 5x
Type 4	Minimal or No WBCs	Activated	A: 5x or > B: < 5x
Type 5	Not Reported	Not Reported	Not Reported

Dr. Allan Mishra (Presented at WOS meeting 2010)

ArthroIt can get VERY complicated

HELPING SURGEONS TREAT THEIR PATIENTS BETTER



A true view of the possible iterations

Blood Banks = 2X

Marx's definition of PRP concentration

- Often incorrectly quoted as dogma
- Whole blood baseline – $1.5 - 2 \times 10^5$ platelets / μL
- Minimum 1×10^6 platelets / μL = **5x PRP**

Anitua's definition of platelet concentration

- Minimum 3×10^5 platelets / μL = **2x PRP**
- Drs. Anitua and Sanchez have been researching PRP for >10 yrs
 - >20 publications on PRP alone, based out of Spain
 - PRGF system: ~2X platelets, minimal WBCs and RBCs; proven clinical efficacy

High concentrations (6-11x) may have a paradoxically inhibitory effect on bone regeneration (osteoblast activity)¹

Viability and proliferation of cells was suppressed by high concentrations but increased by moderate concentrations.²

Optimal fibroblast and osteoblast proliferation with 2.5x PRP³

- Compared with plasma, 1x PRP, 3.5x PRP, 5x PRP

1. Weibrich G et al. Effect of platelet concentration in platelet-rich plasma on peri-implant bone regeneration. *Bone* 2004; 34(4): 665-671.

2. Choi et al. Effect of PRP concentration on the viability and proliferation of alveolar bone cells. *Int J Maxillofac Surg*. 2005

3. Graziani F et al. The in vitro effect of different PRP concentrations on osteoblasts and fibroblasts. *Clin Oral Impl Res* 2006; 17: 212-219.