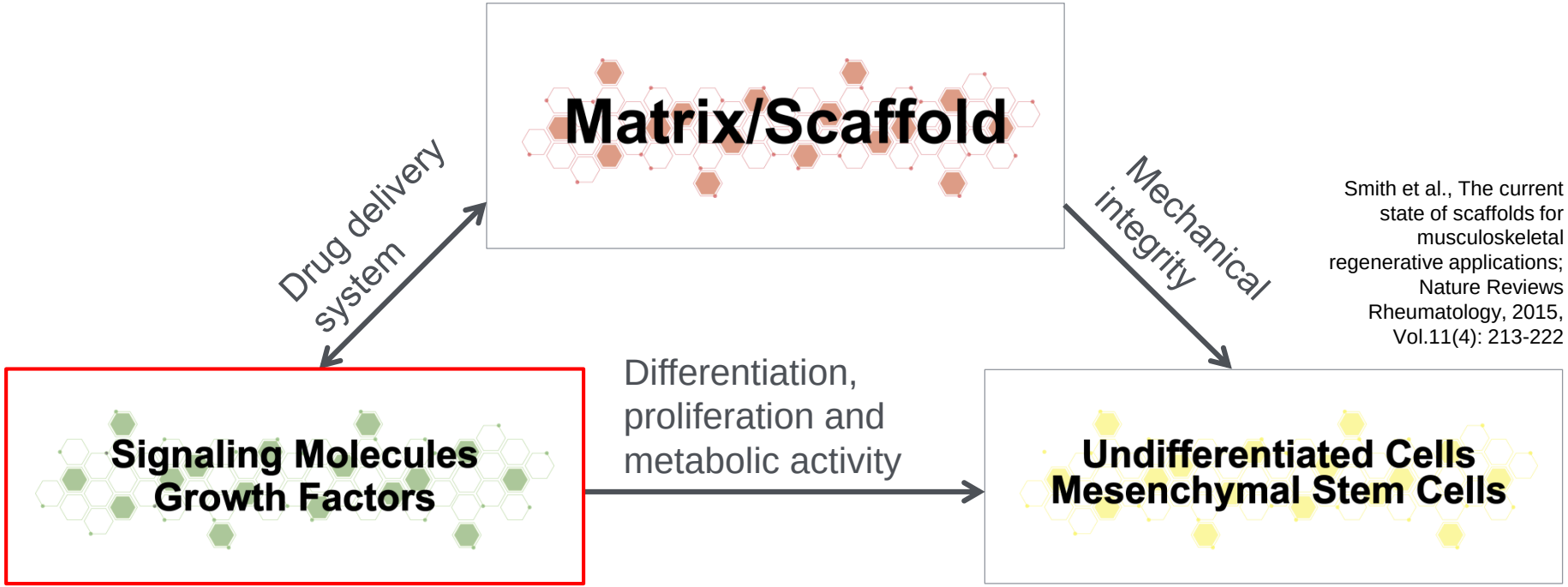
ACP/PRP – Present knowledge and evidence

ACP Tendo, New Generation of Tendon Healing

Sabine Schaumann

Arthrex®

Orthobiology
Healing Triad



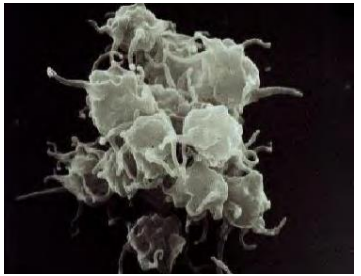
Smith et al., The current state of scaffolds for musculoskeletal regenerative applications; Nature Reviews Rheumatology, 2015, Vol.11(4): 213-222

Healing Triad
Platelets – Source of Growth Factors

High Concentration of Platelets Found in:
Bone Marrow
Whole Blood

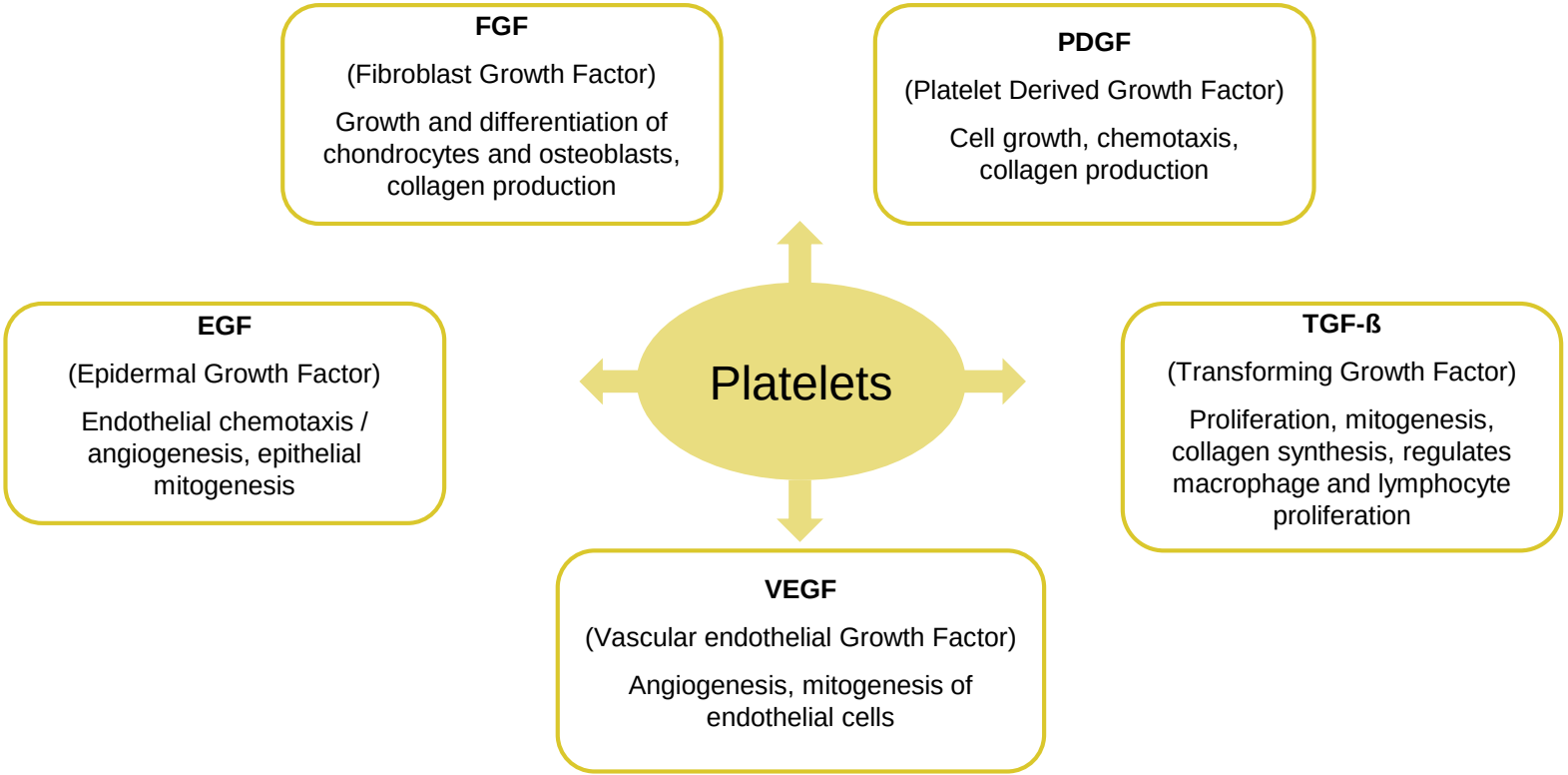
Platelets Contain ~4000 Proteins
α-granules: > 300 different growth factors
D-granules: serotonin, ADP

Activation



Rubio-Azpeitia, Andia et al., Partnership between platelet-rich plasma and mesenchymal stem cells: in vitro experience; Muscles, Ligaments and Tendons Journal, 2014, Vol.4(1):52-62

Growht Factors in Platelets



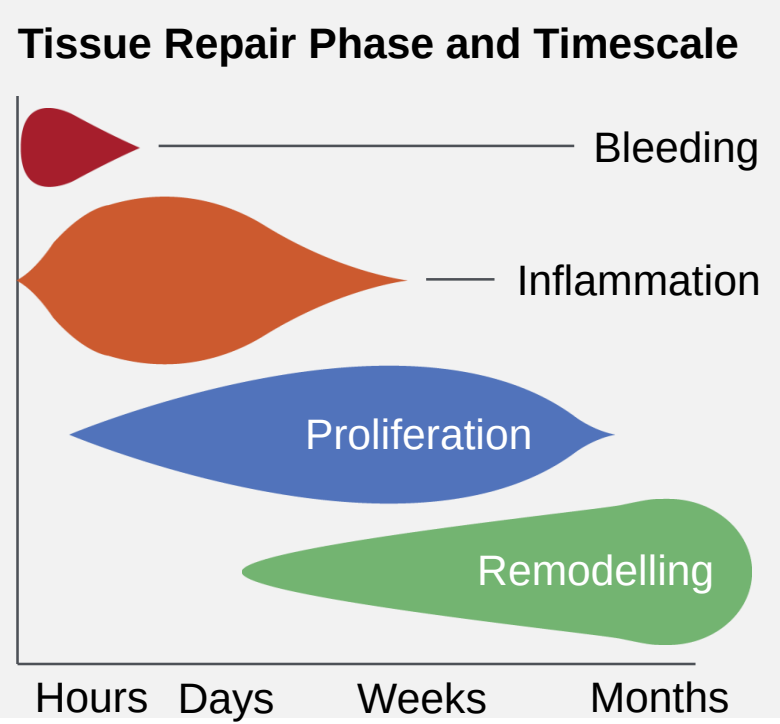
Growth Factors in Plasma

679 proteins documented

- Fibronectin, fibrin, vitronectin
  - ➢ promotion of chemotaxis of stem cells
- Plasma calcium
  - ➢ activator, regulator for extracellular reactions
- Hormones, IGF-1
  - ➢ enhance tendon and cartilage healing
- Glucocorticoids
  - ➢ decrease production or activity of inflammatory mediators

Boswell et al.: „Platelet-Rich Plasma: A Milieu of Bioactive Factors”, Arthroscopy 2012

Healing Cascade – Role of Platelets / Growth Factors



Inflammation

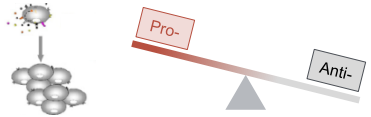
Leukocyte traffic,
CXCL7, CXCL5, CXCL1, PF4
Macrophage activation PF4, CD40L
Termination of inflammation HGF, TGFb

angiogenesis

Vascular cells:
pericytes, smooth muscle
endothelial cells

Pro-angiogenic: VEGF, CXCL12, HGF, angiopoietins, FGF, PDGF, MMP-1, -2, -9, CD40L, EGF
Anti-: TIMP1-4, TSP-1, PF-4, angiostatin, endostatin

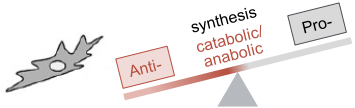
Migration, proliferation



Mitogenic factors:
PDGF (A, B and C), EGF, IGF-I, II, CTGF, VEGF, HGF, IGFBP3, BMP-2

Proteases and fibrinolytic:
MMP-1, -2, -4, uPA, PAI-1

Local cells/fibroblasts



Extracellular matrix
Anabolism/catabolism
TGFb, IGF-I, -II, MMPs, ADAMT13, 10,17

Andia et al.: Basic Science: Molecular and Biological Aspects of Platelet-Rich Plasma Therapies, Oper Tech Orthop, 2012

Inflammation to Proliferation

Secretion of cytokines
- e.g. CXCL-7-precursor
- Chemoattractant and activator for neutrophils

Trafficking of Leukocytes and Monocytes
- PF 4
- Prevention of monocyte apoptosis, promotion of macrophage differentiation

Dying cell removal / matrix destruction

Secretion of cytokines
- HGF, VEGF, TGF-ß
- Restoring cells to noninflammatory phenotype

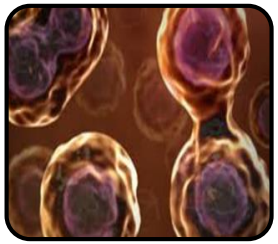
Decrease pro-inflammatory proteins / increase anti-inflammatory proteins
- HGF
- Decrease of IL-6 ←→ Increase of IL-10
  Inhibits NFκB

Termination of the inflammation

HGF is primarily found in plasma – consider ratio of platelets to plasma in your PRP

Andia et al.: Basic Science: Molecular and Biological Aspects of Platelet-Rich Plasma Therapies, Oper Tech Orthop, 2012

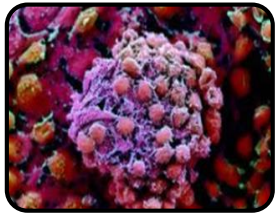
Proliferation



Fibrinolytic Factors

(e.g. uPA)

- Regulation of pericellular environment
- Modify pathways that impact proliferation / migration



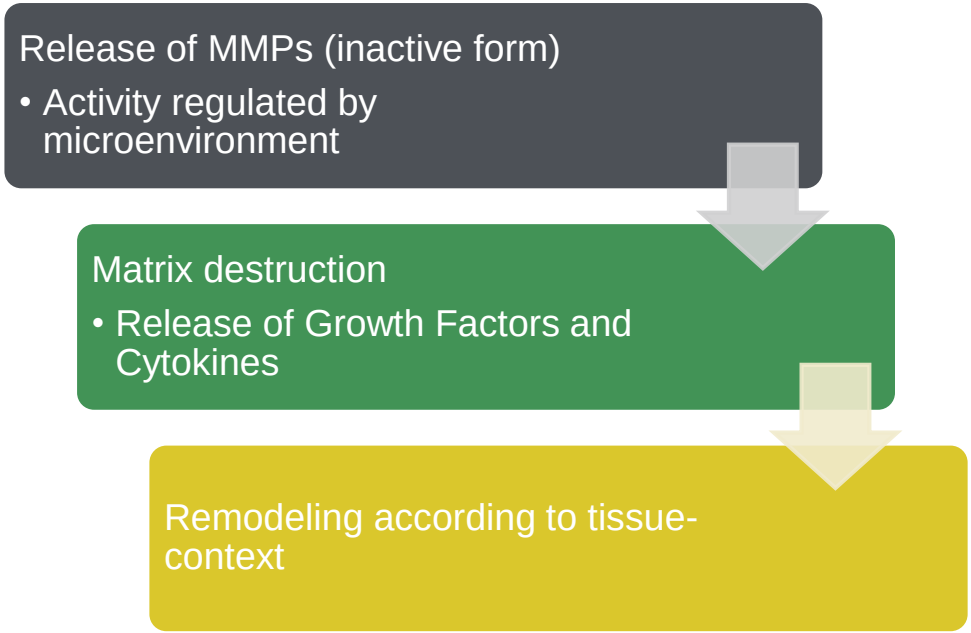
Growth Factors

(e.g. TGF-ß, IGF, FGF)

- Induce differentiation of progenitor cells
- Induce angiogenesis

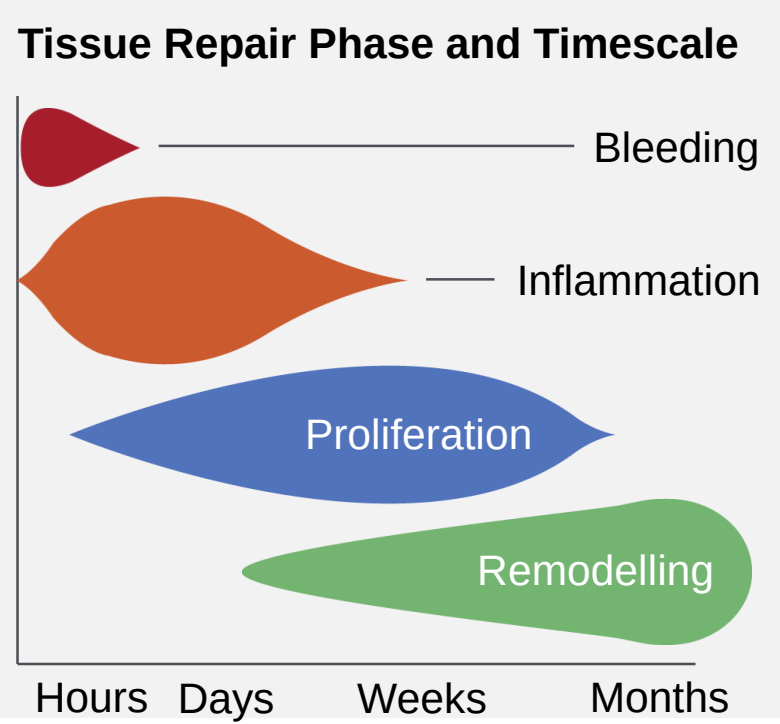
Andia et al.: Basic Science: Molecular and Biological Aspects of Platelet-Rich Plasma Therapies, Oper Tech Orthop, 2012

Remodeling



Andia et al.: Basic Science: Molecular and Biological Aspects of Platelet-Rich Plasma Therapies, Oper Tech Orthop, 2012

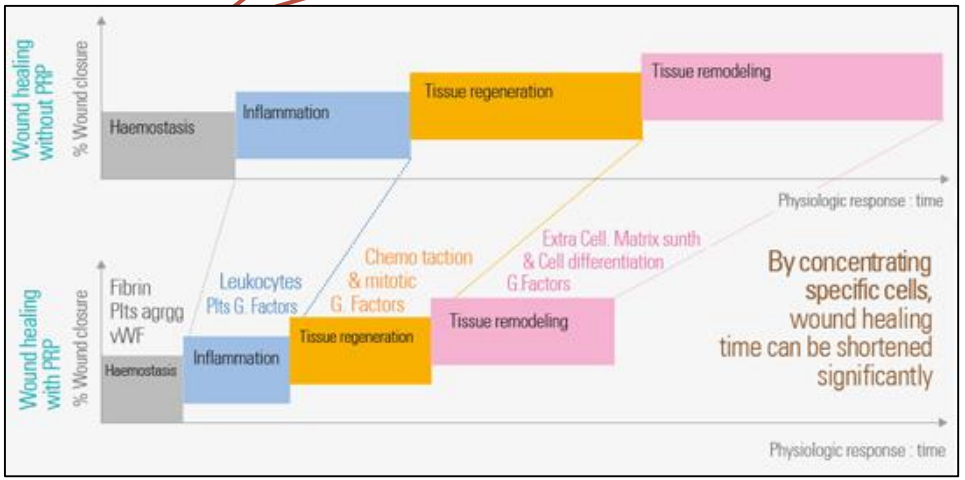
PRP – Mode of Action



Goal:

Create a „Healing Cocktail“ for enhanced tissue repair

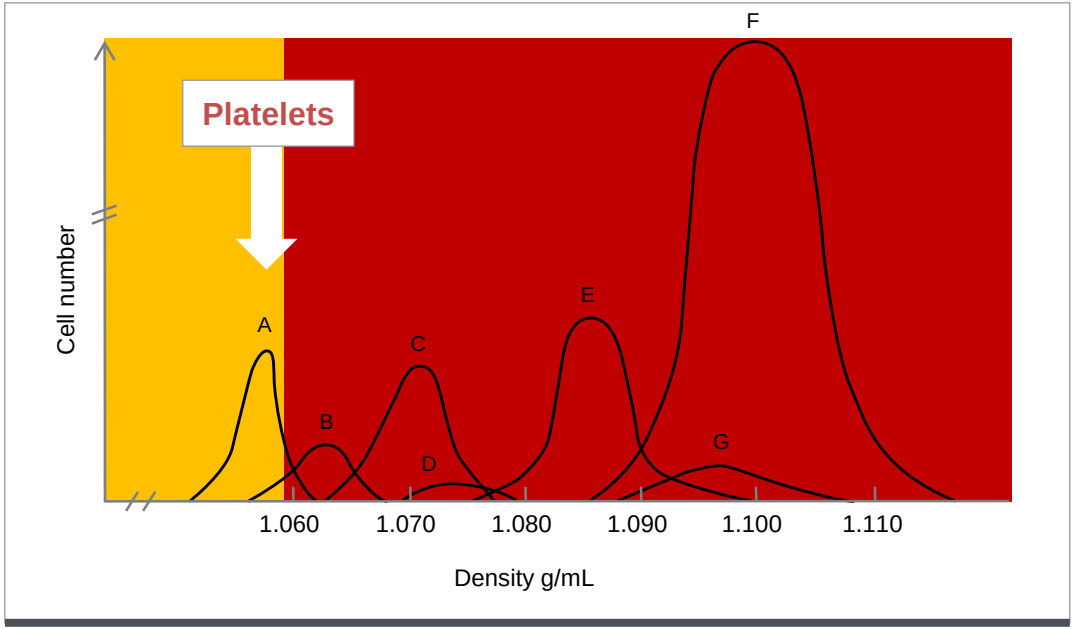
PRP = Platelet Rich Plasma



Arthrex

PRP – How is it done and what to consider?

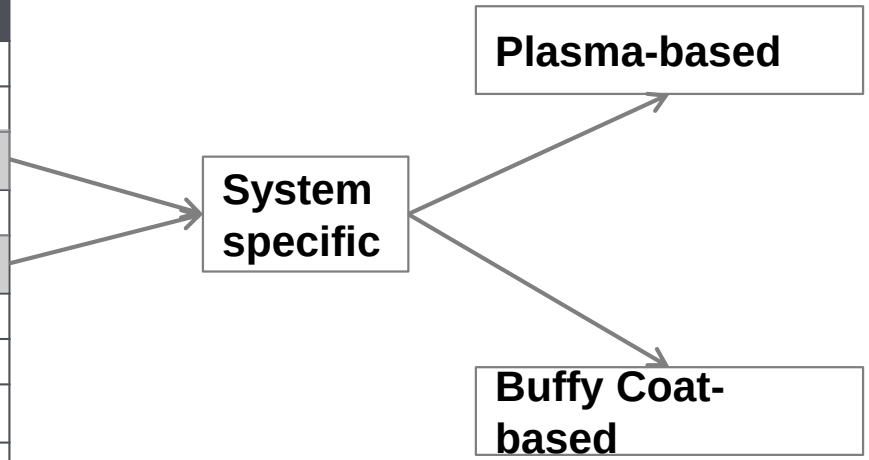
Mass density distribution of blood components
A – Platelets
B – Monocytes
C – Lymphocytes
D – Basophils
E – Neutrophils
F – Erythrocytes
G – Eosinophils



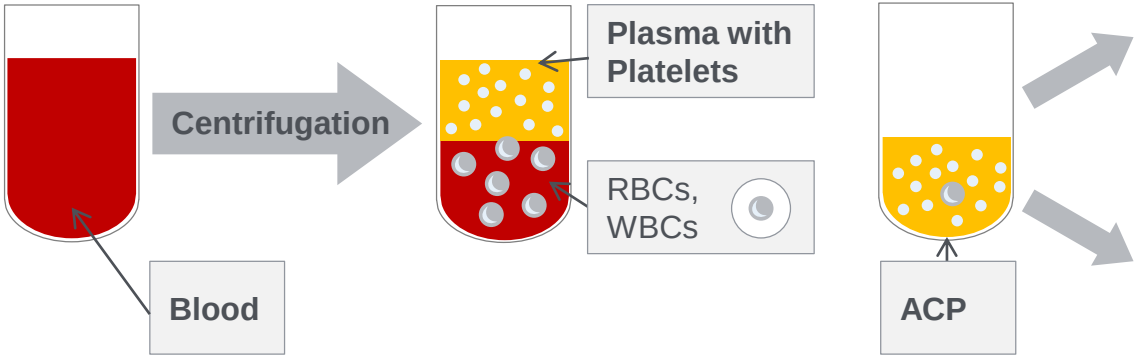
Frequently asked questions

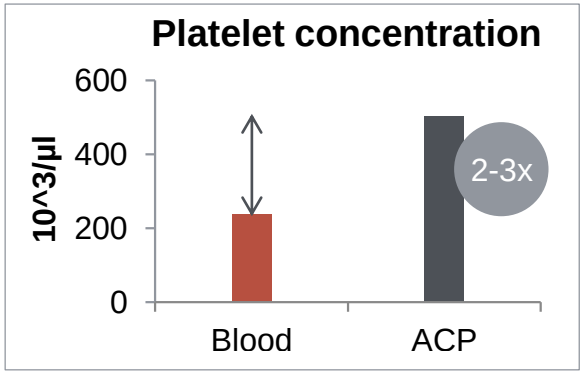
TABLE 1 Variables in PRP treatment
Preparation method
Needle gauge for blood harvest and injection
Platelet concentration
Platelet granule secretion (e.g., GFs)
Leukocyte (and subtype) concentration
Platelet storage (vs. Immediate injection)
Anticoagulant use
Platelet preactivation
Local anesthetic use
Palpation vs. Image guidance
Injection volume
Injection frequency
Preinjection and postinjection protocol (e.g., NSAID/activity restriction)
Type and severity of disease being treated
Patient-specific factors (e.g., age, sex, platelet disorders)

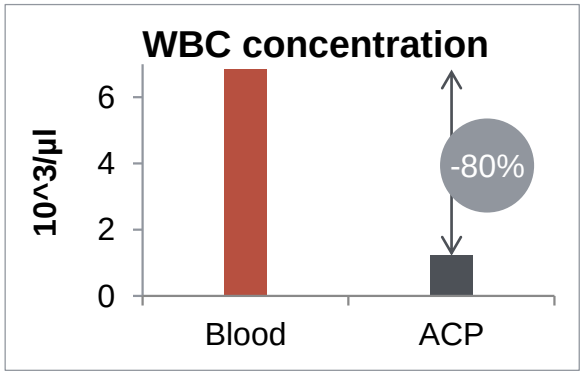
Pourcho et al., 2014



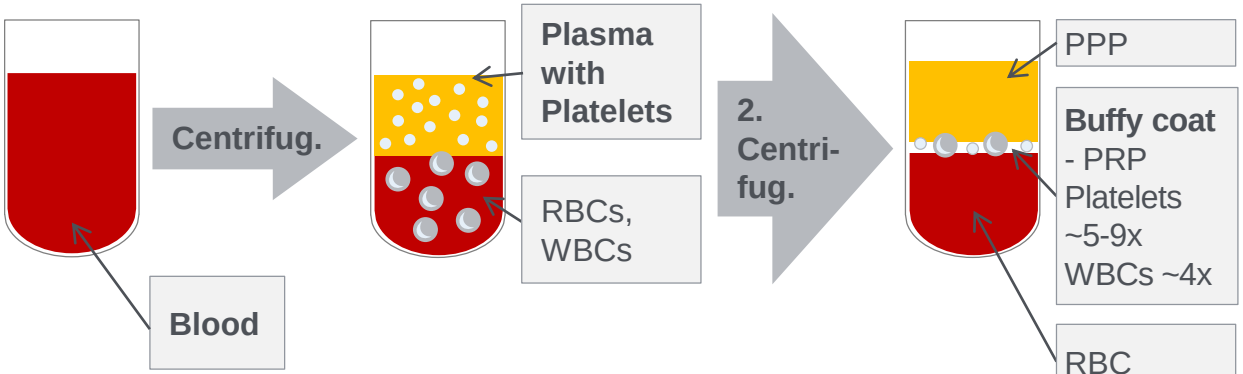
Plasma-based PRP

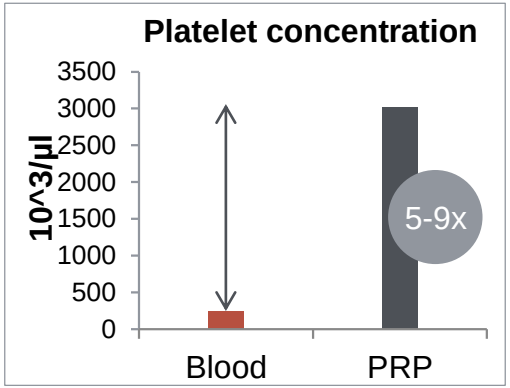


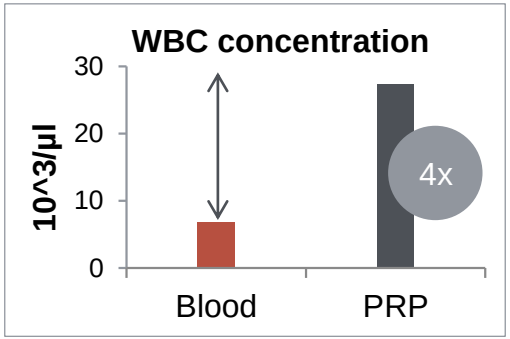




Buffy-coat PRP

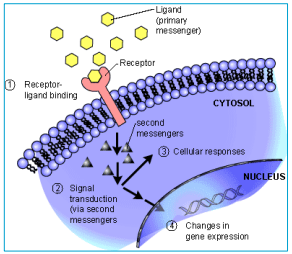




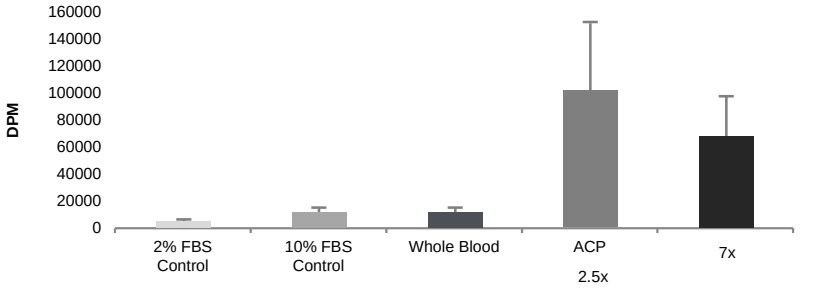


1. Platelet concentration

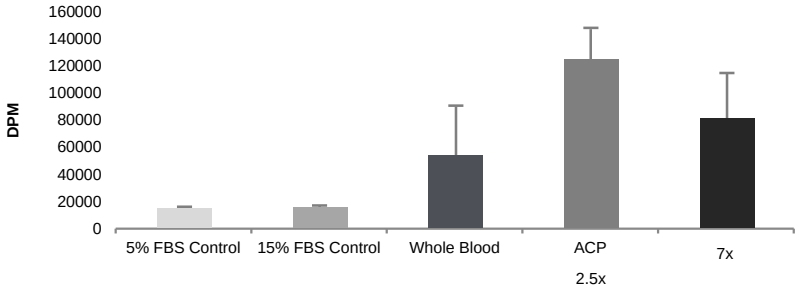
2. Leukocyte concentration



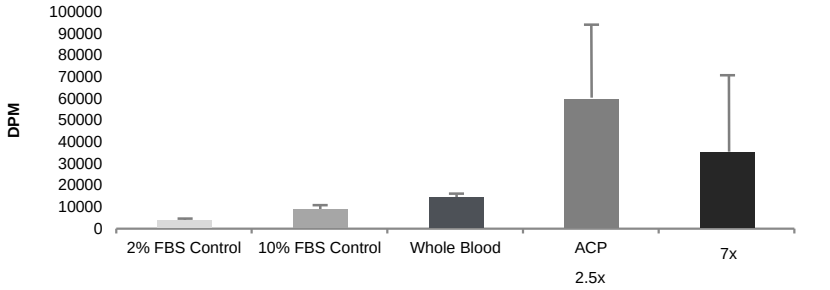
Tenocyte Proliferation



Osteoblast Proliferation



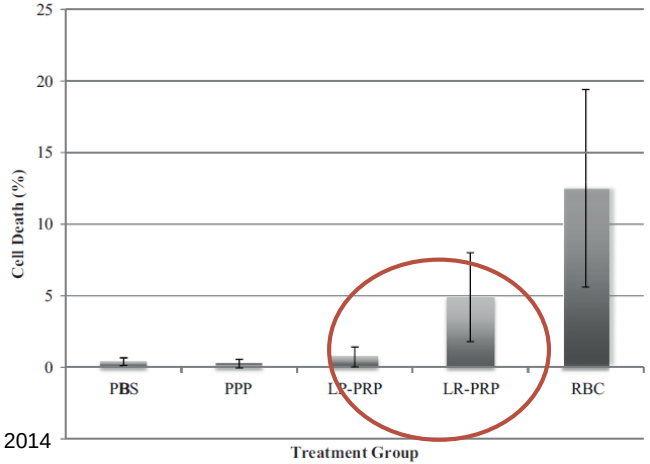
Myocyte Proliferation



Mazzocca et al., ESSKA 2010

1. Platelet concentration
2. **Leukocyte concentration**

„The Effect of Platelet-Rich Plasma Formulations and Blood Products on Human Synoviocytes”



Braun et al., 2014

- Treatment of synovial cells with **leukocyte-rich PRP and red blood cells resulted in significant cell death** and proinflammatory mediator production
- “Clinicians should consider using leukocyte-poor, red blood cells-free formulations of PRP when administering intraarticularly”

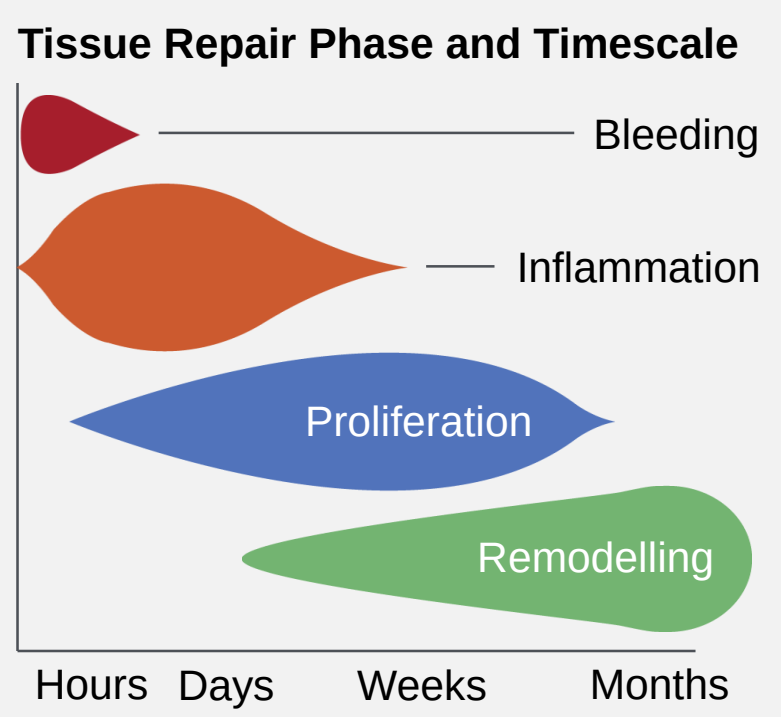
1. Platelet concentration
2. **Leukocyte concentration**

- Leukocytes increase signal molecules for catabolic processes
- When activated, neutrophils release non-specific, toxic agents [1,2,3]
- The toxic agents will destroy everything in contact, injured or healthy
- Neutrophils can delay its regenerative capabilities and healing capacity[4]
- Neutrophils cause destruction of muscle through cytotoxic effect[5]

➢ **Concentrated WBCs at the site of injury may be detrimental toward the healing progression**

1. Diegelmann RF et al. Wound healing: an overview of acute, fibrotic and delayed healing. Front Biosci 2004; 9: 283-9.
2. Martin P et al. Inflammatory cells during wound repair: the good, the bad and the ugly. Trends Cell Biol 2005; 15(11): 599-607.
3. Scott A et al. What do we mean by the term "inflammation"? A contemporary basic science update for sports medicine. Br J Sports Med 2004; 38(3): 372-80.
4. Toumi H et al. The inflammatory response: friend or enemy for muscle injury? Br J Sports Med 2003; 37(4): 284-6.
5. Schneider BS et al. Neutrophil infiltration in exercise-injured skeletal muscle: how do we resolve the controversy? Sports Med 2007; 37(10): 837-56.

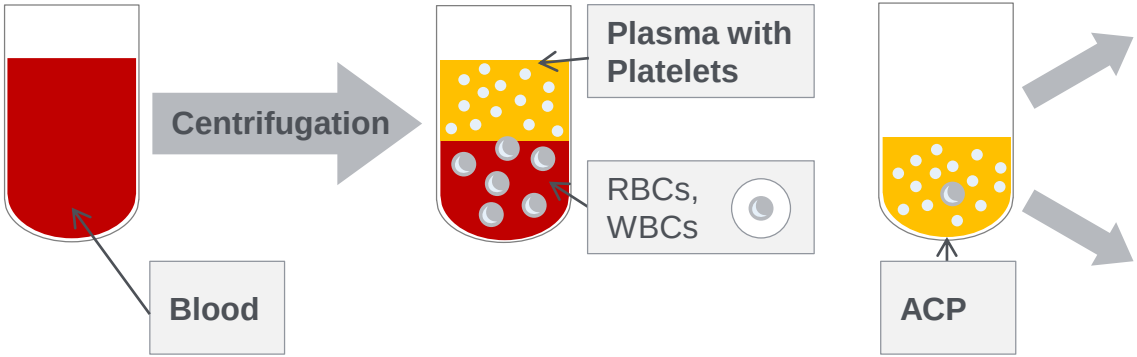
PRP Growth Factors – Mode of Action

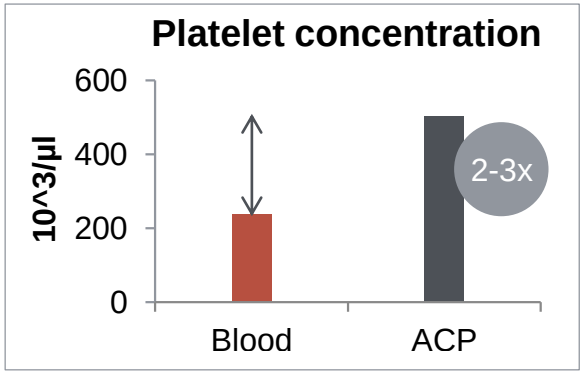


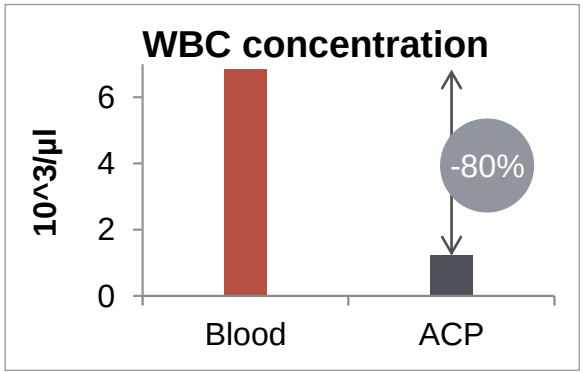
- Platelets active in all phases of tissue healing
- Too high amounts of leukocytes might promote an undirected tissue destruction
- Recent research suggests that the switch from proinflammatory to prohealing activities is key for efficient repair

Isabel Andia et al. 2012; Molecular and Biological Aspects of Platelet-Rich Plasma Therapies

ACP – The Healing Composition

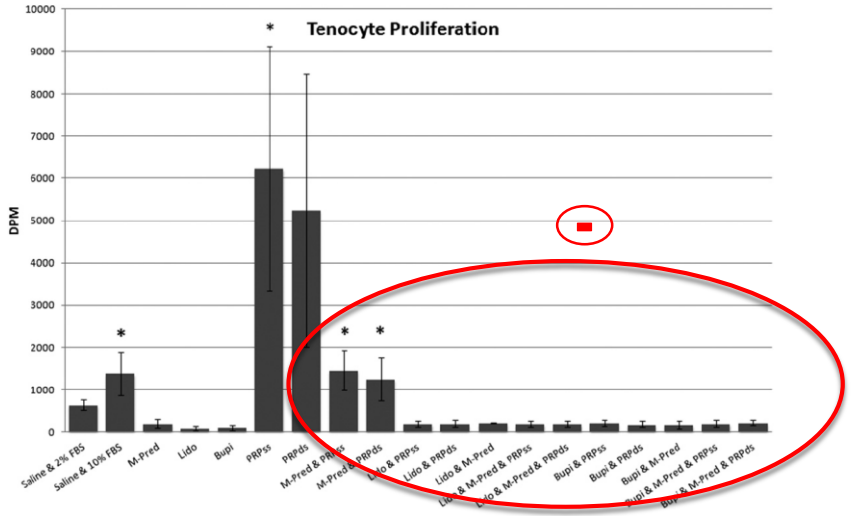


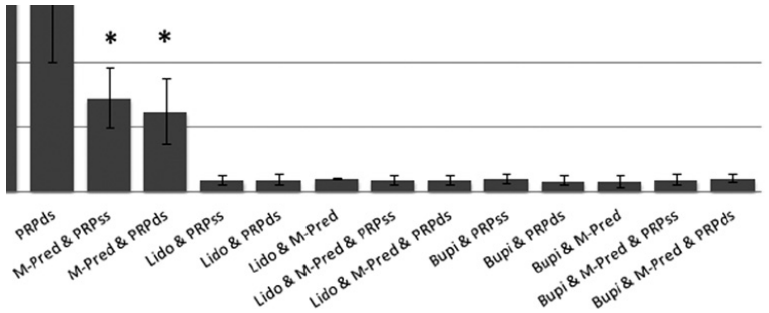




Treatment considerations

How to use ACP – Local Anesthetics, Corticosteroids



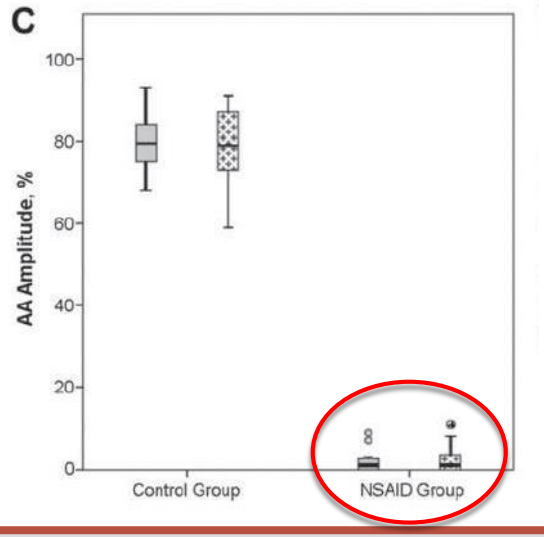


Carofino et al., Corticosteroids and local anesthetics decrease positive effects of PRP_an in vitro study on human tendon cells, Arthroscopy, 2012

→ Reduction of cell proliferation

→ **Recommendation: Injection of ACP without local anesthetics or corticosteroids (alternatively, cooling or subcutaneous application)**

How to use ACP - NSAIDs



Platelet aggregation

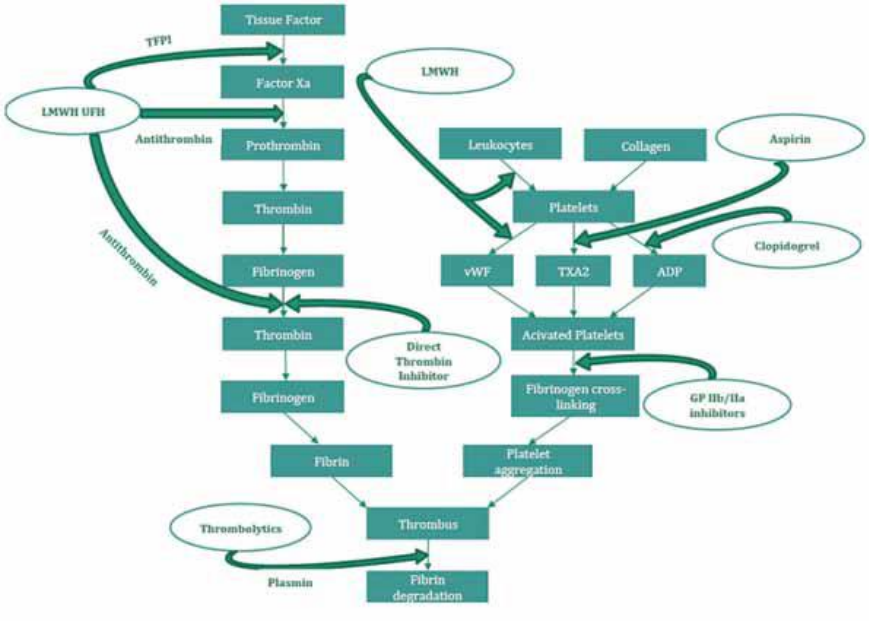
Study group: NSAID (diclofenac or dexibuprofen) taken twice daily (3 days)
Control group: no NSAID history within the previous 2 weeks
Platelet activation performed with standard inductors of platelet aggregation (e.g. Arachidonic acid)

Schippinger et al., Autologous Platelet-Rich Plasma Preparations-Influence of NSAIDs on Platelet Function, The Orthopaedic Journal of Sports Medicine, 2015

→ Significantly impaired platelet function in PRP from subjects after NSAID medication

→ **Recommendation: If required, the administration of NSAIDs should be performed after blood collection for the preparation of autologous PRP;**

How to use ACP – Antithrombotic Therapy



Drug	Half-life	Before PRP	After PRP
Warfarin	20-60 h	4-5 days	2h
Heparin	1.5h	2-4h	1h
Low molecular weight Heparin: Therapeutic dosing		>24h	24h
Low molecular weight Heparin: Prophylactic dosing		10-12h	6-8h
Fondaparinux (factor Xa inhibitor)	17-21h	36-42h	6-8h
Rivaroxaban (factor Xa inhibitor)	5-9h	22-26h	4-6h
Apixaban (factor Xa inhibitor)	9-14h	26-30h	4-6h
Dabigatran (thrombin inhibitor)	12-17h	7days	5days
Clopdogrel	7-8h	7days	
Aspirin (irreversibly inhibits platelet cyclooxygenase)		7days	

Ramsook et al., Timing of Platelet Rich Plasma Injections During Antithrombitc Therapy, Pain Physician 2016

Multiple Injections

Better outcome?

Marketing story?

Multiple Injections – ACP for Patellar Tendinopathy

Zayni, MLTJ, 2015

	At baseline			At 34 monthmean FU		
Clinical scores	**VAS (SD)**	**Tegner score (SD)**	**VISA-P (SD)**	**VAS (SD)**	**Tegner score (SD)**	**VISA-P (SD)**
Group a: 1 PRP injection	7.1 (1.6)	4.1 (1.3)	36.7 (10.6)	3.6 (1.2)	5.9 (5.9)	65.7 (19.8)
Group b: 2 PRP injections	6.7 (1.7)	4.8 (0.94)	35.7 (9.4)	1.07 (1.5)	8.1 (1.7)	93.2 (14)
***p* value**	ns	ns	ns	0.0005	0.0003	< 0.0001

- Randomized prospect. consec. series, level II
- 40 athletes
- Single vs. Two injections (2 weeks apart)
- VISA-P, VAS, Tegner

Results

PRP injection improved clinical outcomes in almost 77% of patients and allowed them to return to their pre-symptom activity level in 86% of cases.

Two consecutive ultrasound-guided intratendinous PRP injections showed a better improvement in their outcomes when compared to a single injection

Multiple Injections – LP-PRP for Knee OA

Görmeli et al., KSSTA, 2015

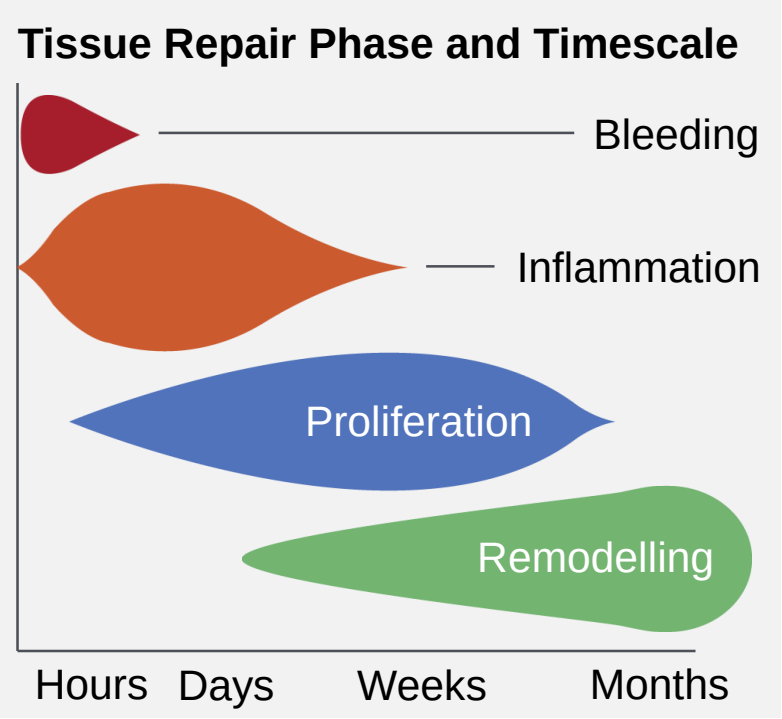
Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis

Results:
Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis

- RCT, level I
- 162 patients, grade I-IV
- Single vs. 3 injections (weekly interval) vs. HA (3, weekly interval) vs. saline (3, weekly interval)

Increased Effect with Multiple Injections
Recommendation:
OA, tendinopathies: 3-5 injections with ACP at weekly intervals
Muscle: up to 5 injections with ACP every 2-3 days

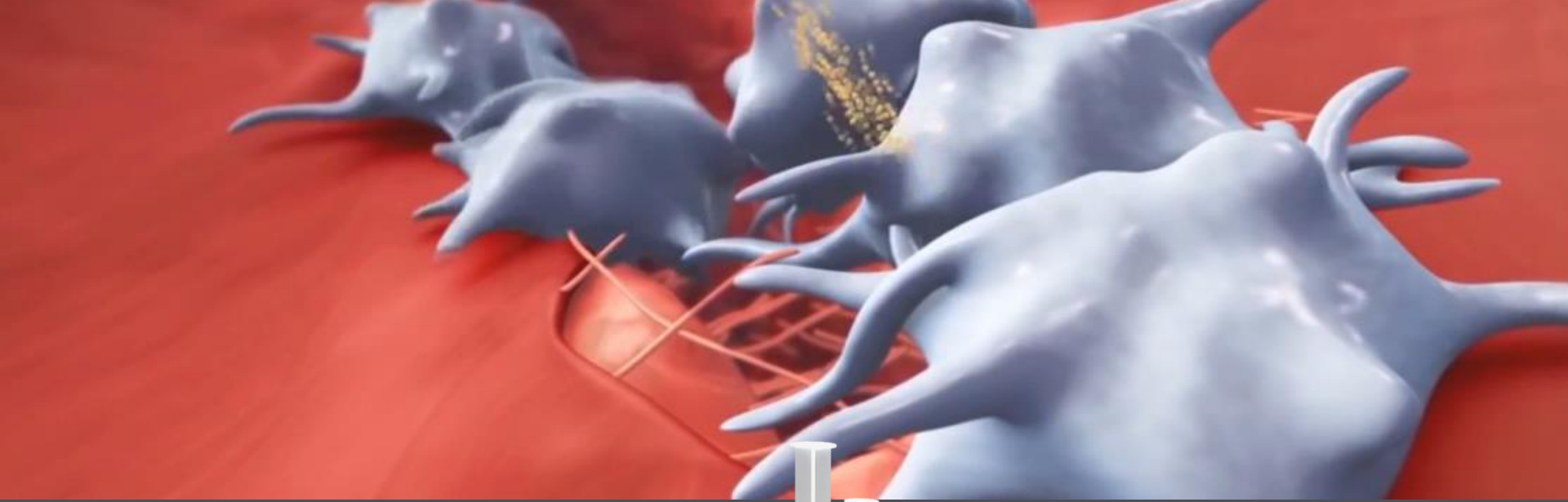
Multiple Injections - Weekly interval



Recent research suggests that the switch from proinflammatory to prohealing activities is key for efficient repair

Platelets have a lifespan of ~ 1 week

Growth factors have a lifespan of max. 24h



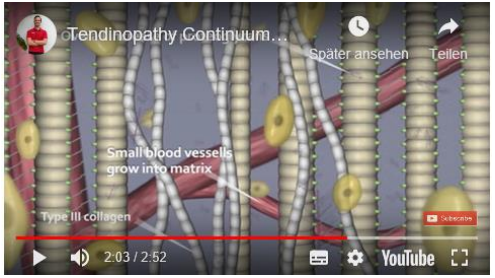
Scientific Evidence
Tendinopathy

Arthrex®

Tendon Pathology

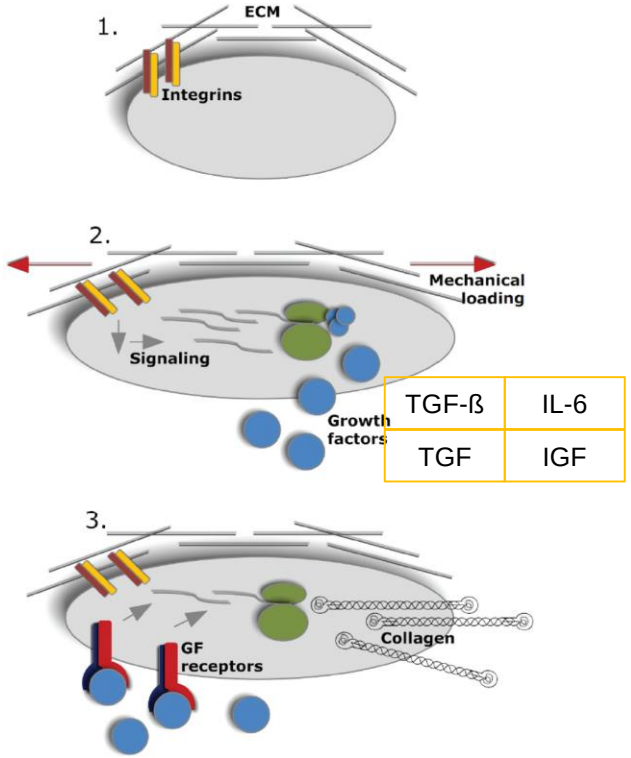
- Overload
- Microtears
- Discontinous / disorganised collagen fibers
- Degenerative changes (lipid deposition, proteoglycan accumulation, calcification)
- Decreased collagen content (increased collagen type III/I ratio)
- Increased MMP expression

Progress of tendinopathy



Role of Growth Factors in Tendon Healing

- Promote tenocyte / stem cell proliferation
- Induce stem cell differentiation
- Increase collagen synthesis
  (platelets increase collagen Type I, Leukocytes increase collagen Type III → Leukocytes may negatively anabolic effects of PRP and increase scar formation)
- Reduce pro-inflammatory mediators



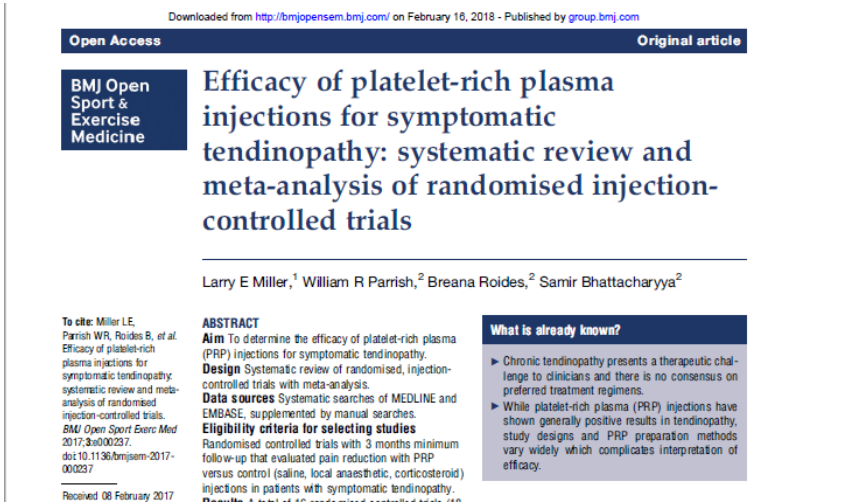
Fibroblast connected to extra cellular matrix

Transcription / Synthesis of growth factors induced by mechanical loading

Increased collagen transcription and synthesis

Heinemeier KM, Kjaer M et al, 2011 / Zhou et al, 2016

PRP for tendinopathy - Review



Open Access Original article

BMJ Open Sport & Exercise Medicine

Efficacy of platelet-rich plasma injections for symptomatic tendinopathy: systematic review and meta-analysis of randomised injection-controlled trials

Larry E Miller,[1] William R Parrish,[2] Breana Roides,[2] Samir Bhattacharyya[2]

To cite: Miller LE, Parrish WR, Roides B, *et al*. Efficacy of platelet-rich plasma injections for symptomatic tendinopathy: systematic review and meta-analysis of randomised injection-controlled trials. *BMJ Open Sport Exerc Med* 2017;3:e000237. doi:10.1136/bmjsem-2017-000237

Received 08 February 2017

ABSTRACT

Aim To determine the efficacy of platelet-rich plasma (PRP) injections for symptomatic tendinopathy.

Design Systematic review of randomised, injection-controlled trials with meta-analysis.

Data sources Systematic searches of MEDLINE and EMBASE, supplemented by manual searches.

Eligibility criteria for selecting studies Randomised controlled trials with 3 months minimum follow-up that evaluated pain reduction with PRP versus control (saline, local anaesthetic, corticosteroid) injections in patients with symptomatic tendinopathy.

What is already known?

- Chronic tendinopathy presents a therapeutic challenge to clinicians and there is no consensus on preferred treatment regimens.
- While platelet-rich plasma (PRP) injections have shown generally positive results in tendinopathy, study designs and PRP preparation methods vary widely which complicates interpretation of efficacy.

- Lateral epicondylar, Achilles, Patellar, Rotator cuff
- 16 randomized controlled trials
- Control groups: LA, Saline, Corticosteroid

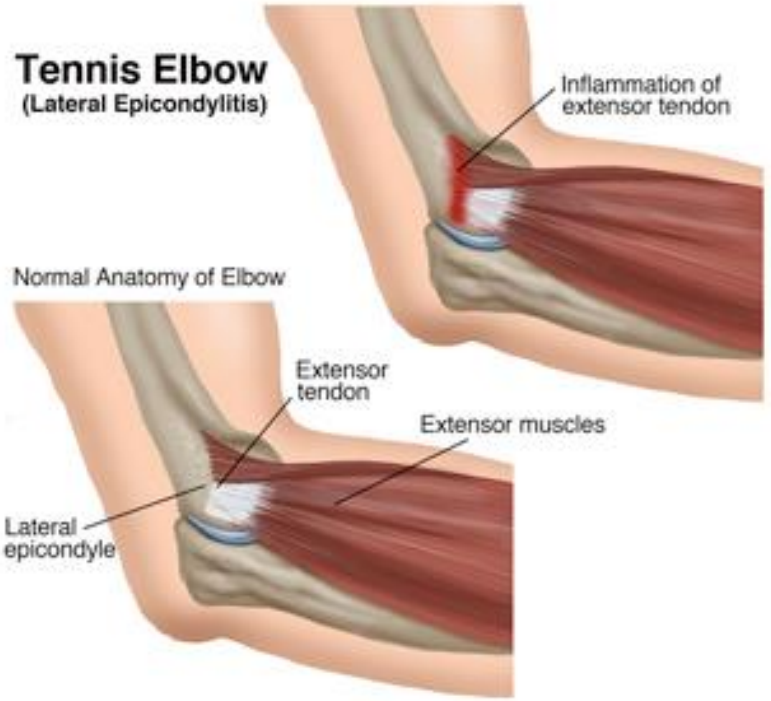
Results

PRP is more efficacious than control injections in patients with symptomatic tendinopathy

PRP injections may be more efficacious in woman than men

01 Epicondylitis

Epicondylitis



7 positive RCT studies

4 vs. steroids; 2 vs. LA; 1 vs. blood

1 ACP vs. Steroid RCT study

3 Review concluding

PRP superior to steroids

Review – Murray

„Platelet-Rich-Plasma Injections in Treating Lateral Epicondylosis: a Review of the Recent Evidence" (Murray, JHM, 2015)

Author	Year	No	PRP Injection vs	Comments
Mishra A K	2013	225	Active control	Significant pain improvement at 24 weeks compared with control group
Gosens	2011	100	Cortico-steroid (CCS) Injection	Significant improvement VAS and DASH at 2 years
Krogh	2013	60	Glucocorticoid & Saline	No significant improvement in pain at 3 months compared to saline or CCS.
Thanasas	2011	28	Autologous whole blood Injection	Significant pain improvement at 6 weeks. No significant difference in function
Creaney	2011	150	Autologous blood injection	No significant difference at 6 months. Higher conversion rate to surgery in ABI group
Peerbooms	2010	100	Cortico-steroid (CCS) Injection	Significant decrease in pain and increase in function compared to CCS

- Most studies carried out with leukocyte-rich PRP

Results

PRP **superior to AWB** injections

PRP **superior to placebo/dry needling** procedures

Benefit of PRP versus steroid injections at level II evidence

"**Steroid injections** are reported to give short-term pain relief, however the **proven recurrence rates and complications should limit their use"**

Epicondylitis – ACP

ACP vs. steroid betamethasone (Lebiedzinski, SICOT, 2015)

	ACP group; n=53		Betamethasone group; n=46	
	Range	Mean	Range	Mean
Before treatment	22.5–94.2	53.2±15.5	27.8–88.7	58.6±14.8
At 6 weeks	2.5–66.7	32.2±18.2	0–68.2	20.6±21.5
At 6 months	0–42.5	14.2±13.4	0–68.8	14.7±22.0
After 1 year	0–66.7	9.9±17.1	73.0	14.4±25.2

- Randomized study
- 99 patients
- Single injection
- DASH

Results

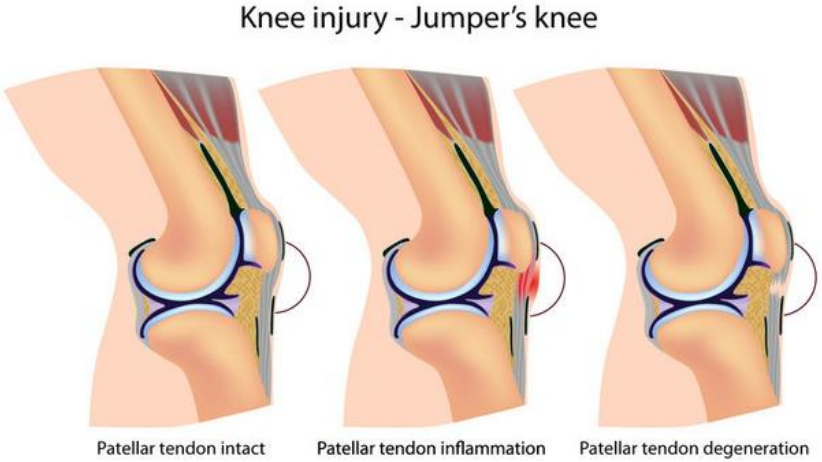
After 6 weeks and six months mean DASH significantly better in steroid group

After 1 year ACP was significantly better

ACP therapy of LE allows better results to be obtained at 12 months, **effect is longer lasting**

02 Patellar Tendinopathy

Patellar Tendinopathy



2 positive RCT studies

1 vs. ESWT; 1 vs. Dry needling

2 ACP

Case series (level IV)

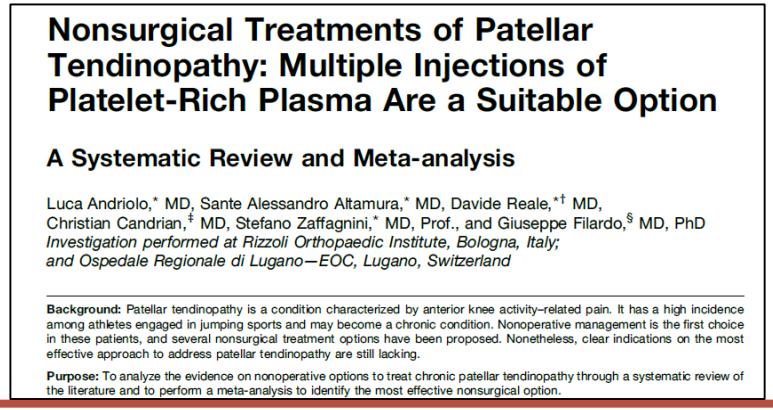
Randomized prospective series (level II)

Review concluding

PRP injection is an effective treatment for patellar tendinopathy

Review – Andriolo

„Nonsurgical Treatments of Patellar Tendinopathy: Multiple Injections of Platelet-Rich Plasma Are a Suitable Option" (Andriolo, AJSM 2018)



Nonsurgical Treatments of Patellar Tendinopathy: Multiple Injections of Platelet-Rich Plasma Are a Suitable Option

A Systematic Review and Meta-analysis

Luca Andriolo,* MD, Sante Alessandro Altamura,* MD, Davide Reale,*† MD, Christian Candrian,‡ MD, Stefano Zaffagnini,* MD, Prof., and Giuseppe Filardo,§ MD, PhD
Investigation performed at Rizzoli Orthopaedic Institute, Bologna, Italy; and Ospedale Regionale di Lugano—EOC, Lugano, Switzerland

Background: Patellar tendinopathy is a condition characterized by anterior knee activity–related pain. It has a high incidence among athletes engaged in jumping sports and may become a chronic condition. Nonoperative management is the first choice in these patients, and several nonsurgical treatment options have been proposed. Nonetheless, clear indications on the most effective approach to address patellar tendinopathy are still lacking.

Purpose: To analyze the evidence on nonoperative options to treat chronic patellar tendinopathy through a systematic review of the literature and to perform a meta-analysis to identify the most effective nonsurgical option.

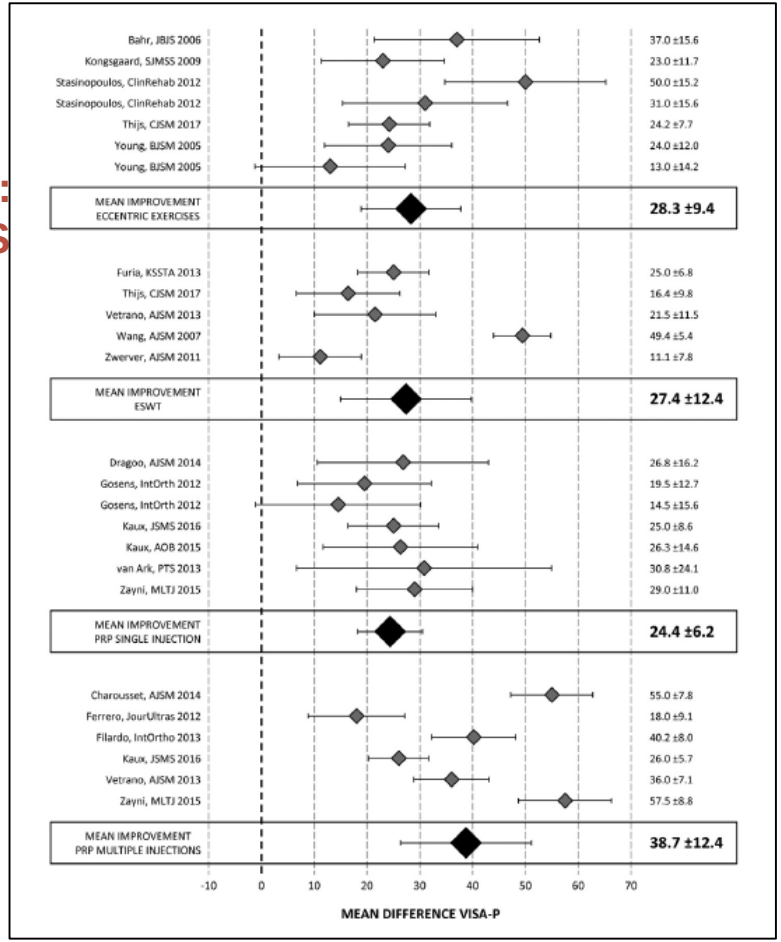
- 70 studies, 2530 patients
- Treatment groups: eccentric exercise, extracorporeal shockwave therapy, Platelet Rich Plasma (single, multiple)

Review – Andriolo

„Nonsurgical Treatments of Patellar Tendinopathy: Rich Plasma Are a Suitable Option" (Andriolo, AJS

Results

- **Multiple injections of PRP obtained the best results at long-term follow-up** (>6 months)
- It **seems advisable to combine PRP treatment with** rehabilitation and specifically **eccentric protocols**
- the results of the available literature suggest that **multiple PRP injections may be considered a suitable option for complex cases** with patients with more serious symptoms or when conservative rehabilitative approaches fail to treat chronic patellar tendinopathy



Patellar tendinopathy – ACP

Zayni, MLTJ, 2015

	At baseline			At 34 monthmean FU		
Clinical scores	**VAS (SD)**	**Tegner score (SD)**	**VISA-P (SD)**	**VAS (SD)**	**Tegner score (SD)**	**VISA-P (SD)**
Group a: 1 PRP injection	7.1 (1.6)	4.1 (1.3)	36.7 (10.6)	3.6 (1.2)	5.9 (5.9)	65.7 (19.8)
Group b: 2 PRP injections	6.7 (1.7)	4.8 (0.94)	35.7 (9.4)	1.07 (1.5)	8.1 (1.7)	93.2 (14)
***p* value**	ns	ns	ns	0.0005	0.0003	< 0.0001

- Randomized prospect. consec. series, level II
- 40 athletes
- Single vs. Two injections (2 weeks apart)
- VISA-P, VAS, Tegner

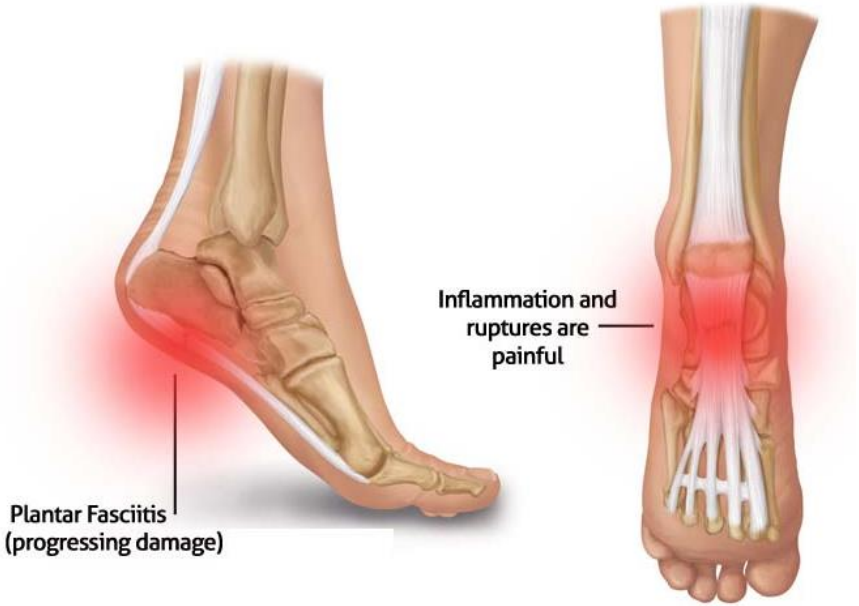
Results

PRP injection **improved clinical outcomes in almost 77% of patients** and allowed them to return to their pre-symptom activity level in 86% of cases.

Two consecutive ultrasound-guided intratendinous PRP injections showed a better improvement in their outcomes when compared to a single injection

03 Plantar Fasciitis

Plantar Fasciitis



4 positive RCT studies

4 vs. steroids

2 ACP

Prospective series (level IV)

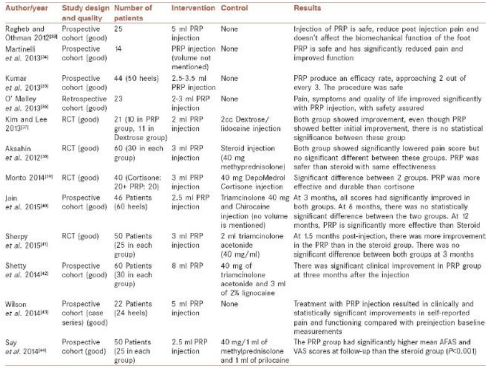
Randomized trial (level II)

2 reviews concluding

PRP superior to steroids

Review – Chiew

„ Effectiveness and relevant factors of platelet-rich plasma treatment in managing plantar fasciitis: A systematic review” (J Res Med Sci, 2016)



Author/year	Study design and quality	Number of patients	Intervention	Control	Results
Ragheb and Othman 2014[39]	Prospective cohort (good)	25	5 ml PRP injection	None	Injection of PRP is safe, reduce post injection pain and doesn't affect the biomechanical function of the foot
Martinelli et al. 2013[34]	Prospective cohort (good)	14	PRP injection (volume not mentioned)	None	PRP is safe and has significantly reduced pain and improved function
Kumar et al. 2013[33]	Prospective cohort (good)	44 (50 heels)	2.5-3.5 ml PRP injection	None	PRP produce an efficacy rate, approaching 2 out of every 3. The procedure was safe
O' Malley et al. 2013[36]	Retrospective cohort (good)	23	2-3 ml PRP injection	None	Pain, symptoms and quality of life improved significantly with PRP injection, with safety assured
Kim and Lee 2013[37]	RCT (good)	21 (10 in PRP group, 11 in Dextrose group)	2 ml PRP injection	2cc Dextrose/ lidocaine injection	Both group showed improvement, even though PRP showed better initial improvement, there is no statistical significance between those group
Aksahin et al. 2012[38]	RCT (good)	60 (30 in each group)	3 ml PRP injection	Steroid injection (40 mg methylprednisolone)	Both group showed significantly lowered pain score but no significant different between these groups. PRP was safer than steroid with same effectiveness
Monto 2014[35]	RCT (good)	40 (Cortisone: 20+ PRP: 20)	3 ml PRP injection	40 mg DepoMedrol Cortisone injection	Significant difference between 2 groups. PRP was more effective and durable than cortisone
Jain et al. 2015[40]	Prospective cohort (good)	46 Patients (60 heels)	2.5 ml PRP injection	Triamcinolone 40 mg and Chirocaine injection (no volume is mentioned)	At 3 months, all scores had significantly improved in both groups. At 6 months, there was no statistically significant difference between the two groups. At 12 months, PRP is significantly more effective than Steroid
Sheepy et al. 2015[41]	RCT (good)	50 Patients (25 in each group)	3 ml PRP injection	2 ml triamcinolone acetonide (40 mg/ml)	At 1.5 months post-injection, there was more improvement in the PRP than in the steroid group. There was no significant difference between both groups at 3 months
Shetty et al. 2014[42]	Prospective cohort (good)	60 Patients (30 in each group)	8 ml PRP	40 mg of triamcinolone acetonide and 3 ml of 2% lignocaine	There was significant clinical improvement in PRP group at three months after the injection
Wilson et al. 2014[43]	Prospective cohort (case series) (good)	22 Patients (24 heels)	5 ml PRP injection	None	Treatment with PRP injection resulted in clinically and statistically significant improvements in self-reported pain and functioning compared with preinjection baseline measurements
Say et al. 2014[44]	Prospective cohort (good)	50 Patients (25 in each group)	2.5 ml PRP injection	40 mg/1 ml of methylprednisolone and 1 ml of prilocaine	The PRP group had significantly higher mean AFAS and VAS scores at follow-up than the steroid group (P<0.001)

PRP = Platelet-rich plasma

- 4 RCTs, 8 cohort studies, 455 patients
- PRP vs. corticosteroids
- Various PRPs and injection protocols

Results

Improvement during the first 3 months

Significant improvement was also noted when the patient was followed up till 12 months postinjection

Regardless of PRP variations, **superiority of PRP treatment compared to steroid was reported in all studies**

PRP therapy might provide an effective alternative … with **no obvious side effects or complication**

Plantar fasciitis– ACP

Martinelli, SICOT, 2013

Platelet-rich plasma injections for chronic plantar fasciitis

Nicola Martinelli · Andrea Marinozzi · Stefano Carrì · Ugo Trevisio · Alberto Bianchi · Vincenzo Denaro

- single-centre, uncontrolled, prospective study
- 14 patients
- 3 injections, weekly interval
- Roles&Maudsley Score, VAS; 12 months

Results

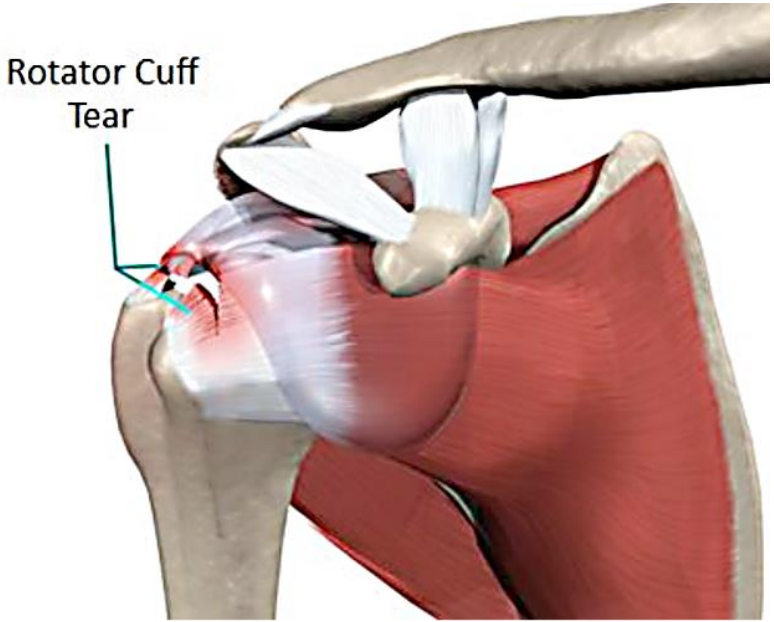
4 of 5 athletic patients returned to same sport activity within 3 months after last injection

79% rated results as excellent and good

VAS decreased significantly from 7.1 to 1.9 at the last follow-up

04 Misc.

Rotator cuff tears



Von Wehren et al. KSSTA 2015
Therapeutic study Level III
50 patients, partial rotator cuff tear
3 ACP injections (weekly) vs. 1 cortisone
VAS and shoulder scores (ASES, SST and CMS) statistically significant better after 3 months in ACP group, trend after 6 months

Werthel et al. 2014, Hak et al. 2014
ACP resulted in lower pain but no improvement regarding functional/structural outcome

ACP Tendo – Next Generation ACP for Tendinopathies

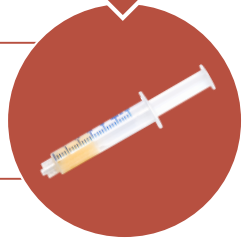
Arthrex®

ACP Tendo – Growth factor depot for the treatment of tendinopathies

Vergenix STR
Scaffold

ACP
Growth factors

ACP Tendo
Growth factor depot



Vergenix STR – New Generation Collagen Scaffold

Col1α1
Col1α2

P4Hα
P4Hβ
LH-3

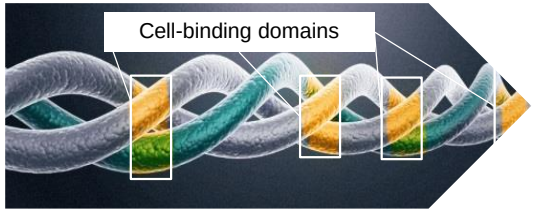
Tobacco plant

Recombinant, ultra pure, human collagen type 1 (rhCol)

rh – Col 1

Vergenix STR – New Generation Collagen Scaffold

Plant-Derived



rhCollagen

- Intact triple helix
- High cell-binding domains

Fully functional 3-D matrix
Thin fibers / high surface area

Fast cell proliferation
and fast tissue repair

Arthrex

ACP Tendo – Mode of Action

Interaction of ACP and Vergenix STR

- Adhesion and Activation of platelets
- Clot formation

Local growth factor release

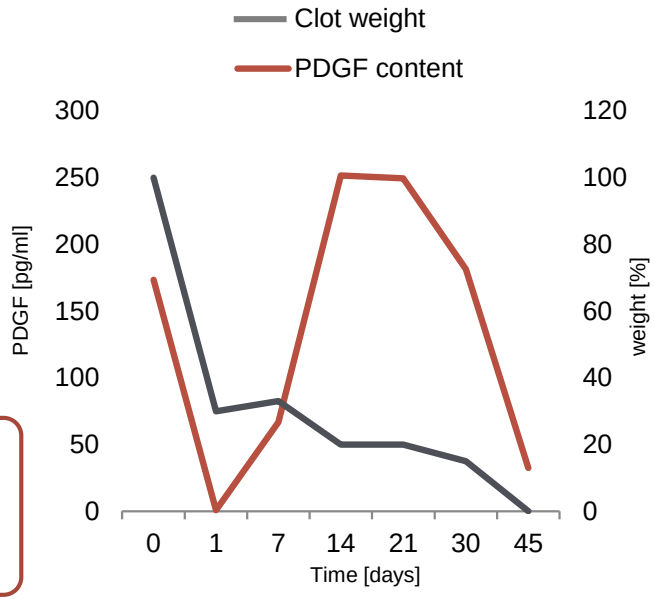
- Elevated levels of growth factors for a prolonged time
- Chemotaxis

Scaffold

- Cell adhesion (fibroblasts, endothelial cells)
- Bildung extrazellulärer matrix

Biodegredation of Vergenix STR

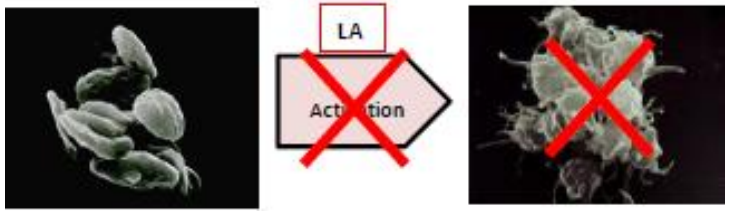
- Maturation of fibrotic tissue
- Arrest of the inflammation process



Subcutaneous injection (mouse model)

Combination with local anesthetics – why is it possible?

Local anesthetics inhibit platelet aggregation → growth factors cannot be released



→ Pure ACP should NOT be combined with local anesthetics

When using **ACP Tendo** platelets get activated during mixing process with the collagen → growth factors are released and embedded in the clot

→ No negative effect of LA on platelet aggregation and growth factor release

ACP Tendo preparation

Indications

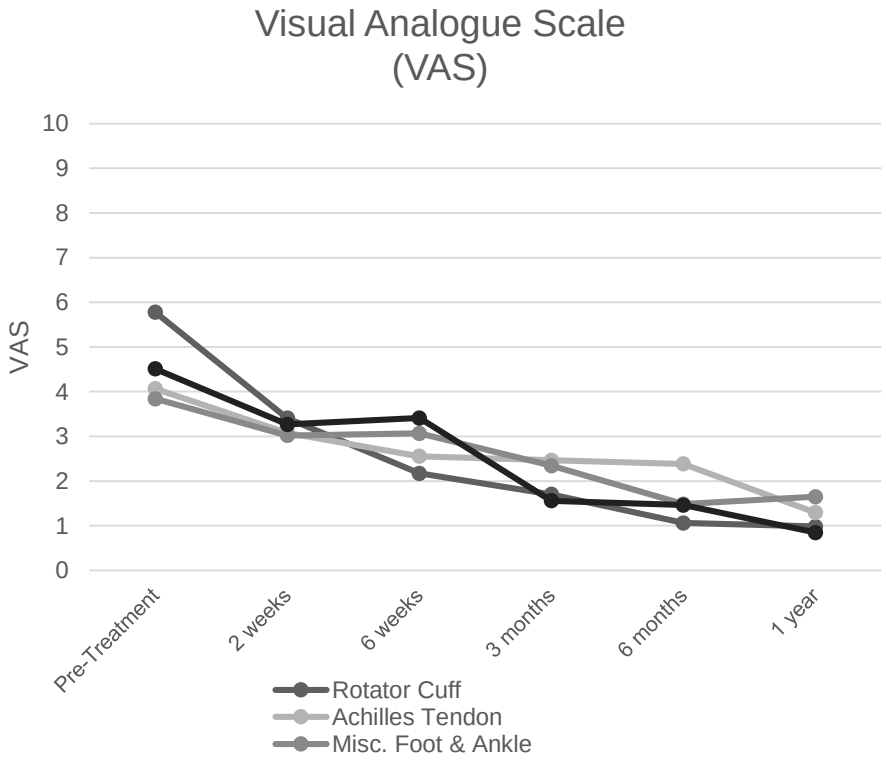
All Types of Tendinopathies / Tendon repairs
Epicondylitis
Patellar tendon
Achilles tendon
Supraspinatus tendon (rotator cuff)
Plantar fasciitis

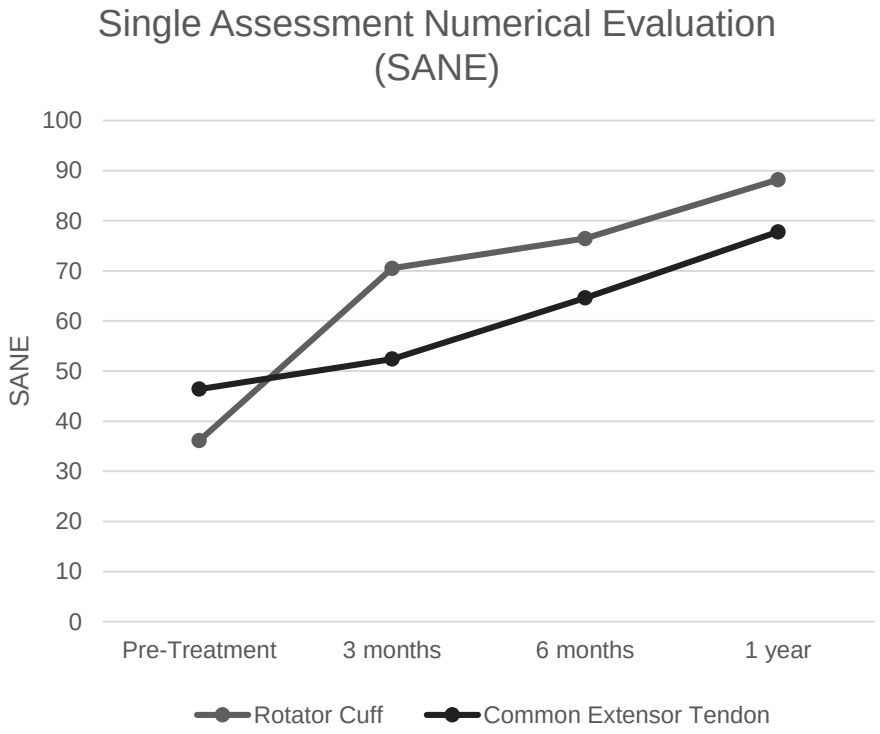
First results

Surgical Outcomes System

Advancing **Evidence-Based** Medicine

Simply and inexpensively quantify patient outcomes.





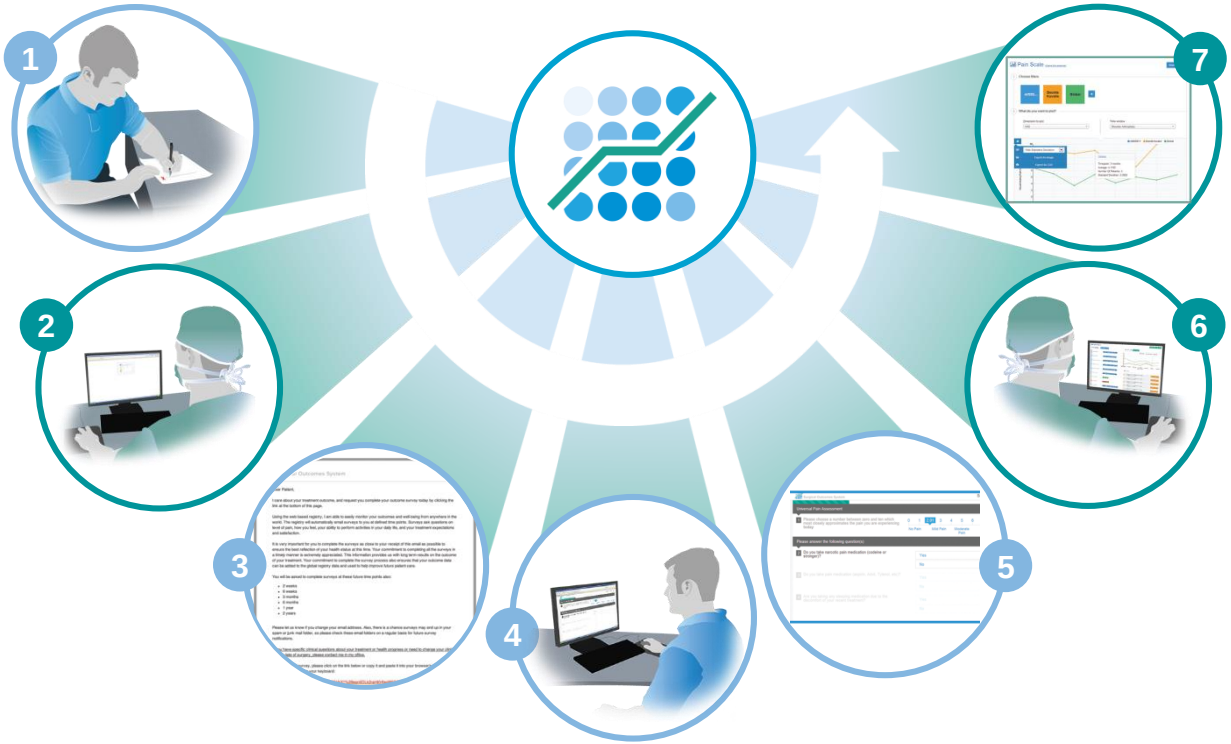
Arthrex

Surgical **O**utcomes **S**ystem

The First Global Registry in Orthopaedics

Arthrex®

Process



SOS – Numbers

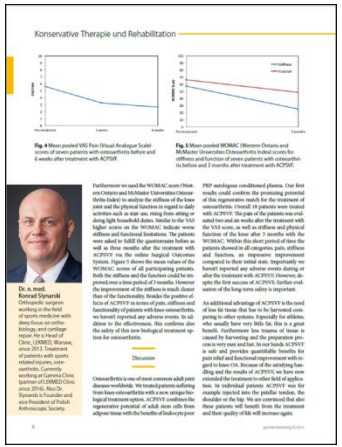
~1000 Users

47 validated Scores

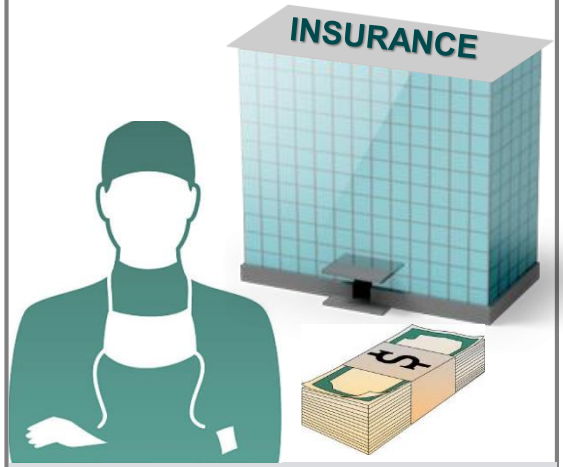
>100 000 Patients

23 Countries

Benefits


Konservative Therapie und Rehabilitation

Publications, presentations or marketing



Convince colleagues, payers and insurance companies of new treatment options

Patient education & engagement

SOS Homepage

www.surgicaloutcomesystem.com

Arthrex ACP® Tendo – Take Aways

- Innovative treatment option
- Especially for structural tendon defects (tears, degenerative tissue)
- Injection directly into the defect (don´t overfill)
- Ultrasound guidance mandatory

Thank you!