**Intralesional Autologous Platelet Rich Plasma Injection Compared to Corticosteroid Injection for the Treatment of Chronic Plantar Fasciitis. A Prospective, Randomised, Controlled Trial.**

**Principle Researcher**
Dr. William Craddock  
Eastern Suburbs Sports Medicine  
South Sydney Sports Medicine

**Co-Workers**
Dr. Greg Lovell  
Flinders Medical Centre Department of Orthopaedics

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**Brief Description of the Project**

**Aim**
This study aims to compare the efficacy of ultrasound guided intralesional injection of autologous platelet rich plasma (PRP) with corticosteroid injection for plantar fasciitis present for more than six weeks that has failed to settle symptomatically with conservative management.

**Introduction**
PRP injection is used to introduce platelets into tissue to stimulate a supra-physiologic release of growth factors in an attempt to ‘jump-start’ healing in chronic injuries and reduce pain.

**Study Design**
This will be a prospective, randomised, controlled, patient blinded study performed over an eighteen month period.

**Subjects**
Adult patients who present to South Sydney Sports Medicine and Eastern Suburbs Sports Medicine between October, 2010, and October, 2011, with plantar fasciitis of more than 6 weeks duration will be considered for the study. Eligible subjects have to satisfy the inclusion and exclusion criteria.

**Protocol**
Each heel will be randomly allocated to receive three injections, either three intra-fascial PRP injections (2 mL PRP each) or a peri-facial cortisone injection (1 mL Celestone Chronodose) followed by two saline injections.
Prior to injection the plantar fascial thickness at the site of maximal tenderness will be assessed under ultrasound as part of the inclusion criteria. All injections will be performed by the first author guided by ultrasound, by a medial approach following injection of local anaesthetic into the skin, and at weekly intervals.

**Outcome Measures**
All patients will be assessed before intervention and then weekly for the first six weeks and then at three and six months. The outcome measures will be measured using the American Orthopaedic Foot and Ankle Society (AOFAS) Hindfoot and Ankle Clinical Rating Scale, Foot Function Index (FFI), Manchester Foot Pain and Disability Index (MFPDI), Foot Health Status Questionnaire (FHSQ), and VISA-A assessment tools. Daily analgesic requirements will be monitored and the plantar fascia thickness will be reassessed under ultrasound at three and six months.

**Detailed Description of the Project**

**Background**
Plantar Fasciitis (PF) is defined as a localised inflammation and degeneration of the proximal plantar aponeurosis. It is thought that mechanical overload produces microtears within the plantar fascia which incites an inflammatory response. Repeated loading results in incomplete repair with chronic inflammation followed by degeneration. \[1\]

PF is of insidious onset characterised by 'start-up' pain which is localised to the plantar medial aspect of the heel and occurs when arising from bed in the morning or from a chair after sitting for a long period. \[1\]

Physical examination reveals localised tenderness to palpation of the plantar fascia at its origin at the plantar medial tubercle of the calcaneal tuberosity. \[1\]

Imaging rarely plays a role in diagnosis of PF. \[1\] Imaging may be required to confirm the diagnosis in patients with atypical features or refractory to initial conservative management. \[2\] Ultrasound findings include localised tenderness, fascial thickening greater than 4 mm, hypoechoigenicity, and hyperaemia. \[2,3,4,5\] Ultrasound has the additional benefit of guiding injections. \[6,7\]

Corticosteroid injection into the origin of the plantar fascia is the current standard of management. Cortisone has been shown to have no or only short term advantage over placebo. \[6,9\] Corticosteroid injection is associated with increased risk of plantar facial rupture, infection, and fat pad atrophy. \[10,11\] The risk of plantar fascial rupture is between 0-5%. \[10,11\] The risks may be minimized by the use of a careful aseptic ultrasound guided injection technique, avoidance of impact activity for 10 days, \[11\] and infrequent repeated use.

Platelet rich plasma (PRP) is defined as a volume of the plasma fraction of
autologous blood having a platelet concentration above baseline. [12]

Platelets contain bioactive proteins responsible for attracting macrophages, mesenchymal stem cells, and osteoblasts which not only promote removal of necrotic tissue, but also enhance tissue regeneration. [12] Alpha granules are storage units within platelets which contain pre-packaged growth factors in an inactive form including transforming growth factor beta (TGFbeta), vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and epithelial growth factor (EGF). [12] The lifespan of a platelet is about 5-10 days.

PRP injection is used to introduce platelets into tissue to stimulate a supra-physiologic release of growth factors in an attempt to 'jump-start' healing in chronic injuries and reduce pain. [12,13] The additional advantage of PRP therapy is the antibactericidal effects of the antibacterial and fungicidal proteins stored in platelets, which may help prevent infection. [13]

PRP can be obtained cheaply, safely, and effectively through commercial and non-commercial methods of centrifugation. Commercial methods can increase platelet concentration 1.65-4.4 times that of whole blood whereas one non-commercial method can increase it up to 6 times. [14,15]

The platelets in the PRP can be activated, causing release of the alpha granule contents, in-vivo by exposure to tendon-derived collagen or in-vitro through the addition of calcium, allowing for administration through a small gauge needle. [16]

There are limited clinical studies in the literature looking at the effect of PRP on PF and tendinopathy. The one study in the literature looking at the effect of PRP on PF, a non-controlled pilot study with a small sample size of nine patients, found US guided PRP injection achieved complete symptomatic relief in six patients at two months. One of the three unsuccessful patients eventually found relief following an additional PRP injection. At one year 77.9% patients had complete resolution of symptoms. [17] A second looked at a cohort of twenty patients with chronic lateral epicondylitis of the elbow where fifteen were treated with one PRP injection and five, the control group, with local anaesthetic. The treatment group noted 60% improvement in pain at eight weeks compared to 16% in the control group. After eight weeks 60% of the control group dropped out preventing further direct comparison. Nonetheless pain reduction was 81% at six months, and 93% at final follow-up at 12-38 months with no adverse effects or complications. The major limitation to the study was the 60% attrition rate of the control group. [18] A third study, a double-blind, placebo controlled trial, involved randomization of 54 patients with Achilles tendinopathy into two groups. At 24 weeks there was no difference in the main outcome measures, pain and function, between the group who received a single PRP injection and the control group that was injected with local anaesthetic. [19]
This study aims to examine the effectiveness of three ultrasound guided intralesional injections of autologous PRP at weekly intervals, produced using a non-commercial and inexpensive system, in reducing pain and improving function compared to corticosteroid injection in the treatment of plantar fasciitis present for more than six weeks duration that has failed to settle symptomatically with conservative management. This study will use corticosteroid as a ‘placebo’ group considering it is the current standard of management but has limited long term benefit. In the treatment group three PRP injections will be performed rather than a single injection as the one well designed study available indicates single injections are not effective.

**Description of Subjects and Recruitment Process**

Adult patients who present to South Sydney Sports Medicine and Eastern Suburbs Sports Medicine between October, 2010, and October, 2011, with plantar fasciitis of more than 6 weeks duration will be considered for the study. Eligible subjects have to satisfy the inclusion and exclusion criteria. All subjects will be fully informed about the nature of the trial and its rationale, and the potential adverse effects of both platelet rich plasma and corticosteroid injections, and consent to take part in the study and to be randomized to either treatment group will be obtained. A total of 75 patients will be enrolled over 12 months.

**Inclusion and Exclusion Criteria for Participation**

**Inclusion Criteria**

1. presenting complaint of plantar heel pain worse on rising in the morning and/or after periods of sitting or lying, which have been present for longer than 6 weeks
2. on examination, site of maximal tenderness at the attachment of the plantar fascia on the medial tubercle of the calcaneus
3. plantar fascial thickness > 4 mm at the area of maximal tenderness
4. failed conservative management of at least 4 weeks duration consisting of calf stretching, tibialis posterior and flexor hallucis longus strengthening, and the use of an off-the-shelf orthotic with heel cut-out and plantar fascial groove

**Exclusion Criteria**

1. previous injections or surgery for heel pain
2. nerve-related symptoms
3. regional pain syndrome
4. achilles tendon pathology
5. rheumatoid arthritis
6. spondyloarthropathy (incl. ankylosing spondylitis, reactive arthritis, enteropathic arthritis, and psoriatic arthritis)
7. diabetes mellitus
8. local infection
9. peripheral vascular disease
10. gout
11. coagulopathy or anti-coagulant therapy
12. pregnancy
13. dysfunction of the knee, ankle, or foot
14. work-related or compensable injury

Protocol
Upon enrollment in the study, data collection will be done on each subject using a standard form, providing background information and a history profile of the heel pain. Background information will include age, gender, weight, height, occupation, hours spent standing during the day, duration of symptoms, types of prior treatment.

Each heel will be randomly allocated to receive three injections, either three intra-fascial PRP injections (2 mL PRP each) or a peri-fascial cortisone injection (1 mL Celestone Chronodose) followed by two non-therapeutic placebo injections of saline.

The 3 mL of platelet rich plasma will be obtained using a single step centrifugation procedure and XC-2000 laboratory benchtop centrifuge. Twenty five point five mL of autologous blood will be divided equally between three 8.5 mL ACD BD Vacutainer venous blood collection tubes and centrifuged at 2,000 rpm (447 g) for 10 minutes. The lowest 1 mL of the plasma, the platelet rich plasma (PRP), is then harvested from each tube avoiding contamination by the buffy coat and red cell layers. Two mL will be collected for injection into the patient and 1 mL will be collected for laboratory analysis of platelet numbers. Each sample will be ‘activated’ with 0.05 mL calcium chloride 10% per 1 mL plasma.

Prior to injection the plantar fascial thickness at the site of maximal tenderness will be assessed under ultrasound as part of the inclusion criteria.

All injections will be performed by the first author guided by ultrasound, by a medial approach following injection of local anaesthetic into the skin, and at weekly intervals.

Patients will be advised to avoid impact activities for 1 week following injection and use cryotherapy and simple analgesics for post-injection pain. The patients will be encouraged to continue with their stretching and strengthening programs and orthotic use but non-steroidal anti-inflammatory medications, extra-corporeal shock-wave therapy, and night splints will not be permitted.

A second set of injections will be offered at three months if the patient still experiences symptoms, with the patient given the opportunity to refuse.

Outcome Measures
All patients will be assessed before intervention and then weekly for the first six weeks and then at three and six months. The outcome measures will be measured using the American Orthopaedic Foot and Ankle Society (AOFAS) Hindfoot and Ankle Clinical Rating Scale, Foot Function Index (FFI), Manchester Foot Pain and Disability Index (MFPDI), Foot Health Status Questionnaire (FHSQ), and VISA-A assessment tools. Daily analgesic requirements will be
monitored and the plantar fascia thickness will be reassessed under ultrasound at three and six months.

**Statistical Analysis**
For statistical analysis, tests will be conducted using the Student t test for continuous data and Pearson chi-square test with Yates' correction for discrete data to assess the similarity of the groups on baseline measures. The two groups will be compared using generalized linear models for repeated measures of VAS scores. An overall significance level will set at $p < 0.05$. The software package used will be SPSS for Mac version 17.0.

**References**
14. Rutkowski JI, Thomas JM, Bering CL, Speicher JL, Radio NM, Smith DM, Johnson DA. Analysis of a rapid, simple, and inexpensive technique used to


