**The Basics**

**Jimi Bradley M.D.**
Clinical Professor Orthopedics UPMC
Head Team Physician – Pittsburgh Steelers
Consultant – Miami Marlins

**Justin Arner MD**
Resident UPMC

**Cellular Treatment Hierarchy**

- **Platelet Rich Plasma**
- **Buffy Coat**
- **Leukocyte Enriched**
- **Leukocyte Poor**
- **Stem Cells**
- **Autologous**
- **POC vs. Expanded**
- **Marrow**
- **Adipose**

**Algorithm of Orthobiologics 2018**

**The Bio Buzz...**

Platelet Rich Plasma  Stem Cells  Orthokine/Regenokine/IRAP
**The Top 10 Things you need to know about PRP & Stem cells**

**#1 There are Critical Obstacles to Widespread Biologic Tx**

**Regulatory Pathway**
- Point of care cellular Tx
- Minimal manipulation
- Autologous
- Efficacy not related to the metabolic activity of the cells

**Research**
- High level comparative studies (millions $$$)
- Used in many applications, need data on all indications

**Reimbursement**
- Coding for some products in not available
- Deemed “Experimental” by Ins. Co.
- Individual approvals

**FDA**

**INDICATIONS TO DATE: “AN ORTHOPEDIC SURGICAL SITE”**
#2 Definition of PRP

There is none Platelet-Rich Plasma

Plasma fraction with a concentration of at least 1,000,000 platelets/μL.2

Autologous plasma fraction that has a concentration of platelets above baseline (200,000 platelets/μL).1


Definition of PRP

- Robert Marx, D.D.S. "definition" of PRP platelet concentration "incorrectly quoted as dogma"
- 2001 White Paper in Implant Dentistry
  - Minimum 1,000,000 platelets/µL = 5x PRP
  - Whole blood baseline – 1.5 - 2 x 10^5 platelets µL

NO supporting citations or references

Optimal Concentration of Platelets is Unknown !!!

High concentrations (6-11x) may have a paradoxically inhibitory effect

Viability & proliferation of cells was suppressed by high concentrations but increased by moderate concentrations.

It may be different for different pathologies

What is the Optimal Concentration of Platelets?

1. Concentration of platelets to bind the available GF receptors without oversaturation
2. Triggering a positive proliferative response
3. Without inducing a negative feedback inhibition
4. Receptor levels may vary between tissues therefore ideal PRP concentrations may as well
#3 All Current Systems are NOT the same
ACP, Biomet GPS, PReP, MTF cascade, Harvest & Magellan

- Differences in blood volume, centrifuge rate/time, delivery method, activating agent, WBC count, PRP volume, Platelet & GF concentration

What do we have today?

- Buffy coat based PRP systems
  - GPS
  - Harvest
  - Magellan
- Plasma based PRP systems
  - ACP
  - Cascade
  - BTI (Anitua/Sanchez)

- All use platelet GF release
- What differs is WBC’s, RBC’s & plasma concentrations

#4 PRP is EXTREMELY Complex

- Delivery methods
  - Activate +/-
- Plasma-based vs. Buffy coat
  - White cells +/-
- Dozens of commercially available systems (40)
  - Variable spin protocols & cellular milieu product
- Significant variability in cellular concentrations
  - Vs. systems
  - Vs. individuals
  - Vs. SAME individual
- Frequency of dosing
  - Acute vs. Chronic?
  - Anatomic site specific?
Multitude of Variables Contribute to Mixed Results

- Platelet activators
- Clotting factors
- Baseline Levels

- Exogenous activation
- Endogenous activation
- Platelet activators
- Clotting factors

- Alpha granules
- Dense granules

- CaCl
- Thrombin

- Neonphil rich
- Neonphil poor

- Platelet-rich plasma
- Platelet-poor plasma

- WBC content
- Type I Collagen

- > 1,250,000 platelets/μL
- > 750,000 to 1,250,000 platelets/μL
- > Baseline to 750,000 platelets/μL

- Platelet aggregation
- Growth factor kinetics

- pH
- Local anesthetics

- Anticoagulants
- Anti-oxidant response

- Delivery technique
- Delivery platform

- Mixed Results

#5 PRP: A Previous Decade of Flawed Research Methodology??

The American Journal of Sports Medicine

#6 The Fundamentals Have Been Missed!!

Back to the Fundamentals: the beginning of the PAW system
… and It can get VERY complicated


#7 Where?

OVERALL Office Experience

- OVERALL Office Experience
  - Total > 450 patients
  - 90% athletes
  - > 900 injections
  - 250 lower extremities injuries
  - 200 upper extremities injuries
  - NFL, MLB, NHL (30%)
  - Only injection code used
  - Recently had to charge $200/injection
Clinical Applications
My Experience

Knee Disorders
• DJD
• MCL/LCL sprains
• Patellar Tendonitis
• Symptomatic Bipartite Patella

Ankle/LE Disorders
• Achilles Tendonitis
• Ankle Sprain (ATFL)
• Peroneal tendons
• Soleus Muscle Strain
• High Ankle Sprains

Soft Tissue LE Disorders
• Rectus Strain
• Proximal Hamstring Strain (CG guided)
• Mid/Distal Hamstring Strains

Shoulder Disorders
• Shoulder DJD
• Rot (prox) Cuff Tears
• Rotator Cuff Tendinoaphy
• SLAP Lesions
• AC Separation

Elbow Disorders
• UCL (partial) tear
• Med/Lat Epicondylitis
• OCD lesions

My Clinical Protocol
ACP - 1 injection a wk for 3wks if better after 2 no more
Start 24-48 hrs after acute injury
No changes rehab protocol
Office Overall Outcomes

Successful outcome = Resolution of symptoms, asymptomatic return to play, no surgery

Poor outcome = Recurrence of symptoms, inability to return to play, surgery

Outcomes/Success Rate

Knee

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Formulation</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCL</td>
<td>100%</td>
<td>Good</td>
</tr>
<tr>
<td>DJD</td>
<td>74%</td>
<td>Good</td>
</tr>
<tr>
<td>Patellar</td>
<td>43%</td>
<td>Good</td>
</tr>
</tbody>
</table>

Formulation Specific Results

<table>
<thead>
<tr>
<th>Author</th>
<th>Diagnosis</th>
<th>Formulation</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patel, AJSM 2013</td>
<td>Knee OA</td>
<td>Leukocyte poor</td>
<td>Significant difference</td>
</tr>
<tr>
<td>Filardo, Musk. Disord 2012</td>
<td>Knee OA</td>
<td>Leukocyte rich</td>
<td>No difference</td>
</tr>
<tr>
<td>Cerza, AJSM 2012</td>
<td>Knee OA</td>
<td>Leukocyte poor</td>
<td>Significant difference</td>
</tr>
<tr>
<td>Sanchez, Arthro 2012</td>
<td>Knee OA</td>
<td>Leukocyte poor</td>
<td>Significant difference</td>
</tr>
<tr>
<td>Filardo, KSTTA 2012</td>
<td>Knee OA</td>
<td>Leukocyte rich</td>
<td>No difference</td>
</tr>
</tbody>
</table>
Intra-articular Autologous Conditioned Plasma Injections Provide Safe and Efficacious Treatment for Knee Osteoarthritis

An FDA-Sanctioned, Randomized, Double-blind, Placebo-controlled Clinical Trial

Patrick A. Smith, MD

Investigation performed at the Columbia Orthopedic Group, Columbia, Missouri, USA

- ACP is safe & provides quantifiable benefits for pain relief & functional improvement with regard to knee OA.
- No adverse events were reported for ACP administration.
- After 1 yr, WOMAC scores for the ACP subjects had improved by 78% from baseline score, whereas placebo group had improved by 7%.

Other joints affected with OA may also benefit from this Tx.

PRP use in Osteoarthritis

A Systematic Review of Randomized Controlled Trials

Sherman M, Bradley J, Mandelbaum B

- Systematic review of level I evidence of PRP for knee OA
- 5 RCT’s with 575 pts
- 4 studies PRP vs. HA, 1 study 1 vs 2 PRP vs saline

Overall they showed sig. improvements in pain, stiffness, & joint function vs baseline HA, & saline

Platelet-Rich Plasma as a Treatment for Patellar Tendinopathy

A Double-Blind, Randomized Controlled Trial

Jaron L. Dragon, MD, Amy S. Reardon, MD, Hillary J. Brout, BA, and Kevin T. Neat, MFN

Investigation performed at Stanford University, Redwood City, California, USA

- Level 1, RCT
- US guided PRP/dry needling vs dry needling alone
- 12 wk f/u
  - PRP with significantly better VISA score
  - 25.4 improved vs 5.2 with needling alone
- No treatment failures in PRP group
Are Multiple Platelet-Rich Plasma Injections Useful for Treatment of Chronic Patellar Tendinopathy in Athletes? A Prospective Study

- Level 4, Case series
- 28 athletes
  - 17 professional
  - 11 semiprofessional
- *Chronic, failed conservative tx
- PRP injection x 3
- 2 yr f/u
- Significantly improved VISA, VAS, and lysholm scores
- 16 pts (57%) returned to completely normal
- Only 3 needed surgery

My top 4 LE office favorites

1. Early OA
2. MCL/LCL sprains
3. Early splits in the post/med menisco-capsular junction
4. Elbow partial UCL

What does the Literature say about shoulder & PRP?
### Positive effect

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Design</th>
<th>Level of Evidence</th>
<th>Investigation</th>
<th>Effect</th>
<th>N</th>
<th>Avg F/U</th>
<th>Limitations</th>
</tr>
</thead>
</table>

### Positive effect

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Design</th>
<th>Level of Evidence</th>
<th>Investigation</th>
<th>Effect</th>
<th>N</th>
<th>Avg F/U</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>D'Ambrosi 2016</td>
<td>Muscul Res</td>
<td>1 PRP effect on muscle performance: improved muscle strength &amp; power.</td>
<td>1</td>
<td>U/S: Markedly improved muscle strength &amp; power.</td>
<td>20</td>
<td>2</td>
<td>PRP components not measured or reported. Non-randomized. No control group.</td>
<td>Small sample size. Short f/u.</td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
<td>Journal</td>
<td>Level of evidence</td>
<td>Topic</td>
<td>Effect</td>
<td>N</td>
<td>Avg f/u (mo.)</td>
<td>Limitations</td>
</tr>
<tr>
<td>-----------------</td>
<td>------</td>
<td>---------------</td>
<td>-------------------</td>
<td>-----------------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td>----</td>
<td>---------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Holtby 2016</td>
<td>OJSM</td>
<td>PRP on Full</td>
<td>1 PRP effect on</td>
<td>Level of evidence: PRP significantly</td>
<td>PRP group showed better clinical outcomes compared to control group</td>
<td>50</td>
<td>8</td>
<td>PRP sample size not measured in control group</td>
</tr>
<tr>
<td></td>
<td></td>
<td>thickness</td>
<td>Full thickness</td>
<td>improved perioperative pain short-term</td>
<td>(days 8-11). PRP group also reported taking less painkillers than</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PRP on Full</td>
<td>Full thickness</td>
<td>PRP group showed better clinical outcomes compared to control group (days 8-11). PRP group also reported taking less painkillers than control group (days 0-30). But no significant impact on patient satisfaction.</td>
<td></td>
<td></td>
<td>PRP sample size not measured in control group</td>
<td></td>
</tr>
<tr>
<td>Zhang 2015</td>
<td>Act</td>
<td>PRP on Small</td>
<td>PRP effect on</td>
<td>Local PRP injection: Double-row RC repair resulted in lower recurrence rates than RC repair control without PRP.</td>
<td>RC repair control without PRP.</td>
<td>82</td>
<td>6</td>
<td>PRP components not measured or reported. Limitation of small sample size in the double-row RC repair study.</td>
</tr>
<tr>
<td></td>
<td>Orthop</td>
<td>to Medium</td>
<td>RC repair</td>
<td>local PRP injection: Double-row RC repair resulted in lower recurrence rates than RC repair control without PRP.</td>
<td>RC repair control without PRP.</td>
<td>82</td>
<td>6</td>
<td>PRP components not measured or reported. Limitation of small sample size in the double-row RC repair study.</td>
</tr>
<tr>
<td></td>
<td>Traumatol</td>
<td>RCTs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Turc</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shams 2016</td>
<td>Eur</td>
<td>PRP vs.</td>
<td>PRP vs.</td>
<td>PRP group showed better clinical outcomes compared to control group (days 8-11). PRP group also reported taking less painkillers than control group (days 0-30). But no significant impact on patient satisfaction.</td>
<td>40</td>
<td>6 wks</td>
<td>PRP sample size not measured in control group</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ortho</td>
<td>Corticosteroids</td>
<td>PRP group showed better clinical outcomes compared to control group (days 8-11). PRP group also reported taking less painkillers than control group (days 0-30). But no significant impact on patient satisfaction.</td>
<td>40</td>
<td>6 wks</td>
<td>PRP sample size not measured in control group</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Surg</td>
<td>PRP vs.</td>
<td>PRP group showed better clinical outcomes compared to control group (days 8-11). PRP group also reported taking less painkillers than control group (days 0-30). But no significant impact on patient satisfaction.</td>
<td>40</td>
<td>6 wks</td>
<td>PRP sample size not measured in control group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pandey 2016</td>
<td>JSES</td>
<td>Moderate</td>
<td>PRP for medium to</td>
<td>PRP improved clinical and structural outcomes. Major enhancement of healing phase. PRP improved clinical and structural outcomes. Major enhancement of healing phase.</td>
<td>PRP improved clinical and structural outcomes. Major enhancement of healing phase. PRP improved clinical and structural outcomes. Major enhancement of healing phase.</td>
<td>102</td>
<td>24</td>
<td>PRP sample size not measured in control group</td>
</tr>
<tr>
<td>Cross 2015</td>
<td>AJSM</td>
<td>PRP &amp; cuff</td>
<td>PRP &amp; cuff repair</td>
<td>Positive effect for reduced rate of re-tear. PRP on healing of non-tear cuff tendinopathy</td>
<td>Positive effect for reduced rate of re-tear. PRP on healing of non-tear cuff tendinopathy</td>
<td>20</td>
<td>6</td>
<td>PRP sample size not measured in control group</td>
</tr>
<tr>
<td>Cross 2015</td>
<td>AJSM</td>
<td>PRP &amp; cuff</td>
<td>PRP &amp; cuff repair</td>
<td>Positive effect for reduced rate of re-tear. PRP on healing of non-tear cuff tendinopathy</td>
<td>Positive effect for reduced rate of re-tear. PRP on healing of non-tear cuff tendinopathy</td>
<td>20</td>
<td>6</td>
<td>PRP sample size not measured in control group</td>
</tr>
<tr>
<td>Scarpone 2013</td>
<td>Glob</td>
<td>PRP &amp; cuff</td>
<td>PRP &amp; cuff repair</td>
<td>Positive effect for reduced rate of re-tear. PRP on healing of non-tear cuff tendinopathy</td>
<td>Positive effect for reduced rate of re-tear. PRP on healing of non-tear cuff tendinopathy</td>
<td>17</td>
<td>12</td>
<td>PRP sample size not measured in control group</td>
</tr>
<tr>
<td>Gumina 2012</td>
<td>JBJS</td>
<td>PLM &amp; large</td>
<td>Improved repair</td>
<td>Improved repair integrity but no difference in outcomes.</td>
<td>Improved repair integrity but no difference in outcomes.</td>
<td>80</td>
<td>13</td>
<td>&lt;2 yr f/u.</td>
</tr>
<tr>
<td>Zumstein 2014</td>
<td>JSES</td>
<td>Leukocyte &amp;</td>
<td>Significantly</td>
<td>Significantly better clinical outcomes.</td>
<td>Significantly better clinical outcomes.</td>
<td>20</td>
<td>3</td>
<td>Small sample, no long term f/u.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>platelet rich</td>
<td>improved vascularizat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>fibrin &amp; cuff</td>
<td>&amp; cuff repair</td>
<td>PRP group showed better clinical outcomes compared to control group (days 8-11). PRP group also reported taking less painkillers than control group (days 0-30). But no significant impact on patient satisfaction.</td>
<td>20</td>
<td>3</td>
<td>Small sample, no long term f/u.</td>
<td></td>
</tr>
<tr>
<td>Jo 2013</td>
<td>AJSM</td>
<td>PRP gel &amp;</td>
<td>Improved retear</td>
<td>Improved retear rates, cross sectional area</td>
<td>Improved retear rates, cross sectional area</td>
<td>46</td>
<td>12</td>
<td>Small sample, short f/u, arbitrary concentration of PRP.</td>
</tr>
<tr>
<td>Rha 2013</td>
<td>Clin</td>
<td>PRP vs dry</td>
<td>Superior</td>
<td>Superior outcome scores and pain</td>
<td>Superior outcome scores and pain</td>
<td>39</td>
<td>6</td>
<td>Short f/u.</td>
</tr>
<tr>
<td>Rehabil 2013</td>
<td></td>
<td>needle in</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
<td>Journal</td>
<td>Level of evidence</td>
<td>Topic</td>
<td>Effect</td>
<td>N</td>
<td>Avg f/u</td>
<td>Limitations</td>
</tr>
<tr>
<td>------------</td>
<td>------</td>
<td>---------------------</td>
<td>-------------------</td>
<td>--------------------------------------------</td>
<td>--------------------------------------------</td>
<td>----</td>
<td>---------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Barber</td>
<td>2011</td>
<td>Arthroscopy</td>
<td>3</td>
<td>PRFM &amp; Cuff repair</td>
<td>Improved retear rates and Rowe scores w/PRFM</td>
<td>40</td>
<td>31</td>
<td>Sample size, lack of randomization</td>
</tr>
<tr>
<td>Randelli</td>
<td>2011</td>
<td>JSES</td>
<td>1</td>
<td>PRP &amp; Rotator cuff repair</td>
<td>Reduced pain in first few postoperative months</td>
<td>53</td>
<td>24</td>
<td>Unknown quantity of platelets &amp; growth factors</td>
</tr>
<tr>
<td>Gwinner</td>
<td>2016</td>
<td>Arch Ortho Trauma &amp; Surg</td>
<td>3</td>
<td>Two-staged PRP application to RC repair</td>
<td>No significant improvement but trend for lower retear rates</td>
<td>36</td>
<td>24</td>
<td>???</td>
</tr>
<tr>
<td>Flury</td>
<td>2016</td>
<td>AJSM</td>
<td>1</td>
<td>PRP vs. Ropivacaine (local anesthetic)</td>
<td>PRP group showed no significant functional improvement</td>
<td>120</td>
<td>24</td>
<td>No description of growth factor concentration, irreversible dilution with NaCl</td>
</tr>
<tr>
<td>Say</td>
<td>2016</td>
<td>J Ortho Surg</td>
<td>3</td>
<td>Single dose of PRP vs. steroid for subacromial impingement syndrome</td>
<td>Steroid injection was more effective than PRP in Constant score and VAS pain</td>
<td>60</td>
<td>6 wks</td>
<td>6 mo, PRP was prepared manually using single spin rotation. Reported 4 fold increase but did not report actual [platelets/μL]</td>
</tr>
<tr>
<td>Verhaegen</td>
<td>2016</td>
<td>JSES</td>
<td>2</td>
<td>Arthroscopic needling for RC augmented with PRP</td>
<td>PRP group showed no beneficial effect on RC healing</td>
<td>40</td>
<td>3 mo</td>
<td>6 mo, 1 yr, No description of growth factor concentration, leukocyte-rich PRP, short F/U</td>
</tr>
<tr>
<td>Wehren</td>
<td>2015</td>
<td>KSSTA</td>
<td>3</td>
<td>ACP vs cortisone subacromial injections for partial RTC tears</td>
<td>Early improvement in outcomes w/ACP but no difference at 6 months</td>
<td>50</td>
<td>6 No description of growth factor concentration</td>
<td></td>
</tr>
<tr>
<td>Hak</td>
<td>2015</td>
<td>Sports Health</td>
<td>2</td>
<td>PRP &amp; Rotator cuff repair</td>
<td>No diff in outcomes</td>
<td>23</td>
<td>6 wks</td>
<td>No description of growth factor concentration, short f/u</td>
</tr>
<tr>
<td>Wang</td>
<td>2015</td>
<td>AJSM</td>
<td>1</td>
<td>PRP &amp; Rotator cuff repair</td>
<td>No improvement in outcomes/tendon healing</td>
<td>60</td>
<td>16 wks</td>
<td>No exact determination of growth factor concentration, short f/u</td>
</tr>
<tr>
<td>Carr</td>
<td>2015</td>
<td>AJSM</td>
<td>1</td>
<td>Leukocyte rich PRP &amp; acromioplasty</td>
<td>No diff in outcomes, reduced cellularity &amp; vascularity</td>
<td>60</td>
<td>24</td>
<td>Leukocyte rich PRP, one injection, biopsy 12 weeks post injection</td>
</tr>
<tr>
<td>Malavolta</td>
<td>2014</td>
<td>AJSM</td>
<td>1</td>
<td>PRP liquid w/thrombin</td>
<td>No improvement in retear rates or clinical outcomes</td>
<td>54</td>
<td>24</td>
<td>Platelet poor plasma used, injected before portals were closed</td>
</tr>
<tr>
<td>Werthel</td>
<td>2014</td>
<td>Int J Shoulder Surg</td>
<td>2</td>
<td>Leukocyte poor ACP &amp; cuff repair</td>
<td>No improvement in retear rates or outcomes</td>
<td>65</td>
<td>19</td>
<td>No description of growth factor concentration, differing amts of ACP injected</td>
</tr>
<tr>
<td>Charousset</td>
<td>2014</td>
<td>Arthroscopy</td>
<td>3</td>
<td>PRP &amp; Rotator cuff repair</td>
<td>No diff in outcomes, recurrent tear rate or healing rate</td>
<td>61</td>
<td>28.6</td>
<td>No description of growth factor concentration, underpowered, single injection</td>
</tr>
<tr>
<td>Antuna</td>
<td>2013</td>
<td>Acta Orthop Belg</td>
<td>1</td>
<td>PRF and large/massive cuff repairs</td>
<td>No diff in clinical outcomes/retear rates</td>
<td>28</td>
<td>&gt;24</td>
<td>Small sample size</td>
</tr>
<tr>
<td>Weber</td>
<td>2013</td>
<td>AJSM</td>
<td>1</td>
<td>PRFM &amp; cuff repair</td>
<td>No improvement in structural integrity, perioperative morbidity or outcomes</td>
<td>60</td>
<td>16 wks</td>
<td>No description of growth factor concentration, short f/u</td>
</tr>
</tbody>
</table>
### Neutral/Negative effect

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Journal</th>
<th>Level of Evidence</th>
<th>Topic of Interest</th>
<th>Effect</th>
<th>n</th>
<th>Avg. f/u (Mos)</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruiz-Moneo</td>
<td>2013</td>
<td>Arthroscopy</td>
<td>1</td>
<td>Leukocyte poor PRGF &amp; cuff repair</td>
<td>No diff in healing or postop outcomes</td>
<td>36</td>
<td>12</td>
<td>No exact determination of growth factor concentration, small sample, short f/u</td>
</tr>
<tr>
<td>Kesikburun</td>
<td>2013</td>
<td>AJSM</td>
<td>1</td>
<td>PRP &amp; cuff repair</td>
<td>Negative effect on healing, no diff in postop outcomes</td>
<td>38</td>
<td>12</td>
<td>No description of growth factor concentration, short f/u</td>
</tr>
<tr>
<td>Rodeo</td>
<td>2012</td>
<td>AJSM</td>
<td>2</td>
<td>PRFM and cuff repair</td>
<td>Negative effect on healing, no diff in outcomes</td>
<td>79</td>
<td>12</td>
<td>No description of growth factor concentration, short f/u</td>
</tr>
<tr>
<td>Bergeson</td>
<td>2011</td>
<td>AJSM</td>
<td>3</td>
<td>PRFM and cuff repair</td>
<td>No diff in outcomes, Higher retear rates and infection rates</td>
<td>37</td>
<td>27 (13 in PRFM group)</td>
<td>No description of growth factor concentration, small sample, large diff in f/u between groups</td>
</tr>
<tr>
<td>Castricini</td>
<td>2011</td>
<td>AJSM</td>
<td>1</td>
<td>PRFM &amp; cuff repair</td>
<td>No improvement in retear rates or tendon healing</td>
<td>88</td>
<td>16</td>
<td>No description of growth factor concentration</td>
</tr>
<tr>
<td>Jo</td>
<td>2011</td>
<td>AJSM</td>
<td>2</td>
<td>PRP gel &amp; cuff repair</td>
<td>No improvement in retear rates or tendon healing</td>
<td>42</td>
<td>19</td>
<td>Short f/u, arbitrary use of PRP volume, PRP collected 1 day before surgery</td>
</tr>
</tbody>
</table>

---

**Every Study shown - positive, negative & neutral has flaws & some fatal**

"It basically has been 10 years of failed methodology"

---

**So, where does this leave us?**

- Decrease in retear rates for small & medium sized RC tears.
- Large & Massive…still a problem
#8 Practical Basic Science studies over the last 6 years

Basic Science University of Connecticut
Human Soft Tissue Research Lab

Mazzocca G, McCarthy B, Romeo A, Bradley J, Arciero R
2009-17

PRP the basics
Use plasma based (low WBC's)
Platelet # does not make a difference (3X)
GF's vary everyday
Platelet to WBC ratio is key (2000:1)
Steroids deactivate AG
Caines kill everything
NSAIDs don't make a difference
Antibiotic & Anti-inflammatory
Modifies post op pain
Multiple injections better one /wk x 3
ACP HA Toradol work synergistically in OA
O.R. Experience
Have used all the major PRP systems in the OR

Top 3 UE ACP OR favorites
1. RCR
2. RC revision
3. Revision Labral repairs

- Post-op Pain relief is the major indication
- Significant reduction in narcotic use

#9 Stem Cells are here to stay!
My Clinical Protocol

BMAC - 1 injection with or without scope usually mild to mod OA knee
2% Hct 7ccs + PRP 3cc

Classification of Stem Cells

MSC’s What the heck are they?

- Unspecialized cells with a self renewal potential which can differentiate into different adult cell types (mesenchymal tissue)
- Can exert regulatory effect on local & distant cells
- Can be isolated from almost every tissue
- Found as perivascular cells
- Secrete massive levels of immunomodulatory & trophic substances
  
Modulate T-cell response
Improve healing by a synergistic Triple Action Mechanism

1. Direct participation in repair (diff into damaged or lost cells)
2. Stimulation of local cells via paracrine mechanism (indirectly promote vascularization, proliferation & differentiation via soluble factors)
3. Anti-inflammatory or immunomodulatory activity (modulate inflammatory cascade)

It May not be their ability to differentiate

MSC’s are the body’s “Drug Store”

Trophic properties

- Anti-inflammatory, Anti-apoptotic, Anti-microbial
- Induce cell proliferation & angiogenesis, reduce scar formation
- Locally derived SC maybe more effective than other sources

MSC’s most relevant contribution maybe is to provide a suitable microenvironment for tissue repair not direct repair

Recent In vivo MSC studies

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>F/U</th>
<th>Mean Age</th>
<th>Cells</th>
<th>Result</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koh et al. 2014</td>
<td>37</td>
<td>28.6</td>
<td>36.5</td>
<td>Buttock Fat pad, IRI I</td>
<td>WOMAC improved from 50 to 33 (P &lt; .001)</td>
<td>Despite lack of lesion healing, improvement in pain &amp; function</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PRP</td>
<td>Lysholm improved from 40 to 73 (P &lt; .001)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>High dose group only</td>
<td>VAS improved from 4.8 to 2.0 (P &lt; .005)</td>
<td></td>
</tr>
<tr>
<td>Jo et al. 2014</td>
<td>18</td>
<td>6</td>
<td>66</td>
<td>Abdominal Fat</td>
<td>WOMAC improved at 6 months</td>
<td>Intra-articular injection of AD MSC is effective in improving pain &amp; function</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Low 1.0x10⁷</td>
<td>Size of cartilage defect decreased (arthroscopy)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Med 5.0x10⁷</td>
<td>Volume of cartilage increased (histology)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>High 1.0x10⁸</td>
<td>High dose group only</td>
<td></td>
</tr>
<tr>
<td>Xie et al. 2014</td>
<td>42</td>
<td>12 weeks</td>
<td>42.5</td>
<td>Rabbit 1. BMSC + PRP</td>
<td>BMSC + PRP showed: High proton density &amp; higher cartilage regeneration than MSC</td>
<td>PRP as a scaffold for stem cells is synergistic for chondrocyte proliferation &amp; viability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2. ADSC + PRP</td>
<td>Higher proton density &amp; higher cartilage regeneration than MSC</td>
<td></td>
</tr>
</tbody>
</table>
Why Concentrate Bone Marrow?

BMA at 96 hrs.  Angel BMC at 96 hrs.

HEALING TRINITY: Cell, Signal, Scaffold

#10

“Biologics are here to stay & will be a mainstay of many operative & non-operative treatment protocols.”
- JPB, 2011

Thank you