STUDY PROTOCOL

Full Title:	**Dorsal Wrist Ganglia; Aspiration alone vs Aspiration and Injection of Platelet Rich Plasma**
Sponsor:	**NHS Grampian**
Sponsor Reference Number:	1/091/17
Funder:	Arthrex
Chief Investigator:	Mr David Lawrie
REC Reference Number:	17/WA/0425
R&D Reference Number:	205497/1153695/14/232

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PROTOCOL APPROVAL

Dorsal Wrist Ganglia; Aspiration alone vs Aspiration and Injection of Platelet Rich Plasma Signatures

The protocol has been reviewed by:

Mr David Lawrie, Orthopaedic Consultant – Chief Investigator

Signature*:*

Mr Patrick Ashcroft, Orthopaedic Consultant – Internal Peer Review for study
Mr Scott Barker, Orthopaedic Consultant – External Peer Review
Mrs Carol Carnegie, Research Nurse - External Peer Review
Miss Katharine Hamlin, Orthopaedic Registrar – Principle Investigator and Author
Research Team Arthrex -
Funder

LIST OF ABBREVIATIONS

GCP	Good Clinical Practice
ISF	Investigator Site File
TMF/SMF	Trial/Study Master File
SOP	Standard Operating Procedure
CRF	Case Report Form
CNORIS	Clinical Negligence and Other Risks Scheme
PRP	Platelet Rich Plasma
DWG	Dorsal Wrist Ganglia/Ganglion
US	Ultrasound
PEM	Patient Evaluated Measure Score
DFML	Mr David Lawrie (Chief Investigator)
KH	Miss Katharine Hamlin
RN	Research Nurse
OR	Orthopaedic Registrar
SOS	Surgical Outcomes System
CM	Miss Clare Miller

SUMMARY

We propose to undertake a study where we examine the efficacy of Platelet Rich Plasma (PRP) to reduce recurrence in dorsal wrist ganglia (DWG). PRP is produced by centrifugation or spinning of a sample of the patient's blood, which separates out the different components. DWG are cystic collections arising from the wrist joint. Most common treatment is aspiration or reassurance as they have a high recurrence rate with any current treatment.

We will compare aspiration alone and aspiration with injection of PRP. We plan to recruit a maximum of 200 patients. We will assess the efficacy by contacting the patients by email or telephone at 6 weeks and 12 months. Adverse events will be screened for/ managed by a telephone call +/- review as necessary between 7 and 14 days. They will be asked to complete a questionnaire and a Patient Evaluated Measure score (PEMS).

1. INTRODUCTION

1.1. Background

Ganglia are soft tissue tumours which consist of a cavity with a collagen wall and filled with mucin rich in hyaluronic acid, glucosamine, globulin and

albumin[1]. The wall consists of collagen fibres arranged into sheets, with occasional mesenchymal cells. The lining is largely acellular with scattered fibroblasts[2]. The cavity communicates with the joint. Although the aetiology is unclear, it is thought to arise from a rent in the capsule allowing escape of synovial fluid. 50% have underlying joint pathology on Arthroscopy[3].

The vast majority of ganglia present around the wrist, with 60-70% located on the dorsal aspect[4]. The prevalence is men 25/100,000 and females 43/100000[5]. MRI studies have shown that they are present in 51% of the asymptomatic population and 19% of patients presenting with wrist pain[6].

They are the second commonest referral to a hand surgeon[7]. The most common reasons people present with their DWR are: cosmesis (38%), fear of malignancy 28%, pain 26% and 8% reduced function or sensation[8]. Pain has been reported to be present in 89% of ganglia but only 19% felt it was significant[3]. They are readily detectable by Ultrasound and MRI but the diagnosis is usually clinical[9-10].

Many solutions have been sought for dorsal wrist ganglia, but each has been troubled by recurrence. Non-surgical methods such as bursting it with firm pressure, simple aspiration +/- multiple puncture and aspiration plus steroid, hyaluronic acid or sclerosant all have similar rates of recurrence, but widely ranging between studies with rates from 18-93% reported and a 5% complication rate. Similarly surgical excision including the whole tract, which can be performed open or arthroscopically, is reported to have recurrence rates of 0-59% and up to 25% complication rate. When this is considered in the light that 49% of ganglia spontaneously resolve it is clear the solution has not yet been found[3].

Platelet rich plasma has been shown useful in many conditions and further studies are underway from bone, soft tissue and skin grafting, to tendinopathies, nerve injuries and even hair regrowth[,12,13]. It is defined as autologous plasma with a platelet count of 1,000,000 platelets/µl. It contains seven native growth factors plus cell adhesion molecules contained within a normal clot[11]. Platelet function includes increasing cell mitosis, increasing collagen production, recruitment of inflammatory cells, initiating angiogenesis, and inducing cell differentiation[14].

Platelet rich plasma would be harvested from a sample of the patient's blood at the same visit as the aspiration and undergo the double centrifugation technique. Once activated the platelets secrete 70% of their stored growth factors in 10 minutes and the evacuation is almost complete after hour. They then synthesize additional factors until they die after about 8 days[11].

Autologous material is inherently safe and acceptable to patients. There is no risk of immune reaction or transmission of blood borne disease. It is never been associated with increased, or decreased, infection rates or induction of malignancy[15].

No prior studies on the use of PRP to prevent dorsal wrist ganglia recurrence have been found.

1.2. Rationale for Study

We believe that by injecting platelet rich plasma into ganglia after aspiration of the contents, the platelets would be activated by exposure to the collagen wall[14] and adherent clot would form in the cavity. It is plausible that the growth factors would cause differentiation of the mesenchymal cells within the walls and draw in inflammatory cells and thus from a relatively acellular position the means for healing have been provided. If the walls became scarred together obliterating the space then recurrence would be reduced. Aspiration is commonly performed and we do not believe any additional risk is posed to the patient from injection of PRP. Ganglia usually recur by 6 months so 1 year is adequate follow up.

2. STUDY OBJECTIVES

2.1. Objectives

2.1.1 Primary Objective

- To assess if injection with Platelet Rich Plasma prevents recurrence after aspiration of dorsal wrist ganglia compared to aspiration alone?

2.1.2 Secondary Objectives

- Does aspiration of dorsal wrist ganglia with or without injection of Platelet Rich Plasma alter PEM Score after 6 weeks and 12 months?

2.2. OUTCOMES

2.2.1 Primary Outcome

- Presence or absence of ganglion recurrence as reported by the patient at 6 weeks and 12 months.

2.2.2 Secondary Outcomes

- Patient reported outcome measure - PEM score which includes patient reported assessments of:

    1. Stiffness
    2. Pain
    3. Cosmesis

3. STUDY DESIGN

3.1. Study Description

1. Patient selection

   All hand referrals vetted by Mr Lawrie or Miss Miller, those for dorsal wrist ganglia sent a letter of invitation and patient information. Patients responding to the letter with interested given an appointment at a special trial clinic.

   Contact details will be provided to allow any issues to be clarified discussed before attendance at clinic if the patient desires.

2. Assess eligibility/ enrolement in study – clinic visit 1

   a) All patients assessed by the chief investigator Mr David Lawrie (DFML) or Miss Katharine Hamlin (KH).

   b) Clinical assessment of presence of ganglion.

   c) Ensure not meeting exclusion criteria.

   d) If eligible and willing to complete study commitments discuss study and answer questions.

   e) Once we are happy the patient has understanding of the study and its risks then the patient will be asked if they wish to enrol or if they would like more time to consider.

   f) If they are willing to participate they will then be offered treatment in the same visit or a return visit

3. Intervention – clinic visit 1 or 2

   a) Check understanding and continuing desire to participate in study if 2nd visit.

   b) Complete consent form.

   c) Patient fills out a PEM score and demographics collected on SOS.

   d) Randomisation.

   e) If in PRP group 15ml blood sample taken with Arthrex ACP double syringe and processed (see processing instructions in Appendix.9.

   f) Aspiration.

g) If in PRP group - Injection of PRP (the same volume as aspirated).

h) Pressure dressing with gauze, wool and crepe for 48 hours.

4. Adverse event screening/ management

Patients are offered two options at the treatment visit.

1. Routine review at 10 – 14 days at the clinic

   or

2. Telephone review at 7 days by Miss Katharine Hamlin who will have performed the procedure.

On telephone review if the patient is entirely happy that there are no concerns then follow up will proceed by email or telephone as below.

If any concerns are raised, or if the patient desires, a face to face review will be arranged ideally within 24 hours but no longer than 72 hours. Recurrence or other outcomes will not be assessed at this time.

5. SOS/ Email/ Telephone interview - 1 (6 weeks)

   a) Ganglion questionnaire

   b) PEM score

   c) Note any adverse events

6. SOS/ Email /Telephone interview - 2 (12 months)

   a) Ganglion questionnaire

   b) PEM score

   c) Note any adverse events

3.2. Study Flowchart

See Appendix 8.

4. STUDY POPULATION

4.1. Number of Participants

We would like to recruit a maximum of 100 patients who have a solitary dorsal wrist ganglion to each treatment arm. A total of 200 patients.

4.2. Inclusion Criteria

Solitary dorsal wrist ganglion.
Over 16 years of age.

4.3. Exclusion Criteria

Underlying wrist or ipsilateral arm pathology.
Unable to consent to treatment.
Unable or unwilling to attend follow up visits.

5. PARTICIPANT SELECTION AND ENROLMENT

5.1. Identifying Participants

Mr David Lawrie (DFML) or Miss Clare Miller (CM) will vet all GP patient referrals for DWG. Each patient will be sent a letter of invitation and patient information. Patients will be asked to telephone DFML secretary for an appointment at a special trial clinic. At the clinic patients will have a history and examination performed to confirm the presence of the ganglion clinically and ensure no other pathology present. The study will be discussed, any questions answered and assess willingness to participate.

5.2. Consenting Participants

To ensure that patients have adequate access to information and discussion prior to a potential 'one-stop' visit a letter will be sent to the patient prior to the clinic visit including the patient information. The patient information leaflet contains contact information allowing potential participants to contact a team member prior to attendance if they wish to clarify any issues or ask questions. On the day each patient will be seen by a member of the research team (Miss Katharine Hamlin) and eligibility assessed. If eligible the study will be discussed and a further opportunity to ask questions. Once we are happy the patient has understanding of the study and its risks then the patient will be asked if they wish to enrol or if they would like more time to consider. If they are willing to participate they will then be offered intervention in the same visit or a return visit and they will be able to choose. Consent will be taken at the treatment visit if a second appointment is desired. If they are uncertain they will be provided with contact details and asked to call for an appointment if they decide they would like to participate in the future.

Mr David Lawrie (DFML) or Miss K Hamlin (KH) will consent all patients prior to intervention being performed visit and record this on a written consent form (see attached documents). The form will be copied in triplicate for the patient, their medical notes and the trial file. All researchers taking consent have under gone Good Clinical Practice Training and are familiar with the procedure and its

risks. The participants GP will be informed of the study with their consent.

5.3. Screening for Eligibility

Clinical screening for presence of ganglion.

5.4. Ineligible and Non-Recruited Participants

Ineligible and non-recruited patients will have only a standard GP clinic letter recorded. No other data will be taken or stored.

6. RANDOMISATION AND BLINDING

6.1. Randomisation Details

Once consent and understanding have been checked the patients will be allocated to one of the two groups randomly.

The study will be block randomized at a 1:1 ratio. We will create a block randomization scheme utilizing http://www.randomization.com/. All blocks will contain an increment of 10 subjects per group and there will be 20 blocks.

The randomization scheme will be enclosed in envelopes with each individual envelope containing one procedure per the block randomization process (see Section 3 for details on study groups). The exterior of the envelope will be marked with the study title and a number (1 through 200); however, the contents of the envelope will not be visible.

The randomization will be performed by Miss Alexandra Haddon, who will also create the envelopes. Her only other role will be ensuring compliance with the follow up schedule.

For a particular subject, prior to the procedure, the investigator will select the next consecutive envelope and open the envelope to determine the procedure for the particular subject. Miss Katharine Hamlin is the contact point for randomization. The appropriate procedure will be performed, and the procedure along with the envelope number will be recorded in the study file.

6.2. Blinding

Blinding will not be performed to save the patients in aspiration alone group the unnecessary discomfort of blood sampling. We feel this is justifiable as the return of the ganglion or not is a physical finding and not influenced by other factors. The assessor and analyst will be blinded.

6.3. Withdrawal Procedures

A patient may withdraw from the trial at any time. A withdrawal form will be completed and filed in the trial folder. If the patient grants permission at the time of withdrawal data will be retained for inclusion in analysis as appropriate. Patients will be replaced if they have not completed either follow up time points.

7. STUDY AND SAFETY ASSESSMENTS

No specific safety requirements are required PRP is already commonly used for injections and as a product generated from the patient's own blood has an excellent safety profile. Blood will be sampled, processed and re-injected by the same person in the same visit, with only one patient at a time receiving the intervention to ensure no mistakes regarding patient identity can be made.

The sample is taken, processed and injected from the same specially designed syringe so that the internal contents maintain sterility. This is routinely performed in the out-patient clinic setting rather than theatre, although every effort at sterility will be maintained with sterile dressing packs, gloves and dressings being used. All the procedures will be performed by Miss Katharine Hamlin who has been trained in venepuncture and aspiration of ganglia via her role as orthopaedic registrar and has undertaken additional training from Nursing/ Medical Staff trained and practiced at processing the samples at the Orthopaedic Out-patient clinic.

Adverse Events (AE) anticipated may include localised minor pain or swelling of short duration (24-72hrs), minor cellulitis requiring oral antibiotics treated by GP.

The patients will be offered clinicial or telephone review (which may proceed to urgent clinical review if concerns to monitor for the presence of adverse events and to ensure they are recognised and treated promptly. The patient information leaflet contains instructions on when and where to seek medical help if concerns at any time. Patient reports will be requested at each follow up with space for recording on each CRF. The patients will also be able to inform the study of AE on SOS. Finally, the GP will be advised to inform Mr Lawrie of any study related patient contact with them. Clinic follow up by Mr Lawrie or his registrar will be arranged as required. As a new indication for PRP we plan to collate and report on all AE.

Serious Adverse Events (SAE) such as hospitalisation for major cellulitis requiring IV antibiotics, abscess formation or septic arthritis requiring surgical management will be reported immediately to the sponsor. These are anticipated to be rare events (<1%) in line with major infective complications from other Orthopaedic procedures.

Upon recognition of any event an Adverse event an Adverse Event Form should be completed and placed in the study file. The file will also contain an AE log.

8. DATA COLLECTION AND MANAGEMENT

8.1. Data Collection

Data will be collected as both electronic files and paper questionnaires and letters. Electronic files will be collected with the Surgical Outcomes System, a research registry run by Arthrex. All data will be kept secure and confidential, see appendix 11. Paper files will be kept in a locker filing cabinet in the Upper Limb Unit Secretaries office.

All participants will be assigned a unique identifier for the duration of the study. A separate log will be kept linking the ID number to the participant which will be kept and stored confidentially.

Surgical outcome system is an online bespoke database containing the data as shown on the case report forms in Appendix 6 and 7. Patients will be identified only by their unique study ID and demographic information (age at time of study and sex) will be entered. Access is password protected on an individual basis. The database is a Microsoft SQL Server database using transparent data encryption. Plausibility data validation is in place, data is checked upon saving. There is a daily full back up of the data. Data enquires will be handled by Miss Katharine Hamlin.

SOS is hosted on servers operated exclusively for Arthrex by Amazon Web Services, Inc. (AWS). The servers are located in a data centre in Virginia, United States, until 2018 when SOS will be separated into two systems, EMEA and USA. EMEA data will then be stored on an AWS Server in Germany. The data centre has multiple layers of operational and physical security to ensure the integrity and safety of the data. The data centre utilizes state-of-the-art electronic surveillance and multi-factor access control systems. The data centre is staffed 24 / 7 by trained security guards and access is authorized on a least privileged basis. See also appendix 11. An anonymised database will be stored on secure shared NHS Grampian drive, with access only to research team.

Data files from SOS will be extracted onto NHS computers as password protected excel files will be stored on secure shared NHS Grampian drive, with access only to research team.

9. LABS AND SAMPLE ANALYSIS

9.1. There is no laboratory requirement. Blood samples will be processed by centrifuge (spinning) in the clinic to produce PRP with sterile technique. No further analysis or storage will be undertaken. Any remaining blood products will be safely disposed of in the clinic.

10. STATISTICS AND DATA ANALYSIS

10.1. Sample Size Calculation

90 participants in each arm would give a 90% power to detect a change in recurrence rate of 25%. We believe this is adequate as current recurrence rates are 59%. This would need to be increased to 100 participants recruited per arm to allow for 10% drop out from follow-up.

As the recurrent rate is so large recruiting 90 patients would detect up to a 25% difference in recurrence rate. To ensure the trial is not extended beyond the point of answering our question we have also calculated numbers to allow for the trial to be closed early if we have sufficient data.

62 participants completing follow-up in each arm would give 90% power to detect a change in recurrence rate of 30%. This would need to be increased to 69 per arm to allow for 10% drop out from follow-up.

46 participants completing follow-up in each arm would give 90% power to detect a change in recurrence rate of 35%. This would need to be increased to 51 per arm to allow for 10% drop out from follow-up.

Therefore we will undertake initial data analysis after 51 and 69 participants have completed their 6 week review and if the difference in the recurrence rate is more than 35% or 30% then we will conclude the trial, but all outstanding follow up will be completed and data included in final analysis.

10.2. Proposed Analysis

Statistical analysis will be performed to assess homogeneity of the study groups and efficacy of treatment. The primary outcome will use chi-squared test (with or without continuity correction). The secondary outcome will be assessed using independent T test if normally distributed or Mann-Whitney test if not.
The difference between the two groups will be significant if the p values are less than 0.05.

The analysis will be performed by Sarah Henrich who is a Clinical Specialist on the Arthrex Research team based in Germany.

10.3. Missing Data

Any patients with missing all follow up data will be deemed to have not completed follow up and will be excluded with a withdrawal form completed. If partial follow up data is available we will use this in analysis.

10.4. Transfer of Data

There is no plan for patient identifiable data to be transferred between collaborators, de-identified data could be sent via NHSmail to other NHSmail accounts. All analysis will be performed on secure password protected computers with data extracted from Surgical Outcomes System. All data is de-identified – see appendix 11. This is a single site study.

11. TRIAL/STUDY MANAGEMENT AND OVERSIGHT ARRANGEMENTS

11.1. Trial/Study Management Group

The trial/study will be co-ordinated by Mr Lawrie, Mr Ashcroft and Miss Hamlin. They will form the trial steering committee (TSC). Mr Lawrie as Chief Investigator, Mr Ashcroft is an Orthopaedic Consultant experienced in research and Miss Hamlin as Principle Investigator. The TSC will meet annually and operate as per sponsors SOP.

11.2. Trial/Study Management

Miss Hamlin will oversee the study and will be accountable to Mr. Lawrie. The Clinical Research Fellow/Orthopaedic registrar/Research Nurse will be responsible for checking the CRFs for completeness, plausibility and consistency. However, this remains the overall responsibility of the CI. Any queries will be resolved by the CI or delegated member of the study team.

A study-specific Delegation Log will be prepared for the site, detailing the responsibilities of each member of staff working on the study.

12. INSPECTION OF RECORDS

The CI, PIs and all institutions involved in the study will permit study related monitoring, audits, and REC review. The CI agrees to allow the Sponsor or, representatives of the Sponsor, direct access to all study records and source documentation.

13. GOOD CLINICAL PRACTICE

13.1. Ethical Conduct of the Study

The study will be conducted in accordance with the principles of good clinical practice (GCP).

In addition to Sponsorship approval, a favorable ethical opinion will be obtained from the appropriate REC and appropriate NHS R&D approval(s) will be obtained prior to commencement of the study.

13.1. Confidentiality
1.

All evaluation forms, reports, and other records will be identified in a manner designed to maintain participant confidentiality. Patient CRFs will only contain study specific data and study identification.

All paper records will be kept in a secure storage area with limited access to study staff only. Anonymised patient data (written on case report forms) will be stored in a locked filing cabinet in the Upper Limb Unit Secretaries office, which is itself secured. Only the research team will have access to this data.

Electronic records will be stored in Arthrex Surgical Outcomes System (SOS). SOS is hosted on servers operated exclusively for Arthrex by Amazon Web Services, Inc. (AWS). The servers are located in a data centre in Virginia, United States, until 2018 when SOS will be separated into two systems, EMEA and USA. EMEA data will then be stored on an AWS Server in Germany. The data centre has multiple layers of operational and physical security to ensure the integrity and safety of the data. The data centre utilizes state-of-the-art electronic surveillance and multi-factor access control systems. The data centre is staffed 24 / 7 by trained security guards and access is authorized on a least privileged basis. See also appendix 11.

Data files from SOS will be extracted onto NHS computers as password protected excel files will be stored on secure shared NHS Grampian drive, with access only to research team.

Clinical information will not be released without the written permission of the participant, except as necessary for monitoring and auditing by the Sponsor or its designee. The CI and study staff involved with this study will not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the study. Prior written agreement from the Sponsor or its designee will be obtained for the disclosure of any said confidential information to other parties.

This study will be using a specially designed outcomes portfolio and as such our data will not be available for global comparison.

The investigator will keep a record of the study ID to enable his research team to track patients involved in the study.

13.1. Data Protection

2.

The CI and study staff involved with this study will comply with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. The CI and study staff will also adhere, if appropriate, to the current version of the NHS Scotland Code of Practice on Protecting Patient Confidentiality. Access to collated participant data will be restricted to the CI and appropriate study staff.

Computers used to collate the data will have limited access measures via user names and passwords.

Published results will not contain any personal data that could allow identification of individual participants.

13.1. Insurance and Indemnity

3.

The NHS Grampian Health Board are Sponsoring the study.

Insurance –

- Grampian Health Board will maintain its membership of the Clinical Negligence and Other Risks Insurance Scheme ("CNORIS") which covers the legal liability of Grampian in relation to the study].

Indemnity: The Sponsors do not provide study participants with indemnity in relation to participation in the Study but has insurance for legal liability as described above.

14. STUDY CONDUCT RESPONSIBILITIES

14.1. Protocol Amendments, Deviations and Breaches

The CI will seek approval for any amendments to the Protocol or other study documents from the Sponsor, REC and NHS R&D Office. Amendments to the protocol or other study docs will not be implemented without these approvals.

In the event that a CI needs to deviate from the protocol, the nature of and reasons for the deviation will be recorded in the CRF, documented and submitted to the Sponsor. If this necessitates a subsequent protocol amendment, this will be submitted to the Sponsor for approval and then to the appropriate REC and lead NHS R&D Office for review and approval.

In the event that a serious breach of GCP is suspected, this will be reported to the Sponsor immediately using the form "Breach Report Form".

14.2. Study Record Retention

Archiving of study documents will be maintained for 7 years, in accordance with the sponsors archiving SOP and the documents will be stored off site using the dedicated NHSG achieve by Removal Services Scotland. After this time they will be securely disposed of. De-identified data will be available on SOS unless a patient or user unsubscribes, the study will be unsubscribed after 7 years and the data deleted.

14.3. End of Study

The end of study is defined as last patient last visit (LPLV). The Sponsor, CI and/or the TSC have the right at any time to terminate the study for clinical or administrative reasons.

The end of the study will be reported to the Sponsor and REC within 90 days, or 15 days if the study is terminated prematurely. The CI will ensure that any appropriate follow up is arranged for all participants.

A summary report of the study will be provided to the Sponsor and REC within 1 year of the end of the study

15. REPORTING, PUBLICATIONS AND NOTIFICATION OF RESULTS

15.1. Authorship Policy

Ownership of the data arising from this study resides with the study team and their respective employers. On completion of the study, the study data will be analyzed and tabulated, and a clinical study report will be prepared.

15.2. Publication

The clinical study report will be used for publication and presentation at scientific meetings. Investigators have the right to publish orally or in writing the results of the study.

Summaries of results will also be made available to Investigators for dissemination within their clinical areas (where appropriate and according to their discretion).

15.3. **Peer Review**

Internal peer review has been undertaken by Mr Scott Barker, Consultant Orthopaedic Surgeon and Mrs Carol Carnegie, Research Nurse. The study was also reviewed by Arthrex during the funding application.

16. FUNDING and EQUIPMENT

Arthrex, an orthopaedic medical device company, is providing funding in the form of supply of disposable material and research support. They will provide up to 100 units of the ACP double syringe. This is used to collect the blood sample, process the PRP and inject the PRP into the ganglion (see Appendix 3). The processing is performed by a centrifuge, provided by Arthrex, in the Orthopaedic out-patient department. This is already in place. Arthrex provide indemnity for the centrifuge (Indemnity number MIA No: 310/13). Both the ACP double syringe and the centrifuge are already in use in NHS Grampian. PRP injections are currently performed for other conditions i.e. Tennis Elbow and Achilles Tendonitis.

Research support will be provided in the form of data management via SOS and statistical support and final analysis.

There are no other additional costs out with the usual treatment costs.

APPENDIX 1: References

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APPENDIX 2: Patient Reported Measure

PATIENT EVALUATED MEASURE SCORE (PEMS)

Part 1 – Treatment:

Please put a circle around the number that is closest to the way you feel about how things have been for you. There are no right or wrong answers.

1. **Throughout my treatment I have seen the same doctor:**

1 2 3 4 5 6 7
Every time Not at all

2. **When the doctor saw me, he or she knew about my case:**

1 2 3 4 5 6 7
Very well Not at all

3. **When I was with the doctor, her or she gave me the chance to talk:**

1 2 3 4 5 6 7
As much as I wanted Not at all

4. **When I did talk to the doctor, he or she listened and understood me:**

1 2 3 4 5 6 7
Very much Not at all

5. **I was given information about my treatment and prognosis:**

1 2 3 4 5 6 7
All that I wanted Not at all

Part two – How is your hand now?

Hand Health Profile

1. **The feeling in my hand is now:**

1 2 3 4 5 6 7
Normal Absent

2. **When my hand is cold and/or damp, the pain is now:**

1 2 3 4 5 6 7
Non-existent Unbearable

3. **Most of the time , the pain in my hand is now:**

1 2 3 4 5 6 7
Non-existent Unbearable

4. **The duration my pain is present is:**

1 2 3 4 5 6 7
Never All the time

5. **When I try to use my hand for fiddly things, it is now:**

1 2 3 4 5 6 7
Skilful Clumsy

6. **General, when I move my hand it is:**

1 2 3 4 5 6 7
Flexible Stiff

7. **The grip in my hand is now:**

1 2 3 4 5 6 7
Strong Weak

8. **For everyday activities, my hand is now:**

1 2 3 4 5 6 7
No problem Useless

9. **For work, my hand is now:**

1 2 3 4 5 6 7
No problem Useless

10. **When I look at the appearance of my hand now, I feel:**

1 2 3 4 5 6 7
Unconcerned Embarrassed & self-conscious

11. **Generally, when I think about my hand I feel:**

1 2 3 4 5 6 7
Unconcerned Very upset

Part three – overall assessment

1. **Generally, my treatment at the hospital has been:**

1 2 3 4 5 6 7
Very satisfactory Very unsatisfactory

2. **Generally, my hand is now:**

1 2 3 4 5 6 7
Very satisfactory Very satisfactory

3. **Bearing in mind my original condition, I feel my hand is now:**

1 2 3 4 5 6 7
Better than expected Worse than expected

APPENDIX 3: Processing Procedure for PRP

APPENDIX 4: Study Flow Diagram

Appendix 5

See attached documents:

Patient Information Leaflet

GP Letter

Consent Form

Case Report Forms

Trial Steering Committee Charter

SOS_FAQ

EMEA SOS Privacy and Security Flyer