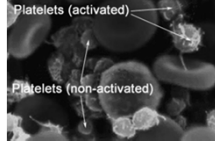


PLATELET RICH PLASMA UPDATE




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Annette M. Zaharoff, M.D.

Financial Disclosure

Dr. Annette Zaharoff has no relevant financial relationships with commercial interests to disclose.


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Regenerative Medicine

- Replacing or regenerating human cells, tissues, organs to restore or establish normal function
- MSK medicine
 - Repair injuries, facilitate healing
 - Cartilage cells, stem cells, collagen, platelets


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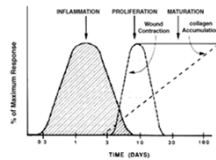
Blood

- Whole Blood
 - Plasma, 93%RBC, 1%WBC
 - 6%Platelets
- PRP
 - 94% Platelets (4-6 fold increase)
 - 5% RBC, <1% WBC, Plasma
 - Increase stimulus for connective tissue healing



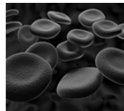
Connective Tissue Healing

- Sequential cascade, systematic process in acute injuries
- Regulation by various cells in different phases
- Phases
 - Inflammation
 - Proliferation
 - Remodeling

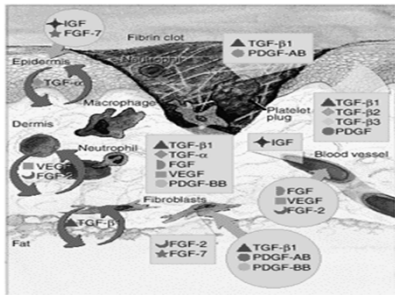


Inflammatory Phase

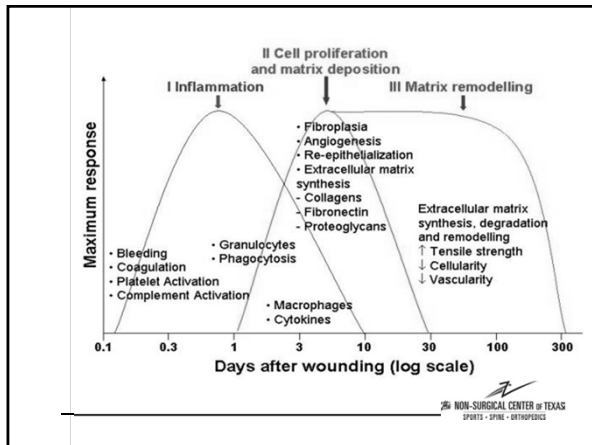
- Hemostasis
- Platelet aggregation
- Platelet degranulation
 - GF's, cytokines, adhesion molecules, > 30 bioactive factors
 - Cell proliferation, chemotaxis, cell differentiation, angiogenesis



Growth Factors



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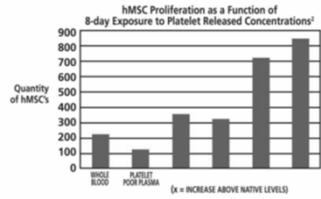
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Platelet Rich Plasma

- Increase platelet concentration
 - 4-6 fold increase (1,000,000 / μ L)
 - Increase hMSC's
 - Increase proliferative activity of cells (fibroblasts, chondrocytes, osteoid, collagen, matrix)
- No mutagenic activity

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Healing Cascade



Relationship of differing platelet concentrations and human mesenchymal stem cell (hMSC) migration and proliferation. From: Haynesworth, Stephen et al. American Academy of Orthopedic Surgery, March 2001

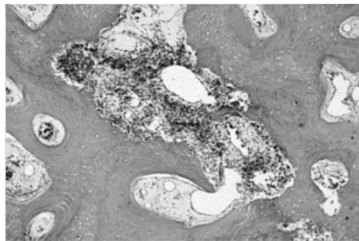


PRP in Clinical Setting

- History
 - Ferrari (1987), autologous transfusion
- Other specialties
 - Maxillofacial, cosmetic, dentistry, spine, neurosurgery, wound healing, podiatry, orthopedics, urology, ENT, Cardiology

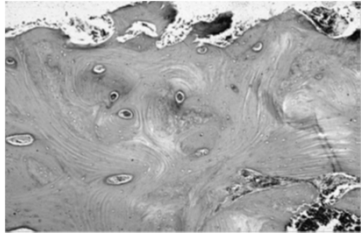


Seeing is Believing



Human bone graft histology at 4 months without platelet rich plasma. There is a 59% trabecular bone density, active resorption remodeling, and a preponderance of immature bone





Human bone graft histology at 4 months with platelet-rich plasma enhancement. There is an 80% trabecular bone density, the bone is mature, and there is no evidence of active resorption remodeling

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Seeing is Believing



Split thickness skin graft 6 days.

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45 days

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MSK Medicine

- MSK injuries
 - Long term pain, disability
 - 45% soft tissue
- Standard treatment
 - NSAID
 - Corticosteroids
 - Pharmaceuticals most commonly prescribed
 - Surgery

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PRP in MSK Medicine

- Chronic degenerative tendinopathies
- Acute injury
 - Muscle, ligament, tendon
- Articular cartilage, intra-articular damage
- Bone and periosteum healing
- Kon et al (2011)
 - Pre-clinical effects of PRP on MSK tissue and injuries

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PRP Literature

- Basic Science
 - In vitro and animal studies
- Low evidence
 - Controlled trials, Cohort and case studies
 - Level 3, 4
- High evidence
 - Systematic reviews, met-analysis of RCT's,
 - Level 1, 2



PRP Literature

- **J Bone Joint Surg Am. 2012**; literature search
 - 895 relevant citations. 33 studies-23 randomized controlled trials and 10 prospective cohort studies, 32 proved eligible for inclusion
- **Conclusions: The current literature is complicated by a lack of standardization of study protocols, platelet-separation techniques, and outcome measures.** As a result, there is uncertainty about the evidence to support the increasing clinical use of platelet-rich plasma and autologous blood concentrates as a treatment modality for orthopedic bone and soft-tissue injuries.
- **Level of Evidence: Therapeutic Level 2** evidence



PRP in Sports Medicine

- Increasing prevalence of regenerative injections
- >86,000 athletes use in U.S.
- WADA approved (2011)
- Pro sports



“Spinning Blood Isn’t Just for Athletes Anymore”

• Wall Street Journal - March 2010



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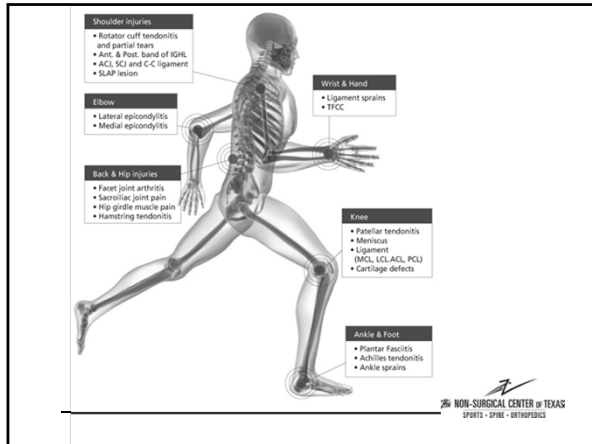
PRP Literature

- Review articles
 - Everts (2006): 28 human studies
 - + outcomes = 21
 - - or no effect = 7 (small sample size, platelet processing compromised)
 - Kon et al (2011): 15 studies
 - Level 1-4 evidence
 - + outcomes = 13

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Table 2 PRP applications in humans: clinical evidence for the treatment of sports lesions

Pathology	Study	Level	Patients	F up	Results
Elbow tendinopathy	Milks Perrella (2006)	2	20	2 years	+ Enhanced healing and functional recovery vs. hyaluronic injections
	Pereboom et al. (2010)	1	100	1 year	+ Reduced pain and increased function, exceeding the effect of corticosteroid injection (short term); none declined
Rotator cuff tear	Machirado et al. (2008)	4	1	6 months	+ Pain relief and ROM recover after surgical repair
	Randelli et al. (2008)	4	14	2 years	+ Complete integrity of the rotator cuff under the fibrous sheath by MRI
Achilles tendon tendinopathy	Sanchez et al. (2007)	3	12	32–50 months	+ No wound complications in surgically repaired tendons
	Filardo et al. (2010)	4	1	18 months	+ Earlier recovery of ROM and a faster return to jogging and sport
	De Vos et al. (2010)	1	54	24 weeks	+ Lower cross-sectional area
Patellar tendinopathy	Filardo et al. (2010)	4	1	18 months	+ Fast tissue repair and return to competitive sports activity in patellar tendon tear
	Kon et al. (2009)	4	20	6 months	+ Same results in pain and activity improvement compared with a saline injection
ACL tear	Orrego et al. (2008)	2	108	6 months	+ Marked improvement in knee function and quality of life
	Silva et al. (2009)	3	40	3 months	+ PRP has to be associated with physiotherapy
Cartilage histology/regeneration	Balciro et al. (2010)	3	30	3–12 months	+ Marked clinical improvement in chronic refractory patellar tendinopathy, compatible with less severe cases
	Sanchez et al. (2000)	4	1	6 months	+ Greater improvement in the level of sports activity in PRP group
	Sanchez et al. (2008)	3	60	5 weeks	+ Enhanced maturation (MRI)
ACL tear	Orrego et al. (2008)	2	108	6 months	+ No effect on tunnel widening
	Silva et al. (2009)	3	40	3 months	+ No MRI difference compared to controls
	Balciro et al. (2010)	3	30	3–12 months	+ 45% reduction in the time required to achieve a complete homogeneous graft signal when PRP was used for surgical ACL augmentation
Cartilage histology/regeneration	Sanchez et al. (2000)	4	1	6 months	+ Rapid resumption of symptom-free athletic activity after surgical treatment for knee cartilage evolution
	Sanchez et al. (2008)	3	60	5 weeks	+ Better pain control and physical function improvement vs. hyaluronic ligatures
ACL tear	Kon et al. (2010)	4	91	1 year	+ Clinical improvement
					+ Better results in early degeneration and younger patients



Muscle and Tendon Healing

- Mishra (2006)
 - Prospective study, lateral epicondylitis
 - PRP vs bupivacaine
 - 98% improved at 2 yrs.
- Peerbooms (2010)
 - **Level 1**, lateral epicondylitis
 - PRP vs corticosteroid injection
 - Increased function, decreased pain

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Muscle and Tendon Healing

- Sanchez (2007)
 - Earlier return to function and impact activities post-op Achilles repair
 - N = 12
- De Vos (2010)
 - Eccentric exercise with PRP or saline injection of Achilles tendinopathy
 - Similar improvement

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Muscle and Tendon Healing

- Barrett (2004)
 - Retrospective study, N = 9
 - + U/S changes of plantar fascia at 1 year
 - 7 of 9 patients with 100% relief
- Kon (2009)
 - Prospective, cohort study, chronic patellar tendinosis, failed treatment
 - Decrease pain, increase function with PRP 3x, administered q15 days



Muscle and Tendon Healing

- Randelli (2008)
 - **Level 1**
 - PRP augmentation of RC repair vs standard
 - Earlier decrease of post-op pain and increase function
 - No MRI differences at 2 yrs, sustained improvement



Muscle and Tendon Healing

- Sanchez
 - 20 professional athletes with hamstring injuries
 - Full recovery in half the expected time **without any fibrosis** or re-injury
- Ligaments
 - MCL, ACL have mixed reviews



Articular Cartilage

- Van Buul
 - Human OA chondrocytes inflammatory factors (interleukin-1 β) inhibited by PRP
- Sampson (2010)
 - PRP 3x q4 weeks, reduced pain, increased function compared to baseline at 1 year



Articular Cartilage

- Kon (2009)
 - 115 patients
 - Moderate-severe knee OA, failed conservative care
 - Majority with statistically significant objective, subjective improvement



Articular Cartilage

- Kon (2010)
 - PRP vs low and high molecular weight HA viscosupplementation
 - ≤ 50 y.o.-all improved at 6 mos; PRP most effective to \downarrow pain, \uparrow function
 - > 50 y.o.-PRP and low molecular weight similar improvement, high m.wt. worst
- PRP safe, effective alternative to HA



State of the Research Art

- Basic science
 - Animal and in vitro studies
- Clinical science
 - Larger sample sizes
 - Randomized controlled studies
 - Standardized protocols, preparations and techniques



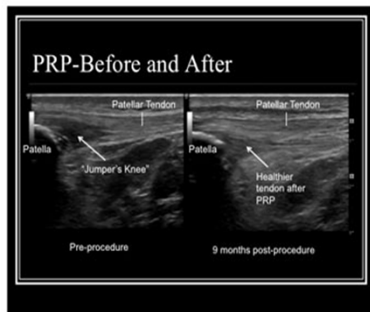
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Achilles tear

Post PRP - 2 months

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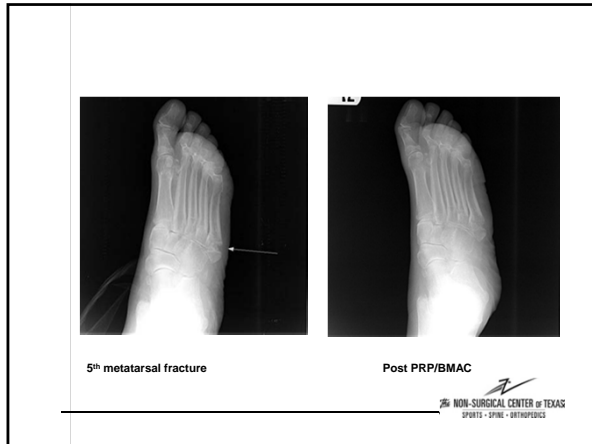


PRP-Before and After

Patellar Tendon
Patella
"Jumper's Knee"
Pre-procedure


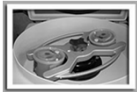
Patellar Tendon
Patella
Healed tendon after PRP
9 months post-procedure


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PRP Preparation



- Venous blood draw
 - Anticoagulated, 30-60ml
- Graft preparation centrifuges

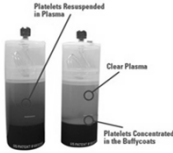






PRP Preparation

- Platelet concentrates (4-6 fold) into small amount of plasma with leucocytes



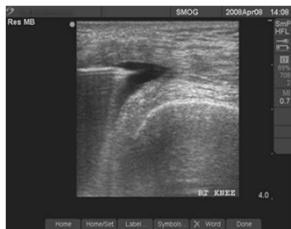


PRP Process

- Injection
 - Activation of platelets
 - Image-guided




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Risks

- Allergic reactions (medication only)
- Percutaneous needle technique
 - Image guidance
- Infection (no transmissible factors)
 - 1:50,000 risk
- Pain
 - Temporary, short duration


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Contraindications

Table 1. Absolute and relative contraindications to PRP use

Absolute	Relative
<ul style="list-style-type: none"> • Platelet dysfunction syndrome • Critical thrombocytopenia • Hemodynamic instability • Septicemia • Local infection at procedure site • Patient not willing to accept risks 	<ul style="list-style-type: none"> • Consistent use of NSAIDs within 48 hours of procedure • Corticosteroid injection at treatment site within 1 month • Systemic corticosteroid use within 2 weeks • Tobacco use • Recent fever or illness • Cancer, especially hematopoietic or bone • Hemoglobin level < 10 g/dL • Platelet count < 105μL

PRP: platelet-rich plasma.
Adapted from Platelet Rich Plasma (PRP) Guidelines, International Cellular Medicine Society, 2011.²⁴



Treatment Course

- Average 2-4 injections
- Frequency: q2-6 weeks
- Post injection
 - No NSAID's or corticosteroids
 - Tylenol or Rx pain medications prn



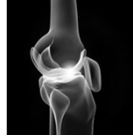
Treatment Course

- ADL's as comfortable, braces and crutches prn
- No heavy resistive exercise or excessive motion at injection area for 2 weeks
- Light exercise as tolerated
- >2-4 weeks: transition into exercise/activity guided by exam and functional status



Conclusions

- Important to understand the body's healing process to make rational decisions for treating MSK injuries
- When indicated, seek non-surgical treatment options with emphasis on long term repair



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Conclusions

- PRP may be an effective long term, non-surgical treatment option for MSK injuries, when indicated
- Safe, simple, cost effective procedure vs. surgery
- Ability to demonstrate objective healing
- Great potential in MSK medicine



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Figure – Platelet-rich plasma treatment offers the potential for a safe, convenient, and effective option for athletes and other active persons with musculoskeletal injuries. Platelets contain more than 30 bioactive proteins responsible for hemostasis and tissue healing.

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