Does Soft Tissue Balancing Using Intra-Operative Pressure Sensors Improve Clinical Outcomes in Total Knee Arthroplasty? A Multi-Centre Randomised Controlled Trial

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Table of Contents

ABSTRACT

Introduction

Although dissatisfaction following total knee arthroplasty (TKA) is a multifactorial problem, surgical causes are commonly related to soft tissue imbalance or malalignment. Achieving a balance of soft tissues through a range of motion is now considered a primary goal to optimise patient outcomes. Balancing techniques commonly include gap balancing, computer-assisted navigation and subjective varus and valgus ligament stressing. The advent of sophisticated intra-operative sensors, however, allows surgeons to quantify knee compartment pressures and tibiofemoral kinematics, thereby optimising coronal and sagittal plane soft tissue balance and tibiofemoral positioning through a range of motion.

Methods and Analysis

A multi-centred, randomised controlled trial was designed to compare the clinical outcomes in 222 patients undergoing TKA. Patients will be randomly allocated to either pressure sensor-guided balancing or standard manual balancing. The sensor will be used in both arms for purposes of data collection, however surgeons will be blinded to the pressure data of patients randomised to the manual balancing group. The primary outcome of the study will be the change from baseline to one year post-operatively in the mean of the four subscales of the Knee Injury and Osteoarthritis Outcome Score ($KOOS_4$) that are most specific to TKA recovery: pain, symptoms, function and knee-related quality of life. (The sports/recreation subscale has a significant floor effect in this population.) Normality of data will be assessed, and a Student's t-test and equivalent non-parametric tests will be used to compare differences in means amongst the two groups. Secondary outcomes will include intra-operative data, radiographs, functional assessment and three other patient-reported outcome measures.

Ethics and Dissemination

Ethics approval was obtained from South Eastern Sydney Local Health District, Approval 18/135 (HREC/18/POWH/320). Results of the trial will be presented at orthopaedic surgical meetings and submitted for publication in a peer-reviewed journal.

Trial Registration Number

Australian New Zealand Clinical Trials Registry (ACTRN#12618000817246); pre-results.

Keywords

Total knee arthroplasty; intra-operative sensors; soft-tissue balance

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This will be a large, multi-centre, randomised controlled trial that will provide clinicians with important information about whether there are significant benefits to using intra-operative pressure sensors for soft tissue balancing in TKA surgery.
- The study will be investigator-initiated, theoretically minimising selection and reporting bias.
- It will be pragmatic, aiming to include all patients who routinely undergo TKA in the general population.
- The secondary outcomes will provide rich multi-modal data, including objective radiological and functional information and significant patient-derived evidence.

Does Soft Tissue Balancing Using Intra-Operative Pressure Sensors Improve Clinical Outcomes in Total Knee Arthroplasty? A Multi-Centre Randomised Controlled Trial

INTRODUCTION

Total knee arthroplasty (TKA) is a successful operation in alleviating pain and improving function for the majority of people with end-stage knee osteoarthritis. However, up to 20% of patients undergoing TKA internationally report some dissatisfaction following their surgery [1-3]. The Australian Clinical Outcomes Registry (ACORN) [4], and the Swedish Knee Arthroplasty Registry [5] report similar results in terms of patients who rate their knee as either 'fair', 'poor' or 'unknown/no answer' at follow-up.

Dissatisfaction following total knee arthroplasty is a multifactorial problem. The surgical causes are commonly related to soft tissue imbalance or malalignment. Both of these can result in knee stiffness, instability, asymmetric joint laxity and patellofemoral maltracking. Malalignment may also result in early component failure, implant loosening, polyethylene wear or osteolysis [3, 5-8].

Achieving balance of soft tissues through a range of motion is now considered a primary surgical goal to optimise patient outcomes. The main surgical technique for surgeons to determine knee balance is by subjective intra-operative assessment using varus and valgus stressing of the ligaments in different degrees of flexion. However, a recent study at our institution found that surgeon-determined assessment of knee balance prior to ligament releasing was poor, with a positive predictive value of 59.2% and a negative predictive value of 54% [9]. Other methods that have been used to optimise balance have included gap balancing methods, (where femoral extension and flexion osteotomies are made based on ligament tension), and computer-assisted navigation, which can assess ligament elongation. However, none of these methods is able to quantify knee compartment pressures and tibiofemoral kinematics.

Intra-operative pressure sensors have been recently introduced for use during TKA to quantify soft tissue balance and tibiofemoral kinematics (Figures 1a and 1b). The Verasense™ System (OrthoSensor, Dania Beach, FL) uses micro-electronic sensors embedded in a standardised tibial trial spacer to determine pressures at peak contact points in the medial and lateral tibiofemoral compartments during TKA component trialling. Providing real time analysis of compartmental loads with wireless connectivity to a computer monitor, a combination of ligamentous releases and bone readjustments may be performed to optimise coronal and sagittal plane soft tissue balance. The sensor also allows dynamic optimisation of tibiofemoral positioning through a range of motion [10].

Figure 1a. Verasense™ inserts

Figure 1b. Wireless graphical display of compartmental loads and tibiofemoral contact points in real time

In 2013, Gustke and colleagues evaluated 176 patients from eight sites using the Verasense™ knee system for soft tissue balancing [11]. The cohort was separated into balanced versus unbalanced groups based on recorded intercompartmental pressure differentials. At six months, the balanced cohort demonstrated significantly better patient reported outcome scores compared to the unbalanced group. However, there was no control group in this study (both groups used Verasense™ data), and the number of patients in the unbalanced group (13%) was significantly smaller than those in the balanced cohort (87%). A two-year follow-up report found that satisfaction scores were significantly higher in the balanced cohort (96.7% satisfied) versus the unbalanced group (82.1% satisfied) [12].

Elmallah and colleagues reported in 2016 on a series of 22 patients who received either a sensor-guided assessment using the Verasense™ system (n=10) or manual gap balancing techniques (n=12) by an experienced knee arthroplasty surgeon [13]. Patients with sensor-guided balancing had significantly lower medial compartmental loads at 10˚, 45˚ and 90˚, compared to the manual gap balance cohort. Additionally, the sensor group had a lower mean difference between medial and lateral compartment loads and a greater need for soft tissue releases to balance the knee.

This study also found improved tibiofemoral congruence in the sensor group versus the manual balancing group, but it did not include patient-reported outcomes.

As soft tissue imbalance may lead to poor patient outcomes and potentially to revision knee surgery (with its associated morbidity and economic impact), it is important to determine whether improvements in soft tissue balance during TKA significantly improve clinical outcomes. There are no published randomised controlled trials that have quantified knee balance and determined whether surgical balancing using sensors improves knee pain and function compared to manual techniques.

The primary aim of this study is to determine if there is benefit in using intra-operative sensors to achieve knee balance in TKA surgery. In addition, we aim to define whether surgeons will be able to accurately determine knee balance, and whether the use of the sensor improves the functional and radiographic outcomes of TKA. Our primary hypothesis, using an intention-to-treat analysis, is that achieving knee balance with use of the sensor will improve $KOOS_4$ outcomes at 12 months in patients undergoing total knee arthroplasty when compared to current manual surgical balancing techniques.

METHODS AND ANALYSIS

Study Design

We will conduct a multi-centred, investigator-initiated, randomised controlled trial (RCT) comparing the clinical outcomes of Sensor-Guided Balancing (SGB) versus Manual Balancing (MB) in patients undergoing TKA. Sensors will be used in both arms for analysis of balance, however in the MB group, the surgeon will be blinded to the data provided by the insert. The sensor data will be recorded by a non-surgical team member.

Eight surgeons will undertake surgeries at 11 different sites, in both public and private hospitals. In order to increase pragmatism of this study, we will aim to include all patients who would routinely undergo elective TKA surgery in the general population. As such, we will include both unilateral and bilateral procedures, patients who have extra-articular deformity from prior fracture or osteotomy surgery, or those with severe stiffness or deformity. All of these variables will be analysed in regression models.

Eligibility

Inclusion Criteria

1. All patients suitable for TKA aged 20-85 years
2. Patients who meet the indications for primary unilateral or bilateral total knee arthroplasty using the Legion or Genesis II cruciate-retaining or posterior-stabilised total knee arthroplasty system (Smith & Nephew, Memphis, TN).
3. Subjects diagnosed with one or more of the following conditions:

- Osteoarthritis
- Rheumatoid or other inflammatory arthritis
- Post-traumatic osteoarthritis

Exclusion Criteria

1. Any surgery where constrained prostheses are required due to significant ligament deficiencies (such as constrained condylar or rotating hinge prosthesis)
2. Any surgery performed for acute fracture or tumour
3. Participants unable to provide consent or complete questionnaires due to cognitive incapacity or English language deficiency
4. Participants unable to commit to full follow-up schedule over two years due to geographic distance or physical challenges

Allocation

Allocation (1:1) per patient via randomisation will occur immediately prior to the commencement of surgery. A member of the surgical team will contact the National Health and Medical Research Council (NHMRC) Clinical Trial Centre's centralised randomisation service by telephone. Stratification factors in the randomisation include patient age, surgeon and gender.

For those patients undergoing bilateral, simultaneous TKA, or sequential unilateral TKA at different time points during the trial, both knees will be allocated to the same arm, as randomisation will be done at the level of the patient, not the knee. The reason for this allocation strategy is that the primary outcome instrument partly measures function and quality of life, and these outcome subscales are unable to discern which limb underwent either intervention.

Although the surgeons will not be blinded to the allocation, the participants, assessors and statisticians will be blinded to enable unbiased collection and analysis of outcomes. Sensor data will be concealed from the surgeon whilst the initial blinded assessment of knee balance is undertaken. Data will then available to the surgeon for knee balancing in those patients allocated to the SGB group. Concealment of sensor data will be maintained in the MB group until study completion.

Unblinding will occur only when knowledge of the treatment allocation is essential for further clinical management. Rationale for unblinding will include a need for revision knee surgery for instability or malalignment, or cases in which the treating surgeon believes that the knowledge of sensor data is clinically necessary.

Interventions

Intervention (Sensor-Guided Balance, SGB) Group

In the SGB group, surgeons will be allowed to use intra-operative sensor data to balance the knee as per the surgical protocol. The compartmental pressure loads will be recorded prior to, and then upon completion of knee balancing at 10˚, 45˚ and 90˚ of flexion.

Control (Manual Balance, MB) Group

In the MB group, surgeons will utilise their method of choice to achieve knee balance, including measured resection techniques with manual soft tissue balancing or gap balancing methods. The compartmental pressure loads will be recorded prior to, and then upon completion of knee balancing with the sensor in situ, but the sensor data will not be viewed or used during knee balancing.

Baseline Measures

Baseline Data

Baseline data will include age at time of surgery; gender; side of surgery; unilateral versus bilateral surgery; body mass index and primary diagnosis (osteoarthritis, rheumatoid or other inflammatory arthritis, post-traumatic osteoarthritis). In addition, description of extra-articular deformities (degree of deformity, diaphyseal versus metaphyseal location); prior knee ligament surgeries (ligament involved, open versus arthroscopic) and prior osteotomy surgeries (femoral, tibial or tibial tubercle) will be recorded.

Pre-operative Radiographic Data

Routine pre-operative radiographs will include hip-to-ankle 4-foot standing films and knee x-rays with AP erect, lateral and patellar skyline views.

Radiographic data to be recorded will include:

1. Hip-knee-ankle (HKA) angle
2. Lateral distal femoral angle (LDFA)
3. Medial proximal tibial angle (MPTA)
4. Any extra-articular femoral or tibial angular deformities, measured in the coronal and sagittal planes

Operative Data

Operative data to be recorded will include type of prosthesis by stability (cruciate-retaining, posterior-stabilised); size and fixation method of each implant. Other operative details will include total operating time (wound incision to skin closure); alignment technique; surgical approach and intra-operative complications. The American Society of Anaesthesiologists (ASA) grade [15] will be recorded.

Primary Outcome Measure

The primary outcome measure will be change from baseline to one year in the mean of the four subscales of the Knee Injury and Osteoarthritis Outcome Score ($KOOS_4$) that are most specific to TKA recovery: pain, symptoms, function in daily living [ADL] and knee-related quality of life [QoL]. The fifth subscale, function in sport/recreation has a significant floor effect in this population, and therefore will not be included [16, 17]. The $KOOS_4$ is an aggregated mean of the four subscales (each scored 0 [worst] to 100 [best]), with this method of analysis based on recommendations from the instrument designers for use in RCT's [16].

Secondary Outcome Measures

In-Hospital Data

In-hospital data to be obtained will include:

1. Total length of stay (from day of surgery to day of discharge)
2. Discharge destination
   - home
   - in-patient rehabilitation unit
   - nursing home facility

Patient-Reported Outcome Measures

1. *Knee Osteoarthritis Outcome Score (KOOS)* - To assess longitudinal progress, the $KOOS_4$ (and each separate subscale for secondary analysis) will be measured again at six months and two years. [16, 17].
2. *Knee Society Score (KSS 2011)* – The KSS is both patient- and physician-derived, and assesses pain, function and objective clinical and radiographic outcomes. It will be measured pre-operatively and at one and two years post-operatively.
3. *Forgotten Joint Score* - The FJS-12 focuses on patients' awareness of their knees in everyday life. Low ceiling effects and good relative validity allow monitoring of longer term outcomes, particularly in well-performing groups after total joint arthroplasty [19]. The FJS-12 will be measured pre-operatively and at one year and two years post-operatively.
4. *EQ5D-5L* – The EQ5D is a standard measure of overall health status that provides a simple descriptive profile and a single index value for health status [20, 21]. The EQ5D-5L will be measured pre-operatively and at one year and two years post-operatively.

Strategies for improving adherence to protocol outcomes will include clear elucidation during the consenting process of the importance of committing to the schedule of follow-up visits, PROMs, and x-rays. Participants will have the opportunity to ask questions, and key messages about the study will be reinforced at each follow-up visit. In order to prevent missing data and avoid associated complexities in study analysis

and interpretation, administrative systems will be employed to diligently schedule follow-up appointments, provide reminders and monitor retention.

Intra-operative Outcome Measures

Surgeon Determination of Knee Balance – Prior to performing knee balancing (for both SGB and MB groups), the computer screen will be turned away from the surgeon. The surgeon will be asked if they believe the knee is balanced or unbalanced at 10˚, 45˚ and 90˚ of knee flexion with the sensor in situ (Balanced: Yes or No). Agreement with the sensor is defined as the agreement at two out of three knee positions.

Tibiofemoral Compartmental Pressure Loads - Initial and final medial and lateral compartmental pressure loads will be compared in both groups at 10˚, 45˚ and 90˚ of knee flexion. 'Balanced' using the sensor will be defined as a pressure difference of less than 15 psi between medial and lateral compartments at 10˚, 45˚ and 90˚ of knee flexion, with no pressure exceeding 40 psi as per Gustke and colleagues [10].

Tibiofemoral match - Tibiofemoral match will be compared in both groups at 10˚, 45˚ and 90˚ of knee flexion. External rotation will be recorded as a negative value and internal rotation as a positive value. Any deviation of more than 5˚ from neutral rotation will be defined as a mismatch. Optimal rotation will be defined as the rotational coupling within 5˚ at two out of three knee positions.

Radiographic Measures

A routine series of knee radiographs will be performed postoperatively (before discharge) and at one and two years after surgery. This series will include the following views: AP erect, 30° lateral and patellar skyline views. Additionally, routine hip-to-ankle 4-foot standing films will be performed at post-operative time points.

Functional Outcome Measures

Knee Range of Motion – This will be measured at six to ten weeks and six months post-operatively. Measurement will be performed in the supine position based on the photographic method of Naylor and co-workers [24]. This method was found to be superior to goniometry alone, and a photographic record allows repeatability and blinding. This will allow the surgeons and their assistants to image active range of motion, but not record it at the time, to exclude observer bias. Markers will be placed on the greater trochanter, lateral epicondyle of the femur and lateral malleolus. Knee flexion will be recorded as a positive value and knee hyperextension as a negative value. The following will be recorded: maximal active extension (with hyperextension being negative, full extension as zero and flexion contracture as positive) and maximal active flexion. From these two values, the arc of knee motion will be recorded (flexion minus extension).

Timed Up and Go (TUG) Test - Participants will be asked to stand up from a standard chair (seat height between 44 and 47cm), walk a distance of 3m (marked on the floor) at a comfortable pace, turn, walk back and sit down. Participants will be permitted to use routine walking aids and will be instructed not to use their arms to stand up. No physical assistance will be given. The time to complete the task will be measured with a stopwatch. Timing commences on the command 'go' and will stop when the subject's back is positioned against the back of the chair after sitting down. Usually the task will be performed twice. Shorter times indicate better performance. This will be measured at six months post-surgery [25].

Six Minute Walk Test (6MWT) - A 25-metre section of the outdoor footpath will be demarcated for this test. The participant will be instructed to walk as far as possible for six minutes, up and down the demarcated footpath, pivoting to turn at the end of each lap. Timing will commence as the participant steps over the start line. Standardised encouragement will be given to the patient after each minute. The participant will be instructed to stop at six minutes. If they are unable to complete six minutes, they will be instructed to maintain their position whilst the assessor measures the final partial lap with a trundle wheel. The use of a walking aid and standing rests will be permitted. One test will be performed for each participant. This will be measured at six months post-surgery. High repeatability of the 6MW test has been established in patients awaiting TKA [26].

Complications

Recorded complications will include serious adverse events related to the operation (e.g. stiffness requiring manipulation under anaesthesia [reoperation] or total or partial component exchange [revision]), and adverse events unrelated to the operation (see Table 1). Intra- and post-operative complications will be assessed and recorded at all time points (Table 2), and as necessary at unscheduled times. The study coordinator will notifiy SESLHD HREC (for public sites) and the local sites' Research Governance Offices (for private sites) of serious adverse events within 72 hours of notification by site co-investigators.

Patient-reported outcomes will be monitored throughout the study to supplementally inform the clinical care of individual participants, but their timing will coincide with scheduled clinical assessment in any case.

Sample Size

Roos and colleagues recommend the minimum clinically important change in $KOOS_4$ to be between 8 and 10 on a scale of 0-100 with a standard deviation of 15. The four scores, each a score out of 100, are aggregated as a mean value [16, 27]. An RCT on TKA versus non-operative treatment for osteoarthritis by Skou and colleagues similarly used the $KOOS_4$ with subscales of Pain, Symptoms, Function and QoL. They

found a one-year change in $KOOS_4$ of 32.5 points (95% CI 26.6-38.3) in the TKA group [28].

Using a one-to-one allocation, 5% significance, a standard deviation of 15 and a 90% power to detect the minimum 8-point difference in change on the $KOOS_4$ score, a sample size of 75 patients per group will be required to test the primary hypothesis. Assuming a 10% loss to follow-up, a minimum of 167 patients in total will be required to ensure adequate sample size with an intention-to-treat analysis of SGB versus MB.

However, previously published data from the principal investigator noted that use of an intra-operative pressure sensor results in an additional 46.5% of surgical adjustments beyond what the surgeon believed was required on manual assessment to achieve knee balance [9]. Hence, we anticipate that there will be approximately half of TKA's in the MB group that will be balanced, and that all knees in the SGB group will be balanced.

Assuming any difference in clinical outcomes between groups will most likely result from improvement in knee balance as opposed to use of the pressure sensor, a further sample size calculation was undertaken on an as-treated basis comparing balanced versus unbalanced knees. With a three-to-one allocation of balanced to unbalanced knees (three of four knees being balanced once treated), a standard deviation of 15 and a 90% power to detect the minimum 8-point difference in change on the $KOOS_4$ score, we will require 150 patients in the balanced group and 50 in the unbalanced group if the null hypothesis were to be rejected. A total sample size of 200 patients will be required, with a 10% loss to follow-up requiring a total sample size of 222.

Data Collection and Monitoring

All PROM data will be obtained from patients at pre-operative and post-operative consultations in paper form, and then stored centrally in a secured, password protected database accessed only by the study coordinator. Intra-operative data will be collected by members of the surgical team and forwarded to the study coordinator. Post-operative follow-ups will be completed by the treating surgeons and their assistants. A research physiotherapist who is blinded to patient allocation will be recruited to undertake functional outcome measures at the relevant time points.

No formal data monitoring committee is deemed necessary for this trial because of its minimal risks and because both trial arms will offer standard, accepted surgical interventions. The accumulating data, however, will be monitored continuously by the principal investigator and the study coordinator to determine if the trial should be modified or discontinued.

Auditing of trial conduct will be carried out by South Eastern Sydney Local Health District Human Research Ethics Committee.

Stopping Rules

This trial will not involve a primary safety endpoint, nor activities of high risk to study participants. It will use a device that is already entered onto the Australian Register of Therapeutic Goods (ARTG). The risks of participating in the study will be comparable to standard medical care, and the sensor-guided pressure device will be used within its approved product indications by experienced clinicians performing an established intervention in line with local, national and international protocols (Type A Risk Category of the Office of Economic Cooperation and Development).

In the course of a routine total knee arthroplasty, trial tibial inserts are used to provisionally determine the correct size of the final tibial insert to be cemented into the joint. The pressure sensor takes the place of the usual trial insert, performing the same indicative sizing function, while also providing measurements of pressure within the tibiofemoral compartments.

For these reasons, formally articulated stopping rules for harm will be considered unnecessary for this study. Similarly, because the trial investigates outcome data associated with a device that is approved and already being used routinely, and because recruitment will be finished before the primary outcome measure is collected, it is not anticipated that there will be a need for stopping rules for benefit.

Interim monitoring for a pattern of unexpected serious adverse effects will be conducted weekly by the Study Coordinator to determine if the trial should be modified or discontinued early.

Data Analysis

Normality of data distribution will be assessed, and Student's t-test will be used to compare differences in means with continuous variables. Chi-squared test and Fisher's exact test will be used for categorical data analysis as appropriate. Intention-to-treat analysis will be performed in the primary analysis. In addition, an as-treated analysis including participants according to treatment received will be added as a secondary analysis. If greater than 20% of data are missing from the randomised sample, the missing data will be imputed. However, attempts will be made to minimise missing data by contacting patients directly by phone or via mail follow-up.

Ethics and Dissemination

Safety considerations

As the two groups being analysed will be offered current routine standards of care, we do not anticipate either the intervention or control arm will be associated with any adverse events beyond those that patients are normally exposed to during total knee arthroplasty surgery.

All sites where the trial is conducted will have provisions for liability insurance, and it will be a requirement for each site to maintain their own indemnity insurance related to performing this study. There will be additional information in the Patient Information Sheet and Consent form instructing participants to notify the principal investigator of any adverse events or complications that arise during the course of the trial.

Ethics

This study protocol received approval from the South Eastern Sydney Local Health District Human Research Ethics Committee (HREC). The trial has been registered with the Australian New Zealand Clinical Trials Registry (ACTRN#12618000817246p).

Important modifications to the protocol that may impact the conduct of the study will be communicated to South Eastern Sydney Local Health District Human Research Ethics Committee HREC and the individual site governing boards as necessary for their approval.

The investigators believe that conducting a randomised trial to determine if there is any benefit to using intra-operative sensors to achieve knee balance will be an ethical way to investigate the question, as the potential benefits of this study to society will outweigh the potential risks to the individuals involved. Because both groups will be receiving an accepted standard of care for knee surgical balance, we see no significant risks to the patient that are outside the norm for patients undergoing total knee arthroplasty surgery.

None of the participants in this study will be paid. None of the investigators has any financial or other conflicts of interest in the process of outcomes of this trial.

Participants will be clearly instructed in the Patient Information and Consent Form to contact the treating doctor as soon as possible if they suffer any injuries or complications they believe are related to the trial, and they will be informed about their legal rights to compensation for any serious harm resulting from participation. They also will be assured verbally and via the Patient Information and Consent Form that their clinical follow-up will continue on a regular basis after the conclusion of this study.

Data Management

Data will be collected by local site investigators, but then submitted securely to the study coordinator and stored electronically in a central password-protected database in the chief investigator's rooms. All records that contain names or other personal identifiers will be stored separately from study records identified by code numbers. The electronic database will be maintained on a password-protected computer and any papers are locked in a filing cabinet will be accessible only to the study

coordinator. At the end of the study period all paper copies will be scanned and destroyed.

During the trial period, only the study coordinator will have access to the full trial data set.

Dissemination

The aggregate, de-identified results of this research will be presented at both national and international orthopaedic surgical meetings, and submitted to a high impact medical or surgical journal for publication. Additionally, the authors will publish a de-identified, participant-level data set and statistical code after journal publication to enable verification and replication of the study.

NOTES

Contributors

SJM, DBC, IAH, were involved in the conception and trial design. SJM and JW were involved in drafting this article and will draft the study report. DBC, IAH, ADD, AB, AWRB, AKLL, RBM, JSM, and RMW were involved in critical revision of this article for important intellectual content. All the authors will be involved in final approval of the study report. IAH provided statistical expertise. Preparing the study design; collection, management, analysis and interpretation of data; and the decision to submit the report for publication will be the responsibility of all the authors.

Funding

This work will be supported by a grant from OrthoSensor (Dania Beach FL, USA) to cover costs of additional personnel (data analyst, physiotherapist, radiographer), and by Smith and Nephew, who will provide the inserts needed to conduct this trial at no cost. The grant will be held in a dedicated research account and administered through the Ingham Institute of Applied Medical Research (Liverpool, NSW).

Competing Interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: the project as a whole will receive a research grant from OrthoSensor for the submitted work, but no individual author will receive support for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three

years; no other relationships or activities that could appear to have influenced the submitted work.

Provenance and Peer Review

Not commissioned; not yet externally peer reviewed.

TABLES

Table 1. Complications

- Bleeding
- Cardiac event
- Cellulitis
- Death
- Deep venous thrombosis (specify index leg, other leg, both legs)
- Delirium
- Dislocation or joint instability requiring bracing or surgery
- Drug Reaction
- Fall
- Fat embolus
- Fracture
- Index joint reoperation/revision during study period
- Joint or lower limb swelling
- Joint stiffness requiring surgery (manipulation or revision)
- Leg length discrepancy
- Muscle weakness
- Nerve injury
- Parasthaesia or numbness
- Pressure Area
- Pulmonary embolus
- Respiratory Infection
- SSI requiring IV antibiotics
- SSI requiring oral antibiotics
- SSI requiring surgery with prosthetic removal
- SSI requiring surgery without prosthetic removal
- Stroke
- Unexpected pain
- Urinary infection or retention
- Wound dehiscence
- Other, specify

Table 2. Schedule of Study Assessments

	Pre-op	Intra-op	Index Admission	6-10 weeks	6 months	1 year	2 years
Written informed consent & PICF	X						
PICF	X						
Demographics	X						
Intra-op Data		X					
Intra-operative Pressure Data		X					
Clinical Assessment	X			X		X	X
KOOS Score	X				X	X	X
KSS Score	X					X	X
FJS Score	X					X	X
EQ5D-5L Score	X					X	X
In-Hospital Data			X				
Functional Assessments					X		
Knee Range of Motion	X			X	X		
Radiographs AP, Lat, Skyline (and 4-ft films at pre-op)	X		X			X	X
Adverse Event Reporting		X	X	X	X	X	X

Table 3. SPIRIT 2013 Checklist with SPIRIT-PRO Extensions

SPIRIT 2013 Checklist with SPIRIT-PRO Extensions				
SPIRIT Section	**Item No.**	**Item Description**	**SPIRIT-Pro Extension**	**Addressed on Page No.**
Administrative Information				
Title	1	Descriptive title identifying study design, population, interventions, and if applicable, trial acronym		Title page
Trial registration	2a	Trial identifier and registry name (if not yet registered, name of intended registry)		4, 18
	2b	All items from the World Health Organization Trial Registration Data Set		N/A
Protocol version	3	Date and version identifier		Footer
Funding	4	Sources and types of financial, material and other support		18
Roles and responsibilities	5a	Names, affiliations and roles of protocol contributors		4, 18
	5b	Name and contact information for trial sponsor		1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities		N/A
	5d	Composition, roles and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team and other individuals or groups overseeing the trial, if applicable		N/A
Introduction				
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Description of the PRO-specific research question and rationale for PRO assessment. Summary of PRO findings in relevant studies	4, 6-8 11-12
	6b	Explanation for choice of comparators		8
Objectives	7	Specific objectives or hypotheses	Statement of PRO objectives or hypotheses (including relevant PRO concepts/domains)	8 11-12
Trial design	8	Description of trial design, including type of trial (e.g. parallel group, crossover, factorial, single group), allocation ratio, and framework (e.g. superiority, equivalence, non-inferiority, exploratory)		8
Methods: Participants, Interventions and Outcomes				
Study setting	9	Description of study settings (e.g. community clinic, academic hospital) and list of countries where data will be collected; reference to where list of study sites can be obtained		1
Eligibility criteria	10	Inclusion and exclusion criteria for participants; if applicable, eligibility for study centres and individuals who will perform the interventions (e.g. surgeons, psychotherapists)	Specify any PRO-specific eligibility criteria (e.g. language/reading requirements or pre-randomisation completion of PRO). If PROs will not be collected from the entire sample, provide rationale and describe the method for obtaining the PRO sub-sample.	8-9
Interventions	11a	Interventions for each group with sufficient data detail to allow replication, including how and when they will be administered		10

SPIRIT 2013 Checklist with SPIRIT-PRO Extensions

SPIRIT Section	Item No.	Item Description	SPIRIT-Pro Extension	Addressed on Page No.
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (e.g. drug dose change in response to harms, participant request, or improving/worsening disease). (Stopping rules)		15
	11c	Strategies to improve adherence to intervention protocols and any procedures for monitoring adherence (e.g. drug tablet return, laboratory tests)		N/A (Interventions are intra-operative.)
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial		N/A
Outcomes	12	Primary, secondary and other outcomes, including the specific measurement variable (e.g. systolic blood pressure), analysis metric (e.g. change from baseline, final value, time to event), method of aggregation (e.g. median, proportion), and time point for each outcome	Specification of the PRO concepts/domains used to evaluate the intervention (e.g. overall health-related quality of life, specific domain, specific symptom) and for each one, the analysis metric (e.g. change from baseline, final value, time to event) and the principal time point or period of interest	11-13
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments and visits for participants; a schematic diagram is highly recommended	Inclusion of a schedule of PRO assessments, providing a rationale for the time points and justifying if the initial assessment is not pre-randomisation. Specification of time windows, whether PRO collection is prior to clinical assessments and if using multiple questionnaires, whether order of administration will be standardised.	11-13, 20
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumption supporting any sample size calculations	When a PRO is the primary end point, statement of the required sample size (and how it was determined) and recruitment target (accounting for expected loss to follow-up). If sample size is not established based on the PRO end point, then discuss the power of the principal PRO analyses.	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size		9
Methods: Assignment of Interventions (for Clinical Trials)				
Allocation Sequence generation	16a	Method of generating the allocation sequence (e.g. computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (e.g. blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions.		9
Concealment mechanism	16b	Mechanism of implementing the allocation sequence (e.g. central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned		9
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions		9
Blinding (masking)	17a	Who will be blinded after assignment to interventions (e.g. trial participants, care providers, outcome assessors, data analysts) and how		9

SPIRIT 2013 Checklist with SPIRIT-PRO Extensions

SPIRIT Section	Item No.	Item Description	SPIRIT-Pro Extension	Addressed on Page No.
	17b	If blinded, circumstances under which unblinding is permissible and procedure for revealing a participant's allocated intervention during the trial		10
Methods: Data Collection, Management and Analysis				
Data Collection Methods	18a	Plans for assessment and collection of outcome, baseline and other trial data, including any related processes to promote data quality (e.g. duplicate measurements, training of assessors) and description of study instruments (e.g. questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Justification of the PRO instrument to be used and description of domains, number of items, recall period and instrument scaling and scoring (e.g. range and direction of scores indicating a good or poor outcome). Evidence of PRO instrument measurement properties, interpretation guidelines and patient acceptability and burden if available, ideally in the population of interest. Statement of whether the measure will be used in accordance with any user manual, and specification and justification of deviations if planned.	12-13
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Specification of PRO data collection management strategies for minimising avoidable missing data. Description of process of PRO assessment for participants who discontinue or deviate from the assigned intervention protocol.	13
Data management	19	Plans for data entry, coding, security and storage, including any related processes to promote data quality (e.g. double data entry, range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol		19
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol		17
	20b	Methods for any additional analyses (e.g. subgroup and adjusted analyses)		N/A
	20c	Definition of analysis population relating to protocol non-adherence (e.g. as randomised analysis) and any statistical methods to handle missing data (e.g. multiple imputation)		17
Methods: Monitoring				
Data monitoring	21a	Composition of data monitoring committee; summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a data monitoring committee is not needed		16
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial		16-17
Harms	22	Plans for collecting, assessing, reporting and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	State whether or not PRO data will be monitored during the study to inform the clinical care of individual trial	15, 18

SPIRIT 2013 Checklist with SPIRIT-PRO Extensions				
SPIRIT Section	**Item No.**	**Item Description**	**SPIRIT-Pro Extension**	**Addressed on Page No.**
			participants, and if so, how this will be managed in a standardised way. Describe how this process will be explained to participants (e.g. in the Participant Information Sheet and Consent Form)	
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and sponsor(s).		16
Ethics and Dissemination				
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board approval		18
Protocol amendments	25	Plans for communicating important protocol modifications (e.g. changes to eligibility criteria, outcomes, analyses) to relevant parties (e.g investigators, research ethics committees/institutional review boards, trial participants, trial registries, journals, regulators)		18
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates and how (see item 32)		9
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable		N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared and maintained to protect confidentiality before, during and after the trial		19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site		18
Access to data	29	Statement of who will have access to the final trial data set and disclosure of contractual agreements that limit such access for investigators		19
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who are harmed by trial participation		18
Dissemination policy Trial results	31a	Plans for investigators and sponsor(s) to communicate trial results to participants, health care professionals, the public and other relevant groups (e.g. via publication, reporting in results databases, or other data-sharing arrangements), including any publication restrictions		19
Authorship	31b	Authorship eligibility guidelines and any intended use of professional writers		19
Reproducible research	31c	Plans, if any, for granting public access to the full protocol, participant-level data set, and statistical code		19
Appendices				
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates		32
Biological specimens	33	Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable		N/A

APPENDICES

Appendix 1. Surgical Technique (As Per Verasense™ Protocol)

Establish Tibial Tray Rotation

Select and position the appropriately sized trial tibial tray. Align the tray to the anatomy (mid-medial third of the tubercle), as recommended by the manufacture's surgical technique. Insert a single anterior or posterior pin (medially or laterally) into the trial tray to allow for internal/external rotational adjustment while maintaining optimal medial/lateral coverage. (Figure 2.)

Figure 2. View of proximal tibia referencing the mid-medial third of tibial tubercle

Sensor Insertion

Insert the sensor with the appropriately sized shim attached to replicate the thickness of the standard trial insert. In a tight knee capsule, it may be necessary to insert the sensor prior to insertion of the femoral trial. DO NOT utilise excessive force or impact the sensor directly with a mallet. (Figure 3.)

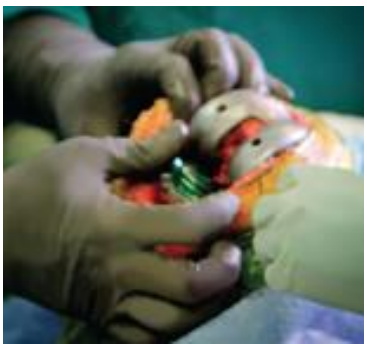


Figure 3. Verasense™ Sensor activated and inserted into the knee

Establish Tibial Tray Rotation Using Contact Points

With the leg supported in 10° flexion, rotate the tibial tray to the most posterior contact point (internally or externally) as needed to horizontally align the medial and lateral contact points within 5° of each other. See reference protocol found in Appendix I for how to hold the leg using Verasense™. A positive (+) value in the Contact Point Rotation (CP Rotation box) indicates internal rotation (IR); a negative (-) value indicates external rotation (ER). (Figures 4-6.)

When preferred tray rotation is achieved (within 5° Contact Point Rotation):

- Add additional pin to stabilize tray
- Flex knee and confirm patellar tracking
- Record the final value

Figure 4. Sensor as displayed on graphical user interface. CP (Contact Point) Rotation degree [in red box] references the degree of tibiofemoral incongruity. Yellow circles correspond to femoral contact points. The number 8 represents total pounds of pressure in the medial and lateral compartments.

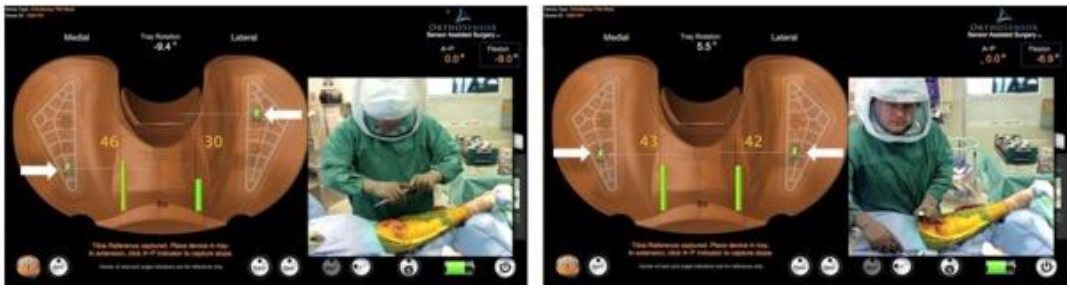


Figure 5. Left: Medial and lateral femoral contact points (indicated by white arrows) demonstrate tibiofemoral rotational incongruency, due to excessive IR of the tibial tray. Right: After correcting for IR, the femoral contact points demonstrate symmetry (indicated by white arrows).

Figure 6. Left: Example of excessive ER (indicated by white arrows), as a result of referencing the mid-third of the tibial tubercle, shown by the sensor interface. Middle: Trial tibial/femoral components in place with the sensor; tibial tray visually and digitally exhibiting external rotation. Right: The tibial tray is rotated to improve congruency, as seen by the parallel contact points (indicated by white arrows) on the sensor interface.

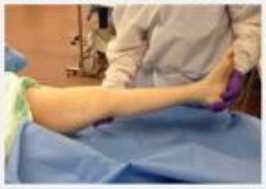
Balance Soft Tissue Sleeve

Once tibial tray rotation has been assessed, the medial and lateral compartment pressures are evaluated in the coronal and sagittal planes. The soft tissue gaps are evaluated and recorded at 10°, 45°, and 90° of flexion, with the hip in neutral rotation and the femur supported just proximal to the knee. The capsule must be closed provisionally during assessment at each pose using a towel clip placed above and below the patella in the medial retinaculum. Incremental balancing using a pie-crusting technique with an 18-gauge needle is recommended to address ligamentous tension when necessary. Additional bony resections may be necessary for excessive loading (refer to Surgical Reference Guide in Appendix 2 and 3). Previous research evaluating the use of Verasense™ during TKA suggests a load differential of up to 15 psi or less between the medial and lateral condyles is indicative of soft-tissue balance [11] (Figure 7). These balancing parameters are the target in the SGB group.

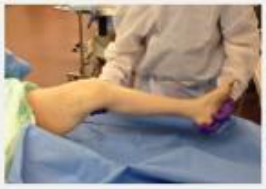
Figure 7. Left: The mediolateral inter-compartmental difference, pre-release, is 42 psi. This value exceeds the 15 psi limit, thus classifying this joint as 'unbalanced.' Right: The mediolateral inter-compartmental difference, post-release, is 1 psi, and was classified as 'balanced' upon closing.

Appendix 2. Holding the leg for Verasense™ Pressure Calculations

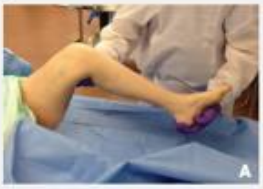
HOLDING THE LEG For the correct depiction of intra-articular loading, in extension and flexion, the leg must be held with posterior support:

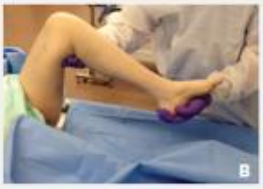


Step 1.
With the leg in extension, one hand is placed on the heel of the operative leg; one hand is placed under the backside of the knee, at the posterior capsule.



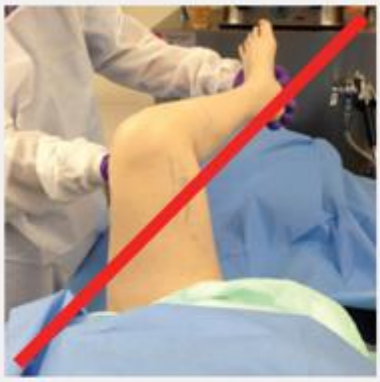
Step 2.
Initial evaluation of soft tissue should always be assessed with the leg flexed in 10° with the posterior capsule relaxed and the screw home mechanism disengaged. Failure to do so could result in the over-releasing of soft-tissue, as loads tend to increase during terminal extension due to the screw home mechanism.



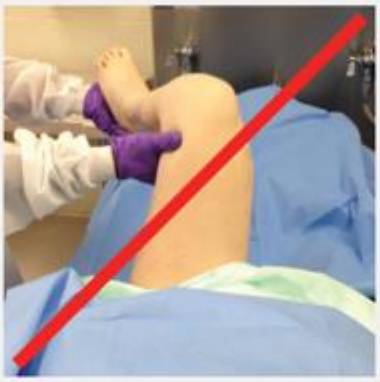


Step 3.
Soft tissues should continue to be evaluated at 45° (FIG A) and 90° of flexion (FIG B). If using a cruciate retaining component, an intraoperative posterior drawer test will allow the surgeon to assess PCL stability using the VERASENSE tracking option (FIG C).

HOLDING THE LEG (CONTINUED)



INCORRECT
Abducted/Externally Rotated



INCORRECT
Adducted/Internally Rotated

CORRECT
Neutral Position

Appendix 3. Balancing of the Varus Knee

SURGICAL TECHNIQUE QUICK REFERENCE

Authored By: Martin W. Roche, M.D.
Holy Cross Hospital, Fort Lauderdale, FL
Patrick A. Meere, M.D.
NYU Langone Medical Center, New York, NY

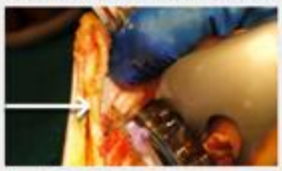
Assess soft-tissue load references with **joint reduced and capsule closed**. Only address soft-tissues after loads have been assessed in both **extension and flexion (10°-90°)**. After any tissue release, the **leg should be "cycled"** (taken through the range of motion) several times.

APPROACH TO VARUS KNEE

TIGHT IN EXTENSION - MEDIALLY

SENSOR PRESENTATION:

SURGICAL CONSIDERATION:



Evaluate MCL

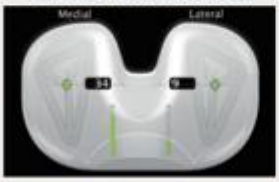
Palpate fibers of MCL to assess tension. Release **posterior fibers of MCL** (both deep and superficial).

Evaluate Medial Posterior Capsule

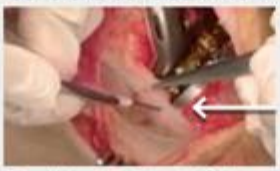
Release medial posterior capsule and/or semimembranousus at tibial attachment site.

TIGHT IN FLEXION - MEDIALLY

SENSOR PRESENTATION:



SURGICAL CONSIDERATION:



Condition 1. **Evaluate MCL**

Palpate fibers of MCL to assess tension. Release **anterior fibers of MCL** (both deep and superficial).

SENSOR PRESENTATION:

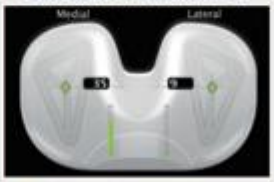
SURGICAL CONSIDERATION:

Condition 2. **Evaluate PCL**

If medial femoral contact point exhibits excessive tension and posterior positioning, release **anterolateral bundle PCL fibers.**

TIGHT IN FLEXION AND EXTENSION - MEDIALLY

SENSOR PRESENTATION:



SURGICAL CONSIDERATION:

Condition 1. **Loads 20-40 lbs.**

Extension Balancing:

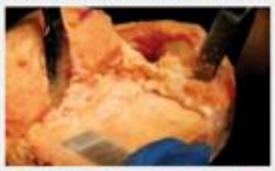
- Posterior MCL fibers released if in tension; loads rechecked.
- Posterior medial capsule checked for tension and released, if needed; loads re-checked.
- If necessary, semimembranosus can be released.

Flexion Balancing:

- Anterior MCL fibers released if in tension; loads rechecked.

SENSOR PRESENTATION:

SURGICAL CONSIDERATION:



Condition 2. **Loads > 40 lbs.**

If loads beyond 40 lbs. are displayed, consider recutting the tibia plateau **to add additional varus** alignment.

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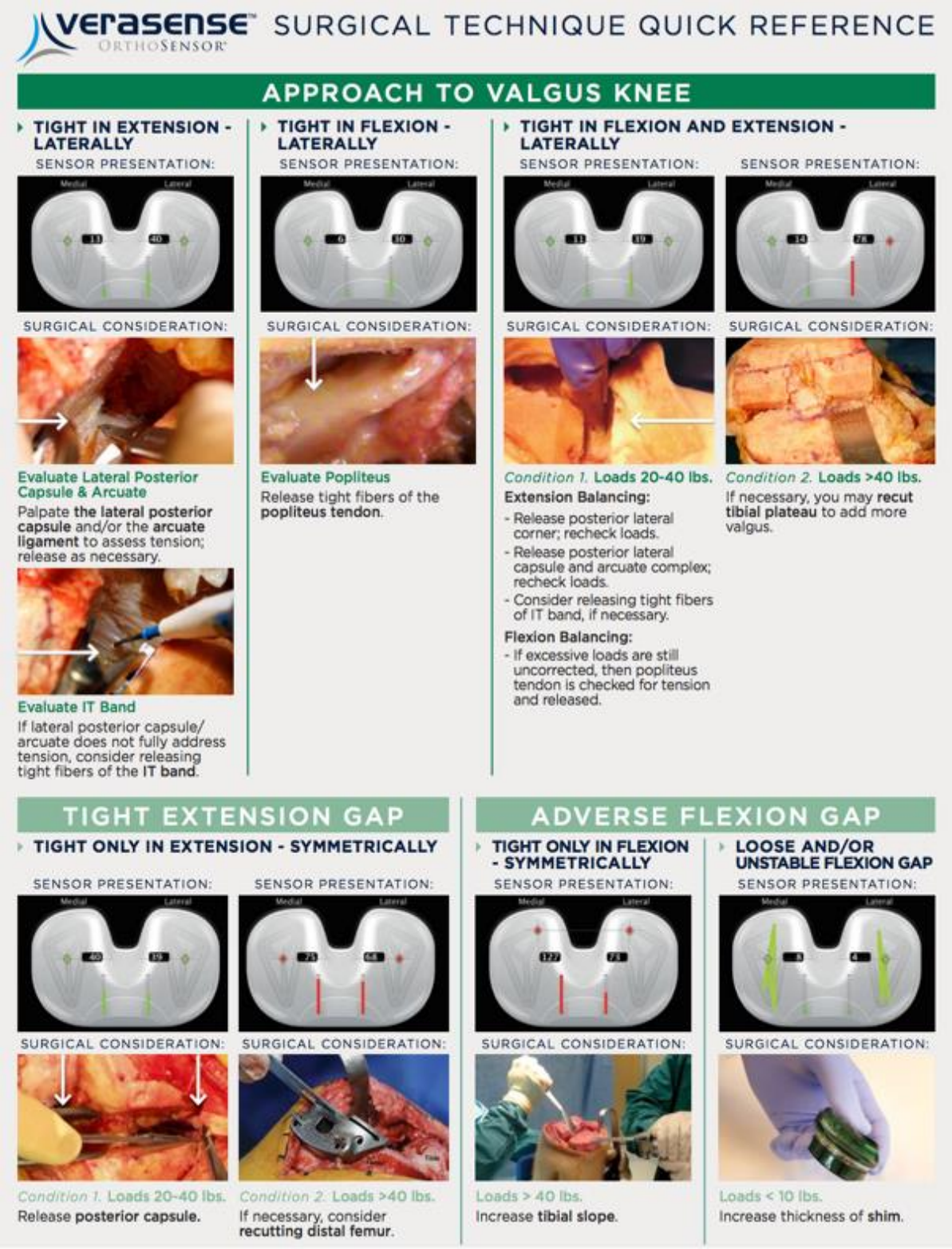
Training and Education Training@OrthoSensor.com

Appendix 4. Balancing of the Valgus Knee



Appendix 5. Participant Information Sheet and Consent Form

See link at Sydney Knee Specialists website: http://www.sydneyknee.com.au/.

REFERENCES

1. Ali, A., et al., *Dissatisfied patients after total knee arthroplasty: a registry study involving 114 patients with 8-13 years of followup.* Acta Orthop, 2014. **85**(3): p. 229-33.
2. Choi, Y.J. and H.J. Ra, *Patient Satisfaction after Total Knee Arthroplasty.* Knee Surg Relat Res, 2016. **28**(1): p. 1-15.
3. Williams, D.P., et al., *Early postoperative predictors of satisfaction following total knee arthroplasty.* Knee, 2013. **20**(6): p. 442-6.
4. ACORN, A.C.O.R. *ACORN Annual Report, 2015*. 2015 2015; Available from: http://www.acornregistry.org/images/ACORN_AnnualReport_2015.pdf.
5. Dunbar, M.J., G. Richardson, and O. Robertsson, *I can't get no satisfaction after my total knee replacement: rhymes and reasons.* Bone Joint J, 2013. **95-b**(11 Suppl A): p. 148-52.
6. Sakellariou, V.I., et al., *Risk Assessment for Chronic Pain and Patient Satisfaction After Total Knee Arthroplasty.* Orthopedics, 2016. **39**(1): p. 55-62.
7. Nam, D., R.M. Nunley, and R.L. Barrack, *Patient dissatisfaction following total knee replacement: a growing concern?* Bone Joint J, 2014. **96-B**(11 Supple A): p. 96-100.
8. Scott, C.E., et al., *Predicting dissatisfaction following total knee arthroplasty in patients under 55 years of age.* Bone Joint J, 2016. **98-B**(12): p. 1625-1634.
9. MacDessi, S. and M. Gharaibeh, *Accuracy of Manual Surgeon-Defined Assessment of Soft Tissue Balance in TKA In Comparison to Sensor-Guided Measures and its Effect on Final Balance.* Orthopaedic Journal of Sports Medicine, 2017. **5**(5_suppl5): p. 2325967117S00161.
10. Gustke, K., *Use of smart trials for soft-tissue balancing in total knee replacement surgery.* J Bone Joint Surg Br, 2012. **94**(11 Suppl A): p. 147-50.
11. Gustke, K.A., et al., *A new method for defining balance: promising short-term clinical outcomes of sensor-guided TKA.* J Arthroplasty, 2014. **29**(5): p. 955-60.

12. Gustke, K.A., et al., *Increased satisfaction after total knee replacement using sensor-guided technology.* Bone Joint J, 2014. **96-b**(10): p. 1333-8.
13. Elmallah, R.K., et al., *Can We Really "Feel" a Balanced Total Knee Arthroplasty?* J Arthroplasty, 2016. **31**(9 Suppl): p. 102-5. Fix numbers hereafter.
15. Doyle, D.J. and E.H. Garmon, *American Society of Anesthesiologists Classification (ASA Class)*, in *StatPearls*. 2017, StatPearls Publishing LLC.: Treasure Island (FL).
16. Roos, E.M. *The 2012 User's Guide to: Knee injury and Osteoarthritis Outcome Score (KOOS)*. 2012 [cited 2018 29th April]; Available from: http://www.koos.nu/index.html.
17. Roos, E.M. and L.S. Lohmander, *The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis.* Health Qual Life Outcomes, 2003. **1**: p. 64.
18. Scuderi, G.R., et al., *The new Knee Society Knee Scoring System.* Clin Orthop Relat Res, 2012. **470**(1): p. 3-19.
19. Hamilton, D.F., et al., *Validation of the English language Forgotten Joint Score-12 as an outcome measure for total hip and knee arthroplasty in a British population.* Bone Joint J, 2017. **99-b**(2): p. 218-224.
20. *EuroQol--a new facility for the measurement of health-related quality of life.* Health Policy, 1990. **16**(3): p. 199-208.
21. Herdman, M., et al., *Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L).* Qual Life Res, 2011. **20**(10): p. 1727-36.
22. Chauhan, S.K., et al., *Computer-assisted total knee replacement. A controlled cadaver study using a multi-parameter quantitative CT assessment of alignment (the Perth CT Protocol).* J Bone Joint Surg Br, 2004. **86**(6): p. 818-23.
23. Sikorski, J.M., *Alignment in total knee replacement.* J Bone Joint Surg Br, 2008. **90**(9): p. 1121-7.
24. Naylor, J.M., et al., *Validity and reliability of using photography for measuring knee range of motion: a methodological study.* BMC Musculoskelet Disord, 2011. **12**: p. 77.

25. Podsiadlo, D. and S. Richardson, *The timed "Up & Go": a test of basic functional mobility for frail elderly persons.* J Am Geriatr Soc, 1991. **39**(2): p. 142-8.
26. Ko, V., et al., *The six-minute walk test is an excellent predictor of functional ambulation after total knee arthroplasty.* BMC Musculoskelet Disord, 2013. **14**: p. 145.
27. Collins, N.J., et al., *Knee Injury and Osteoarthritis Outcome Score (KOOS): systematic review and meta-analysis of measurement properties.* Osteoarthritis Cartilage, 2016. **24**(8): p. 1317-29.
28. Skou, S.T., et al., *A Randomized, Controlled Trial of Total Knee Replacement.* N Engl J Med, 2015. **373**(17): p. 1597-606.