**RESEARCH PROPOSAL SUMMARY DOCUMENT:** Version 1.0

**STUDY TITLE**:

Influence of Prosthesis Alignment: Does Kinematic Alignment result in a more balanced Total Knee Arthroplasty?

**ABBREVIATED TITLE**

Verasense TKA: K vs M

**PROJECT SUMMARY**

The primary aim of this project is to determine the influence of two different prosthesis alignment techniques in total knee arthroplasty (TKA) on the soft tissue balance of the knee by using a novel intra-operative pressure sensor device. Our hypothesis is that the kinematic alignment of total knee prosthesis creates a more balanced knee without the need for soft tissue release when compared to mechanical alignment. We aim to investigate this hypothesis by performing a multicentre, multi-surgeon, prospective randomized control trial in patients undergoing unilateral TKA for advanced osteoarthritis (OA).

**STUDY IDENTIFICATION**

Registered with ANZCTR (Australian and New Zealand Clinical Trials Registry)

Registered by Dr Peter McEwen

**SPONSOR**

ORIQL (Orthopaedic Research Institute of Queensland)

**ADMINISTERING INSTITUTION**

ORIQL

Street Address: 7 Turner Street, Pimlico, QLD 4812

Telephone: 0413 685 331

Website: [www.oriql.com.au](http://www.oriql.com.au)

Email: research\_coordinator@oriql.com.au

**Investigators and Institutions**

Dr Peter McEwen ORIQL, James Cook University

Dr Ben Parkinson ORIQL, James Cook University

Dr Mike Reid ORIQL, James Cook University

Dr Matthew Wilkinson ORIQL, James Cook University

Andrea Grant ORIQL

Dr Ryan Faruque ORIQL

**GLOSSARY OF ABBREVIATIONS:**

CR – Cruciate Retaining

HKA- Hip knee angle

JCU – James Cook University

LCL – lateral collateral ligament

LDFA – lateral distal femoral angle

MCL – Medial Collateral Ligament

MPTA – medial proximal tibial angle

OA – Osteoarthritis

PCL – Posterior cruciate ligament

PSI – Patient specific instrumentation

ROM – Range of movement

ITB – Iliotibial band

SM- Semimembranosus tendon

TKA – Total knee arthroplasty

**RATIONALE AND BACKGROUND INFORMATION**

Traditionally TKA alignment is perpendicular to the mechanical axis of the femur and tibia to produce a neutral overall limb alignment with a knee joint line parallel to the ground (mechanical alignment). Native limb alignment however is in slight varus and mechanical alignment of a total knee prosthesis results in tighter soft tissue on the medial side of the knee that requires release to achieve a “balanced” knee(1,2). The reliability of the average surgeon to achieve an accurate soft tissue release to gain a balanced knee is relatively unknown. It has been proposed that soft tissue imbalance around the knee may be in part, responsible for the dissatisfaction after TKA (3–5).

A recent study has utilised a novel pressure sensor insert (Verasense) during TKA to provide objective data on the medial and lateral soft tissue balance of the knee(5). The surgeons in this study aimed to align the prosthesis mechanically and achieve equal pressures on each side of the knee through a full range of motion. Balance of the knee was achieved by either soft tissue release and/or adjustment of the angles of the bony cuts to align the knee. This study demonstrated a satisfaction rate of 96.7% in knees that were balanced vs a satisfaction rate of only 82.1% in knees that could not be balanced.

Contrary to mechanical alignment, kinematic alignment involves individualizing the alignment of the prosthesis to match a patient’s native knee alignment in an effort to achieve a balanced knee without the need for soft tissue releases. A randomized control trial of mechanical vs kinematic alignment in TKA has demonstrated improved patient reported outcomes at two years with kinematic alignment (4). The improved functional outcomes with kinematic alignment are thought to be due to a better “balanced” knee with this technique, but as of yet there are no studies demonstrating that kinematic alignment actually results in a more balanced knee.

Concern exists for the potential of premature wear and early failure of the prosthesis if the components are aligned in significant deviations away from the neutral axis (6). Long-term clinical studies at a minimum of 15 years follow-up have however demonstrated no increased failure rate in prostheses aligned in more than 3° from neutral (7,8). In reality, the safe limits for prosthesis alignment are currently unknown. A recent study has compared the joint line restoration in mechanical and kinematically aligned TKAs(9). This study found that only kinematic TKA alignment restored a natural knee joint line for the majority of patients. Mechanical alignment resulted in a significant change in knee joint line obliquity with only approximately 1/3 of mechanically aligned TKAs having a joint line parallel to the floor.

This complex relationship between prosthesis alignment techniques in TKA and the effects on overall limb alignment, joint line obliquity and soft tissue balance of the knee is yet to be determined. This study aims to investigate these factors and determine the influence on patient outcomes.

**STUDY HYPOTHESIS**

Kinematic alignment of total knee prosthesis creates a more balanced knee without the need for soft-tissue release.

**AIMS**

**Primary Aim:**

To quantify the influence of prosthesis alignment on the balance of the soft tissue envelope of the knee

**Primary Outcome:**

* Difference in medial vs lateral compartmental pressures and rollback patterns as measured by the Verasense insert.
* The frequency and type of soft tissue releases and/or bone cut adjustments required to gain a balanced knee.

**Secondary Outcome:**

* ­Patient reported outcomes questionnaires
* Limb and joint line alignment
* Knee ROM
* Complication rates  ­
* Long term prosthesis survival

**STUDY DESIGN**

This is a single blinded, prospective, randomised control trial study on unilateral TKA participants to examine the difference in ‘balance’ between kinematic and mechanical alignment through soft-tissue release, verified by the Verasense tensile instrument. 160 consecutive participants will be recruited to this study across three sites; Mater Health Services North Queensland Ltd, Cairns Base Hospital and Cairns Private Hospital. commencing December 2016. Participants will be randomly assigned to either a (1) kinematic group or to a (2) mechanical group. All participantss will receive a PSI Nexgen Cruciate Retaining (CR) Flex TKA prosthesis, manufactured by Zimmer.

**METHODS**

***Setting***

This study will prospectively recruit participants from three sites, who are patients of one of the four Chief and Principal Investigators.

***Population***

The study population will include patients who require TKA for treatment of OA.

***Selection Criteria***

Inclusion criteria:

1. Male or Female
2. Age 45-80
	1. This age range depics the typical population that undergo total knee replacement. participants less than 45 years are not amenable to a total knee replacement and are known to have poorer outcomes and increased rates of failure of prosthesis. Patients older than 80 years often have many co-morbidities and have an increased risk of complications and thus do not typically have total knee replacement surgery.
3. BMI <40
4. Patients who require a primary TKA for treatment of OA.

Exclusion criteria include:

1. No previous open surgery
2. No previous high tibial osteotomy operation
3. No previous ligamentous injury to the collateral ligaments
4. No previous fracture of the tibia or femur
5. Varus or valgus deformity of >15 degrees
6. Fixed tibial subluxation due to severe posterior bone wear
7. Hyperextension deformity

***Recruitment***

Potential participants will be referred to the investigating surgeon for treatment of OA. On consent for surgery, and deemed ‘fit’ for consideration, participants will be provided information on the study, and an opportunity to ask questions. Eligible participants willing to be included will be asked to provide consent for inclusion.

***Consent***

All participants shall provide consent prior to participation. Consent will be obtained verbally, then electronically via FORCE THERAPEUTICS once the Verasense KVM Study Protocol has been assigned to the participant’s profile. A witness must also provide date/time logged signature electronically, as will the consulting surgeon.

***Randomization***

Clinic Research Coordinators (CRC/Nurse) will email ORIQL Research Coordinator via FORCE THERAPEUTICS, to a) provide notification of participant recruitment and b) request participant randomization. Randomization will be performed by Computer Randomization Number generator program, based on the use of complex numerical algorithms. Participants will be assigned a randomization number (to be used for statistical analysis) and will be assigned an alignment protocol for surgery.

***Blinding***

The participant will be blinded as to which prosthesis alignment technique will be used. However, the surgeon cannot be blinded as they will have an MRI requested prior to the surgery to produce to the PSI.

***Time points***

|  |  |  |
| --- | --- | --- |
|  | **Study Visits** |  |
|  | Pre-Surgery | Surgery  | 6 weeks later | 6 months later | 12 months later | 24 monthslater |
| MRI to produce PSI/Informed ConsentRandomization | x |  TKAIntra-operative Data collection  |   |   |   |  |
| Clinical exam | x | x | x | x | x |
| Questionnaires | x | x | x | x | x |
| X-ray | x | x |  x | x | x |

***Participant Information and Demographic Data***

***Primary Outcome (Intra-operative Data Assessment)***

1. Difference in compartmental pressures: medial vs lateral (psi) at 10°, 45° and 90°
2. Roll back patterns:
	1. Lateral rollback (medial pivot)
	2. Equal rollback (neutral pivot)
	3. Medial rollback (lateral pivot)
3. Verasense contact-point rotation number at 00 and 900 - Verasense provides contact point rotation number which quantifies the amount of rollback difference; obtained from a contact point tracking map.
4. Count of soft-tissue structure adjustments and bone resections required.
	1. Ligament structures adjusted- ITB, LCL, lateral retinaculum, popliteus, PCL, MCL, SM
	2. Type of adjustment- pie crusting or complete release
	3. Bone resection adjustments
	- Coronal alignment of distal femoral cut
	- Coronal alignment of proximal tibial cut
	- Sagittal alignment of proximal tibial cut
	- Medial tibia reduction osteotomy

***Secondary Outcome***

1. Assessment of the knee range of motion (ROM; supine and active).
2. HKA and joint line changes obtained from pre-operative and post-operative X-rays
3. Assessment forms include ED-5Q, KOOS (includes WOMAC), Oxford. Knee Society Knee Score (pain and function). See timeline for activities.
4. Long term prosthesis survival/complication rates.

***Radiographic Assessment***

Long leg standing pre-operatively and post-operatively. See timeline

***Study Procedures***

*Preoperative Assessment*

Once the participant have been consented into the study, they will have their pre-operative assessments performed. Participants will then have their preoperative MRI request given to them to have this testing done. This will then be used to manufacture their patient specific instrumentation (PSI)

*Surgical Procedure*

Surgical technique will be standardized with respect to the resection of bone, ligament tension assessment and use of Verasense instrumentation; The Verasense insert will be used intra-operatively to measure the medial and lateral compartment pressures during the prosthesis trialing phase, before any soft tissue releases are performed. If the knee is not balanced, then measured steps will be undertaken to achieve 'balance’. All intra-operative surgical data will be recorded

*Post-operative Assessment*

Post-operative participant review will be conducted at two weeks, six weeks, six months, and then yearly. Standard TKA post-operative radiologic assessment will be undertaken to determine the final prosthesis alignment

***Sample Size***

A recent study(10) looking at kinematic versus mechanical alignment using PSI was found a Knee Society Score change of 12 points and a standard deviation of 18 points. Assuming Type I error (alpha) to 5% (p = 0.05) and Type II error (beta) to 0.2 (power equal to 80%); for a two sided 5% significance level mean difference of 12 points and standard deviation of 12 points, we can use a sample size table to estimate the sample size to 64 knees in each group. We will investigate 70 knees to compensate for 10% expected loss to follow-up. As we have 4 consultants working on the study, for better division of work we will increase this to 80 in each group participants; overall total of 160 participants in the study.

An interim analysis on Verasense intra-operative assessment data between kinematic and mechanical alignment when n=40 will provide an indication on whether the sample size will be sufficient to show significant effect, and after that no further recruitment will be required.

***Statistical analysis***

Statistical analysis will be performed using Statistical Sciences (SPSS, Version 22).

**DATA MANAGEMENT**

Data will be collected by local site investigators electronically and or recorded in Participant Study Files. Any paper source documentation will be scanned or entered electronically onto ORIQL database (FORCE THERAPEUTICS) by the Project Research Coordinator. Participant assessment questionnaires will be entered directly onto FORCE THERAPEUTICS. Data will be stored in a password protected cloud based server as well as password protected ORIQL computer which is housed in locked premises as are any source document files. Data will be kept for a minimum of 15 years post study completion/publication.

**ETHICAL CONSIDERATIONS**

This study will be submitted to the Principal Investigators Ethics Committee, Townsville Hospital Health Services Ethical Governance Human Research Ethics Committee (HREC). Once the study has passed HREC approval, we will send applications for Specific Site Assessment (SSA) approval to the three separate sites where the study will be conducted.

The study will be registered prior to trial commencement with the ANZCTR.

**FEASIBILITY**

The cost involved with utilizing the Verasense instrumentation will not hinder the ability of investigators to complete this project.

**DISSEMINATION OF RESULTS AND PUBLICATION**

The results of the study will be presented at national and international orthopaedic scientific meetings such as the Australian Orthopaedic Association (AOA) Annual Scientific Meeting. Results will be published in a high impact surgical journal and will be disseminated via various forms of media.

Authorship will be under the name of Investigators belonging to ORIQL, and by association to James Cook University.

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