**RESEARCH PROTOCOL**

1. **TRIAL DETAILS**

**TITLE:** A Prospective Evaluation of Arthroscopic All-Inside Meniscal Repair in Paediatric Patients

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**Universal Trial Number:** U1111-1231-2363

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**Trial Summary**

This is a prospective cohort study seeking to investigate the post-operative clinical and radiographic outcomes of ‘all-inside’ meniscal repair in paediatric patients, with or without concomitant knee surgery if indicated. Patient outcomes will be collected over a 24 month post-operative period, and will include a range of subjective and functional outcomes, radiographic measures and patient satisfaction.

1. **STUDY RATIONALE**

The menisci are integral to knee joint health and function, playing a crucial role in load-

bearing, load transmission and shock absorption, as well as lubrication and nutrition of articular cartilage [1]. Meniscal injuries are one of the most common injuries assessed by orthopaedic surgeons [2], generally caused via cutting or twisting movements, hyperextension or actions of great force [3].

In the presence of symptomatic meniscal injuries, despite the high prevalence of meniscectomy there is good evidence to suggest that total or partial meniscectomy is highly deleterious, particularly in paediatric patients, inducing the development of premature osteoarthritis [4, 5]. Therefore, meniscal repair is now more commonly employed when appropriate to try and restore the natural function of the meniscus and possibly prevent early degeneration changes within the knee [6].

Outcomes after meniscal repair are encouraging [7-10], though limited evidence exists in the paediatric population. While a range of surgical methods exist for undertaking meniscal repair, arthroscopically assisted ‘inside-out’ repair techniques had long been considered the gold standard, though limitations include the need for additional surgical assistance to pass sutures, a separate medial or lateral incision and concerns about complications [10]. It has been suggested that ‘all-inside’ meniscal repair techniques may decrease operative time and lower complication rates [10]. However, current reviews report no differences in failure rates, functional outcomes or complication rates between ‘inside-out’ and ‘all-inside’ repair techniques for isolated meniscal tears [6, 10].

Therefore, given the important role of meniscal repair in restoring normal knee mechanics and loading characteristics, the high prevalence of symptomatic meniscal tears in the paediatric population, and the relative lack of research in paediatric patients embarking on meniscal repair, this prospective study seeks to ascertain the post-operative clinical and radiographic outcome of young patients undergoing ‘all-inside’ meniscal repair surgery (with or without concomitant knee surgery if indicated) for symptomatic meniscal tears.

1. **TRIAL OUTCOMES**

Hypotheses:

1. Functional equivalence will be observed at 24 months post-surgery between the operated and non-operated limbs (as demonstrated in the single hop test for distance), in paediatric patients undergoing ‘all-inside’ meniscal repair surgery for symptomatic meniscal tears.
2. Paediatric patients will significantly improve in clinical and radiographic outcomes following arthroscopic ‘all-inside’ meniscal repair surgery.

The primary and secondary outcomes of this trial will be to investigate:

1. Post-operative symmetry/asymmetry in functional capacity (i.e. single limb hop capacity).
2. Post-operative symmetry/asymmetry in active knee range of motion.
3. The improvement from pre-surgery to 24 months post-surgery in patient-reported outcome measures (PROMs) of pain, symptoms, function and activity.
4. Post-operative patient satisfaction up until 24 months post-surgery.
5. Peri- and post-operative complications, knee re-injury and re-operation rates.
6. Quality of meniscal healing on post-operative magnetic resonance imaging (MRI) at 6 and 12 months post-surgery.
7. **TRIAL DESIGN**

**Patient Consent and Recruitment**

This trial has been designed as a single centre study (through the Perth Children’s Hospital) prospective cohort study. Patients who fulfil the inclusion criteria and are undergoing surgery for their symptomatic knee meniscal tears (with or without concomitant pathology which will be addressed at the time of surgery if required), will be invited to participate. That is, all patients as part of this prospective review are already undergoing knee surgery to address their symptomatic meniscal tear, as per the routine clinical pathway. This study has been designed as a robust pre- and post-operative clinical review of this patient cohort undergoing surgery. Therefore, potential participants for surgery will be identified by the orthopaedic hospital team.

All orthopaedic surgeons operating on patients fulfilling the below inclusion criteria (Table 1), will participate in the study. Therefore, upon discussion with the patient and family, and consent for surgery as per the usual clinical pathway, the research study will then be presented to the patient and their respective parents. This will include a verbal discussion and provision of the Patient Information Sheet. Should more time be required, the parents can take the information away and discuss with others, and another time will be made to discuss again and consent if they are willing to participate. While all outcomes collected may also be obtained through a routine clinical pathway anyway, as outlined in the Patient Consent Form, a discussion will take place at this time with the parents of the child (the patient) that they are free to withdraw from the study at any time without prejudice or altered post-operative care.

The Patient Information Sheet and Consent From will be provided by the research team (Mr Peter Annear and Dr Jay Ebert), and discussion with the family (child and parents) will also be with these researchers. These researchers will also be responsible for obtaining consent from the parents (and child), as per the Patient Information and Consent Form.

**Table 1.** Patient inclusion and exclusion criteria (for study participation).

|  |  |
| --- | --- |
| **INCLUSION CRITERIA** | **EXCLUSION CRITERIA** |
| * The individual is between the ages of 8 and 16 years.
* The individual clinically qualifies for meniscal repair surgery based on clinical examination and MRI.
* Multiple meniscal injuries are present.
* The meniscal repair is combined with another knee surgery (or surgeries), such as ligament reconstruction.
 | * The individual (and parent) is unable or unwilling to sign the Patient Informed Consent, specific to this study, and approved by the Institutional Ethics Review Board.
* The individual is classified as morbidly obese (>40 BMI).
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**Study Sample Size**

For this study, a *priori* sample size power calculation has been determined employing G-Power (Dusseldorf, Germany). The primary outcome variable is the Limb Symmetry Index (LSI) of the single hop for distance (cm) at 24 months post-surgery. The LSI is a measure of the operated limb as a percentage of the non-operated limb. An LSI <90% has been regarded as clinically unsatisfactory for a variety of strength and functional tests, including single limb hop capacity [11-13]. We would expect that the LSI in the single limb hop test for distance to be 100% (irrespective of limb dominance), and for the current study accept side-to-side equivalence if the LSI in single limb hop capacity (as per the single hop for distance test – cm) of >90%, as per current clinical recommendations of functional limb restoration after lower limb surgery. Therefore, using these values (i.e. a non-inferiority margin of 10%) and a SD of 15%, 26 patients will be required at alpha 0.05 with 95% power, to test the primary hypothesis that non-inferiority will be observed (in the single hop test for distance) in paediatric patients undergoing ‘all-inside’ meniscal repair surgery for symptomatic meniscal tears at 24 months post-surgery. Therefore, we seek to recruit and assess 30 patients (i.e. an additional 15% to allow for attrition over the 24 month assessment period).

It is anticipated that the patient cohort be recruited over a 12 month period, with follow up over 24 months (i.e. 3 years in total).

**Surgical Technique & Rehabilitation**

All patients will undergo medial and/or lateral meniscal repair using an all-inside surgical technique, under general anaesthetic. Standard arthroscopic portals will be used, and the *TRUESPANTM Meniscal Repair System (DePuy Synthes)* will be employed in all cases.

Concomitant surgery (i.e. anterior cruciate ligament reconstruction etc.) that may also be required will be undertaken as per the routine surgical pathway of the specific orthopaedic surgeon.

Patients will be permitted to touch weight bear initially with crutches, with restricted knee flexion to 90°, for the first 6 weeks. Therefore, pivoting and excessive flexion of the knee that may impair meniscal healing will be avoided. From this time, exercises and activities will be gradually increased, with cycling permitted from 6-8 weeks though sport will not be permitted until 6 months post-surgery and based on clinical progress. The rehabilitation pathway for patients will be standardized (though modified dictated by the nature of any concomitant surgery), and will be provided by the physiotherapy hospital team as per the routine clinical pathway.

**Clinical Evaluation**

Firstly, a thorough patient history will be taken to collect patient demographics (age, height, weight, body mass index), limb dominance, activity history (particularly sports) and information on the injury mechanism.

The following measures will be undertaken at the designated time points, also outlined in Table 2. All clinical reviews will be undertaken at the Perth Children’s Hospital at the designated time-points.

Firstly, a number of PROMs will be undertaken pre-surgery and at 6 weeks, as well as 3, 6, 12 and 24 months post-surgery. These will include the:

1. Visual Analogue Pain Scale (VAS) – this will be used to assess the frequency (VAS-F) and severity (VAS-S) of patients’ pain levels, on a whole number rating scale from 0 (no pain) – 10 (worst pain).
2. International Knee Documentation Committee (IKDC) Subjective Knee Form [14]- the IKDC is a knee-specific outcome measure evaluating patient-perceived symptoms, physical function and sporting activity, and is scored from 0-100 with higher scores indicating a better score.
3. Knee Injury and Osteoarthritis Outcome Score (KOOS) [15] – this is a knee specific questionnaire and will be employed to assess knee pain, symptoms, activities of daily living (ADL), sport and recreation. Each of these five subscales is scored from 0 (worst) to 100 (best).
4. Lysholm Knee Score (LKS) [16] – this has been used previously to evaluate the outcomes of knee ligament surgery, though has been reported in the evaluation of patients following meniscal surgery. It consists of eight functional parameters (limp, using cane/crutch, locking, giving way, pain, swelling, climbing stairs and squatting) that total 100 points in an asymptomatic knee.
5. Tegner Activity Scale (TAS) [16] – this will be employed to grade current sporting activities. This activity score reports on the patient’s activity level on a 0-10 point scale, ranging from sick leave or disability (0 points) through to elite competitive (i.e. soccer) sports (10 points). Patients are required to select one of the levels of participation that best describes their current activity level.

While the aforementioned PROMs have not been specifically validated for use in a paediatric cohort, all have been used extensively in studies evaluating the outcomes of meniscal surgical treatment [6, 9, 10, 17], as well as many in paediatric patients undergoing meniscal repair surgery [18-20].

A Patient Satisfaction Questionnaire (PSQ) will be employed at 6, 12 and 24 months post-surgery to evaluate the patient’s level of satisfaction with their surgery overall, as well as their satisfaction with surgery to relieve their knee pain, improve their ability to perform normal daily activities and improve their ability to return to recreational activities and participate in sport. A Likert response scale will be employed with descriptors Very Satisfied, Somewhat Satisfied, Somewhat Dissatisfied and Very Dissatisfied.

A number of objective clinical assessments will also be undertaken throughout the post-operative period. The active knee flexion and extension range of motion (ROM) will be measured pre-surgery and at 6 weeks, as well as 3, 6, 12 and 24 months post-surgery, using a hand held goniometer. Furthermore, at 6, 12 and 24 months post-surgery patients will undertake a series of validated single-legged hop tests, including: 1) the single hop for distance (primary outcome variable), 2) the triple hop for distance, and 3) the triple crossover hop for distance. Patients will be provided verbal descriptions of each test and will be permitted 2-3 warm-up hops on each limb prior to initiating the hop battery. Each of the hop tests will be initiated on the unaffected limb, and then alternated between the unaffected and operated limbs until the required number of valid test trials is obtained. To avoid fatigue, patients will be given as much time as required between trials; though this time will not standardized and based on the individual patient’s readiness to proceed.

Finally, magnetic resonance imaging (MRI) will be employed pre-operatively to aid in the diagnosis of the mensical tear, as well as at 6 and 12 months post-surgery to evaluate the presence of healing (or failure). Information on the status of the meniscus and meniscal repair (via the 6 and 12 month MRIs) will be provided for all patients. Only patients whereby MRI-based healing is not confirmed will require further MRI after the 12-month post-operative period.

Generally, the aforementioned evaluations are often undertaken as part of the usual hospital standard of care, and the study aims to evaluate the outcomes of patients more comprehensively through this routine management pathway.

**Table 2.** Timeline of patient evaluation throughout the study.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Measure | Pre-surgery | 6 weeks | 3 months | 6 months | 12 months | 24 months |
| VAS (Pain)  | x | x | x | x | x | x |
| IKDC | x | x | x | x | x | x |
| KOOS | x | x | x | x | x | x |
| Lysholm | x | x | x | x | x | x |
| Tegner | x | x | x | x | x | x |
| Satisfaction |  |  |  | x | x | x |
| Knee ROM | x | x | x | x | x | x |
| Hop Capacity |  |  |  | x | x | x |
| MRI | x |  |  | x | x |  |

**Planned Data and Statistical Analysis**

Firstly, the mean (SD, range) of all subjective and objective measures collected will be presented for the designated pre- and post-operative time-points. Repeated measures Analysis of Variance (ANOVA) will be employed to evaluate change over the pre- and post-operative timeline in all PROMs, as well as active knee ROM and functional hop capacity (both absolute scores for the operated and non-operated limbs, as well as LSIs). ANOVA will also be employed to evaluate differences between the operated and non-operated limbs in these tests. LSIs will be calculated for the single limb hop tests by dividing the peak values on the operated limb by that recorded on the unaffected limb. The mean LSIs for each of the aforementioned hop tests will be presented, and further categorized by the number and percentage of patients with LSIs <90% and ≥90% (as per clinical recommendations of unsatisfactory and satisfactory performance, respectively). The number respondents reporting each satisfaction score (Very Satisfied, Somewhat Satisfied, Somewhat Dissatisfied and Very Dissatisfied) across each of the Satisfaction items will be reported. The number (and type) of surgical complications, post-operative adverse events and re-injuries will be presented. The status of meniscal healing as demonstrated on MRI (6 and 12 months) will be reported, though a definitive scoring tool may be employed depending on availability at the time. Where appropriate, statistical analysis will be performed using SPSS software (SPSS, Version 23.0, SPSS Inc., USA), while statistical significance was determined at *p*<0.05.

1. **ASSESSMENT OF SAFETY**

Post-operative monitoring will be conducted by the treating surgeon(s) and the research team at the Perth Children’s Hospital. Any identified adverse events or complications will be reported, recorded and treated accordingly, as per the routine clinical pathway.

1. **DATA MANAGEMENT, STATISTICAL ANALYSIS AND RECORD KEEPING**

All patient data will be stored securely at the Perth Children’s Hospital. Research data will be kept for a period of 15 years and will then be securely erased from the research computer’s hard-drive. Statistical procedures have been outlined above, though may change and the most appropriate statistical procedures will be decided in time, though statistical analysis will be assisted by a trained biostatistician.

1. **MONITORING / AUDIT / TERMINATION**

The trial investigators/institutions will participate in all trial-related monitoring, audits, and regulatory inspections, providing direct access to source data/documents. This may include, but not limited to, review by Human Research Ethics Committees and institutional governance review bodies.

1. **QUALITY CONTROL AND QUALITY ASSURANCE**

The investigators of the trial will conduct it in compliance with the protocol, Good Clinical Practice and the application regulatory requirements.

1. **PUBLICATION**

The results of this research will be made available through medical journals or meetings, but individual patient information will not be identifiable in any of these communications.

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