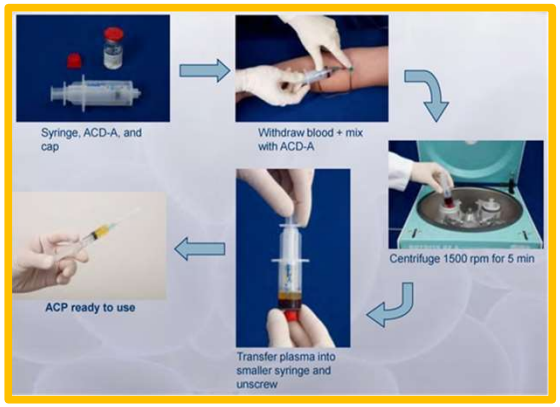
Platelet Rich Plasma – Clinical Applications



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Introduction

- **Presentation Outline**

  - Introduction and history
  - Mechanism of Action
  - Preparation
  - Clinical Utility of PRP
    - Osteoarthritis
    - Tendinopathy
    - Contraindications to therapy
  - Cost
  - Conclusions & clinical practice

Introduction & History

- Definition of platelet rich plasma
  - Autologous blood with a concentration of platelets above baseline values.
- Origins
  - Initially was used in the 1980s – 1990s in oral maxillofacial and periodontal surgery to aid in reducing inflammation and to promote healing[1]
- Contents of platelet rich plasma
  - Beyond platelets, it contains numerous growth factors (GFs) thought to aid in healing and dampening inflammation

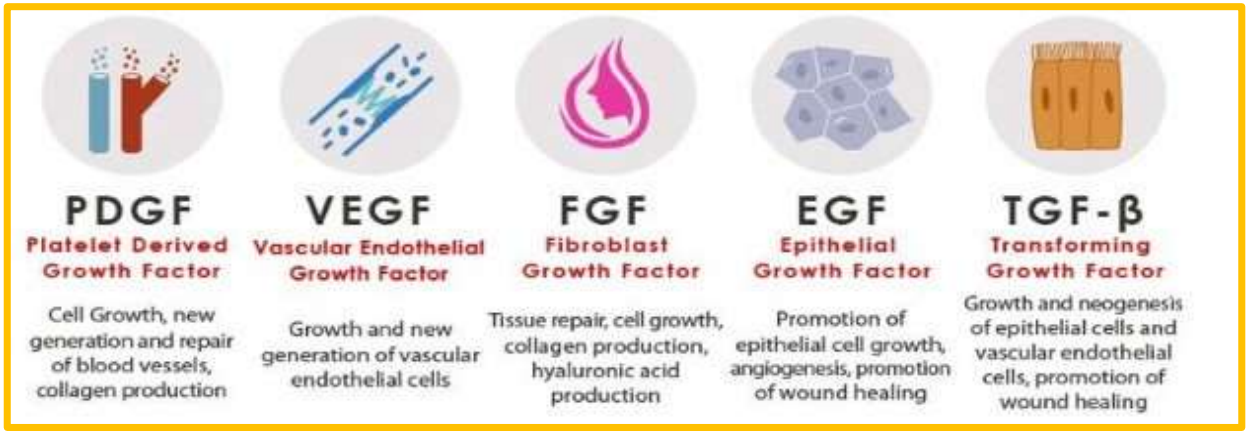
Growth Factor	Source	Function
Platelet-derived growth factor	Platelets	Stimulates cell replication, angiogenesis, mitogen for fibroblasts
Vascular endothelial growth factor	Platelets	Angiogenesis
Transforming growth factor-β1	Platelets	Key regulator in balance between fibrosis and myocyte regeneration
Fibroblast growth factor	Platelets	Stimulates proliferation of myoblasts, angiogenesis
Epidermal growth factor	Platelets	Proliferation of mesenchymal and epithelial cells, potentiation of other growth factors
Hepatocyte growth factor	Plasma	Angiogenesis, mitogen for endothelial cells, antifibrotic
Insulin-like growth factor-1	Plasma	Stimulates myoblasts and fibroblasts, mediates growth and repair of skeletal muscle

Reproduced with permission from Creaney L, Hamilton B: Growth factor delivery methods in the management of sports injuries: The state of play. *Br J Sports Med* 2008;42;314-320.

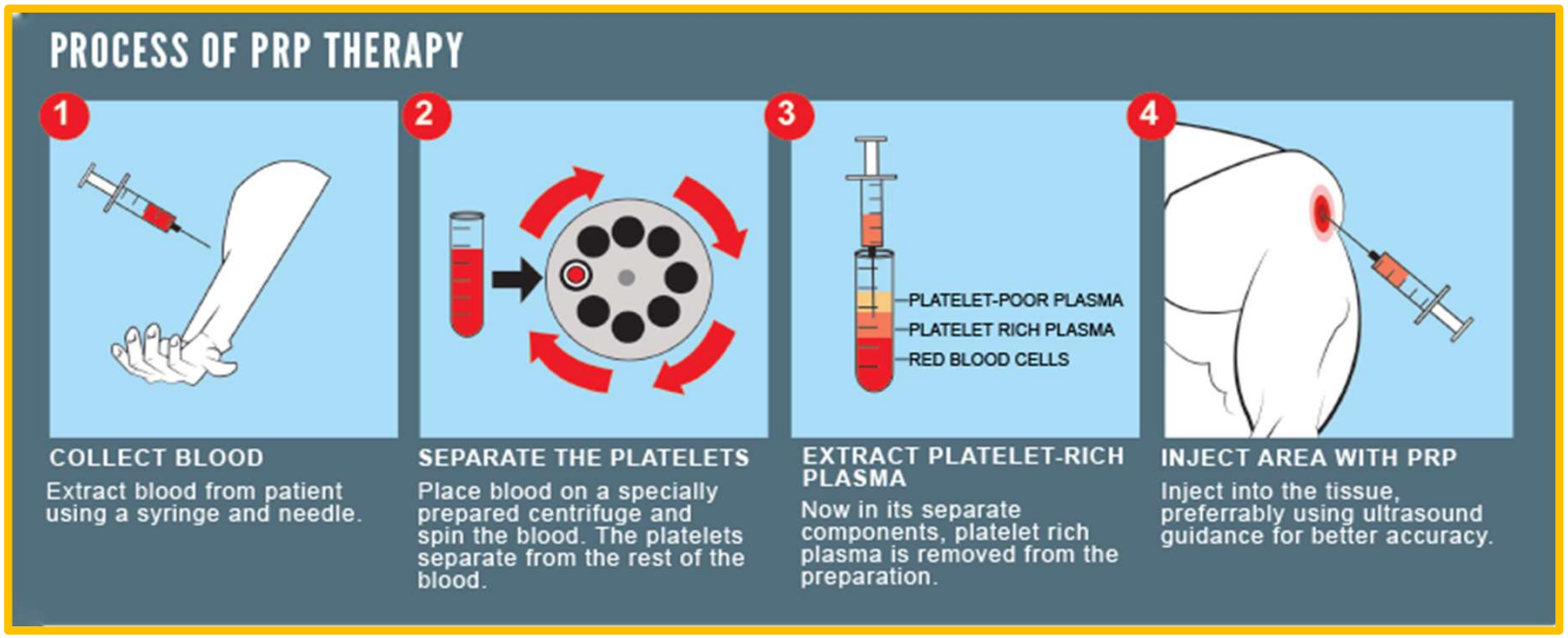
Mechanism of Action

- Anti-inflammatory effects
  - Reduces inflammation by enhancing the expression of an NF-kappa-beta inhibitor, thus reducing NF-kappa-beta signaling and dampening its downstream inflammatory cytokine activation

- Tissue repair augmentation
  - The high concentrations of growth factors including tissue growth factor and platelet-derived growth factors, aid in mediating the proliferation of mesenchymal stem cells and increase matrix synthesis and collagen formation



Preparation



Analysis of Platelet-Rich Plasma Extraction

Variations in Platelet and Blood Components Between 4 Common Commercial Kits

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Paul Robert McCrory,‖ PhD, FFSEM, FACSP, FRACP, MBBS,
Martin D. Richardson,¶ FRACS, MBBS, MS, and Ming Hao Zheng,‡# PhD, DM, FRCPath, FRCPA
Investigation performed at the University of Western Australia,

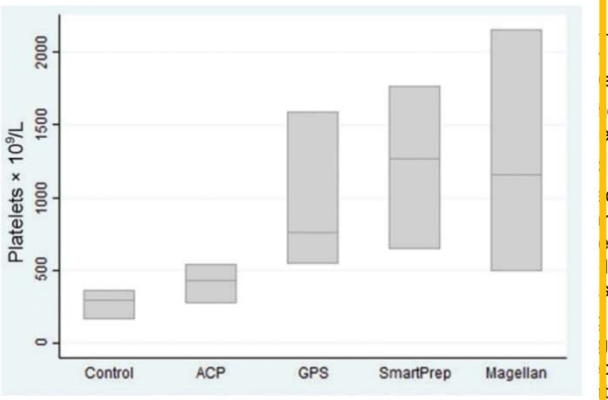

Figure 1. Platelet counts by kit type.

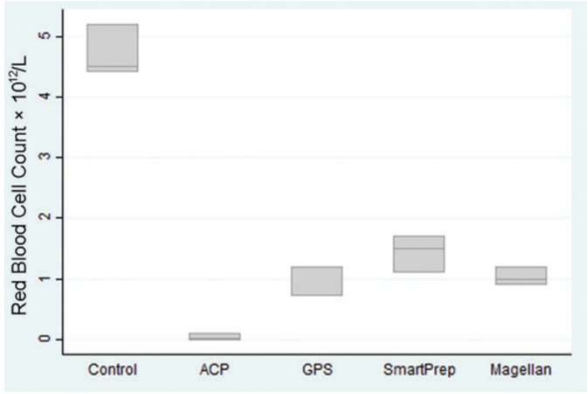

Figure 2. Red blood cell counts by kit type.

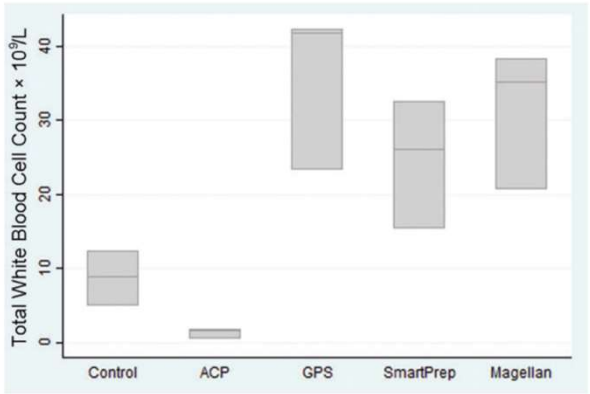

Figure 3. Total white blood cell counts by kit type.

Conclusion: This study reveals the variation of blood components, including platelets, red blood cells, leukocytes, pH, and glucose in PRP extractions. The high concentrations of cells are important, as the white blood cell count in PRP samples has frequently been ignored, being considered insignificant. The lack of standardization of PRP preparation for clinical use has contributed at least in part to the varying clinical efficacy in PRP use.

Clinical Relevance: The variation of platelet and other blood component concentrations between commercial PRP kits may affect clinical treatment outcomes. There is a need for standardization of PRP for clinical use.

Keywords: platelet-rich plasma; PRP; leukocyte; osteoarthritis; tendinopathy

COMMENTARY AND PERSPECTIVE

Rich or Poor? Examining Platelet-Rich Plasma Leukocyte Concentration in Knee Osteoarthritis

Commentary on article by Aazad Abbas, HBSc, et al.: "The Effect of Leukocyte Concentration on Platelet-Rich Plasma Injections for Knee Osteoarthritis. A Network Meta-Analysis"

Vellios, Evan E. MD[1,a]

Author Information

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Clinical Utility – Osteoarthritis of the knee

- The American Journal of Sports Medicine[2]

Hyaluronic Acid Versus Platelet-Rich Plasma

A Prospective, Double-Blind Randomized Controlled Trial Comparing Clinical Outcomes and Effects on Intra-articular Biology for the Treatment of Knee Osteoarthritis

Brian J. Cole,*†‡§||¶ MD, MBA, Vasili Karas,# MD, MS, Kristen Hussey,† MS, David B. Merkow,† BA, Kyle Pilz,†¶ MMS, PA-C, and Lisa A. Fortier,** DVM, PhD, DACVS
Investigation performed at the Rush University Medical Center, Chicago, Illinois, USA

- **Population & Intervention**: 111 patients with unilateral symptomatic knee OA (KL Grade 1-3) with a minimum of 3 mo of knee pain were randomized to PRP vs HA.
- **End Points**: Primary end points were WOMAC pain score, IKDC score and visual analog score were monitored for 1-year.
- **Conclusion**: There was no significant difference in WOMAC score, but IKDC and visual analog scores were statistically improved at 24 and 52 weeks in the PRP group vs HA group.

Clinical Utility – Osteoarthritis of the knee

Figure 3. Mean In
tee (IKDC) score in
plasma (PRP) groups over the course of 52 weeks. *Statistically significant difference (P = .013) between treatment groups at 24 weeks. Error bars demonstrate the standard error.

course of 52 weeks. *Statistically significant difference between treatment groups at 24 (P = .0096) and 52 weeks (P = .0039). Error bars demonstrate the standard error.

PRP Is Better vs HA at 52 weeks or 1year:

IKDC Scores

VAS

Clinical Utility – Osteoarthritis of the knee

- Arthroscopy: The Journal of Arthroscopy and Related Surgery[3]

Intra-articular Injection of Platelet-Rich Plasma Is Superior to Hyaluronic Acid or Saline Solution in the

PRP Is Better vs HA or Saline at 52 weeks or 1year:

IKDC Scores

WOMAC

- **End Points**: WOMAC and IKDC scores were collected at 1,2,6 and 12 months
- **Conclusion**: All three groups showed improvement at 1 mo, but only the PRP group demonstrated statistically significant improvements in WOMAC and IKDC scores at 2, 6 and 12 months. Only the PRP group reached the minimal clinically important difference in both the WOMAC and IKDC. There was no difference between HA and NS during the interval of study.

Clinical Utility – Osteoarthritis of the knee

- The Orthopaedic Journal of Sports Medicine[11]

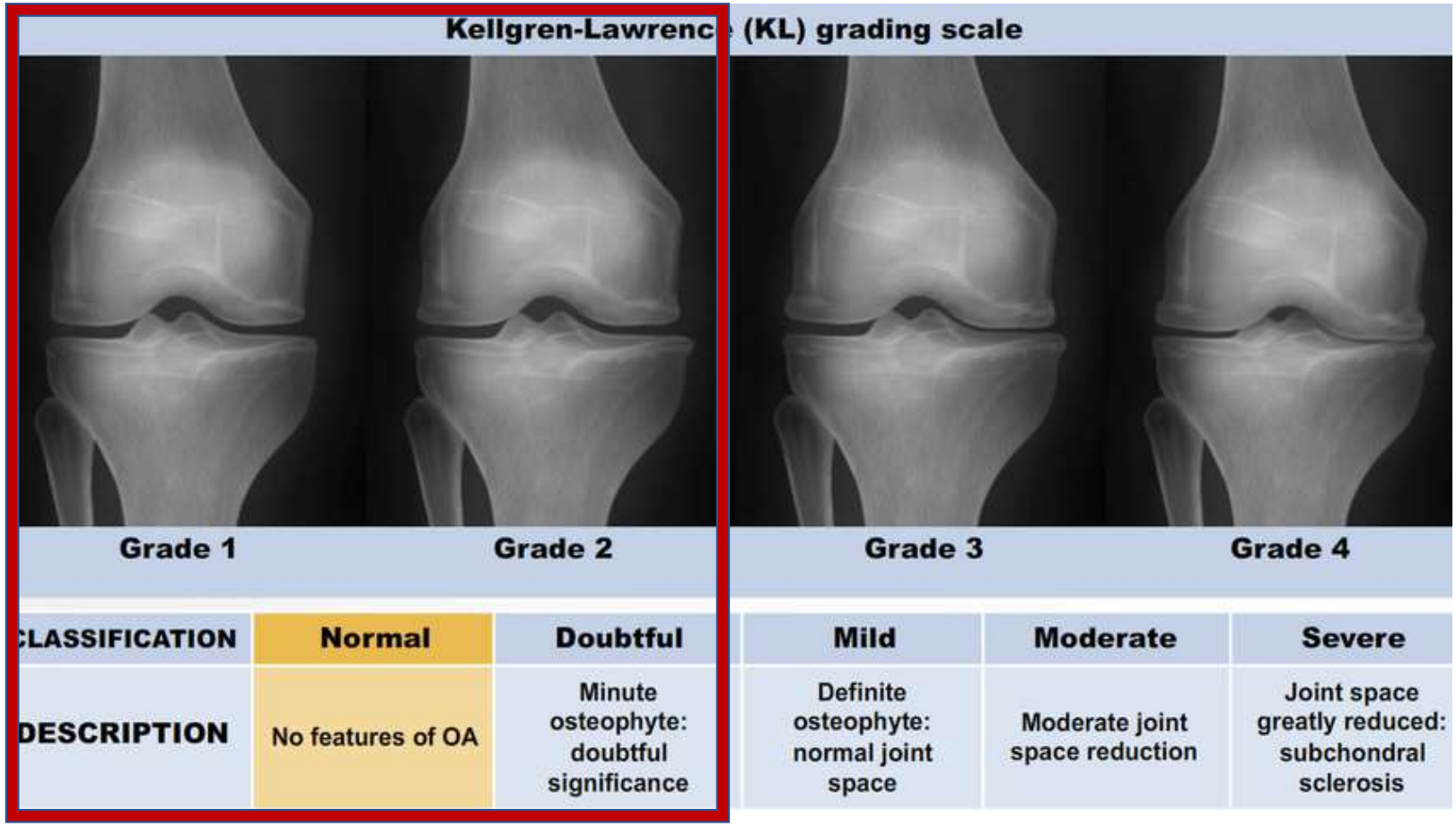
Platelet-Rich Plasma Injections for Advanced Knee Osteoarthritis

PRP vs Saline

NO DIFFERENCE at 6 months!

- were randomized to a single treatment with PRP or CSI.
- **End Points**: VAS, Knee Injury and Osteoarthritis Score (KOOS) and Short Form-36 were at 1, 3 and 6 months.
- **Conclusion**: VAS, KOOS and SF-36 scores all improved during the study interval, but did not reach statistical significance during the study period. They postulated this might be the product of their study population.

KL – Grade Knee OA



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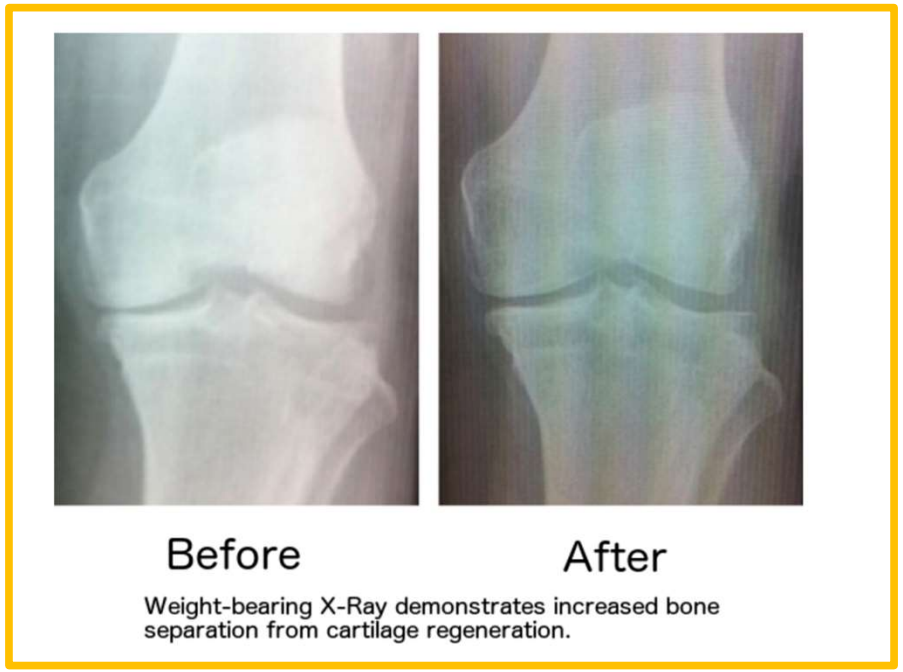
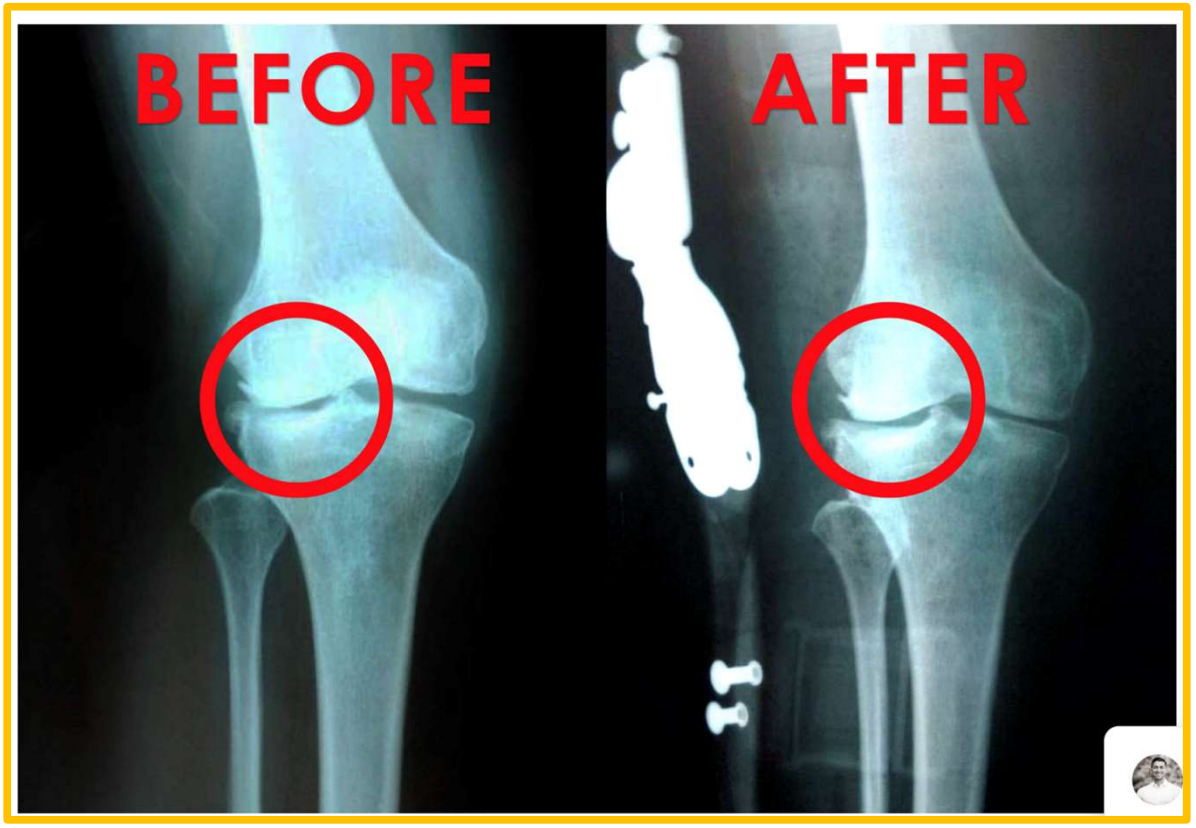




Clinical Utility – Osteoarthritis of the hip

- The American Journal of Sports Medicine[5]

Ultrasound-Guided Injection of Platelet-Rich Plasma and Hyaluronic Acid, Separately and

PRP Is Better vs PRP+HA or HA at 6 months but NOT at 12 months:

VAS

WOMAC

by Kellgren-Lawrence grading who were symptomatic were randomized to receive PRP, PRP+HA, or HA.

- **End Points**: VAS pain score and WOMAC at 2, 6 and 12 months.
- **Conclusion**: The PRP alone group had statistically significant improvements in VAS throughout the duration of the study and WOMAC scores at 2 and 6 months compared to both the PRP+HA and HA groups.

Clinical Utility – Osteoarthritis of the shoulder

?

Clinical Utility – Osteoarthritis of the shoulder

- Case Report
  - Freitag and Barnard published a case report in 2016 of a 62 yo female patient with severe GH arthritis who was able to achieve significant reductions in both VAS pain score DASH score that were sustained for greater than 6 months with a PRP injection.[6]

Clinical Utility – Rotator Cuff Tear (Shoulder)

PRP Is Better vs Steroid at 3 months but NO Difference at 1 year:

VAS

ASES

Results

We followed up 99 patients (47 in the PRP group and 52 in the CS group) until 12 months after injection. There were no

13.6 vs 0.4, $P = .03$), ASES (13.0 vs 2.9, $P = .02$), and WORC (16.8 vs 5.8, $P = .03$) scores. There were no differences in patient-reported outcomes at 6 weeks or 12 months. There was no difference in the rate of failure ($P = .31$) or conversion to surgery ($P = .83$) between groups.

Clinical Utility – Lateral epicondylitis

- The American Journal of Sports Medicine[7]

Positive Effect of an Autologous Platelet Concentrate in Lateral Epicondylitis in a Double-Blind Randomized Controlled Trial

Platelet-Rich P
With a 1-Year

PRP Is Better vs Steroid at 6 months:

VAS

DASH

- **Population & Inte**
  epicondylitis (sympt
  corticosteroid
- **End Points**: VAS and DASH outcome measure scores (success was defined as a 25% reduction/improvement respectively)
- **Conclusion**: There was a statistically significant difference in primary end point in the PRP group vs the CSI group (73% vs 49%, $p<0.001$). Improvement was sustained in the PRP at the end of the study while the CSI group's initial benefit resolved by the studies end.

Clinical Utility – Lateral epicondylitis

- The American Journal of Sports Medicine[7]

Positive Effect of an Autologous Platelet Concentrate in Lateral Epicondylitis in a Double-Blind Randomized Controlled Trial

Platelet-Rich Plasma Versus Corticosteroid Injection With a 1-Year Follow-up

PRP vs Steroid at 6 months:
NO DIFFERENCE!

VAS			
	4	44.2 ± 26.4	55.4 ± 24.2
	8	42.9 ± 29.2	46.9 ± 24.9
	12	44.2 ± 27.1	38.7 ± 27.2
	26	56.6 ± 23.2	32.6 ± 31.5
	52	50.1 ± 28.1	25.3 ± 31.2

Figure 2. Twenty-four of the 49 patients (49%) in the corticosteroid (CS) group and 37 of the 51 patients (73%) in the platelet-rich plasma (PRP) group were defined as *successful* with the visual analog score (VAS), a significant difference ($P < .001$). CI, confidence interval. 0, CS; x, PRP.

	4	97.4 ± 69.0	135.9 ± 78.0
	8	84.7 ± 73.4	113.4 ± 79.6
	12	92.2 ± 68.7	92.0 ± 78.8
	26	117.3 ± 75.6	79.5 ± 80.3
	52	108.4 ± 82.2	54.7 ± 73.2

Figure 3. Twenty-five of the 49 patients (51%) in the corticosteroid (CS) group and 37 of the 51 patients (73%) patients in the platelet-rich plasma (PRP) group were defined as *successful* with the DASH Outcome Measure, a significant difference ($P = .005$). CI, confidence interval. 0, CS; x, PRP.

Clinical Utility – Lateral epicondylitis

- The American Journal of Sports Medicine[8]

Ongoing Positive Effect of Platelet-Rich Plasma Versus Corticosteroid Injection in Lat

A Doub
With 2-

PRP vs Steroid at 2 years:
PRP is better!

- **Population & Intervention**: 100 patients with chronic lateral epicondylitis (symptoms > 6 mo) were randomized to PRP and corticosteroid
- **End Points**: VAS and DASH outcome measure scores (success was defined as a 25% reduction/improvement respectively)
- **Conclusion**: There was sustain continued improvement at 2 years post intervention.

Clinical Utility – Patellar tendonitis

- Knee Surgery and Related Research[12]

Platelet-Rich Plasma Injections as a Treatment for Refractory Patellar Tendinosis: A Meta-Analysis of Randomised Trials

PRP is better vs. Dry Needling and Shockwave Therapy

- extracorporeal shockwave therapy.
- **Population**: First study required completion of 6 weeks of physical therapy with MRI confirmation of diagnosis. The second study required > 6 months of symptoms with confirmatory U/S and patients had to be “athletic”. Age > 18.
- **Conclusion**: PRP demonstrated statistically significant improvements at 6-months up to 1 year compared to alternative techniques of treatment.

Patient selection for PRP

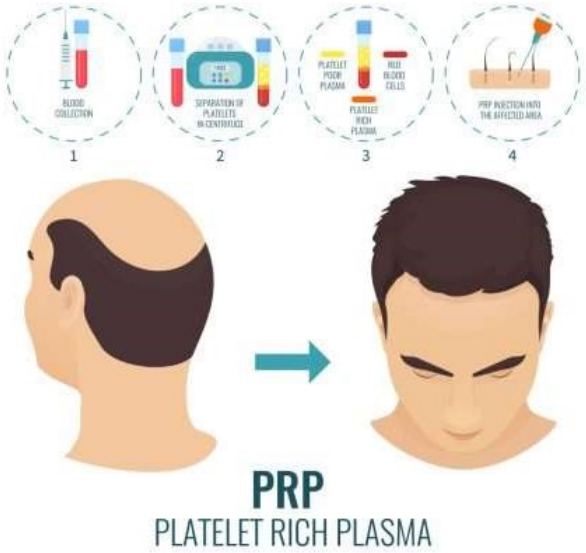
- Who are NOT appropriate candidates for platelet rich plasma injections?
  - Patients with thrombocytopenia
  - Patients on chronic anti-coagulation therapy (that cannot be stopped peri-procedure)
  - Patient with active malignancy or metastatic disease (solid organ cancer or hematologic)
  - Patients with active rheumatologic disorder
  - Patients with a superficial skin infection overlying the area of the injection
  - Patient who are currently ill
  - Pregnant patients or those breastfeeding

Cost of therapies

- Platelet Rich Plasma
  - $500 - $1500

Hartford, CT	$400 - $500
New York City, NY	$400 - $1,000
Rutherford, NJ	$650 - $1,300
Washington, DC	$600
Chicago, IL	$600
Los Angeles, CA	$800
Atlanta, GA	$800
Dallas, TX	$700
Houston, TX	$1,000 - 1,500
Miami, FL	$500 - $1,000

Other PRP Applications



PRP is made by injecting the platelet-rich plasma obtained by centrifugation of the person's own blood to the face. Various growth factors secreted from platelets create a bio-revitalization (skin regeneration) effect on the skin. More successful results are obtained when combined with methods such as fractional laser and chemical peeling. Generally, sessions are in the form of 6-10 applications with 2-3 week intervals.

& Clinical Practice

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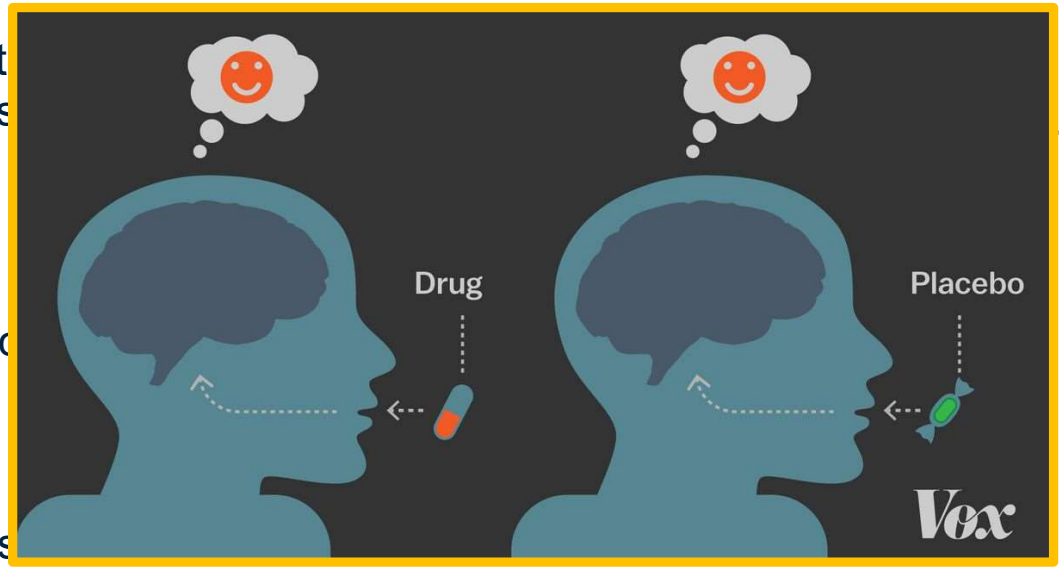

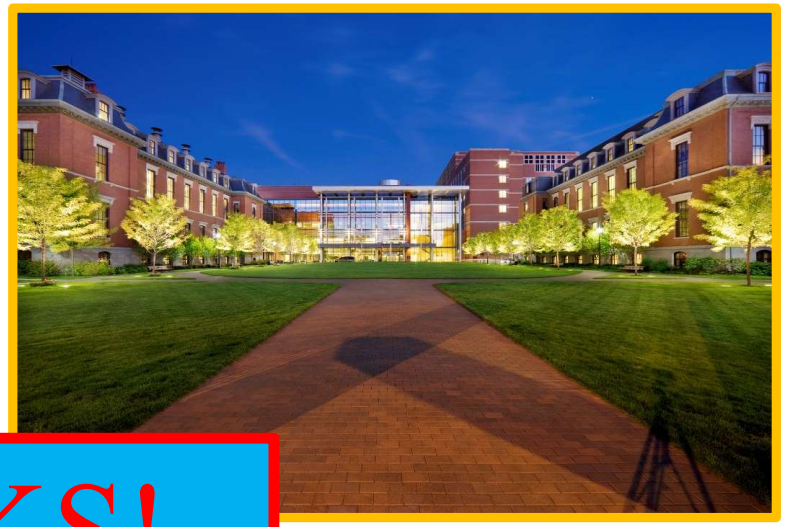

THANKS!