Platelet-Rich Plasma: The PAW Classification System


Abstract: Platelet-rich plasma (PRP) has been the subject of hundreds of publications in recent years. Reports of its effects in tissue, both positive and negative, have generated great interest in the orthopaedic community. Protocols for PRP preparation vary widely between authors and are often not well documented in the literature, making results difficult to compare or replicate. A classification system is needed to more accurately compare protocols and results and effectively group studies together for meta-analysis. Although some classification systems have been proposed, no single system takes into account the multitude of variables that determine the efficacy of PRP. In this article we propose a simple method for organizing and comparing results in the literature. The PAW classification system is based on 3 components: (1) the absolute number of Platelets, (2) the manner in which platelet Activation occurs, and (3) the presence or absence of White cells. By analyzing these 3 variables, we are able to accurately compare publications.

Despite the promising effects of platelet-rich plasma (PRP) therapy, most studies conducted have lacked accurate measurements and documentation of the PRP components and delivery methods used. This lack of standardization and consistency is prevalent throughout the literature and has frustrated attempts to compare results between articles. To determine the efficacy of PRP from system to system and patient to patient, the PRP components and the means by which they are delivered to the target tissue site should be identified and documented. Without these fundamental prerequisites, the evolution of PRP as a safe and effective treatment for orthopaedic disorders may not progress efficiently.

IDENTIFYING CONTENT OF PRP

Several essential factors exist that need to be identified to adequately determine the effects of PRP treatment.

- The most essential factor is to ensure accurate and definitive concentration measurements of platelets. Without precise quantification of the cellular components, validation and accurate comparison of studies will remain extremely difficult, ultimately impeding discovery of optimum dosing. Many studies published in the recent literature lack this most basic requirement.
- The presence or absence of platelet activators, as well as the type of activator used, is another important element requiring documentation. The way in which the platelets are applied to the tissue will undoubtedly affect the response of the tissue. For example, an exogenous platelet activator may be necessary to generate a clot in certain procedures, whereas endogenous platelet activation without the use of an external clotting factor may be ideal in other indications.
- Whether the administered PRP treatment includes highly concentrated leukocytes above baseline.
levels or leukocyte-deficient PRP below baseline should also be documented. This will identify which type of PRP system was used, plasma based or buffy coat. Buffy-coat systems contain both red blood cells (RBCs) and white blood cells (WBCs), whereas plasma-based systems exclude them. There is considerable debate over the necessity of including white cells, with several studies suggesting that they may in fact be harmful to the healing process.²⁻¹¹ Neutrophils, in particular, have been hypothesized to impede healing. It is likely that the need to include WBCs in the PRP preparation will vary by indication, and the WBC concentration should be noted as above or below baseline in the “Methods” section of articles. Further identifying neutrophil levels above or below baseline may prove to be a key in solving the controversy surrounding the efficacy of PRP rich in leukocytes.

- In addition to documentation of the components of the PRP end product, it is also important to record the delivery technique and whether additional factors were distributed to the tissue site.

**UNDERSTANDING PRP METHODS AND SYSTEMS**

PRP can be manufactured in 2 basic formats: plasma-based and buffy-coat preparations. Both begin with whole blood but differ in the centrifugation process, which isolates and concentrates different blood-cell components.¹²

Plasma-based methods work to isolate only plasma and platelet components and remove WBCs. Protocols for these preparations leave some platelets behind and focus on intentionally excluding leukocytes, which are thought to be detrimental to the healing process.²⁻¹¹ The main goal of this method is to capture only platelets during the centrifugation; thus a slower and shorter spin regimen is used. This yields platelet concentration yields are between 2⁻³ and 3⁻³ those of baseline levels (300,000 to 500,000 platelets/L) (Table 1).

Buffy-coat–based methods isolate a platelet-poor plasma layer and a buffy-coat layer, which contains both leukocytes and erythrocytes. Protocols for buffy-coat systems seek to capture all available platelets during the centrifugation and obtain a high concentration of WBCs; thus a slower and shorter spin regimen is used. This yields platelet concentrations typically around 2⁻³ to 3⁻³ those of baseline whole blood levels (300,000 to 500,000 platelets/μL) (Table 1).

To complicate comparisons, each commercially available PRP system uses a different spin protocol. Protocols, number and length of spins, platelet and leukocyte concentrations, and delivery platform vary between these devices.

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**TABLE 1. Plasma-Based and Buffy Coat–Based PRP Systems**

<table>
<thead>
<tr>
<th>Device Name</th>
<th>Centrifuge Time (min)</th>
<th>Initial Blood Volume (mL)</th>
<th>Final PRP Volume (mL)</th>
<th>Platelet Concentration From Baseline</th>
<th>WBC Content</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma-based PRP systems</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthrex (Naples, FL)/ACP (Edison, NJ)</td>
<td>5</td>
<td>16</td>
<td>4-7</td>
<td>2⁻³ - 3⁻³</td>
<td>Minimal to none</td>
<td>22</td>
</tr>
<tr>
<td>Cascade/MTF Fibrinet</td>
<td>6 (plasma)</td>
<td>9</td>
<td>4.5 (plasma)</td>
<td>1.3⁻¹⁻¹.7⁻¹ (plasma)</td>
<td>Minimal to none</td>
<td>14, 23-25</td>
</tr>
<tr>
<td>BTI (Vitoria-Gasteiz, Spain)/PRGF</td>
<td>8</td>
<td>9</td>
<td>2⁻³</td>
<td>2⁻³⁻³</td>
<td>Minimal to none</td>
<td>26-28</td>
</tr>
<tr>
<td>Buffy coat–based PRP systems</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biomet (Warsaw, IN)</td>
<td>12-15</td>
<td>30 or 60</td>
<td>3 or 6</td>
<td>2⁻³⁻⁸</td>
<td>Increased over baseline</td>
<td>29-33</td>
</tr>
<tr>
<td>GPS II/III</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harvest (Plymouth, MA)</td>
<td>12-15</td>
<td>20 or 60</td>
<td>3 or 7-10</td>
<td>3⁻⁻⁷</td>
<td>Increased over baseline</td>
<td>24, 32-35</td>
</tr>
<tr>
<td>Arteriocyte Medtronic</td>
<td>14-20</td>
<td>30 or 60</td>
<td>3-10</td>
<td>3⁻⁻⁷</td>
<td>Increased over baseline</td>
<td>14, 33, 36, 37</td>
</tr>
<tr>
<td>Emcyte (Fort Myers, FL)/Genesis CS/Exactech (Gainsville, FL) Accelerate</td>
<td>12</td>
<td>30 or 60</td>
<td>3 or 10</td>
<td>7⁻⁻¹⁰</td>
<td>Increased over baseline</td>
<td>38-40</td>
</tr>
</tbody>
</table>

Abbreviations: ACP, autologous conditioned platelets; BTI, Biotechnology Institute; GPS, gravitational platelet separation; MTF, musculoskeletal transplant foundation; PRGF, platelet rich growth factor.
devices, making no 2 PRP products identical (Table 1). These variances lead to different amounts of anabolic and catabolic proteins released to the target tissues after injection. For instance, Castillo et al. tested 3 different PRP separation systems, and each system yielded a similar platelet concentration (approximately 600,000 platelets/μL) and RBC, active transforming growth factor (TGF) β1, and fibrinogen levels. However, each system produced significantly different levels of platelet-derived growth factor (PDGF) AB, PDGF-BB, vascular endothelial growth factor (VEGF), and WBC concentration. Although the effects of these bioactive factors on tissue were not tested, it is possible that these variations could result in considerable and dramatically distinct effects on healing. Lack of standardization of PRP preparations may therefore lead to inconsistent results in the literature.

Additives also alter the content and effect of PRP. For example, anticoagulants and local anesthetics alter the pH of PRP; understanding the effect of this alteration on tissue response is important. Variations in pH have been shown to affect in vitro proliferation, and consideration must be given to the desired response before choosing to mix PRP with an additive. Local anesthetics, in particular, appear to produce a negative effect on PRP treatment in vitro and should be avoided when possible.

PRP can even be altered by the metals used in medical devices or implants as well as the centrifuge material. Tanaka et al. studied the effects that various metals had on platelet adhesion. The study found that platelet adhesion and aggregation can both be inhibited and enhanced by different types of metal. Test tube materials are also important. Michelston reported in his comprehensive book on platelets that polypropylene tubes are superior to either polystyrene or polycarbonate when used for platelet preparation and/or storage. In addition, he noted that uncoated glass may artificially activate platelets and affect results. A study conducted by Grottum et al. determined the effect of polystyrene particles on PRP. Incubation of PRP with polystyrene particles induced surface contact between platelets and particles, uptake of particles, and changes in platelet morphology. After injection into rabbits, Grottum et al. identified increased platelet aggregation, which may have resulted from a reduction in platelet surface charge due to interaction with polystyrene. For these reasons, it is imperative that the protocol chosen to manufacture PRP in each study be strictly adhered to, and materials cannot be freely substituted.

### UNDERSTANDING CELLULAR COMPONENTS

#### Platelet Concentration

Few studies have compared the healing effects of different PRP platelet concentrations for the same indication. This may prove to be the most significant aspect in identifying the true effectiveness of PRP and in choosing the proper protocol.

**Low:** Less Than 1× (Less Than Baseline): Platelet concentrations below baseline may not allow for a sufficient cellular response. Often used as a control, platelet-poor plasma has only shown the slightest benefit.

**Moderate:** Greater Than 1× to Less Than 4× (Greater Than Baseline to 750,000 platelets/μL): Plasma-based PRP systems typically produce platelet concentrations between baseline and 3× baseline. The absolute platelet number obtained by this method is generally equal to or less than 750,000 platelets/μL.

In vitro, in vivo, and clinical studies have been conducted and published by Anitua and Sánchez, as well as their colleagues, showing the effectiveness of PRP with a platelet concentration of 2× to 3×, 26,28,43-49 Sánchez et al. injected exogenously activated PRP with a 3× platelet concentration into surgically repaired human Achilles tendons. They found significant improvement and an earlier return to sports as compared with the control group. The same researchers performed an uncontrolled retrospective case study in which they treated 16 aseptic nonunions intraoperatively with a moderate PRP platelet concentration (2× to 3×) with a bone allograft and an autologous fibrin membrane. All subjects went on to bony union. Another study showed enhanced tendon graft ligamentization during anterior cruciate ligament surgery. Histology at the 6- and 24-month marks showed increased connective tissue remodeling when compared with the untreated grafts.

Anitua and Sánchez are not the only researchers who have shown positive responses to PRP in the 2× to 3× baseline range. Graziani et al. evaluated the effect of PRP on the function of osteoblasts and fibroblasts. After a 72-hour incubation period, the 2.5× (approximately 550,000 platelets/μL) PRP group resulted in a statistically significant increase in cell count for osteoblasts and fibroblasts when compared with plasma and the negative control. The authors concluded that a platelet concentration of 2.5× yielded optimal results. In addition, Torricelli et al. evaluated the effect of PRP for the treatment of musculoskeletal overuse injuries in competition horses. With the placebo effect nullified, they found that PRP with a platelet concentration of 750,000 plate-
Platelet-rich plasma classification

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Platelet Count

A single individual’s platelet count can vary considerably on different days. There is also a significant variation in platelet count between individuals. For example, the normal platelet count varies between 150,000 and 350,000 platelets/µL. An individual with a low normal count receiving PRP with a concentration of 1 million platelets/µL would see an approximately 6.5× increase. An individual with a high normal count receiving PRP with a concentration of 1 million platelets/µL would see an approximate 3× increase. Variations in an individual’s baseline platelet count lead to inconsistency in quantifying a “fold” increase, making PRP products different between both individuals and treatments, even when identical protocols are used. For this reason, documenting both the absolute number of platelets per microliter contained in the PRP preparation and the individual’s own platelet count on the day of treatment is important in comparing effectiveness.

Centrifugation force, duration, and frequency are also important elements that may result in varying platelet concentrations and alteration of platelet morphology. jo et al. found optimum PRP gel formation by varying time and gravitational forces during centrifugation. The optimal conditions were found to be 900g for 5 minutes and 1,500g for 15 minutes for the separating centrifugation step and the condensing centrifugation step, respectively. In addition, Barrett and Erredge found that the number of centrifugations varied platelet capture significantly. They determined that a single centrifugation spin produced 1,254,000 platelets/µL whereas a double spin produced 2,017,000 platelets/µL.

The process for measuring platelet count may contribute to variation as well. Most hematology analyzer systems are designed to operate in ranges found within whole blood, and PRP may exceed the upper limit of the linear range of platelets that can be counted. In addition, adequate resuspension of the PRP and proper sample preparation are required for accurate platelet counts. Platelet clumping or lack of even distribution may result in inaccuracies.

Woodell-May et al. determined the average platelet count to be significantly less when samples were measured immediately after preparation of the PRP than when samples were resuspended on a rocker (P < .05). This study suggests that for accurate platelet counts to be achieved, the entire PRP sample must be removed and allowed to sit on a rocker for at least 5 minutes before counting. Furthermore, this study recommends using manual mode in the hematology analyzer because automatic counting modes are more likely to allow the sample to settle, reducing the absolute platelet count.

Leukocyte Content

The effect of highly concentrated WBCs contained within PRP preparations has been hotly debated. PRP systems that use a buffy coat contain an increased concentration of WBCs above baseline levels, whereas plasma-based methods do not. Although normal levels of WBCs have a positive immunomodulatory effect, heightened levels in some PRP preparations may have a deleterious impact. Literature suggests that excessive leukocytes, specifically neutrophils, may be contributing to these undesired results. However, the efficacy of WBCs in PRP treatments still remains unclear and may be
dependent on indication. PRP used to treat open wounds and prevent infection may require supranormal WBC levels,\textsuperscript{61-64} whereas PRP used to minimize scar formation should not contain WBCs.\textsuperscript{7,65} WBC content should always be documented in any classification system.

**UNDERSTANDING DELIVERY METHOD**

**Activation Methods**

Platelets can be activated endogenously or through the addition of an exogenous clotting factor to any commercially available system. Each type of activator may produce varying effects and significantly influence growth factor kinetics. Accurately documenting the delivery method and activation scheme used is another key to a successful classification system.

**Exogenous:** Exogenous activation results in rapid coagulation of platelets and quick clot formation. For this reason, clots formed in this manner are best applied manually to the tissues, rather than administered by injection. They often can be sutured to repairs. Proposed benefits of a preformed clot include the ability to more accurately localize growth factor release, as well as decreased diffusion when used intra-articularly. Advocates of preclotted PRP also theorize a more sustained growth factor release because growth factors are thought to elute from the clot slowly over the span of several days. The effect of exposure of the clot to synovial fluid has not been well documented, and it is possible that the clot is quickly dissolved in the joint.\textsuperscript{66,67}

**Endogenous:** The addition of external clotting factors to PRP may not be needed to significantly activate platelets. Not only will tissue collagen cause activation of platelets but simple agitation of platelets, such as centrifugation, as well as needle-induced bleeding during PRP injection, may provide the appropriate endogenous clotting factors needed for activation. Endogenous activation has the potential for slower aggregation of platelets and release of growth factors by allowing collagen within the tissue to operate as the activator providing a natural release pattern.\textsuperscript{68} Clot formation occurring after injection provides the benefit of administration through a needle and may allow a more precise delivery to, and within, the target tissue.

**Platelet Activators**

**Thrombin:** Thrombin causes rapid aggregation of platelets. Rapid activation may lead to excessive condensing of the fibrin matrix and significant retraction of clots, which may be inferior with respect to cell migration and growth factor enmeshment when compared with less condensed physiological activation.\textsuperscript{69-72} A rapid activation may also lead to a decrease in the total amount of growth factors available at the tissue site over time. Some growth factors have a short half-life (minutes to hours) and will degrade before additional tissue receptors become available if they are not immediately used upon release from a platelet.\textsuperscript{68,73} Additional potential negative effects include an immune-mediated coagulopathy resulting from antibody formation against bovine-derived thrombin.\textsuperscript{68}

**Calcium Chloride:** Calcium chloride has been added exogenously to PRP preparation in lieu of bovine thrombin and may result in the formation of a less condensed fibrin matrix. The fibrin matrix may provide a trapping mechanism for platelets, resulting in smaller amounts of thrombin formation endogenously, allowing a slower release of growth factors over a 7-day period, which may enhance cell migration and healing.\textsuperscript{72,74,75} Injections containing calcium chloride have a low pH and cause significant pain and a burning sensation to the patient.

**Calcium Chloride Plus Thrombin:** Calcium chloride is a citrate inhibitor and allows the plasma to coagulate, and thrombin causes fibrin to polymerize into an insoluble gel; platelets then degranulate and release growth factors.\textsuperscript{57} When calcium chloride and thrombin are combined with PRP, a gel or scaffold matrix is produced. This may offer the benefit of a slower, “time-released” effect of growth factors.

**Type I Collagen:** Endogenous type I collagen has been found to be equally effective as thrombin in activating platelets and stimulating the release of growth factors. In an in vitro study of PRP from human donors, clotting was performed with type I collagen or bovine thrombin. Type I collagen resulted in similar release of PDGF and VEGF but a more extended and overall greater release of TGF-β than thrombin. Clots formed by use of type I collagen also exhibited far less retraction than those formed with bovine thrombin. In addition, both type I collagen and bovine thrombin stimulated similar release of PDGF and VEGF between days 1 and 10, whereas thrombin resulted in a greater release of TGF-β during days 1 to 5.\textsuperscript{76}

**Delivery Technique**

The technique used during delivery of PRP is another fundamental variable that should be understood and addressed. Individual tissues may have ideal an-
atomic locations for delivery of PRP. For example, PRP injection into the osseotendinous, midsubstance, or myotendinous zone of a tendon may produce varying results. An in vivo rabbit model study determined the effect of PRP on insulin-like growth factor (IGF-1) expression in the epitenon and endotenon of rabbit Achilles tendons. At week 4, histologic analysis showed superior expression of IGF-1 in the epitenon of the PRP group versus the saline solution group, which produced superior IGF-1 levels in the endotenon (P < .0001).

The PRP delivery platform (liquid, spray, gel, or clot) should be selected based on procedure type (open vs. arthroscopic) and whether slow or fast activation of platelets is desired (Table 2).

### PAW CLASSIFICATION SYSTEM

With all of the previous information being taken into consideration, the PAW classification system of PRP is based on 3 components: (1) the absolute number of Platelets, (2) the manner in which platelet Activation occurs, and (3) the presence or absence of White cells. By analyzing these 3 variables, we are able to accurately compare publications (Tables 3 and 4).

### Platelets and White Cells

The first part of the classification system identifies the specific cellular components of platelets and white cells contained within the PRP preparation and should be documented as follows (Fig 1). Platelet concentration should be measured in platelets per microliter and categorized as follows: P1, less than or equal to baseline levels; P2, greater than baseline levels to 750,000 platelets/μL; P3, greater than 750,000 to 1,250,000 platelets/μL; and P4, greater than 1,250,000 platelets/μL.

Total WBC content is identified as either above (A) or below/equal to (B) baseline levels. Systems designated with an “A” are buffy-coat systems, whereas plasma-based systems fall under “B.” Because the

### Table 2. Types of PRP Delivery

<table>
<thead>
<tr>
<th>PRP Platform</th>
<th>Specific Activator/Modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liquid injection</td>
<td>Endogenous CaCl₂</td>
</tr>
<tr>
<td>Spray</td>
<td>Endogenous CaCl₂ + thrombin Thrombin</td>
</tr>
<tr>
<td>Gel</td>
<td>CaCl₂ + thrombin Thrombin</td>
</tr>
<tr>
<td>Clot (fibrin matrix)</td>
<td>CaCl₂ + centrifugation CaCl₂ + thrombin Thrombin</td>
</tr>
</tbody>
</table>

Abbreviation: CaCl₂, calcium chloride.

### Table 3. PAW Classification of Plasma-Based Systems and Buffy Coat–Based Systems

<table>
<thead>
<tr>
<th>Device Name</th>
<th>Platelet Concentration</th>
<th>Activation Method*</th>
<th>Total WBC Content</th>
<th>Neutrophil Content</th>
<th>Endogenous</th>
<th>Exogenous</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthrex/ACP</td>
<td>P2</td>
<td>*</td>
<td>B</td>
<td>α</td>
<td>P2-ββ</td>
<td>P2-x-ββ</td>
<td>22</td>
</tr>
<tr>
<td>Cascade/MTF Fibrinet</td>
<td>P2</td>
<td>*</td>
<td>B</td>
<td>β</td>
<td>P2-ββ</td>
<td>P2-x-ββ</td>
<td>14, 23-25</td>
</tr>
<tr>
<td>BTI/PRGF</td>
<td>P2</td>
<td>*</td>
<td>B</td>
<td>β</td>
<td>P2-ββ</td>
<td>P2-x-ββ</td>
<td>26-28</td>
</tr>
<tr>
<td>Harvest SmartPreP 2/DePuy Symphony II</td>
<td>P2</td>
<td>*</td>
<td>A</td>
<td>α</td>
<td>P2-βAα</td>
<td>P2-x-βAα</td>
<td>29-33</td>
</tr>
<tr>
<td>Arteriocyte/Medtronic Magellan</td>
<td>P2</td>
<td>*</td>
<td>A</td>
<td>α</td>
<td>P2-βAα</td>
<td>P2-x-βAα</td>
<td>14, 33, 36, 37</td>
</tr>
<tr>
<td>Emcyte Genesis CS/Exactech Accelerate</td>
<td>P4</td>
<td>*</td>
<td>A</td>
<td>α</td>
<td>P4-βAα</td>
<td>P4-x-βAα</td>
<td>38-40</td>
</tr>
</tbody>
</table>

*Ultimately, researchers can choose to activate platelets endogenously or through the addition of an exogenous clotting factor to any commercially available system.
†Buffy coat–based systems typically produce highly variable platelet concentrations.
<table>
<thead>
<tr>
<th>Condition Treated</th>
<th>Authors</th>
<th>Evidence Level</th>
<th>Study Type</th>
<th>No. of Patients</th>
<th>PRP Outcome</th>
<th>System</th>
<th>Platelets/µL</th>
<th>Activation Method</th>
<th>WBCs</th>
<th>PAW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial/lateral epicondylitis</td>
<td>Hechtman et al.⁷⁸ (Orthopedics, 2011)</td>
<td>IV</td>
<td>Case series, prospective study</td>
<td>PRP group previously unresponsive to nonsurgical treatment (n = 31)</td>
<td>(+) Improved pain and function scores, thus avoiding surgery</td>
<td>Cascade MTF</td>
<td>NA</td>
<td>Exogenous CaCl₂</td>
<td>Below</td>
<td>NA-x-Bβ</td>
</tr>
<tr>
<td></td>
<td>Thanasas et al.⁷⁹ (Am J Sports Med, 2011)</td>
<td>I</td>
<td>Randomized controlled single-blind trial</td>
<td>PRP group (n = 14) vs autologous whole blood group (n = 14)</td>
<td>(+) Effective for chronic lateral elbow epicondylitis</td>
<td>Biomet GPS III</td>
<td>1.292,500</td>
<td>5.5×</td>
<td>Endogenous type I collagen</td>
<td>Above</td>
</tr>
<tr>
<td></td>
<td>Peerbooms et al.⁸⁰ 1-yr follow-up (Am J Sports Med, 2010)</td>
<td>I</td>
<td>Randomized controlled study</td>
<td>PRP group (n = 51) vs corticosteroid group (n = 49)</td>
<td>(+) Reduced pain, increased function</td>
<td>Biomet NA</td>
<td>NA</td>
<td>Endogenous type I collagen</td>
<td>Above</td>
<td>NA-Aa</td>
</tr>
<tr>
<td></td>
<td>Hechtman et al.⁷⁸ (Orthopedics, 2011)</td>
<td>II</td>
<td>Prospective comparative study</td>
<td>PRP group (n = 15) vs bupivacaine group (n = 5)</td>
<td>(+) Reduced pain in chronic severe tenosynovitis in patients in whom nonoperative treatment has failed</td>
<td>Biomet GPS</td>
<td>3,310,000</td>
<td>5.39×</td>
<td>Endogenous type I collagen</td>
<td>Above</td>
</tr>
<tr>
<td>Achilles tendinopathy/rupture</td>
<td>de Jonge et al.⁸³ 1-yr follow-up (Am J Sports Med, 2011)</td>
<td>I</td>
<td>Double-blind randomized placebo-controlled study</td>
<td>PRP group (n = 27) vs placebo-saline solution injection (n = 27)</td>
<td>(Neutral) PRP injection did not result in greater improvement in pain and activity over placebo injection</td>
<td>Biomet GPS III</td>
<td>NA</td>
<td>Endogenous type I collagen</td>
<td>Above</td>
<td>NA-Aa</td>
</tr>
<tr>
<td></td>
<td>Schepull et al.⁸⁶ (Am J Sports Med, 2011)</td>
<td>II</td>
<td>Randomized controlled single-blind study</td>
<td>PRP group (n = 16) vs control group (n = 14)</td>
<td>(+) PRP not useful for treatment of Achilles tendon ruptures; lower Achilles tendon total rupture score, thus suggesting detrimental effect</td>
<td>NA</td>
<td>3.673 ± 1.051 × 10⁷</td>
<td>17×</td>
<td>Endogenous type I collagen</td>
<td>NA</td>
</tr>
<tr>
<td>Patellar tendinopathy</td>
<td>Filardo et al.⁸⁷ (Br J Sports Med, 2011)</td>
<td>IV</td>
<td>Case study</td>
<td>PRP group (n = 1)</td>
<td>(+) Fast tissue repair and return to full function</td>
<td>NA</td>
<td>6.5 × 10⁶</td>
<td>6.1× ± 1.6</td>
<td>Exogenous CaCl₂</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>de Jonge et al.⁸³ 1-yr follow-up (Am J Sports Med, 2011)</td>
<td>III</td>
<td>Case-control, descriptive laboratory study</td>
<td>PRGF athlete group (n = 6)</td>
<td>(+) Earlier ROM recovery and return to activity</td>
<td>BT/PRGF NA</td>
<td>NA</td>
<td>Exogenous CaCl₂</td>
<td>Below</td>
<td>NA-x-Bβ</td>
</tr>
<tr>
<td></td>
<td>Sánchez et al.²⁴ (Am J Sports Med, 2007)</td>
<td>II</td>
<td>Propective comparative study</td>
<td>PRP group with 3 injections (n = 15) vs exercise-only group (n = 16)</td>
<td>(+) PRP has potential to achieve satisfactory clinical outcome, even in difficult cases with chronic refractory tendinopathy after previous classical treatments have failed</td>
<td>NA</td>
<td>6.5 × 10⁶</td>
<td>6.1× ± 1.6</td>
<td>Exogenous CaCl₂</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Randelli et al.⁸⁶ (Int Orthop, 2010)</td>
<td>IV</td>
<td>Prospective study</td>
<td>PRP group (n = 20) evaluated at 6 mo</td>
<td>(+) Aided regeneration of tissue which otherwise has low healing potential</td>
<td>NA</td>
<td>6 × 10⁶</td>
<td>6×</td>
<td>Exogenous CaCl₂</td>
<td>NA</td>
</tr>
<tr>
<td>Rotator cuff reconstruction</td>
<td>Io et al.⁹⁰ (Am J Sports Med, 2011)</td>
<td>II</td>
<td>Prospective cohort study</td>
<td>PRP group (n = 19) vs control group (n = 23)</td>
<td>(Neutral) Did not clearly show accelerated recovery clinically or anatomically</td>
<td>COBE spectra LRS Turbo (Lakewood, CO)</td>
<td>1.400 × 10⁵</td>
<td>(adjusted via saline solution to 1,000 × 10⁵)</td>
<td>Exogenous Calcium Gluconate</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Randelli et al.⁸⁶ (J Shoulder Elbow Surg, 2011)</td>
<td>I</td>
<td>Prospective randomized controlled study, 2-yr follow-up</td>
<td>PRP augmentation group (n = 26) vs control group (n = 27)</td>
<td>(+) Reduced pain in first postoperative months; long-term results of subgroups of grade 1 and 2 tears suggest that PRP positively affected cuff rotator healing</td>
<td>Biomet GPS II NA</td>
<td>NA</td>
<td>Exogenous CaCl₂</td>
<td>Above</td>
<td>NA-x-Aa</td>
</tr>
</tbody>
</table>
**TABLE 4. Continued**

<table>
<thead>
<tr>
<th>Condition Treated</th>
<th>Authors</th>
<th>Evidence Level</th>
<th>Study Type</th>
<th>No. of Patients</th>
<th>PRP Outcome</th>
<th>System</th>
<th>Platelets/μL</th>
<th>Activation Method</th>
<th>WBCs</th>
<th>PAW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subacromial decompression</td>
<td>Everts et al.93 (Eur Surg Res, 2008)</td>
<td>I</td>
<td>Randomized controlled study</td>
<td>Platelet leukocyte gel group (n = 20) v control group (n = 20)</td>
<td>(+) Faster recovery, earlier return to daily activities, took less pain medication</td>
<td>Magellan</td>
<td>NA</td>
<td>Endogenous type I collagen</td>
<td>Above</td>
<td>NA-Aa</td>
</tr>
<tr>
<td>Cartilage regeneration/OA</td>
<td>Kon et al.96 (Arthroscopy, 2011)</td>
<td>II</td>
<td>Prospective comparative study</td>
<td>PRG group (n = 50, 3 injections) v HA low-molecular-weight group (n = 50, 3 injections) v HA high-molecular-weight group (n = 50) evaluated at 2 and 6 mo</td>
<td>(+) PRP greater and longer efficacy than HA injections</td>
<td>NA</td>
<td>6.8 × 10^5</td>
<td>Exogenous CaCl_2</td>
<td>NA</td>
<td>P4-x-NA</td>
</tr>
<tr>
<td>Anterior cruciate ligament reconstruction</td>
<td>Silva and Sampaio96 (Knee Surg Sports Traumatol Arthrosc, 2009)</td>
<td>II</td>
<td>Prospective comparative study</td>
<td>PRP (n = 30) v without PRP (n = 10)</td>
<td>(Neutral) PRP with or without thrombin activation does not seem to accelerate tendon integration</td>
<td>Biomet GPS III</td>
<td>NA</td>
<td>Exogenous thrombin v no thrombin</td>
<td>Above</td>
<td>NA-Aa</td>
</tr>
<tr>
<td>Total knee arthroplasty</td>
<td>Peerbooms et al.97 (Acta Orthop, 2009)</td>
<td>I</td>
<td>Double-blind randomized controlled trial</td>
<td>Platelet gel group (n = 50) v control (n = 52)</td>
<td>(Neutral) Application to wound site did not promote wound healing; no effect on pain, knee function, or hemoglobin values</td>
<td>Biomet</td>
<td>NA</td>
<td>Exogenous CaCl_2 v thrombin</td>
<td>Above</td>
<td>NA-Aa</td>
</tr>
</tbody>
</table>

Abbreviations: CaCl_2, calcium chloride; HA, hyaluronic acid; NA, not applicable; OA, osteoarthritis; PRFM, platelet rich fibrin matrix.

*The data indicate a lack of reporting of platelet concentration, activation method, and WBC content among clinical studies. Of the 23 clinical publications cited, the PAW could only be indicated for 1 study. This clearly shows that adequate comparison between studies is virtually impossible, and documentation and adherence to a classification system are imperative.*
**PRP "PAW" Classification System**

**P**latelets

- **CONCENTRATION** [platelets/μL]
  - $\leq$ baseline
  - >baseline - 750,000
  - >750,000 - 1,250,000
  - >1,250,000
- **METHOD**
  - eXogenous

**A**CTIVATION

**W**hite Blood Cells

- **Total WBC's**
  - Above baseline
  - Below or = to baseline
- **NEUTROPHILS**
  - Above baseline
  - Below or = to baseline

**Example:** P2 - B$\beta$ or P2 - B

**Example:** P3 - x - A$\alpha$

**Figure 1.** PRP PAW classification system.
inclusion or exclusion of neutrophils will become an important variable, a subcategory for neutrophil count has been created for systems that concentrate WBCs. If neutrophils are included in the buffy coat, then \( \alpha \) (above) is added. If neutrophils are filtered out, then \( \beta \) (below) is added. Therefore buffy-coat systems will have a designation of either \( \alpha \alpha \) or \( \alpha \beta \) in our system.

For example, a PRP preparation consisting of 900,000 platelets/\( \mu \)L, with a total WBC and neutrophil content above baseline levels will be documented as P3-A\( \alpha \).

**Activation Method**

Ultimately, researchers can choose to activate platelets endogenously or through the addition of an exogenous clotting factor to any commercially available system. Endogenous activation is not given a designation. However, if an exogenous external activator is used, it is documented with an \( \times \). Combining the previously described PRP preparation with this activation method will provide the complete classification: either P3-A\( \alpha \) for endogenous activation or P3-x-A\( \alpha \) for exogenous activation.

**CONCLUSIONS**

PRP continues to occupy both orthopaedic literature and the lay press, and more funding is being dedicated to unraveling its mysteries; a simple method for comparing published data based on the content of PRP needs to be established. Our system offers a simple, effective method for quickly documenting the cellular components and activation method used. The acronym PAW serves as a pneumonic for Platelets, Activation, and White cells, and the subcategories are thoughtfully organized to enhance recall. Using a classification system will speed the process of identifying the optimal PRP preparation for each indication and allow other investigators to replicate published data or perform meta-analyses.

**Acknowledgment:** The following individuals are acknowledged for their substantial contribution in the development of the classification system: Bryan T. Hanypsiak, M.D., David O. Shepard, M.B.A., C.T.B.S., and Brandon L. Roller, M.D. All are employees of Arthrex, Naples, Florida.

**REFERENCES**

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PLATELET-RICH PLASMA CLASSIFICATION


