

Current evidence and indications for prolotherapy with **PRP** in chronic musculoskeletal conditions

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Prolotherapy

The background of the image is a dark, almost black, space filled with ethereal, flowing smoke or mist. The smoke is rendered in shades of light blue and white, creating a sense of movement and depth. The wisps of smoke are layered and translucent, with some appearing as thin, delicate lines and others as more substantial, billowing clouds. The overall effect is one of soft, organic motion, contrasting with the sharp, clean lines of the text.

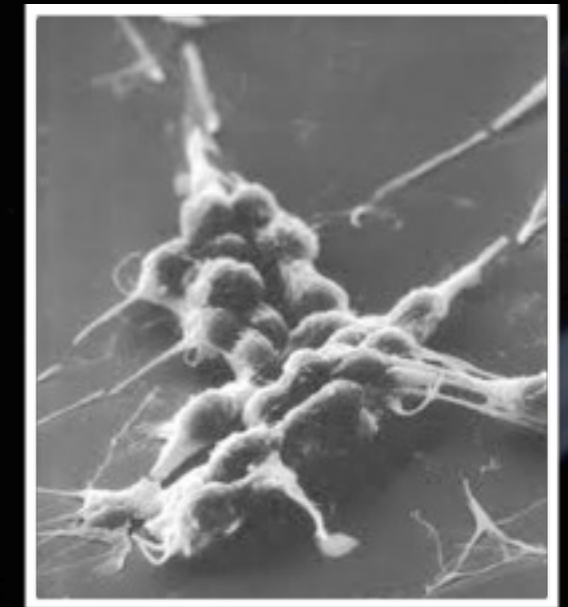
Prolotherapy

- «Proliferation therapy»; «regenerative injection therapy»; «proliferative injection therapy»
- Injection of a ***non-pharmacological*** and ***non-active*** irritant solution
- ***Re-initiate*** the inflammatory process

Platelet-rich plasma

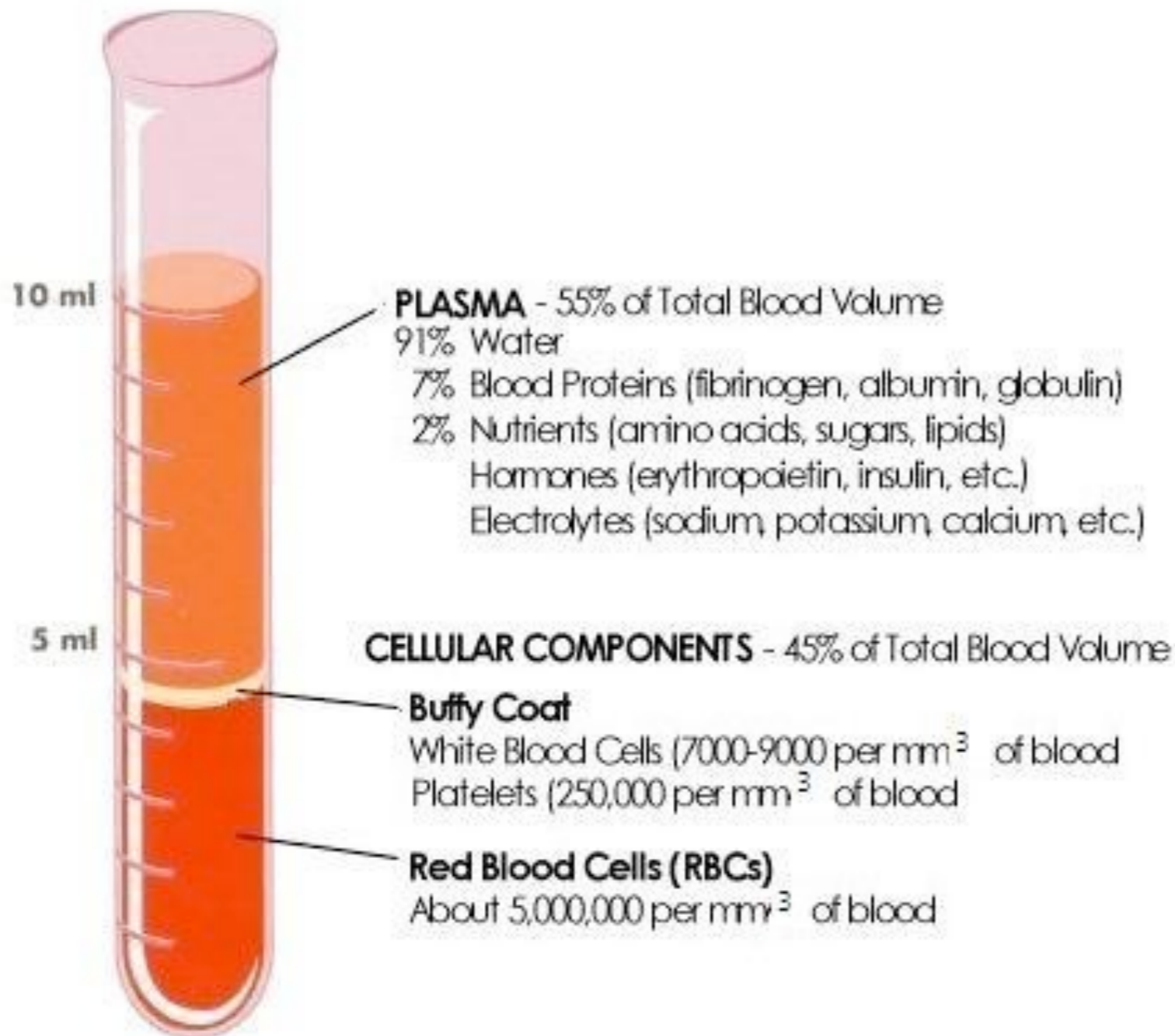


PRP



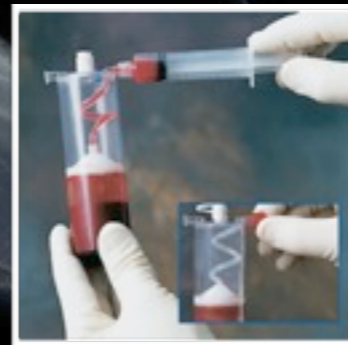
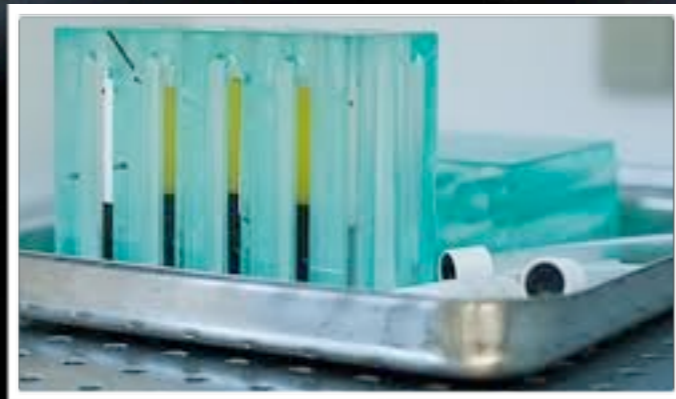
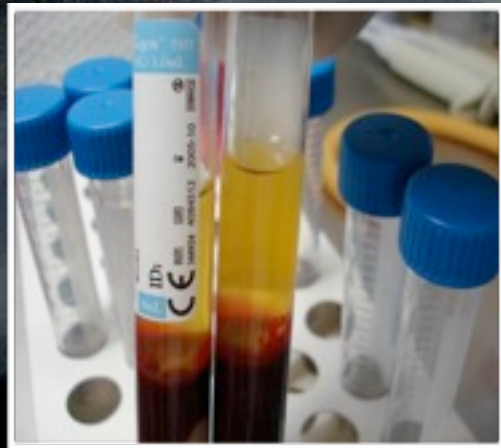
- = Platelet-Rich Plasma
- Centrifugation of **autologous** blood
- **High concentration of platelets** (3-10x)
- Platelets → roles in coagulation, inflammation, immunity modulation, «**restorative**» properties
- Liberation of cytokines and **growth factors** (VEGF, PDGF, TGF- β , IGF-I, HGF)

PRP

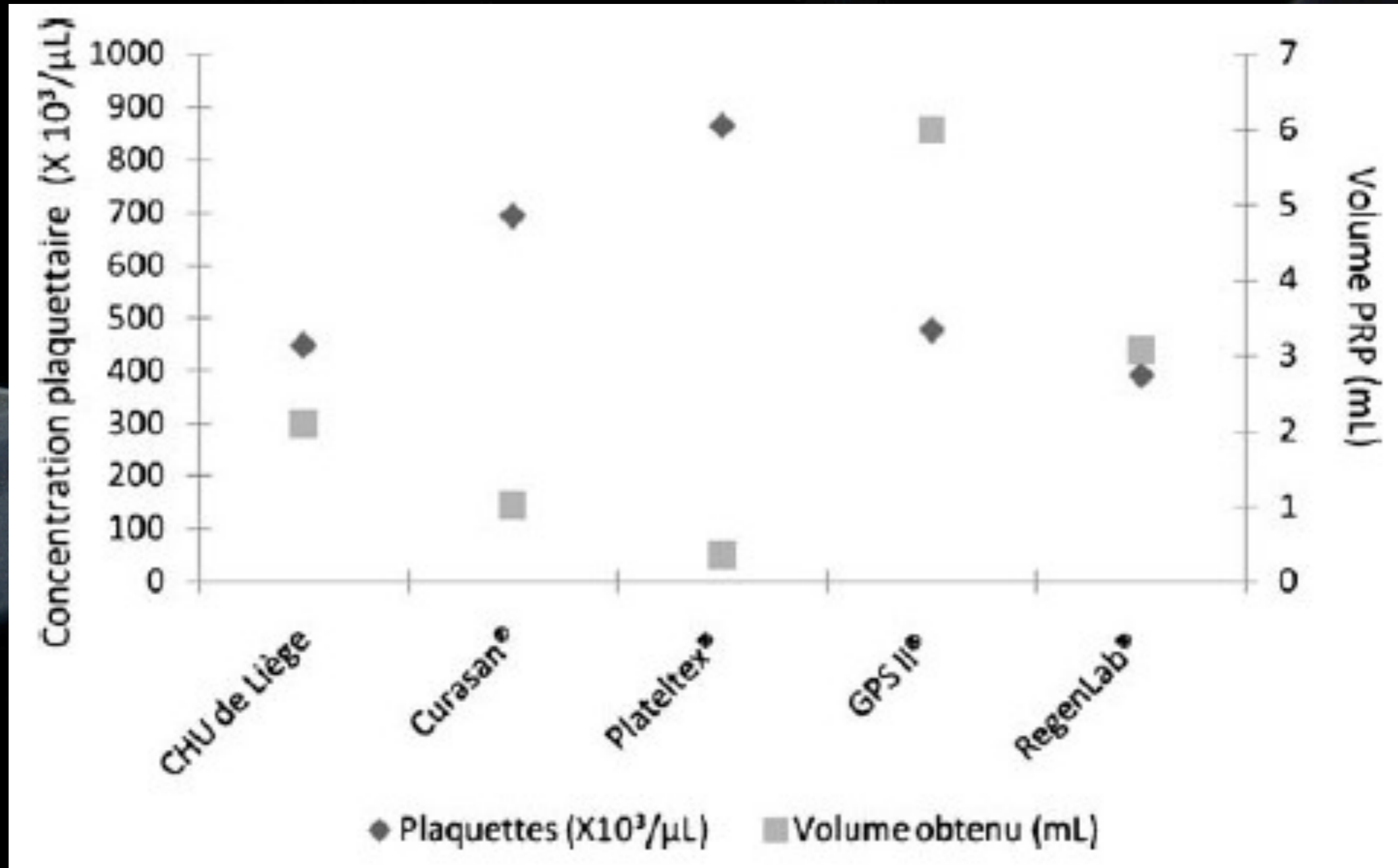


PRP

- Different techniques → different PRP
 - **variations** of platelet concentration
 - presence or not of red and white cells



PRP



PRP

- **Activation** by thrombine, CaCl_2 or collagene in situ → degranulation → liberation of GF
- **Not** really *prolotherapy* !!
- No local anaesthetic
- Avoid NSAIDs
- US guided, Rx guided

PRP

- **No general agreement**
- **Controversed** in litterature
- Very popular in **sport**
- **Removed** form the **doping list** of the WADA





PRP & tendons

PRP & tendons

- Tendons = ***small metabolic index***
- GF → tenocyte proliferation, ***collagen synthesis***, stimulation of angiogenesis, analgesic properties (Anitua et al, *Cell Prolif* 2009; Bosch et al, *Scand J Med Sci Sports* 2011; Kaux et al, *Wound Repair Regen* 2012)
- ***Stimulation*** and ***acceleration*** of tissue ***regeneration***
- The application of ***mechanical loads*** is required to obtain an optimal tissue quality (Virchenko et al, *Acta Orthop* 2006; Kaux et al, *J Orthop Res* 2012)

PRP & tendinopathies

- Tendinopathies **chronic** (more than 3 months)
- Initiate an **acute inflammatory reaction** that quickly move on to the **proliferative phase**
- **NOT** be used for acute tendinitis nor tenosynovitis
- **No side effect** described

Lateral epicondylitis



PRP & tendinopathies

- Lateral epicondylitis

- **PRP** (15) vs local **anesthetic** infiltration (5) + **eccentric** program (8 weeks) → **significant pain regression** in the PRP group over a period of 2 years (Mishra et al, Am J Sports Med 2006)
- **RCT** (51 **PRP** vs 49 **corticosteroid** infiltration) → significant **decrease** of **pain** and **algo-functional score** after 1 and 2 years for PRP group (Peerbooms et al, Am J Sports Med 2010; Gosens et al, Am J Sports Med 2011)

PRP & tendinopathies

- **Lateral epicondylitis**

- **RCT** (150 patients, **blood** vs **PRP**) → **similar** improvement of algo-functional scores after 6 months (Creaney et al, *Br J Sports Med* 2011)
- **RCT** (28 patients, **blood** vs **PRP**, under US guidance) → **PRP** better in the **short term** (6 weeks) ; **no significant difference** in the **longer term** (3 and 6 months), but symptom improvement PRP>blood (Thanassas et al, *Am J Sports Med* 2011)



Rotator cuff tendinopathies

PRP & tendinopathies

- **Rotator cuff tendinopathies**

- **Observational** series (17) PRP infiltration under US guidance → **favorable progression** (Frey, J Traumatol Sport 2009)
- Case report of favorable evolution of a 44-yo woman suffering from **calcific tendinopathy of shoulder** after 3 infiltrations of PRP and a protocol of rehabilitation (Seijas, J Orthop Surg 2012)
- after 1 year, she was still pain-free and regained full range of motion

PRP & tendinopathies

- **Rotator cuff tendinopathies**
- **Long term** observations of **arthroscopic rotator cuff suture** with adjunction of PRP
→ **less pain** in the first month but **no MRI difference** (Randelli et al, *Disabil Rehabil* 2008 & *J Shoulder Elbow Surg* 2011; Maniscalco et al, *Acta Biomed* 2008)
- **No positive effect** of applying PRP during cuff suturing compared to a control group (Castricini et al, *Am J Sports Med* 2011; Rodeo et al, *Am J Sports Med* 2012)



Patellar tendinopathies

PRP & tendinopathies

- **Patellar tendinopathies**

- **Prospective 4-month follow up** 8 high-level athletes → PRP infiltration under US → **significant improvements** in **algo-functional** scores and **MRI + return to sports** after 12 weeks (Volpi et al, *Medicina Dello Sport* 2007)
- 20 athletes → **3 injections of PRP** → **return to competition** at their former level (Kon et al, *Injury* 2009)
 - Importance of complementing the PRP injection with a **mechanical stimulus**

PRP & tendinopathies

- **Patellar tendinopathies**

- 15 athletes (*refractory for 2 years*) vs “control” population (*moderate tendinopathy for 6 months*)
→ **3 injections of PRP** → at 6 months no significant difference (Filardo et al, *Int Orthop* 2010)
 - patients with refractory patellar tendinopathy evolve as favorably as those with less severe pathology
- Case report athlete (9 months) under US guidance (Brown et al, *PM R* 2010)

PRP & tendinopathies

- **Patellar tendinopathies**

- **A *prospective study*** 14 patients (corticoids or ethoxysclerol and/or surgery) vs 22 patients → eccentric ***rehabilitation***, stretching, and eccentric work following PRP injection. After 4 weeks, sports or recreational activities → improvements more pronounced in patients ***who did not receive treatment prior to PRP*** infiltration (Gosens et al. *Int Orthop* 2012)

PRP & tendinopathies

- **Patellar tendinopathies**

- **Prospective study** 20 patients → PRP infiltration without local anesthesia → after 6 weeks **improvement algo-functional scores** and reduced pain during physical tests (without significant performance improvement) → continued for 3 months (Kaou, submitted)
- **RCT** → PRP **improves wound healing** at the donor site during surgery for the anterior cruciate ligament of the knee (de Almeida et al, Am J Sports Med 2012)



Achilles tendinopathies

PRP & tendinopathies

- **Achilles tendinopathies**

- **Series** of 14 patients (without controls) →
PRP infiltration and **eccentric** work →
decrease pain and **improvement**
algo-functional scores and **echo-**
Doppler images after 18 months (Gaweda
et al, *Int J Sports Med* 2010)

PRP & tendinopathies

- **Achilles tendinopathies**

- **RCT PRP vs isotonic saline** (n = 54) + **eccentric** activities for 3 months
→ after 24 weeks algo-functional scores, patient satisfaction, and return to sports activities significantly **improved in both groups** → idem after 1 year + **no US differences** (de Vos et al, JAMA 2010 & Br J Sports Med 2011; de Jonge et al, Br J Sports Med 2010)

- **Critics:**

- no eccentric treatment before study
- injection could cause local bleeding
- change in pressure-volume related to the presence of saline solution
- relatively invasive for a control group,
- PRP quality may not have been optimal

PRP & tendinopathies

- **Achilles tendinopathies**

- 2-year longitudinal **follow-up** of 10 patients → **PRP** → **modest improvement** in function **without** any **MRI** changes (owens et al, *Foot Ankle Int* 2011)



PRP & plantar fasciitis

PRP & plantar fasciitis

- ***Irritation*** of the ***fascia sheathing the tendons*** responsible for maintaining the ***foot arch***
- Not a real tendon structure
- ***Symptoms*** and ***treatment*** are relatively ***similar***

PRP & plantar fasciitis

- **Prospective** study 25 patients followed for 10 months → **PRP** → **88% improvement of pain** and **favorable functional progression** (60%) + **favorable US changes** (Ragab et al, Arch Orthop Trauma Surg 2012)
- 60 patients (2 groups of 30 subjects) **PRP** vs **corticosteroid** infiltration → **no difference** at 3 weeks and 6 months (Aksahin et al, Arch Orthop Trauma Surg 2012)
- A multicenter RCT is in process (Peerbooms et al, BMC Musculoskelet Disord 2010)



PRP & osteoarthritis

PRP & osteoarthritis

- ***Degenerative phenomenon*** of the ***cartilage*** with complex, ***multifactorial pathophysiology***
- Potential healing ***very poor***
- Multitude of ***conservative*** pharmacological treatments (palliative rather than curative)

PRP & osteoarthritis

- **3 PRP injections vs hyaluronic acid** (30 gonarthrosis)
→ at 5 weeks **significant improvement** in **pain** and **algo-functional** questionnaires with **PRP** (Sanchez et al, Clin Exp Rheumatol 2008)
- Different prospective studies **3 PRP injections vs hyaluronic acid** in moderate cases of gonarthrosis
→ **significant improvements** in **pain** and **algo-functional** scores after a follow-up period of up to 1 year (Sampson et al, Am J Phys Med Rehabil 2010; Spakova et al, Am J Phys Med Rehabil 2012; Wang-Saegusa et al, Acta Orthop Trauma Surg 2011; Kon et al, Knee Surg Sports Traumatol Arthrosc 2010; Filardo et al, Knee Surg Sports Traumatol Arthrosc 2011; Kon et al; Arthroscopy 2011)

PRP & osteoarthritis

- **Cohort study** (144 patients) **2 different PRP preparations for gonarthrosis** → **significant clinical improvement** compared to baseline in **both groups** (Filardo et al, *Knee Surg Sports Traumatol Arthrosc* 2011)
 - 1 technique initially produced more pain and swelling
 - best results were observed in younger patients with a low degree of cartilage damage

PRP & osteoarthritis

- **Written debate knee arthroplasty vs PRP injection** (gonarthrosis) → **2 options seem reasonable** in a 60-year-old patient with moderate symptoms who wishes to continue skiing (Klatt et al, PM R 2011)
- because **PRP** infiltration therapy is less costly, less invasive, and less risky than knee arthroplasty → **first line treatment**
- **dissatisfaction** regarding pain control and improved knee function → **arthroplasty**

PRP & osteoarthritis

- **Cohort study** (6-month follow up) of 40 patients with **severe hip osteoarthritis** → **significant improvements** in pain and also functional scores after **three injections of PRP** under **US guidance** (Sanchez et al, *Rheumatology* 2012)
- **Absence of side effects** associated with this treatment



PRP & nonunion

PRP & nonunion

- A fracture will normally fuse
- ➔ nonunion = the **absence of fusion** between bone fragments.
- This produces **pain** and **abnormal movements** of varying degrees.

PRP & nonunion

- **Percutaneous PRP** injection under **fluoroscopic guidance** → unclear and **controversial** (Seijas et al, *Acta Orthop Belg* 2010; Mariconda et al, *J Orthop Trauma* 2008)
- This technique could produce **encouraging results** and provide a **less invasive** alternative to open bone-grafting techniques (Bielecki et al, *Eur Surg Res* 2008)

Side effects of PRP



Side effects

- No side effect reported
- Exuberant local inflammation in an insulin dependant diabetes patient (NAD ?) (Kaush, *submitted*)



Conclusion

Conclusion

- PRP → growth factors
- Easy to prepare, relatively low cost and minimal invasiveness
- New therapeutic option → chronic tendinopathies, plantar fasciitis, osteoarthritis, nonunion
- Currently little tangible clinical evidences
- RCT with appropriate placebo group are needed

Thank you for your attention !



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