What is PRP Therapy ?

Platelet-rich plasma (**PRP**) is blood plasma that has been enriched with platelets. As a concentrated source of autologous platelets, PRP contains (and releases through degranulation) several different growth factors and other cytokines that stimulate healing of bone and soft tissue.

Platelet Rich Plasma: Historical Perspective

The application of PRP has been documented in many fields. First promoted by M. Ferrari in 1987 (*1)* as an autologous transfusion component after an open heart operation to avoid homologous blood product transfusion, there are now over 5200 entries in the NCBI for PRP ranging in fields from orthopedics, sports medicine, dentistry, otolaryngology, neurosurgery, ophthalmology, urology, wound healing, cosmetic, cardiothoracic and maxillofacial surgery.
The initial popularity of PRP grew from its promise as a safe and natural alternative to surgery. PRP advocates promoted the procedure as an organically based therapy that enabled healing through the use of one's own natural growth factors. In recent years, scientific research and technology has provided a new perspective on platelets. Studies suggest that platelets contain an abundance of growth factors and cytokines that can affect inflammation, postoperative blood loss, infection, osteogenesis, wound, muscle tear and soft tissue healing. Research now shows that platelets also release many bioactive proteins responsible for attracting macrophages, mesenchymal stem cells and osteoblasts that not only promote removal of degenerated and necrotic tissue, but also enhance tissue regeneration and healing.

Musculoskeletal practitioners began using PRP for tendinopathy in the early 1990s. These early practitioners were primarily trained in the use of prolotherapy. The popularity of PRP grew as physicians began to see clinical results in concentrating a patient's own blood factors. The PRP procedure is significantly more complex and requires additional equipment to perform successfully, but many practitioners have seen a relatively more robust response, fewer treatments and improved tissue health compared to prolotherapy.

The growth of PRP therapy has relied primarily on anecdotal or case reports. Historically, there have been few controlled trials to prove the efficacy of PRP. Of these existing trials, the sample sizes tended to be too small to allow for generalization of findings. Moreover, lack of concensus on technique, number of injections, spacing of injections, number of platelets, concentration of platelets over baseline, with or without leukocytes in the injection, exogenous activation of injected platelets and even a definition of appropriate candidates for the procedure are lacking and in need of further definition and evaluation. Recently, however, there has been an emerging literature on the beneficial effects of PRP for chronic non-healing tendon injuries including lateral epicondylosis, plantar fasciopathy and cartilage degeneration (2,3).

Platelet Rich Plasma: Definition and Preparation Considerations

By definition, PRP must contain a higher concentration of platelets than baseline, however an increase in platelets is a very gross description of PRP and does not accurately describe the variability among different types of PRP. There are several parameters that need to be taken into account when considering PRP, including: platelet concentration above baseline, whether or not leucocytes are included, whether or not the PRP has been anticoagulated and whether it requires exogenous activation.Platelet count is the first variable to consider. Absolute platelet count varies depending on the platelet concentration in the subjects' peripheral blood. PRP devices can be usually divided into lower (2.5 - 3 times baseline concentration) and higher (5 – 9 times baseline concentration) systems. It would seem intuitive that a higher platelet count would yield more growth factors and better clinical results.

PRP containing white blood cells will have different biologic activity than PRP in which they are absent. The lower platelet count systems separate the whole blood into two components: one with the cellular components and the other consists of serum in which the platelets are suspended. The higher platelet count systems separate the whole blood into three fractions: the red cells, serum and buffy coat. The buffy coat contains both platelets and white blood cells (WBCs).

What is BUFFY COAT ?

The buffy coat is a rich source of cells and proteins that may help optimize
the conditions for healing, including:
Platelets
Growth Factors
White Blood Cells (WBC's)
CD34+ cells as a stem cell marker
Cytokines and Adhesion Molecules

It has been documented in the literature that effective cellular therapy requires a scaffold for cell migration, progenitor cells which can be converted into bone or soft tissue, and signal proteins to modulate the repair and regeneration process.
These key biologic cells are located in the "buffy coat" layer.

Activation of PRP
PRP is activated prior to injection is another parameter that requires further discussion. PRP can be activated exogenously by thrombin, calcium chloride or mechanical trauma. Once PRP is activated, a fibrin network begins to form, solidifying the plasma and creating a fibrin clot or membrane. If PRP is activated too strongly, the fibrin network will be a bivalent, unstable network. If it is activated in a more physiologic manner, a tetramolecular stable network forms that enhances enmeshment of cells and growth factors. (4) Although this can be useful for surgical procedures, it is undesirable to have the PRP overly viscous when injecting into soft tissue.
Activation results in rapid growth factor release, with 90% of the prefabricated factors released in ten minutes. Many growth factors have short half-lives, so greatest effectiveness may result if they are activated at or just prior to injection. Variable half-lives of growth factors also creates a differential PRP make-up depending on how quickly after activation it is used. Most commercial PRP kits do not activate PRP. Some replace calcium that was bound by ACD to create a more physiological state. Employing unactivated PRP may result in a more normal physiologic activation by the injected tissue.To avoid unintentional activation of platelets, most protocols use large bore needles (>22 G) to draw the blood and re-inject PRP.

Once activation has occurred at the injection site, release of growth factors initiates an inflammatory response that lasts approximately 3 days (5). Fibroblasts accumulate at the site of injection, which marks the beginning of the proliferative phase of healing that lasts several weeks. After that, remodeling occurs to the collagen matrix that was laid down by the fibroblasts. This remodeling phase that leads to the formation of mature tissue lasts about 6 months. It takes all three phases for new tissue to form and provide long-term stability to tissue (6).
Collagen is a natural activator of PRP, thus when PRP is used in soft tissue, it does not need to be exogenously activated.
Once activation has occurred at the injection site, release of growth factors initiates an inflammatory response that lasts approximately 3 days (9). Fibroblasts accumulate at the site of injection, which marks the beginning of the proliferative phase of healing that lasts several weeks. After that, remodeling occurs to the collagen matrix that was laid down by the fibroblasts. This remodeling phase that leads to the formation of mature tissue lasts about 6 months. It takes all three phases for new tissue to form and provide long-term stability to tissue (10).

Platelet Rich Plasma: Indications

PRP has been successfully used in a variety of applications including:

- Anti-Ageing
- Wrinkles and Skin Revitalisation
- Hair Loss
- Following Face & Neck Lifts
- Burns
- Scars and Trauma
- Soft Tissue Reconstruction
- Wound Care (e.g. skin ulcers)
- Sports Injuries (e.g. tendon regeneration)
- Stimulation and Acceleration of Bone and Soft Tissue Healing
- Osteoarthritis (OA)

Platelet Rich Plasma: Contraindications

Absolute Contraindications:
- Platelet dysfunction syndrome
- Critical thrombocytopenia
- Hemodynamic instability
- Septicemia
- Local infection at the site of the procedure
- Patient unwilling to accept risks

Relative Contraindications:
- Consistent use of NSAIDs within 48 hours of procedure
- Corticosteroid injection at treatment site within 1 month
- Systemic use of coriticosteroids within 2 weeks
- Recent fever or illness
- Cancer- especially hematopoetic or of bone
- HGB < 10 g/dl
- Platelet count < 105/ul

Platelet Rich Plasma: Protocols, Technique and Safety Recommendations

Protocol/Technique
Generally speaking, the procedure only requires the physician and an assistant to aid in preparation of a PRP graft, maintenance of aseptic technique and saving images on ultrasound (if applicable).
Pre-procedure Considerations
1) There should be a specific indication correlated with physical exam and confirmed with imaging studies such as x-ray, ultrasound, MRI, or CT scan prior to treatment.
2) Appropriate patient education and discussion has occurred with an informed consent signed prior to the initiation of the procedure.
3) Contraindications to the procedure are reviewed prior to initiation (see above).
4) Analgesics (no NSAIDs) or anxiolytics have been administered, if applicable

Graft Preparation

1) The patient is placed in a comfortable seated or recumbent position.
2) Sterile single use needles and syringes should be used with appropriate handling and disposal.
3) Using aseptic technique (see below), an appropriate amount of venous blood is obtained for the given procedure. a. Single-stick draws are preferred to decrease chances of activation.
b. If a vein is passed through completely, blood flow is not smooth, needle comes out of vein or multiple attempts at a single site occur, consideration of a second site should be given.
c. If the patient is a difficult draw, consider using ultrasound to guide the drawing needle.

4) Using sterile technique, the venous blood is transferred to the centrifuge. PRP should be obtained using a separating device designed for autologous blood. Preference is given to a closed system that prevents exposure of the blood and cellular components to the open air in the room and allows for minimal manipulation of the tissue.
5) If multiple patient grafts are prepared concurrently, proper labeling of each graft should be completed to ensure no cross contamination or the graft being used on the wrong patient.

Image Guidance
1) Real-time image guidance using CT, fluoroscopy or ultrasound should be used when injecting PRP.
2) If ultrasound is used, the following considerations should be decided upon in advance: a. Sterile gel. We recommend this for longer procedures, intra-articular injections, and any injections around the spine. Universal use has not been shown to improve infection rates, and in the setting of simple soft tissue injections, judicious use of aseptic technique is sufficient.
b. Sterile probe covers. We recommend probe cover use with longer procedures (percutaneous needle tenotomy, etc). Cleansing of the probe before and after procedures and adherence to aseptic technique is sufficient. Covering the probe with sterile wound products (tegaderm) or using sterile gloves are other options that have been used in the community with success.
c. Scout images and indelible markings of the site of probe position and needle entry should be made prior to final cleansing of the skin.

PRP Injection
1) The patient is placed in an appropriate and comfortable position that allows for sterility and access to the site of injection.
2) All necessary materials for the injection (PRP, additives, 4X4s, needles, US gel) should have been planned and placed on a sterile table adjacent and easily accessible to the physician.
3) The patient's skin is cleansed appropriately and towels or drapes may be used to create an aseptic field.
4) If local anesthetic will be used, it is to be applied with aseptic technique. See above discussion on anesthetic effects on PRP; consider infiltrating only the local subcutaneous area with anesthetic. Consider nerve block for larger/longer procedures (tenotomies).
5) If ultrasound is used, apply gel consistent with markings made previously.
6) Complete the injection with real-time recording of images.
7) Apply a dressing or appropriate bandage to protect the needle entry site.

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Post-Injection

1) Monitor for post-procedure complications (vaso-vagal most common)
2) Patients should be given post-procedure instructions, precautions, and emergency contact information.
3) Protocols for immobilization and post-procedure activity allowed/encouraged vary widely. Future recommendations will be forthcoming once protocols are more widely accepted +/- studied.
4) Post procedure analgesic prescription should be dispensed. Avoid NSAIDs until the patient has healed, is pain free, has full function or has reached a plateau.
5) Contaminated areas should be disinfected in between patients per OSHA guidelines.
6) The procedure should be recorded in detail with a procedure note including: date, pre/post-procedure diagnosis, procedure title, performing physician w/wo assistants, anesthesia, brief indication of procedure, description of graft preparation, description of procedure including guidance and instruments.

Follow-up
1) Patients are generally re-examined 2-6 weeks after the procedure to follow pain, function, injection site and to discuss concerns and future course.
2) Patient response should be recorded using validated outcome measures such Nirschl, VISA, etc.

3) Consideration for re-injection should be a patient centered decision and made based on functional outcome. We do not endorse a specific number of injections at any site.

Safety*:*
1) Universal precautions at all times during the procedure and immediately following the procedure.
2) Infection: PRP is antimicrobial and effective against most bacteria classes except Klebsiella, Enterococcus and Pseudomonas. Standard skin disinfection should be used before injection.
3) This is entirely an autologous graft making eliminating the concern for disease transmission unless the graft were contaminated.
4) Risks to patient from the procedure: a. Infection
b. Bleeding
c. Nerve damage
d. Pain
e. Lack of result
f. Loss of limb and death are very rare but possible.

References:
1. M Ferrari et al. A new technique for hemodilution, preparation of autologous platelet-rich plasma and intraoperative blood salvage in cardiac surgery. *Int J Artif Organs.* 1987 Jan;10(1):47-50.
2. (Mishra and Pavelko. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. *Am J Sports Med.* 10(10):1–5, 2006
3. Barrett and Erredge. *Podiatry Today.* 17:37–42, 2004
4. Dohan et al. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). 2009. *Trends in Biotechnology.* 27(3): 158–67.
5. Kumar et al. Pathologic basis of disease 7th ed. Chapter 2. Copyright 2005. Saunders.
6. Tate KS, Crane D. Platelet rich plasma grafts in musculoskeletal medicine. *Journal of Prolotherapy.* May 2010 2(2):371-376.

EASY PRP is...

...an innovative patented system for simple, easy, safe and effective preparation of highly concentrated PRP

Why EASY PRP

1. Considers initial RBC (Red Blood Cell) and PLT differential > constantly high PRP quality
2. Contains Buffy Coat – highest PRP concentration
3. Adjustable PRP concentration
4. Platelet Poor Plasma (PPP) can be used for additional applications
5. Top price-performance ratio

PRP Applications – Clinical Areas

Aesthetics	skin rejuvenation, wrinkles, acne scars, hair loss, fat graft, post-skinlasertreatment
Plastic Surgery	pressure sores, leg ulcers, burns, wound healings
Orthopedics & Pain	cartilage/ligament repair,arthritis,tendonitis,post-operativepain, inflammation reduction, chronic pain
Dentistry	bone graft including onlay & inlay, sinus lift, bone defects created by teeth removal, small cyst or cleft, dental implant surgery
Ophthalmology	epithelial defects of the cornea, dry eye syndrome, ocular surface damages,post-laser surgery syndrome
Veterinary	tendon and ligament injuries, wound healing, osteoarthritis treatment

PRP Overview Monograph

Reviews cell therapies using platelet rich plasma autologous cellular regeneration

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