RESEARCH PROTOCOL

Date	January 9, 2017
Title	Using Intraoperative Sensing Technology to Evaluate Revision TKA
Research Sponsor	OrthoSensor, Inc., Dania Beach, FL USA
Principal Investigator	William Leone, MD
Department	The Leone Center for Orthopedic Care, Holy Cross Hospital, Fort Lauderdale, FL USA

Project Summary/Abstract

This study will attempt to draw relationships between the soft-tissue related complications contributing to early TKA revision and the loading and positional patterns from intraoperative tibial trial sensors. The data from the sensors may enable the surgeon to address such soft-tissue abnormalities that may otherwise be unknown during traditional total knee revision procedures. The utilization of sensors should in theory, help diagnose the potential causes attributing to soft-tissue imbalance and may lead to a decreased need for an all component revision. Furthermore, the economic implications from converting a total revision to a partial revision could have a profound effect to the patient and healthcare provider such as decreased rehabilitation regimes and opportunity for cost savings. Eligible revision patients who agree to participate will be followed for a period of 12 months following the revision procedure. Patient reported outcomes measures (PROM) such as the 2011 Knee Society Score (KSS) and the Veterans Rand 12-Item Health Survey (VR-12) will be collected at baseline (pre-operatively) and at 6 weeks, 6 months and 12 months post-procedure. All outcomes will be scored to observe changes from baseline at 12-months. Cost-analyses of sensor-assisted revision TKA will be performed to include OR costs, facility and physician fees, as well as payments to post-acute collaborators such as SNFs, rehab hospitals, PT and home care providers. A quantitative analysis of commercial payer claims / usage data (e.g., CMS Medpar data) will be used to examine costs associated with traditional revision TKA procedures.

Purpose of Study

A. Research Objective:

Primary: The objective is to evaluate and link the possible causes of early TKA revision procedures using intraoperative sensors in effort to understand why knees fail in addition to examining the economic implications to the patient and hospital.

Secondary: To observe changes in patient reported outcome measures from baseline at 12-months. Patients will be stratified by diagnosis and revision type (partial / total) to observe changes in outcome measures.

B. Hypothesis or Research Question

This study is observational and not intended to be a hypothesis driven trial. However, it is believed that sensor guidance during revision TKA may lead to a decreased need for all component revision while optimizing post-operative satisfaction and clinical outcomes.

Background and Significance

Several advances in technology have been incorporated into total knee arthroplasty over the past decade to improve clinical outcomes and implant survivorship. Yet despite these advances, revision rates of TKA are expected to rise[1]. While total hip arthroplasty revision rates have steadily declined over the past several years, the revision rate for TKA is projected to increase fivefold by 2030 despite improvements in infection control, surgical methods, innovative prosthesis designs, and accelerated rehabilitation programs[2,3]. "Early" revision is typically defined as occurring within five years of the primary procedure, and is considered a devastating failure for both the patient and physician[4]. Fehring, et al. found that as many as 63% of TKA failures occur within the first five years[4]. Of these early failures, 35% can be attributed to soft tissue imbalances[5]. Ligamentous alignment and component attenuation are intrinsically linked[2]. Imbalance may manifest as stiffness, instability, prosthetic loosening, tibiofemoral incongruency, or as defects in patellofemoral tracking[6]. In a study by Babazadeh, et al., 86% of knees with asymmetrical component wear lacked ligamentous balance. This study also found that balanced knees have a significantly lower rate of prosthetic loosening. Micromotion in an asymmetric joint may result in accelerated osteoclast activity leading to osteolysis and component loosening or failure[6]. Sharkey, et al. reviewed the etiology of revision in 781 failed TKAs and determined that aseptic loosening was most common cause along with a significant number of revisions due to instability[5]. If all total knee replacements exhibited proper soft-tissue balance, the rate of early failures would improve by 40%, and the overall TKA failure rate by 25%.

However, the use of advanced technology to understand why total knee arthroplasties fail today has not been extensively evaluated. A recent development has made it possible to embed microelectronics into the standard tibial trial (VERASENSE, OrthoSensor, Inc., Dania Beach, FL). This array of sensors provides dynamic, intraoperative feedback regarding tibiofemoral position and quantitative pressure at peak contact points in the medial and lateral compartments during total knee arthroplasty (TKA) trialing. Using sensor-derived data, the surgeon can now evaluate intercompartmental loading throughout the range of motion (ROM) and correct for soft-tissue abnormalities while receiving real-time feedback regarding joint position and the tibiofemoral relationship defined by the contact point location. Utilization of these sensors during revision TKA should in theory, help diagnose the potential causes of revision if they relate to soft tissue imbalance.

Research Plan

A. Study Design

- Prospective, multicenter, single-cohort evaluation of patients undergoing sensor-assisted revision total knee arthroplasty
- All eligible patients will be asked to participate and sign informed consent
- The surgeon will use Verasense on all patients. Data will be electronically captured by designated research personnel.
- Patients will be assessed preoperatively and will have standard of care follow up appointments at 6 weeks, 6 months and 12 months.
    - During these visits the following outcome measures will be assessed:
        - ✓ New Knee Society Score (KSS)[7]
        - ✓ The Veterans Rand 12-Item Health Survey (VR-12)

B. Setting

The study will be conducted at institutions within the United States.

C. **Participants**: Patients requiring revision total knee arthroplasty will be recruited from the respective clinical practice at the participating institutions. Up to 200 patients will be enrolled and followed for a period of 12 months in order to assess patient outcomes. Any patient who is a candidate for revision TKA and meets all inclusion and no exclusion will be offered study participation without regard to race, sex, economic status, or religious belief.

Inclusion criteria:

- Patients undergoing revision unilateral total knee arthroplasty within the first 5-years of the index procedure
    a. Include Male and Female subjects
    b. Include subjects 18 years and older
- Patients should present with idiopathic pain and/or instability/stiffness attributed to aseptic loosening, polyethylene wear or malrotation
- Patients able to understand study intent, and agree to study participation
- Patients must be previously implanted with the following cruciate-retaining (CR) or posterior-substituting (PS) total knee systems: Stryker TRIATHLON, Zimmer-Biomet VANGUARD or NEXGEN or Smith and Nephew LEGION or JOURNEY II.

Exclusion criteria:

- No prior revision surgery on operative side
- Ligament insufficiencies, prior surgeries such as PCL reconstructions, posterolateral reconstructions, osteotomies, tibia plateau fractures
- Culture positive aspiration indicating infection of the joint
- ASA class > III
- History of drug or alcohol abuse

Methods/Procedures:

At the time of the revision procedure, the implanted polyethylene will be removed and the corresponding VERASENSE insert type will be placed with the original implanted components still intact. With the patella reduced and the capsule provisionally closed, the knee will be taken through a range of motion to record and observe contact point location and medial and lateral loading at 10, 45, and 90 degrees of flexion as dictated by VERASENSE. Kinematic tracking embedded in the computer software will be engaged to observe femoral rollback patterns in each respective knee. Once the pre-revision “diagnostic” data is recorded, the surgeon will proceed with the standard of care revision procedure. Dependent upon the complexity of the case and output of the VERASENSE data, the surgeon may elect to salvage some or all of the original implanted components or choose to completely revise the knee with the preferred implant system. All revision cases will be cataloged by type (“partial” or “total”). A “partial” revision will be indicated when only the tibial liner is changed or only the tibial liner with the tibial tray or only the tibial liner with the femoral component; A “total” revision will be indicated when all components are completely removed and replaced (tibial tray, femoral component and tibial liner). The VERASENSE sensor will be utilized for final balancing prior to completing the partial or total revision procedures and loading and positional data will be documented once again. All surgical corrections made (i.e.,

bony resections and/or soft tissue releases) during the revision procedure will be documented.

D. Data Collection

- Demos/History/Clinical: Patient's age at time of surgery, gender, ethnicity, height/weight and body mass index, occupational status, health insurance type, tobacco and alcohol use. Patients medical history and comorbidities will be obtained as well as principal / secondary diagnosis and pre-operative plan for revision (i.e., total revision, partial revision). Preoperative radiographs (AP, lateral and skyline views) should be taken as standard of care.

- Intra-operative /discharge data: OR and tourniquet times, surgical technique and approach, operative complications (if applicable), length of stay and discharge destination. Pre and post-revision sensor data will be obtained (operative findings / operative action/surgical correction). Length of stay and discharge status will be captured as well as any post-operative complications and readmissions within 90 days of discharge following the revision procedure.

- Clinical Outcome Measures: Dependent variables or outcome variables will be collected pre-operatively and at 6 weeks, 6 months and 12 months post-operatively. The outcomes measures will include the 2011 Knee Society Score and THE VETERANS RAND 12-ITEM HEALTH SURVEY (VR-12).

- Cost Data: Hospital cost data including OR costs, facility and physician fees, as well as payments to post-acute collaborators such as SNFs, rehab hospitals, PT and home care providers will be collected. MEDPAR data from Centers for Medicare and Medicaid (CMS) will be used as benchmark to understand the national averages of hospital cost, hospital charges and average reimbursement. Implant cost data will be obtained from literary sources and market reports.

***Data Sheet**:* See attached data sheets.

E. Study Device

Verasense™ is developed by Orthosensor Inc., Dania Beach, Florida, USA and is FDA approved for commercial distribution in the United States. The 510(k) number is K090474.

F. Statistical Analysis

Analysis of the data will be performed using SPSS version 21. Comparative Statistics will be run between outcomes data stratified by revision type: Analysis of variance (AVOVA) will be used to assess the difference between groups stratified by reasons for revision, with post-hoc TUMHANE'S test to demonstrate significance. Separate analyses will be performed to evaluate power of sample sizes and any correlative affect that demographic/clinical variables may have on patient outcomes. The alpha value is 0.05 with a lower power threshold of 0.7.

G. Ethical Considerations

a. **Informed consent:** Research assistants/coordinators will obtain patient consent and the consent statements will be kept in a secure location. Copy of the informed consent statement is attached.

b. Privacy information: The data will be stored electronically on a restricted access network folder and will only be accessible to the investigator and research team. The information collected does not include information that may be damaging to the individual should it be wrongfully disclosed. Data sheets may be used in the collection of data, however, will not document PHI. Data analysis will be performed using only the de-identified database. No data will be disclosed to another institution and all identifiers linking to the patient will be destroyed after data collection is complete.

c. **Confidentiality and Management of Data**: The data will be stored and will only be accessible to the investigator, research team and OrthoSensor. Data sheets may be used in the collection of data, however, will not document PHI. Data analysis will be performed using only the de-identified data. Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act (HIPAA). Patient data will be entered into electronic spreadsheets. One spreadsheet (the correlation tool) will contain the patient name, medical record number, and patient study number. The second spreadsheet will contain the patient study number, as well as all of the variables required by the study. The two spreadsheets will be stored as separate files. De-identified data will be provided to the Research Specialist for data analysis. Any paper records will be stored in hard copy in a locked filing cabinet for a minimum of five years. At this time the information will be shredded.

d. Risks/Benefits of participation: There are no risks to participants. This study is intended for observational purposes only. There are no costs to exceed those associated with the standard of care which currently exists. This could potentially benefit those patients who are undergoing traditional revision TKA but this is not yet known.

H. Estimated Period of Time to Complete

When will study begin?	*February 2017*
IRB Approval	*3 weeks*
Data collection	*~2 years*
Data analysis	*1 month*
Presentation development (if applicable)	*1 month*
Manuscript Development (if applicable)	*3 months*
Journal submission process (if applicable)	*3-6 months*
Study closure	*1 year*

When and how will results be disseminated?

- OrthoSensor will notify the Investigator when adequate data have been collected or when the clinical evaluation is terminated for any reason.
- The data collected in this study will be analyzed and compiled into a report for review by the Investigator per the contracted agreement between the Investigator/Institution and OrthoSensor. The results will be published in a scientific medical journal and will be presented at National and International congresses and symposia.

I. Contact Information

For assistance or questions regarding this evaluation, please contact the Department of Clinical Research at OrthoSensor, Inc as indicated below:

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Clinical Research Associate	Leah Elson Phone: 951-577-7343 E-mail: lelson@orthosensor.com

References:

1. Kurtz SM, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg. 2007; 89-A:780--785.

2. Kurtz S, Mowat F, Ong K, Chan N, Lau E, Halpern M. Prevalence of primary and revision total hip and knee arthroplasty in the United States from 1990 through 2002. J Bone Joint Surg Am. 2005;87:1487-97.

3. Bansal A, Khatib ON, Zuckerman JD. Revision Total Joint Arthroplasty: The Epidemiology of 63,140 Cases in New York State. The Journal of Arthroplasty. 2014 Jan; 29(1): 23–27.

4. Fehring TK, Odum SM, Griffin W, et al. Early failures in total knee arthroplasty. Clin Orthop Relat Res 2001;392:315.

5. Sharkey PF, Hozack WJ, Rothman RH, Shastri S, Jacoby SM. Why are total knee arthroplasties failing today? Clin Orthop Relat Res 2002;404:7-13.

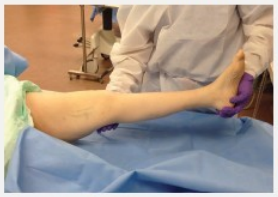
6. Babazadeh S, Stoney JD, Lim K, Choong PF. The relevance of ligament balancing in total knee arthroplasty: how important is it? A systematic review of the literature. Orthop Rev (Pavia). 2009 Oct 10; 1(2): e26.

7. Scuderi GR, et al. The new Knee Society Scoring system. Clin Orthop 2012;470:3-19

Appendix I

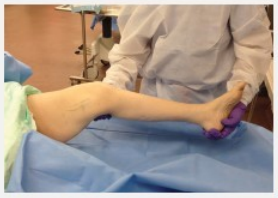
Holding the Leg using Verasense

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



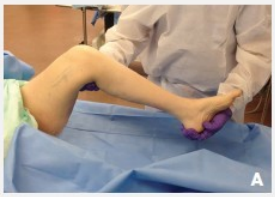
Step 1.

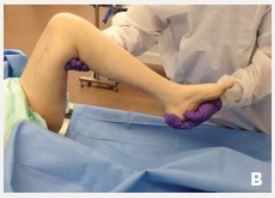
With the leg in extension, one hand is placed on the heel of the operative leg; one hand is placed under the backside of the knee, at the posterior capsule.

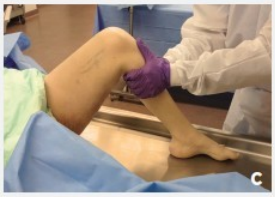


Step 2.

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.



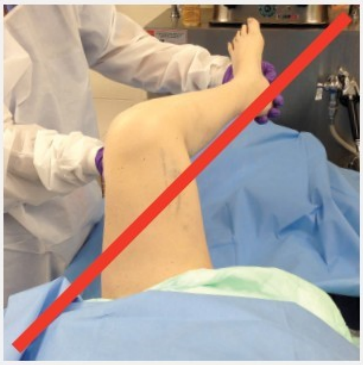




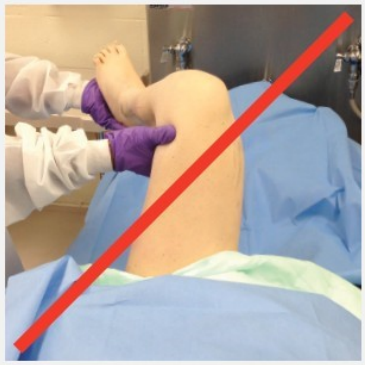
Step 3.

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).

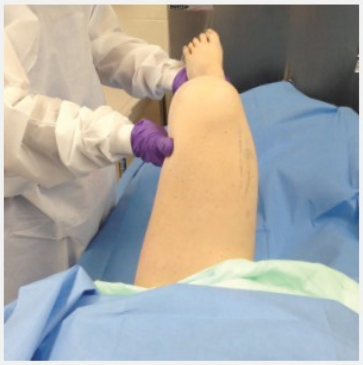
HOLDING THE LEG (CONTINUED)



INCORRECT
Abducted/Externally Rotated



INCORRECT
Adducted/Internally Rotated



CORRECT
Neutral Position