# Tendon & Ligament Application of PRP

*Sang Chul Lee, M.D, PhD.*
*Department of Physical Medicine & Rehabilitation,*
*Myongji hospital, Kwandong University College of Medicine*

# Tendon and Ligament

**Low metabolic rate at baseline**

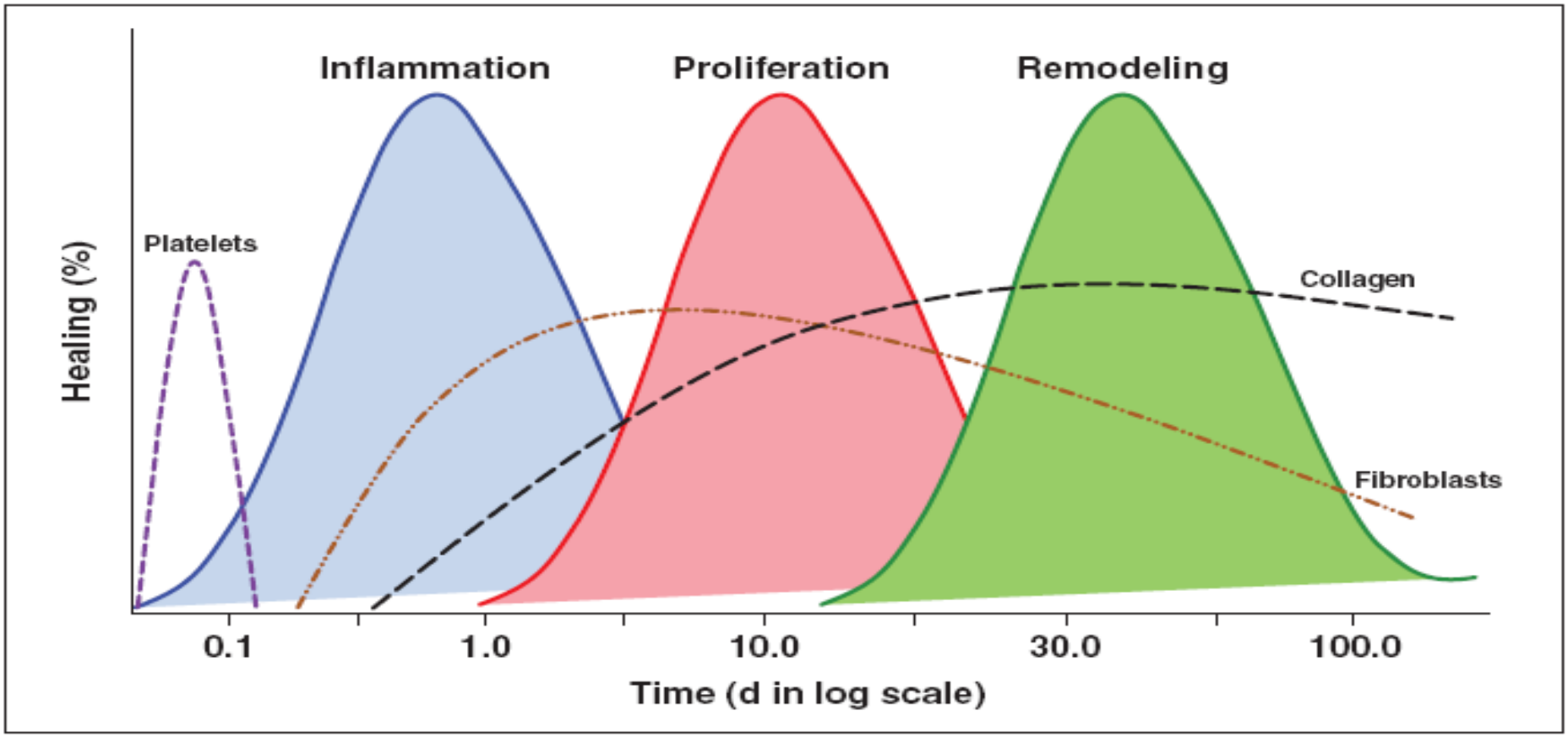
**Predisposed to slow healing after injury**

# Platelet-Rich Plasma

# PRP & Acute Injury

# PRP & Chronic Injury

# PRP & Rotator Cuff




**GF bind to transmembrane receptors on local or circulating cells >intracellular signaling**

**> production of proteins responsible for cellular chemotaxis, matrix synthesis, and proliferation**

# Chronic Injury

Collagen fiber disruption

Mucoid degeneration

Neovascularization

Absenct or less inflammation

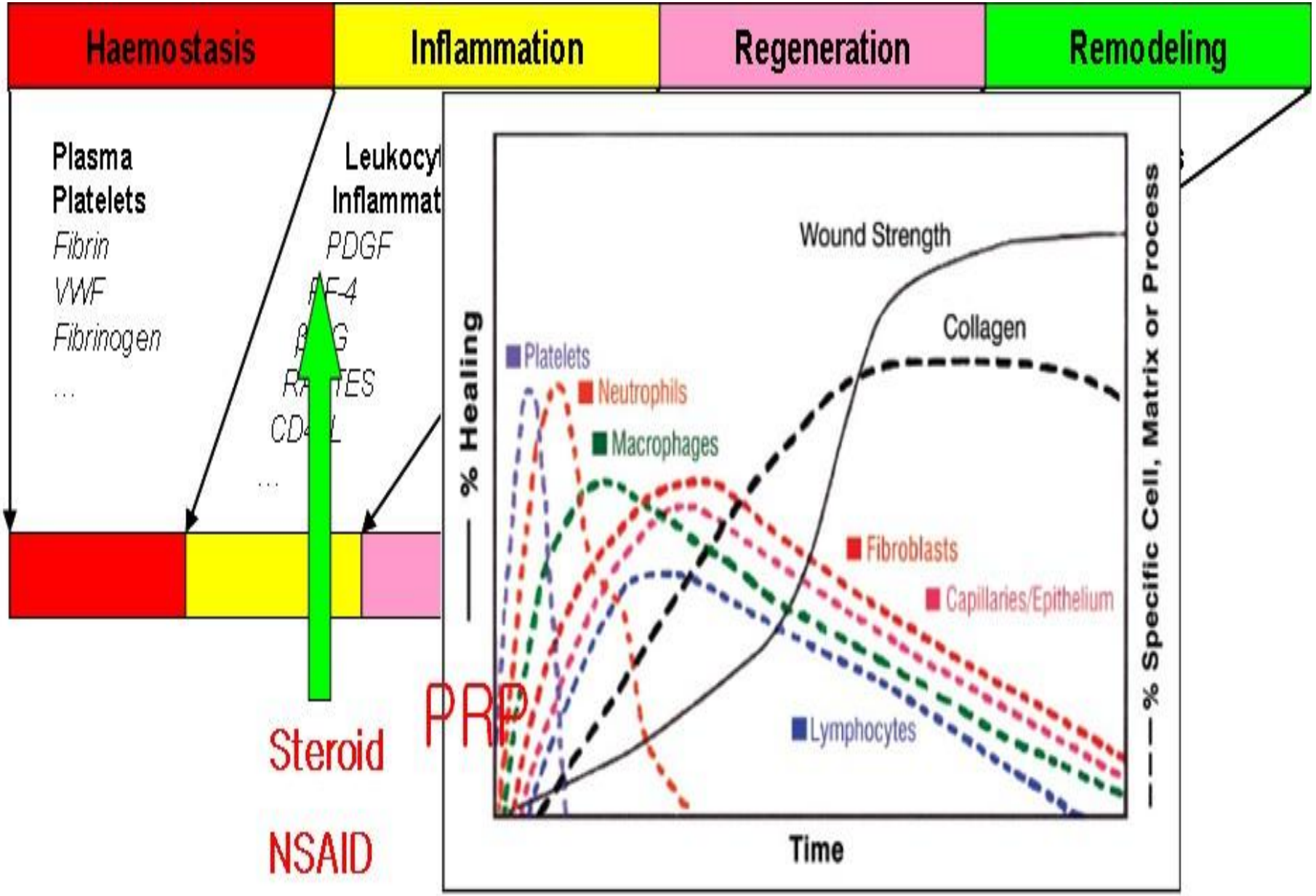

Haemostasis
Inflammation
Regeneration
Remodeling
Plasma
Platelets
Fibrin
VWF
Fibrinogen
...
Leukocyt
Inflammat
PDGF
PF-4
...
Steroid
NSAID
PRP
Wound Strength
Collagen
Platelets
Neutrophils
Macrophages
Fibroblasts
Capillaries/Epithelium
Lymphocytes
% Healing
% Specific Cell, Matrix or Process
Time

**TABLE 4.** Tendinopathy at the Elbow and Platelet-Rich Plasma: Results From a Randomized Controlled Study on Wrist Extensor Tendinopathy by Peerbooms et al[41] Using 1-mL Peppering Technique Injection and a Case–Control Study on Combined Group of Wrist Extensor Tendinopathy and Wrist Flexor Tendinopathy Patients by Mishra et al[40] Using 3-mL Peppering Technique Injection

| | Baseline VAS | VAS Decrease | | | | |
|---|---|---|---|---|---|---|
| | | 4 Weeks (%) | 8 Weeks (%) | 12 Weeks (%) | 26 Weeks (%) | 52 Weeks (%) |
| PRP group (N = 51)[41] | 70.1 (100%) | 14.7 (21%) | 23.2 (33.1%) | 31.4 (44.8%) | 37.5 (53%) | 44.8 (63.9%) |
| Control group (cortisone injection) (N = 49)[41] | 65.8 (100%) | 21.6 (32.8%) | 22.9 (34.8%) | 21.6 (32.8%) | 9.2 (14%) | 15.7 (24%) |
| PRP group (N = 15)[40] | 80.3 (100%) | 33.9 (46%) | 48.3 (60%) | — | — | 74.6 (93%) |
| Control group (bupivicaine injection) (N = 5)[40] | 86 (100%) | 15 (17%) | 3 patients withdrew; 1 of 2 remaining patients showed nil symptoms | — | — | — |

There were no reported significant between-group differences in pain scores in the study by Peerbooms et al, but there was a significant difference in the number of PRP-treated patients who achieved >25% reduction in visual analog pain scores at 1 year (primary outcome measure with a "pre-established analysis plan").

**TABLE 4.** Tendinopathy at the Elbow and Platelet-Rich Pla
Tendinopathy by Peerbooms et al[41] Using 1-mL Peppering
Wrist Extensor Tendinopathy and Wrist Flexor Tendinopath

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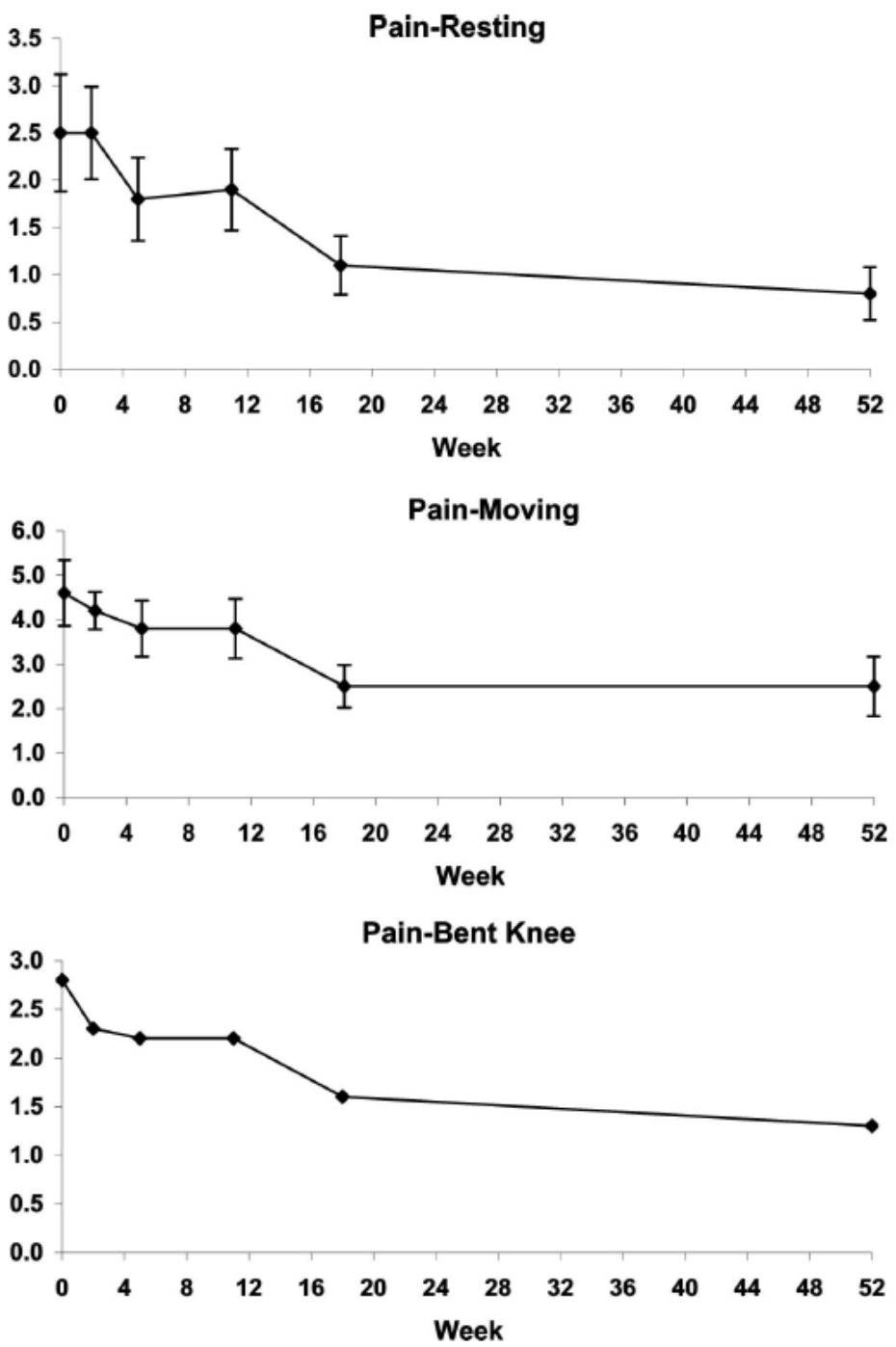



**FIGURE 3** *Brittberg-Peterson Pain VAS results.*

# Properties of PRP

"Biological glue"
Coagulation and hemostasis
Wound healing
Provisional scaffold for stem or primary cell migration and differentiation
Intra-articular restoration of hyaluronic acid
Balances joint angiogenesis
Increases glycosaminoglycan chondrocyte synthesis and cartilage matrix
Anti-inflammatory
Antibacterial
Analgesic

TABLE 1
Growth Factors Identified Within Platelet-Rich Plasma and Their Physiologic Effect[a]

| Factor | Target Cell/Tissue | Function |
|---|---|---|
| PD-EGF | Blood vessel cells, outer skin cells | Cell growth, recruitment |
| | Fibroblasts, and many other cell types | Differentiation, skin closure |
| | | Cytokine secretion |
| PDGF A + B | Fibroblasts, smooth muscle cells, chondrocytes, osteoblasts, mesenchymal stem cells | Potent cell growth, recruitment |
| | | Blood vessel growth, granulation |
| | | Growth factor secretion; matrix formation with BMPs (collagen and bone) |
| TGF-β1 | Blood vessel tissue, outer skin cells | Blood vessel (±), collagen synthesis |
| | Fibroblasts, monocytes | Growth inhibition, apoptosis (cell death) |
| | TGF gene family includes the BMPs | Differentiation, activation |
| | Osteoblasts—highest levels of TGF-βr | |
| IGF-I, II | Bone, blood vessel, skin, other tissues | Cell growth, differentiation, recruitment |
| | Fibroblasts | Collagen synthesis with PDGF |
| VEGF, ECGF | Blood vessel cells | Cell growth, migration, new blood vessel growth |
| | | Anti-apoptosis (anti–cell death) |
| bFGF | Blood vessels, smooth muscle, skin | Cell growth |
| | Fibroblasts, other cell types | Cell migration, blood vessel growth |

[a]PD-EGF, platelet-derived epidermal growth factor; PDGF, platelet-derived growth factor; BMP, bone morphogenetic protein; TGF, transforming growth factor; IGF, insulin-like growth factor; VEGF, vascular endothelial growth factor; ECGF, endothelial cell growth factor; bFGF, basic fibroblast growth factor.

# Platelet-Rich Plasma

GFs: "normal" biologic ratios

Increased cell numbers with increasing PRP concentration from 1% to 10%, Plateau in the dose–response effect

Non-growth factors in the dense granules

Tendon collagen in vivo activate PRP

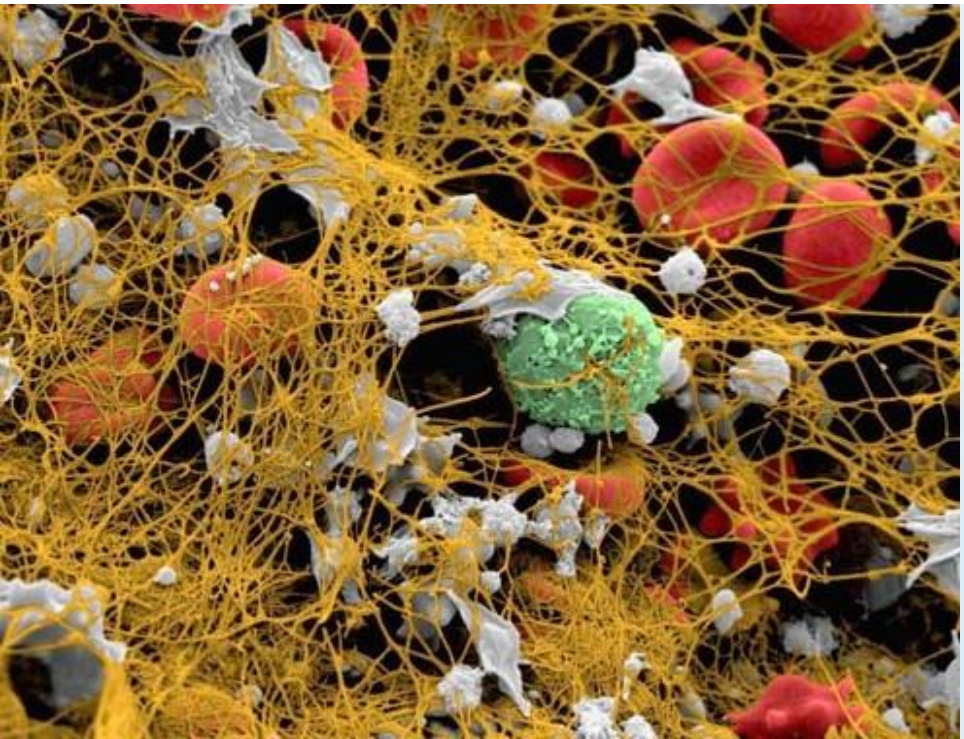
In vitro, rabbit patellar tendon,

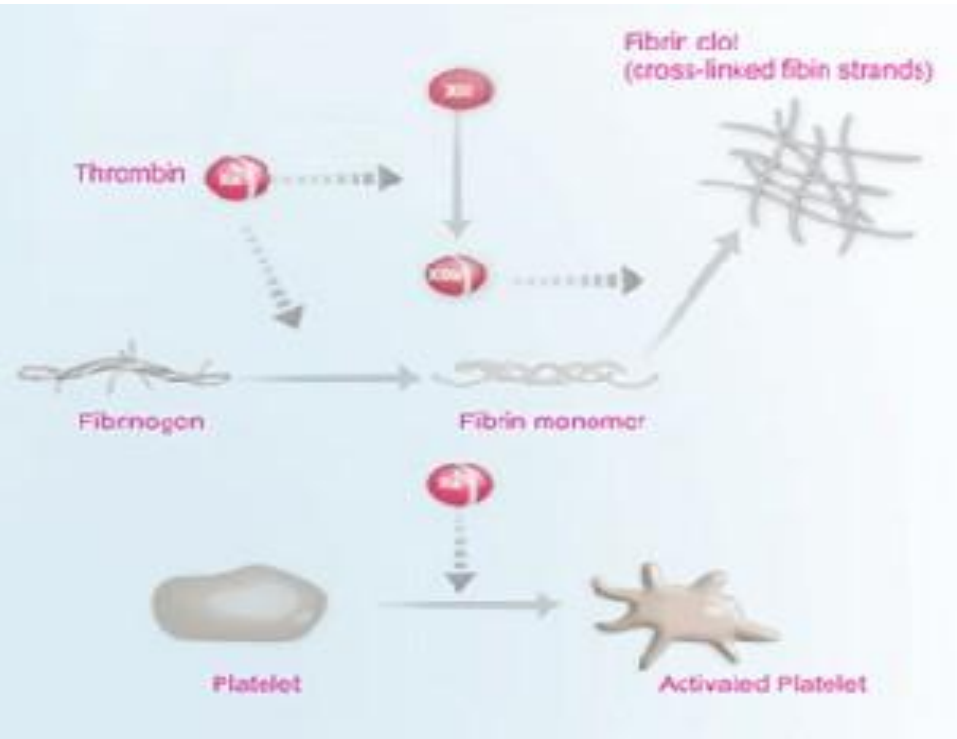
PRP treated tendon stem/progenitor cell differentiate into tenocyte

# Platelet-Rich Plasma

**To synergistically assist inflammatory cascade and healing injured tissue by manipulating GFs and bioactive proteins**

**To create a provisional fibrin scaffold**





# Wound healing:
# Repair of Collapsed Building

**Platelet: relatively passively involved**

**GF: just the messenger/ not giving the orders**

**Macrophage: tissue repair brain**

**Fibroblast, satellite cell: actual builder**

**Fibroblast: produce collagen infrastructure**

**satellite cell: form tenocyte, etc**

# PRP need to be determined

Volume of injection/application

Buffering/activation (lidocaine?)

Timing of injection to injury

Single vs Serial injections

Injection technique (one vs multiple)

Most effective rehabilitation protocol

# Remodelling Phase

Collagen is reorganized and stabilized
by also GH mediation

Tissue is remodeled through normal physiologic turnover in response to loading, stress, and humoral factors
The most important external stimulus is enhancing mechanobiological signaling by means of rehabilitation and physical therapy

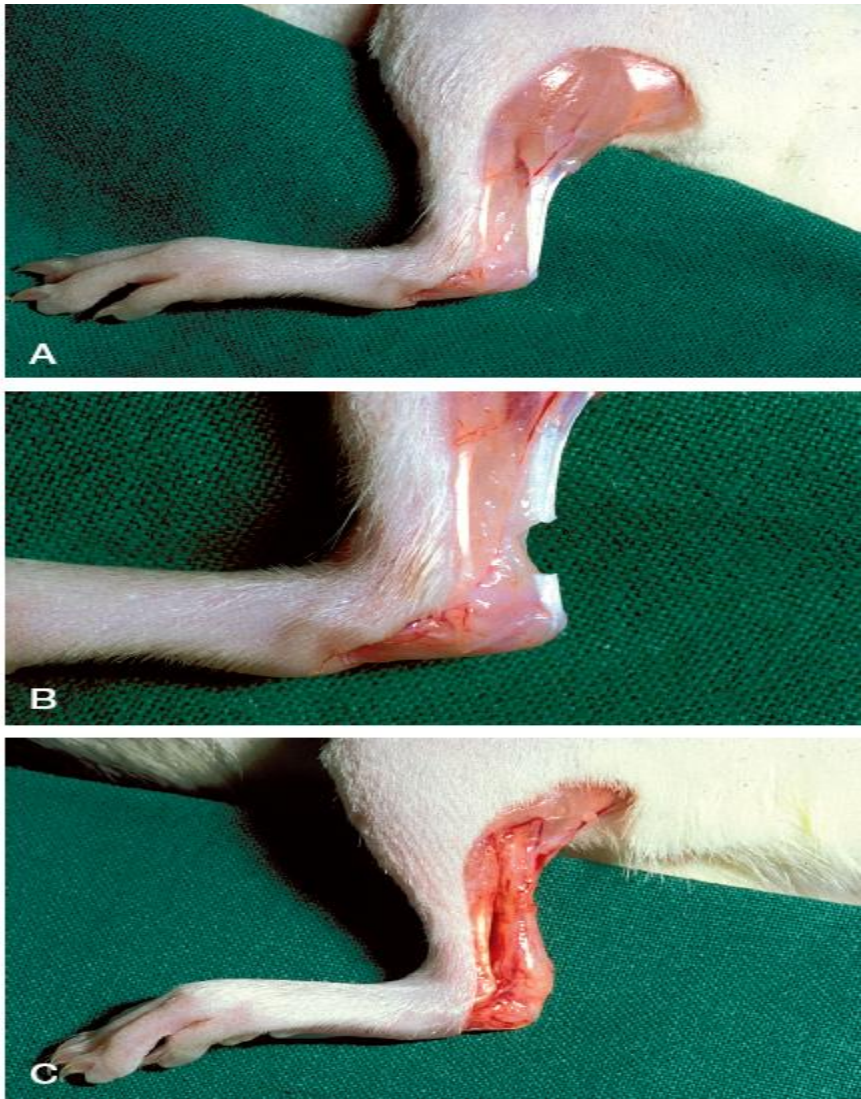
# How can one platelet injection after tendon injury lead to a stronger tendon after 4 weeks?

## Interplay between early regeneration and mechanical stimulation

Olena Virchenko and Per Aspenberg

**At 14 days, unloading (with Botox) abolished any effect of PRP to less than half of normal**

**Mechanical stimulation is a prerequisite for the effect of PRP**



# Acute Injury

# Acute Tendon and Ligament Injury

**Potential to exacerbate inflammation (pain) in the setting of acute injury**

**However,**
**Often slow to heal and are prone to reinjury**

**To promote an increase in healing, level of at least 1,000,000/mL is needed**

# Acute Tendon and Ligament Injury

**PRP may be even more effective for acute injuries than chronic injury**

**Greatest effect: early PRP within 24 hours**

# Acute Tendon and Ligament Injury

**Equine FDS tendon explants cultured in PRP**

gene expression of type I collagen, type III collagen, cartilage oligomeric matrix protein ↑

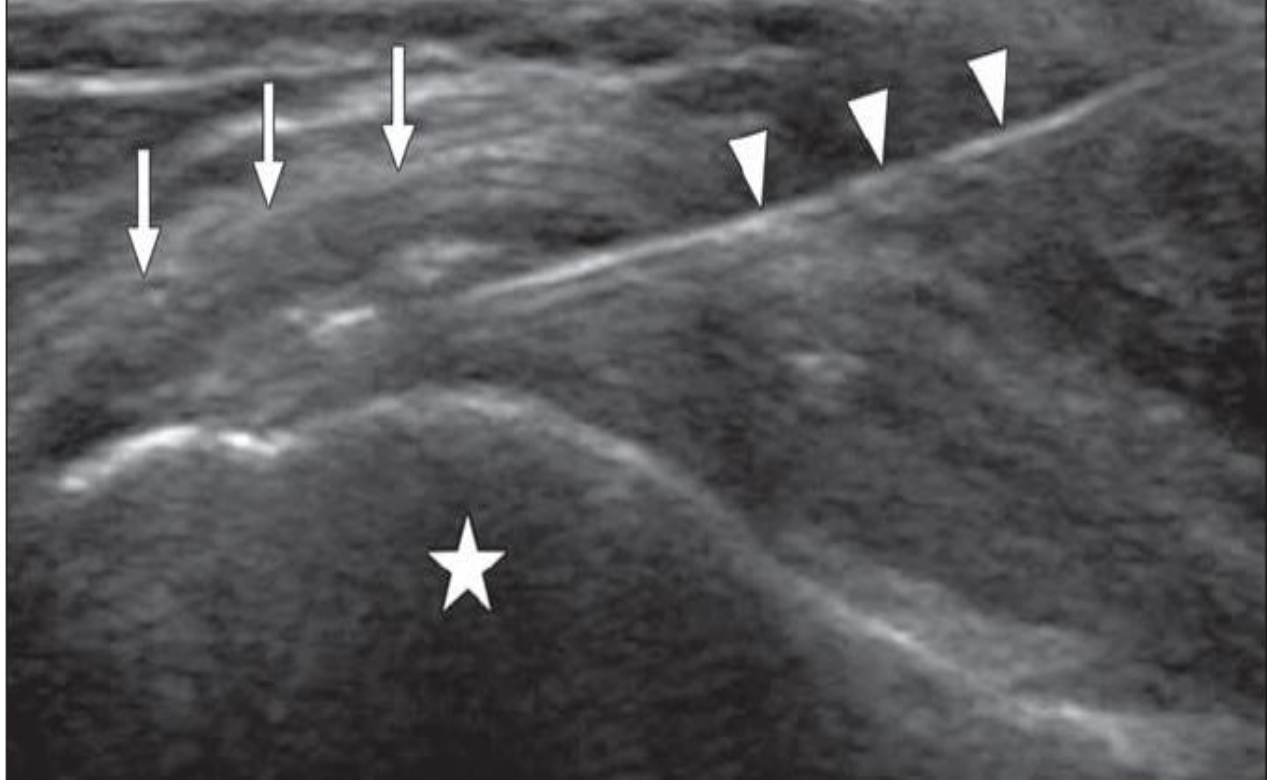
**In vivo, injection, 6 hours after creation of defect in a rat Achilles tendon**

tendon callus strength and stiffness ↑

**PRP injected into patellar tendon injury in a chimeric rat**

recruitment of circulation-derived cells to the injury site ↑

collagen production ↑



# Medial collateral ligament injuries of the knee

**PRP vs Rest & Rehabilitation**

**Professional soccer players with grade 2 acute medial collateral ligament injuries (n=22)**

**PRP injections: within 72 hours of injury**

**Return-to-play time:**

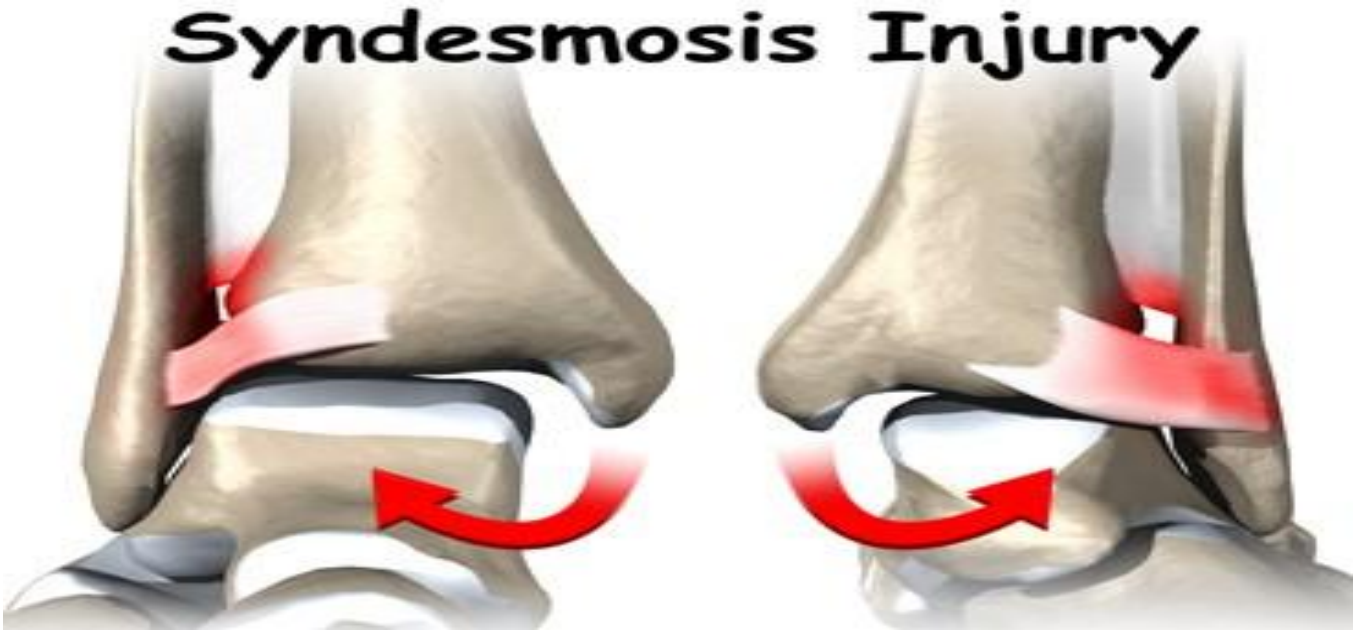
**Shortened by 27% compared to the control group**

# Ankle Injury

**Calcium-activated PRP**

**For type 3 ankle syndesmotic injuries in 11 patients**

**Average time of healing**
**5.18 weeks vs 8.00 weeks**



# Anterior Cruciate Ligament

**Grafts** With and Without PRP

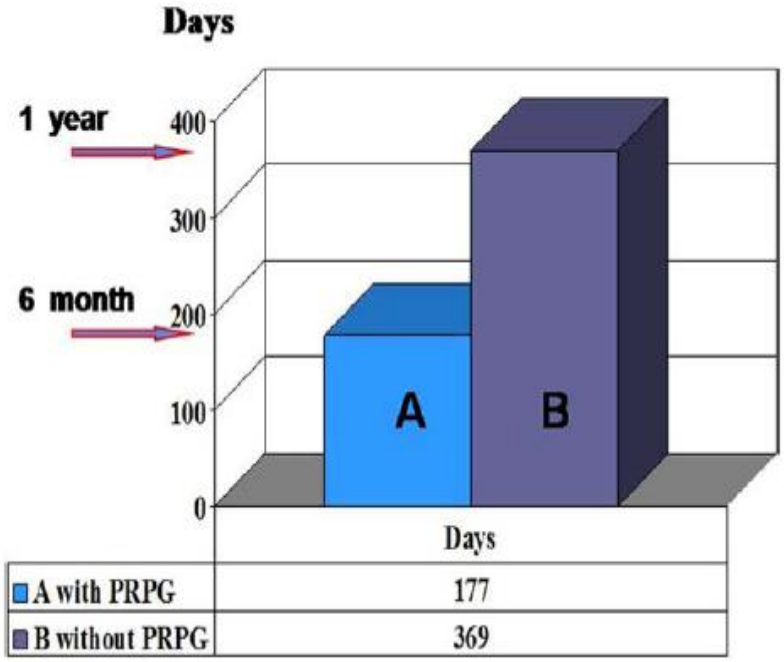
**Mean time** to obtain a completely

PRP group needed only **48%** of time

control group required to achieve

**homogeneous** intra-articular segment

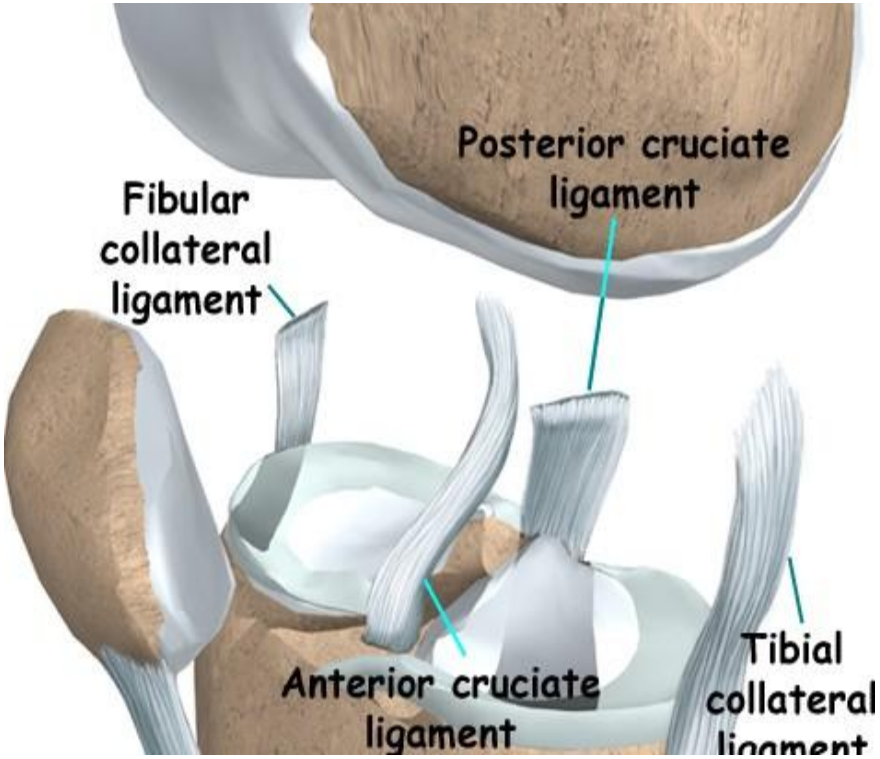
on MRI image



# Anterior Cruciate Ligament

Human RCTs have failed to show effect

PRP application cannot be recommended in combination with ACL reconstruction



# Achilles Tendon Rupture

In case-controlled study of Surgical repair
Significant improvement in the PRP adjunctive group for
- earlier ankle ROM,
- early return to gentle running
- to sports training
- decreased tendon CSA

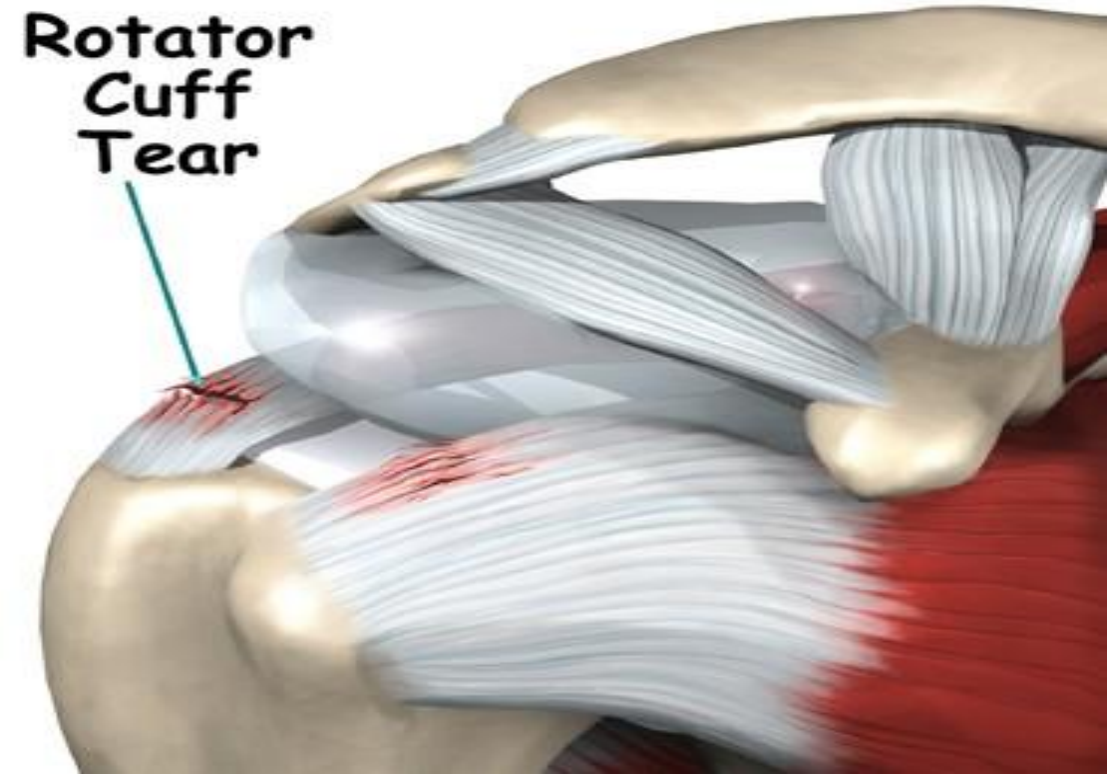
Small patient group numbers (n = 6)

# Achilles tendon rupture

RCT: 30 patients
OP + PRP 10cc

At 1-year follow-up,
No significant difference in heel raise index
However, Achilles tendon Total Rupture Score was significantly lower in the PRP group

# Chronic Injury



# Chronic Tendon Injury

**With chronic injuries, particularly tendon injuries**

- **with no, or minimal, inflammatory component, the rationale for PRP, is less clear**

**A traumatic model was used in the equine study, and the effects of PRP might be different in degenerative tendon tissue**

- **Absence of basic science studies on growth factors and PRP in chronic tendon injury models**

# Chronic Tendon Injury

**Process of wound repair may be inhibited due to**

**Compromised vascularity**

**Limited cellularity**

**Paucity of platelets and decrease in healing potential**

**To stimulate the tissue and restart the inflammatory process,**

**Making the chronic injury into a new acute injury!**

# General Management

## Chronic Tendon Injury

### Eccentric exercises

Promote collagen fiber cross-link formation

within the tendon

>facilitating tendon remodeling

# Steroid: still debated

## Lateral Epicondylitis

**Corticosteroid injection reduced pain in the short term**

**worse in the long term than are most conservative interventions**

**Repeated corticosteroid injections (average of 4.3, 18 months) were associated with a poorer long-term effect on reduction in pain than one injection**

## Rotator cuff tendinopathy

**Short-term efficacy: not clear, inconsistent**

**Of the 416**

- **38 (9%) cases of atrophy**
- **31 (8%) cases of pain**
- **2 (<1%) cases of depigmentation**
- **1 (<1%) case of tendon rupture of the Achilles tendon**

**10 studies in animals :**

- **damage to tendons: not established**

# Extracorporeal Shock Wave Therapy

**Mechanical forces generated directly or indirectly via cavitations**

- **Stimulation of soft-tissue healing**
- **inhibition of pain receptors**

**ESWT or Eccentric training for Achilles tendinopathy**

- **Comparable results in a RCT**

# Extracorporeal shock-wave therapy for tendinitis of rotator cuff

***Speed CA et al***
***JBJS Br 2002***

- Double-blind, randomized, controlled trial, n=74
- Painful arc, impingement sign
- Shoulder pain & disability Index (SPADI)

**Table II.** The number and *percentage* of subjects with improvement of 50% from baseline at three months

| | Group ESWT | Sham | p value | Odds ratio | 95% confidence interval |
|---|---|---|---|---|---|
| SPADI | 12 (*35.0*) | 18 (*45.0*) | 0.479 | 1.176 | 0.809 to 0.711 |
| Subscales | | | | | |
| Pain | 15 (*44.0*) | 13 (*38.0*) | 0.8180 | 0.8726 | 0.3482 to 2.186 |
| Disability | 19 (*47.5*) | 14 (*35.0*) | 0.8122 | 1.150 | 0.4450 to 2.970 |
| Night pain | 14 (*41.0*) | 15 (*37.5*) | 0.814 | 0.941 | 0.650 to 1.362 |

- Significant placebo effect, but no evidence of benefit compare to sham Tx.
- Do not recommend ESWT for the Tx of SS tendinitis!

# Operative Treatment

**To excise fibrotic adhesions**

**To remove or debride areas of failed healing**

**To restore vascularity, and possibly stimulate viable cells to initiate protein synthesis and to promote healing**

**To destruct neovessels**

# US-guided microtenotomy

**Achilles tendon, Tennis elbow**

**Ablation of sensory nerve fibers**

**Needling within the tendon improved tendon structure**

**PRP; to stimulate angiogenesis and remodeling by tenocytes Synergy Effect?**

**Platelet-Rich Plasma : From Basic Science to Clinical Applications**
***Am J Sports Med* 2009**
**Timothy E. et al.**

## Empirical PRP Use

# Achilles Tendinopathy

Conventional conservative therapy : ineffective in around 25%

US guidance for needle localization and confirmation of the PRP directly into the affected area

Immediately after the injection, protection with a brace and removal from athletic activity

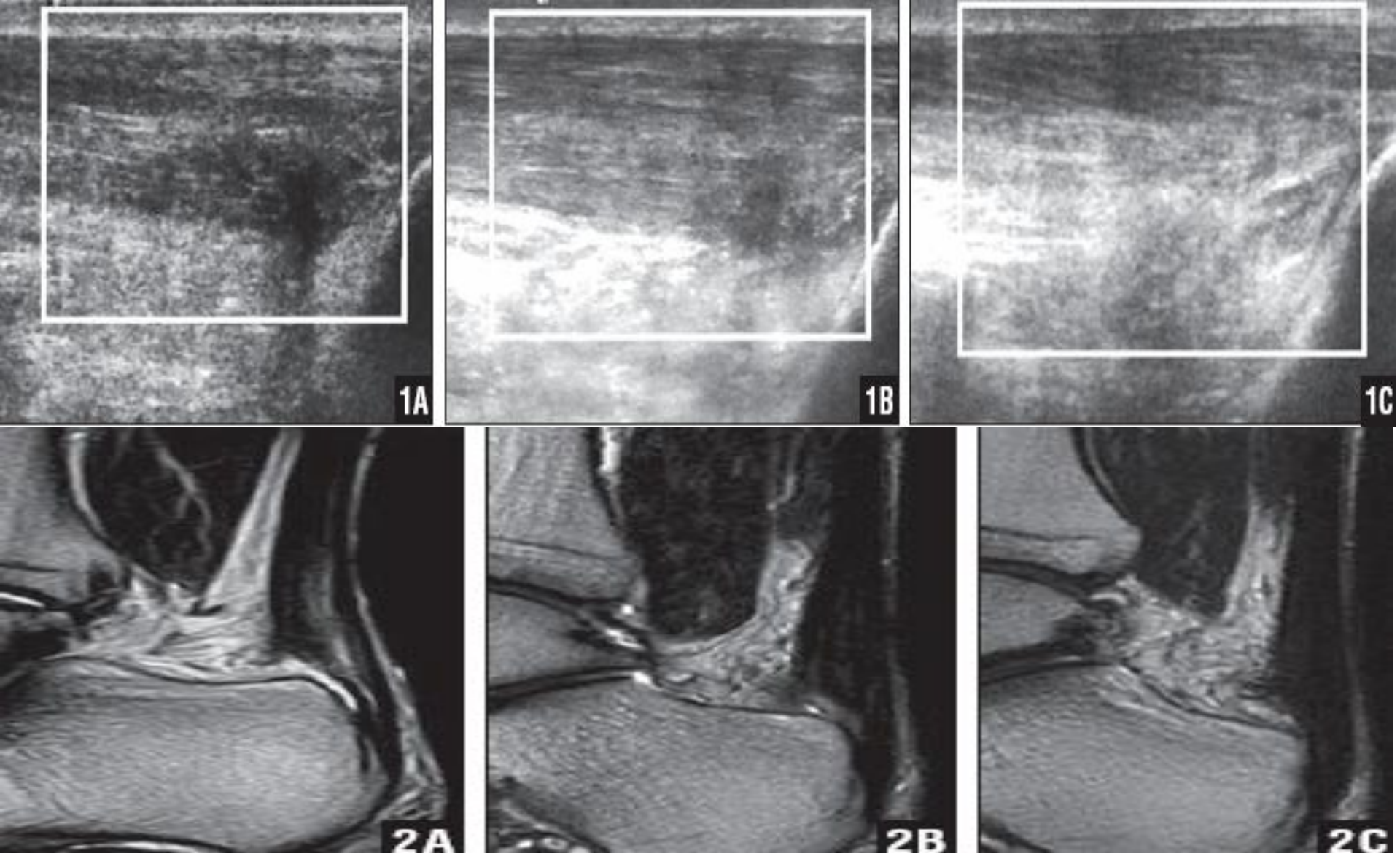
Immediate protocol of active and active-assisted ROM strictly in the PF–DF plane
Gradually progresses with a standard protocol for strength and functional recovery
Gradual return to activities over 6 to 8 weeks

# Achilles Tendinopathy

**De Vos RJ, compared with saline inj:**

**Injecting PRP for treatment of chronic midportion Achilles tendinopathy (one injection, three puncture, five small depots)**
**does not**
**contribute to an increased tendon structure**
**Alter degree of neovascularisation, compared with placebo**

**Eccentric exercise program overshadowed an effect of PRP**




**(A)Initial, (B) reparative process , (C) final follow-up at 3 months**

**MRIs: lesion with disruption of the signal within the tendon and widening of the tendon edges**

# Plantar Fasciitis

Chronic refractory plantar fasciitis

Injection into medial plantar fascia with ultrasound guidance

Post-injection protocol: immediate Wt. bearing, standard rehabilitation program for strength and functional progress

Beneficial for patients with tears of the plantar fascia:
no data

# Plantar Fasciitis

**Barrett and Erredge, 2004**

**Calcium activated PRP in liquid form for injection**

**6/9 patients achieved complete symptomatic relief after 2 months**
**1/3 unsuccessful patients eventually achieved complete resolution of symptoms after 2nd PRP injection**
**Overall, 77.9% complete resolution symptoms at 1yr**

# Patellar Tendinopathy

**PRP treatment for patellar tendinosis are as follows:**
**1) severe symptoms present for more than 3 months unresponsive to physical therapy**
**2) confirmed by US or MRI**
**3) "washout" period from NSAIDs for at least 1 week before PRP injection**

**Avoid NSAID use for 3 to 4 weeks after intervention**
**The postinjection protocol: same**
**Ice, particularly in the early stages, helpful in controlling post injection pain**

# Patellar Tendinopathy

5-mL PRP injections separated by 15 days
3-injection treatment, at the 6-month follow-up
(SF-36 and EQ-VAS; N = 20)
Significant improvement in pain and physical function using health QOL scales

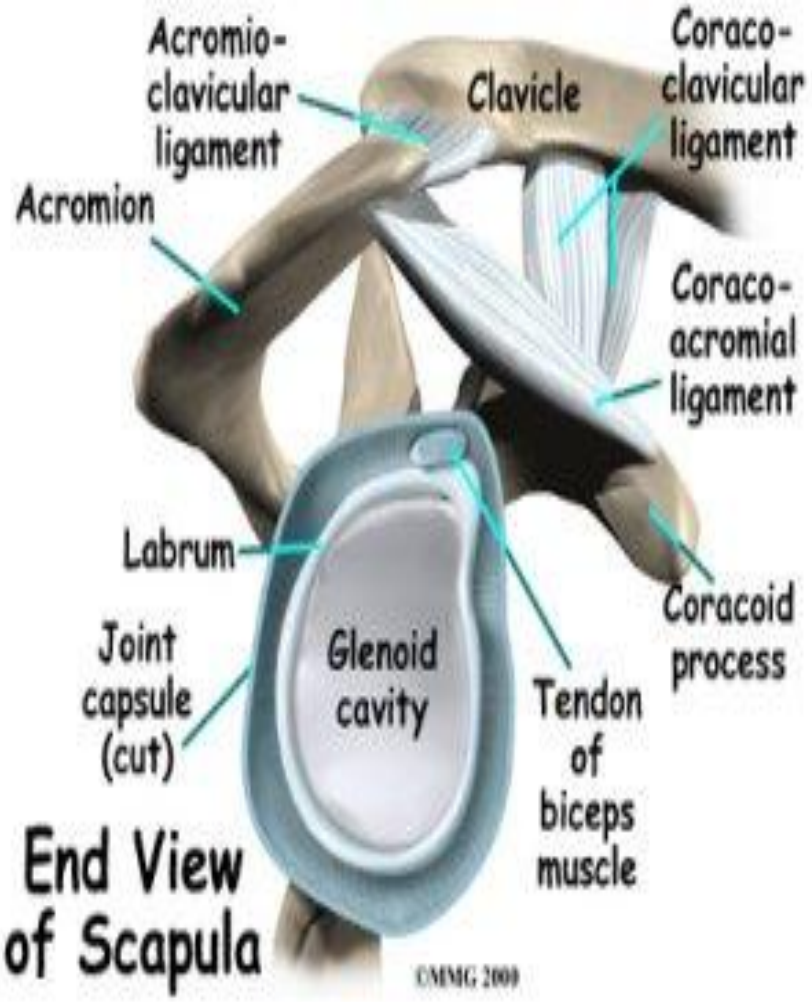
Other study (n=31)
PRP +rehabilitation protocol vs rehabilitation protocol
No between-group difference in VAS score

# Rotator cuff with PRP

**Intrinsic factor: age-related degeneration**

**Extrinsic factor: Hooked acromion, Repetitive microtrauma**

**Postoperative rotator cuff retears : 11 to 94%**



# Rotator cuff with PRP

The area of injury: identified and clearly marked based on physical examination, imaging studies, and area of maximal tenderness

Dynamic musculoskeletal US: for the accurate placement of PRP into the pathologic region of tendon

A multiplanar injection technique (peppering the tendon):
to deliver the platelets to a wider surface area
thus potentially enhance the healing process

Acetaminophen with or without narcotic medication
For post-injection pain
NSAIDs: not be used in the first 2 weeks after injection

**Neer's Test For Impingement**

**Hawkins Test For Impingement**

**Supraspinatus (Empty Can) Test**

**Testing Infraspinatus And Teres Minor (External Rotators)**

**Gerbers Liftoff Test (Subscapularis)**

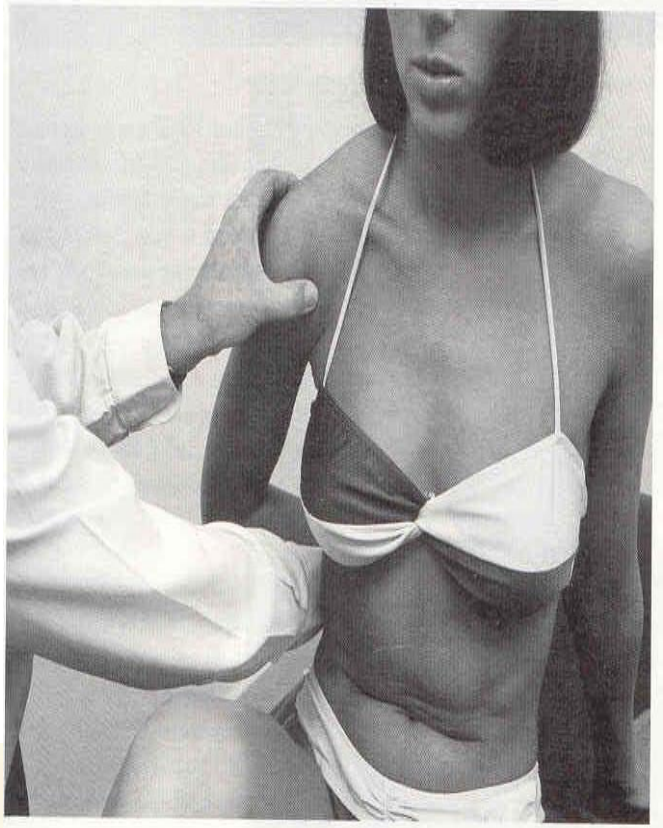
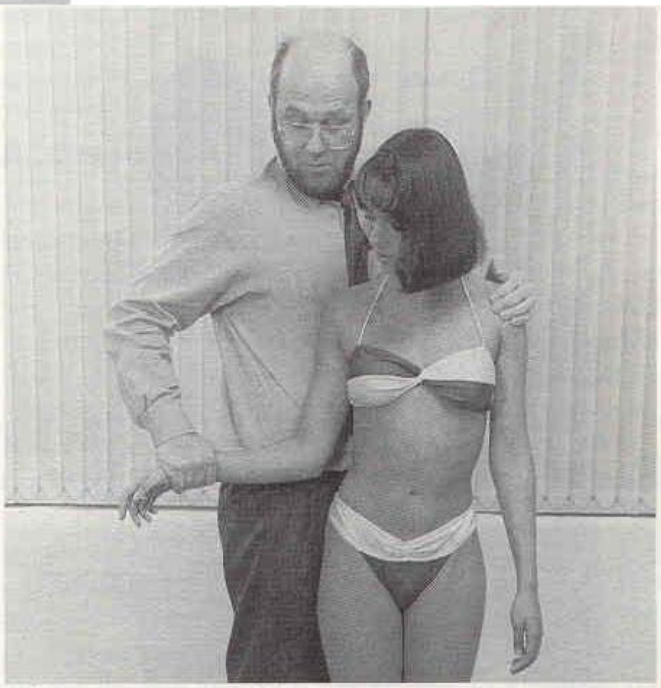


**Figure 29:** Passive horizontal lateral rotation.



# Rotator cuff with PRP

Small and medium rotator cuff tears
arthroscopic rotator cuff repair without (n = 45) or with (n = 43) PRP
follow-up at 16 months
No statistically significant difference in total Constant score & MRI
Operated shoulder: immobilized for 3 weeks using a sling

Significantly fewer narcotics for less than half the time of counterparts

In massive rotator cuff surgery: good results adding PRP gel

SLAP: shown to accelerate healing and reduce pain as compared with controls

**Does the PRP remain within the tendon or muscle injected?**

**How important is tenotomy (needling) in conjunction with PRP?**

**Current study is purposed to verify the effect of PRP itself and to reveal the synergic effect of PRP with dry needling**

Only supraspinatus with rotator cuff lesion confirmed by US

Included Tendinosis or Partial tear

SASD Bursitis -excluded

Dry needling vs PRP+dry needling
Two 3-mL PRP injections separated by 1 month
At the 6-month follow-up

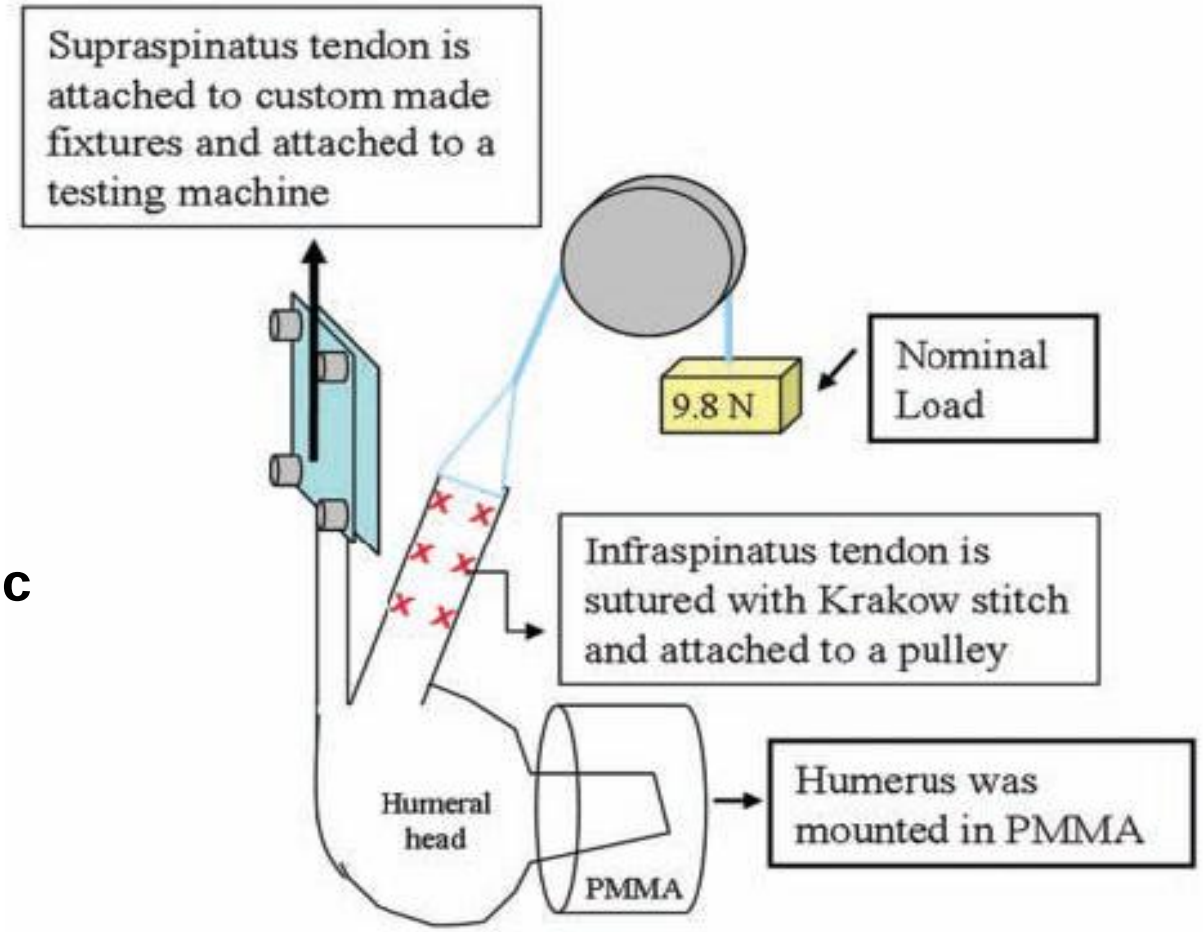
Result: not yet...

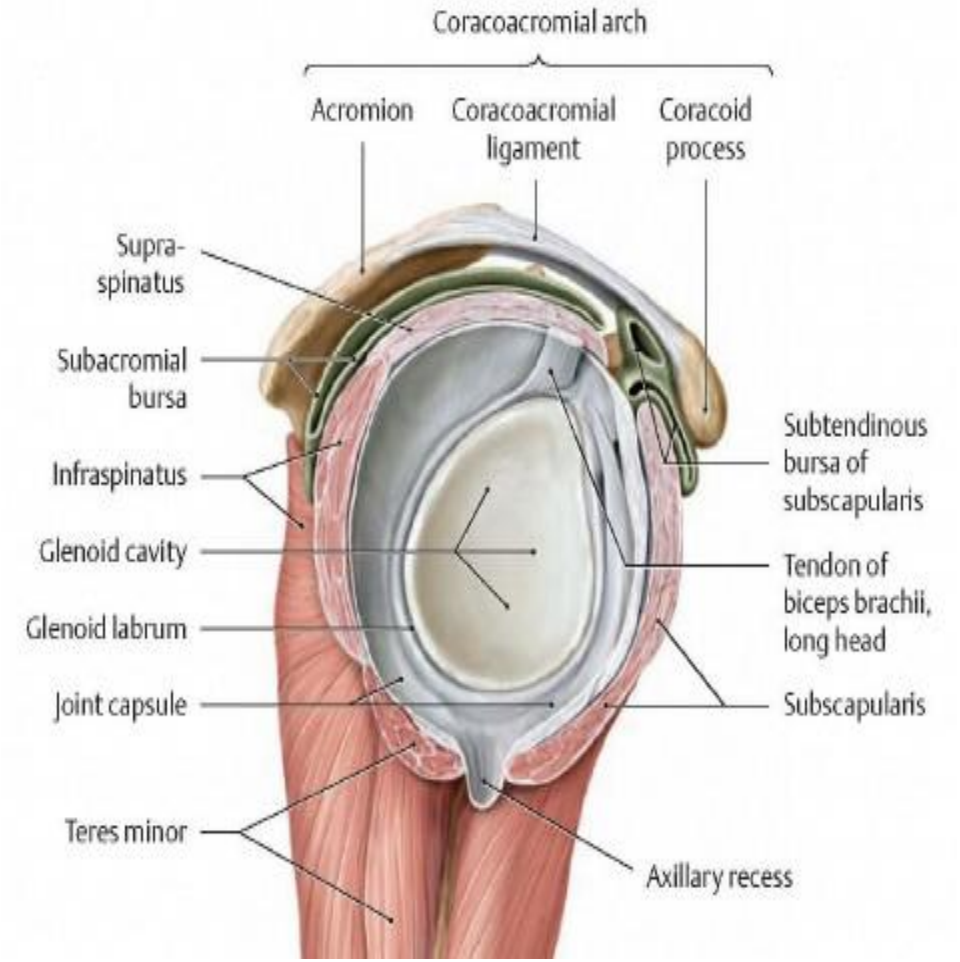
# Interaction Between the Supraspinatus and Infraspinatus Tendons : Effect of Anterior Supraspinatus Tendon Full-Thickness Tears on Infraspinatus Tendon Strain

Nelly Andarawis-Puri, Eric T. Ricchetti and Louis J. Soslowsky

*Am J Sports Med* 2009 37: 1831 originally published online May 29, 2009

**fresh-frozen cadaveric shoulders**




Coracoacromial arch
Acromion
Coracoacromial ligament
Coracoid process
Supra-spinatus
Subacromial bursa
Infraspinatus
Glenoid cavity
Glenoid labrum
Joint capsule
Teres minor
Subtendinous bursa of subscapularis
Tendon of biceps brachii, long head
Subscapularis
Axillary recess

**Conventional Tx is not enough**

**Proceeding to Next step**

**PRP can not take the place of Rehab!**


# Thank you for listening^^