Platelet-Rich Plasma Therapy

Applications of PRPT in Sports and Musculoskeletal Medicine

In 2009, golfer Tiger Woods reportedly received four injections of Platelet-Rich Plasma (PRP) into his knee to augment graft healing following ACL surgery. While this news was overshadowed by other more sensational events in his life, it nevertheless resulted in a moderate ripple of interest in PRP.

Interest in PRP treatment for sports injuries and musculoskeletal healing had, in fact, been building up for the better part of the last decade. Clinics in parts of Europe, notably Spain, have been administering PRP treatments to injured soccer players since the early part of the decade. Word had reached footballers in the English Premier League and there were reports of players from top clubs flying to Spain for PRP treatment when they were injured.

The idea of using platelets for healing is not new. Reports dating back to the 1970's concerning platelet interaction with tissues can be found in medical literature. Autologous PRP was first popularised in maxillofacial surgery by dental surgeons in the 1990's. Current uses include augmentation of healing for bone graft, peri-implant defects, skin-graft healing, and soft tissue healing.

What is PRP?

PRP refers to a concentrate of platelets in plasma that is higher than that of normal circulating platelets in the body. Beyond this concept, however, there is considerable variation in its definition. Robert Marx, one PRP's pioneers in the area of dental surgery, defined PRP as having 1 million platelets of more per microlitre (Marx, 2001). Other definitions include 2 to 6 times the native concentration. Some authors define PRP as a concentrate of (only) platelets in plasma, deliberately leaving out the white cells, which could be counter-productive and cause more inflammation and pain. Others have emphasised the need to include white blood cells in the concentrate as they could play a role in macrophage-mediated tissue regeneration together with platelet-derived growth factors.

Terminologies used also tend to create confusion. While Platelet-Rich Plasma remains probably the most widely used term, some authors or companies producing kits have used the terms "Autologous Conditioned Serum (ACS)", "Autologous Conditioned Plasma (ACP)" or "Platelet-Derived Growth Factors (PDRF)". There are subtle differences, but in essence, all are concentrates of platelets derived from the patient's own blood. The autologous nature of the preparation is one of its key safety points, in that there is no possibility of rejection by a patient.

Platelets have a vital role in the healing of injured tissues. The alpha granules of platelets contain growth factors which result in various biological effects (See table). However, variations in individuals and differences in preparation methods can affect the absolute and relative concentrations of these different factors in PRP, which could account for differences in clinical outcome.

The release of these factors can be rapidly triggered by platelet activators thrombin and calcium. This results in the formation of a gel which can be used in open surgery but is impractical for injection. More gradual activation of platelets is also possible through exposure to damaged collagen, which attracts platelets through cytokine signalling. This fact makes it possible for PRP to be administered without pre-activation into damaged tissues.

Not to be confused with Stem Cells

It is not uncommon for patients or even doctors to confuse PRP treatment with stem cell treatments, due to the autologous nature of the preparation. Unlike stem cells, platelets survive for only 7 to 10 days and are unable to reproduce themselves, as they contain no nuclei. The inability to reproduce eliminates the risk of carcinogenesis, which is a risk in stem cell treatments. Stem cell therapies are still considered experimental whereas PRP has achieved greater mainstream acceptance and far wider usage.

Growth Factors In Platelets

Factor	Name	Effects
PDGF aa PDGF bb PDGF ab	Platelet Derived GF	Mitogens of mesenchymal stem cells, Promote synthesis of extracellular matrix
TGF-α TGF – β	Transforming GF	Stimulation of DNA Synthesis, Proliferation of various cells, Favours synthesis of collagen
IGF – I IGF – II	Insulin-like GF	Stimulates proliferation and differentiation of osteoblasts, Stimulate prolifiration of fibro-blasts
EGF	Epidermal GF	Stimulates Proliferation and differentiation of epidermal cells, co-stimulating angiogenesis
VEGF	Vessel Endothelial Growth Factor	Stimulate Angiogenesis

The author preparing PRP for injection

Experimental and Theoretical Benefit

The biological effects of PRP and the various platelet-derived factors have been the subject of a considerable amount of laboratory-based research. Studies in animals have shown that for ligament repairs, PRP could result in improved maximal ligament load and linear stiffness. For tendon repairs, the addition of PRP resulted in significantly stronger healing, compared with the control side. Various positive effects on cartilage synthesis have also been seen with PRP or its factors. PRP has also shown potential to modulate inflammation.

The theoretical benefit of PRP injection administered locally to an injured tissue, in its simplest reading, is a way of bringing about a faster pace of healing in tissues. But has this translated into a clinically significant benefit?

Most recent reviews on PRP have concluded that there is a sound scientific basis for its use in soft tissue injuries, but have highlighted the lack of robust clinical data. Truly randomised, placebo-controlled, blinded trials are currently lacking. Clinical reports so far tend to be summations of experiences in groups of patients, or comparative studies against a more established treatment method. It has been reported that muscle tears heal twice as fast with PRP. Other clinical reports in medical press or conference proceedings have reported positive effects of PRP in tennis elbow, Achilles tendonitis, ankle sprains and osteoarthritis. While there appears to be overall support for PRP in soft tissue and wound healing, the benefit of PRP for bone repair and bone graft healing, remains controversial.

In the case of soft tissue injuries, the current lack of robust clinical data is somewhat mitigated by the fact that PRP is autologous and therefore considered safe, with patients having nothing to lose, and everything to gain from trying it.

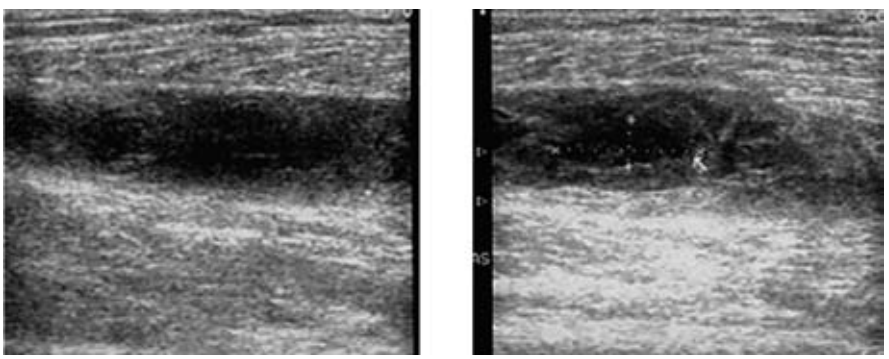
Clinical Applications in Sports and Musculoskeletal Medicine.

A vast majority of sport and exercise-related injuries involve soft tissues and are not severe enough to warrant surgery. Such injuries would usually heal on their own over time. A typical muscle strain, for example, would go through phases of hemostasis, inflammation, regeneration (replacement with original tissue) and repair (scar tissue). The management of such injuries typically involves management of inflammation and pain, combined with physiotherapy to address related issues such as spasm, muscle imbalances or joint stiffness which may have predisposed the patient to the injury. Essentially, the injured tissue is left to heal on its own, as determined by the body's natural pace of healing.

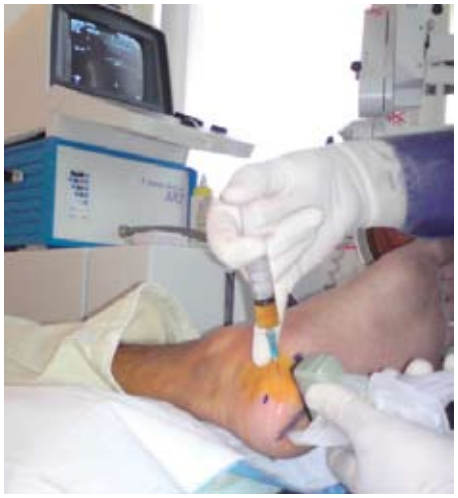
PRP, with its potential to quicken healing, appears to be an attractive option for sportsmen or exercisers wishing to minimise injury downtime from both acute as well as overuse injuries. With an increasing numbers of adults and mid-lifers adopting exercise as a lifelong habit, degenerative and overuse injuries are becoming increasingly commonplace. PRP treatment once again presents itself as being a potential part of the solution for such injuries.

Current uses for PRP in sports medicine include:

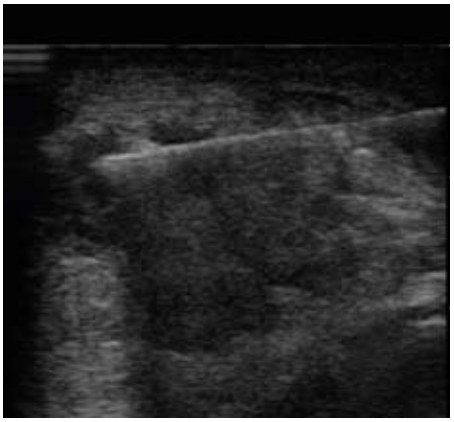
- **Acute Muscle Tears eg. Myoseptal tears of the calf or hamstring**
- **Chronic Insertional or Intrasubstance Tendinopathy with or without tear, Eg. Tennis elbow, Patellar tendinosis, Insertional Achilles Tendinosis, Plantar Fasciitis, Rotator Cuff tendinosis**
- **Cartilage degeneration, and early stages of Osteoarthritis of the knee, ankle and other joints**
- **Ligament Tears, eg. Medial Collateral Ligament (MCL) of the knee, Ankle ligament sprains**
- **Post-surgical augmentation of soft tissue healing, eg. following surgical tendon repairs in tendo-achilles or rotator cuff, meniscus repair, or cartilage surgery in degenerative joint disease**



Left: Ultrasound Scan of 9-day old Calf Muscle Tear with hematoma formation in a 50 year old tennis player, immediately prior to PRP administration. Right: The same tear 1 week later showing evidence of healing.



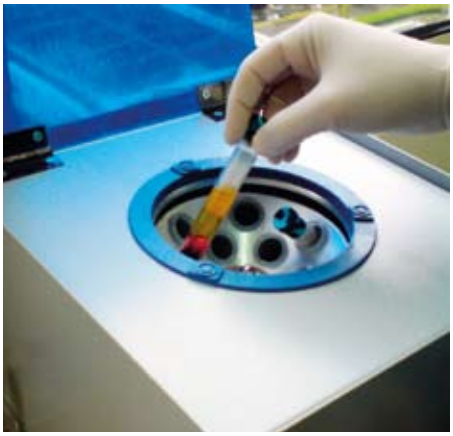
Ultrasound-guided injection of PRP for plantar fasciitis



Ultrasound-guided injection helps ensure PRP is delivered accurately to the site of injury

Side Effects and Risks

The most predictable post-injection complaint is, by far, that of temporarily increased soreness of the injury, which may last several weeks. This tends to occur most commonly with tendon injections and in this author's experience, can usually be minimised by resting and frequent icing of the injured area within the first 24 to 48 hours after injection. Mild muscle spasm and stiffness overlying a site of injection is fairly common. In the long term, excessive fibrous tissue formation at the site of injury is a potential side effect. Infection is a potential risk. Blood drawn and left standing or exposed to the environment could become contaminated and act as a medium for growth of pathogens. Most PRP preparation systems address this through the use of sterile disposable items within a closed system. Other site-specific risks could occur, related to poor injection technique or inaccurate placement of needles. If pre-activated PRP is injected into a blood vessel, there is a theoretical risk of thrombus formation.



Centrifuging separates blood into its various components.

The PRP Procedure

Thanks to the increasing variety of specialised PRP kits being made available, it is now possible to perform such treatments, from start to finish, quickly and simply in the clinic.
Blood drawn from the patient through venipuncture goes immediately into a special tube containing a permitted anti-coagulant, and in certain systems such as the Regenkit™, a gel separator as well. The tube is then spun in a high-speed centrifuge for several minutes in order to achieve a separation of cells and plasma. PRP is then obtained from the plasma layer, with different kit manufacturers adopting slightly different methods of extraction. Some PRP preparation kits employ a filtration method instead of, or in addition to, centrifuging. The PRP preparation is then delivered to the area of damage. This is usually done under ultrasound or other imaging guidance for muscle or ligament tears in order to ensure maximum accuracy. It stands to reason that optimal efficacy with minimum risk would be achieved if PRP can be accurately delivered into the exact site of injury.

Is it Doping?

PRP given as an intramuscular injection is listed in the World Anti-Doping Agency's (WADA) 2010 list of prohibited substances and methods. The basis for this ban appears to be that certain growth factors contained in PRP, such as IGF and VEGF, are regarded as performance enhancing. However, evidence that autologous PRP is able to enhance athlete performance beyond a therapeutic effect is lacking, and as of 2011, WADA has removed this prohibition, making PRP injections permissible for competing athletes.

Conclusion

PRP provides a means of biological stimulation for tissue healing. It has the potential to be a powerful tool in the management of sports injuries, and as such, its popularity is on the rise. Current clinical studies generally show beneficial results, particularly for soft tissue treatment, but high level clinical evidence is lacking at the moment. This could change within the next few years as more prospective controlled trials are carried out. MG

Reference / Further reading
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Dr Patrick Goh obtained his Masters in Sports Science (Sports Medicine) from the US Sports Academy. He was former Deputy Director (Sports Medicine) at Singapore Sports Council's Sports Medicine and Research Centre, and was Team Singapore's CMO for the 2000 and 2004 Olympic Games. Currently in private practice, he is also Chairman of Anti-Doping Singapore, and Co-Chairman of the Sports Medicine Sub-speciality Training Committee under the Ministry Of Health. He was the first sports physician in Singapore to use PRP for sports injuries, and has delivered papers on it both locally and internationally. Dr Goh currently practices at Sports Medicine International in Camden Medical Centre, www.ortho-intl.com/sportsmed/.