TSolution One® Total Knee Arthroplasty Clinical Trial

Protocol Number: 16-PROTO-01

Sponsor: Think Surgical, Inc.

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Version 6.0: 09 SEP 2019

REVISION HISTORY

Ver.	Date	Summary of Changes
1.0	05 JUL 2016	Original Version
2.0	13 JAN 2017	Increased time permitted between baseline and surgery from 30 days to 90 days.
3.0	12 JUL 2017	Moved comparison of pre- and post-op alignment from a secondary effectiveness endpoint to a primary effectiveness endpoint to address study design considerations.
3.1	18 SEP 2017	Added clarification to state that post-operative alignment outcomes will be compared to surgeon's pre-operative alignment goals versus neutral alignment.
4.0	24 OCT 2017	Increased subject follow-up time from 3 months to a minimum of 6 months and a maximum of 12 months. Clarified that all patients with AEs at the final study visit (6M or 12M) will be followed until AE resolution or termination of study. Added clarification for patients who are to be excluded under Exclusion Criterion 'c'. Added Change Summary table after title page.
5.0	07 DEC 2018	Update contact information. Corrected footnote (b) under the Schedule of Procedures to reflect standard of care pre-operative and post-operative blood work.
6.0	09 SEP 2019	Add Continued Access arm to study design. Update Sections 1.0, 5.0, 5.1, 5.2, 6.5, 7.0, 7.1, 7.3, 7.4, 7.5, 7.6, 7.7, 9.1, 9.2, 9.3 and 15.0 to clarify requirements for Continued Access arm. Add Table 3 with Schedule of Procedures for Continued Access arm. Update MCRA CRO address in Section 16.0. Add administrative clarification regarding treatment of patients that withdraw consent or are withdrawn by the PI before surgery in Section 6.5. Add administrative clarification regarding data collection requirements for Unscheduled Visits in Section 7.8. Add administrative clarifications regarding Adverse Event follow up requirements in Schedule of Procedures (Tables 2 and 3) and Sections 8.1, 10.2 and 10.8. Add administrative clarifications regarding stopping rules for safety concerns in Sections 8.5 and 10.7.

PROTOCOL APPROVAL SIGNATURE PAGE

Protocol Number: 16-PROTO-01

Protocol Title: TSolution One Total Knee Arthroplasty Clinical Trial

Protocol Version: Version 6.0

Protocol Date: 09-SEP-2019

This protocol has been read and approved by:

SPONSOR:

Joel Zuhars
Director of Engineering, THINK Surgical Inc.

Date (dd/mmm/yyyy)

CRO:

Iman Ahmad
Director, Clinical Affairs, MCRA, LLC

Date (dd/mmm/yyyy)

Dave McGurl
Director, Regulatory Affairs, MCRA, LLC

Date (dd/mmm/yyyy)

Greg Tullo
Director, Data Management & Biostatistics, MCRA, LLC

Date (dd/mmm/yyyy)

INVESTIGATOR SIGNATURE PAGE

I have read and understand the "TSolution One® Total Knee Arthroplasty Clinical Trial" protocol (16-PROTO-01), and will conduct the study in accordance with this protocol, all attachments and amendments, applicable Food and Drug Administration regulations, HIPAA, and local regulations, and the policies of local IRB and institutions where the study will take place.

In my formal capacity as Investigator, my duties include ensuring the safety of the study patients enrolled under my supervision and providing THINK Surgical, Inc.™ with complete and timely information, as outlined in the protocol. It is understood that all information pertaining to the study will be held strictly confidential and that this confidentiality requirement applies to all study staff at this site.

Protocol Number: 16-PROTO-01

Protocol Title: TSolution One Total Knee Arthroplasty Clinical Trial

Protocol Version: Version 6.0

Protocol Date: 09 SEP 2019

Principal Investigator:

Print Name

Signature Date (dd/mmm/yyyy)

Sponsor:

Print Name

Signature Date (dd/mmm/yyyy)

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1. STUDY SUMMARY

Title	TSolution One Total Knee Arthroplasty Clinical Trial
Sponsor	THINK Surgical, Inc.
Short Title	TSolution One TKA
Protocol Number	16-PROTO-01
Lead Investigator	Bernard N. Stulberg, MD
Methodology	Multi-center, prospective, non-randomized clinical trial
Study Type	Observational
Study Duration	Patients will be consented to participate for a period of no less than 6 months and no more than 12 months. Each study arm will terminate once the last enrolled patient of the study arm completes their 6 month study visit. Patients who are not expected to reach their 12 month visit prior to study arm termination will be exited at 6 months; all others will be exited at 12 months.
Objectives	The goal of this study is to evaluate the safety and effectiveness of robotic-assisted total knee arthroplasty, and to document clinical and radiological outcomes for TCAT-assisted implantation using the TSolution One System for TKA compared to a literature control.
Diagnosis and Main Inclusion Criteria	Primary osteoarthritis of the knee requiring a primary unilateral total knee arthroplasty (TKA)
Number of Patients	IDE Study Arm: The total sample size to be enrolled is 115 patients (103 patients plus 10% for possible loss to follow-up). Continued Access Arm: Once the IDE enrollment is completed, up to 50 patients will be enrolled in a separate arm of the study (Continued Access arm).

Outcome Measurements	**Primary Effectiveness Endpoint -** The primary effectiveness endpoint is alignment of coronal mechanical axis at 3 months defined as achieving varus-valgus alignment less than ±3° in the frontal plane after TKA. A review of 1,376 patients undergoing conventional TKA with manual instrumentation showed a 32% malalignment for mechanical axis greater than 3° (Mason). This study is designed to demonstrate that the investigational device is capable of reducing the malalignment rate by 50%, that is, to 16%. **Primary Safety Endpoint** - The primary safety endpoint is a composite safety endpoint that includes a number of relevant adverse events identified in a literature search, each having an expected incidence $\leq$2.7%. The sum of these relatively rare complications is equal to 7.6%. The percentage of patients with TCAT-assisted implantation using the TSolution One System for TKA experiencing the composite safety event will be compared to 7.6%. **Secondary Safety Endpoints** • Bleeding complications are not rare and will be assessed separately as a secondary safety endpoint based on the incidence of transfusions (allogeneic or autologous). • Complications related to excessive bleeding that require surgical intervention will be assessed and summarized as a subset of the bleeding complications above. • Other secondary safety endpoints include the incidence of the individual adverse events comprising the composite. **Secondary Effectiveness Endpoints** Effectiveness endpoints are considered secondary for this study and are summarized below: • Postoperative function will be evaluated by collecting Knee Society Scores at 3, 6, and 12 (if available) months. • Health related quality-of-life will be assessed by collecting Short Form 12 (SF-12) Health Survey scores at 3, 6, and 12 (if available) months. • Post-operative alignment outcomes will be compared to pre-operative alignment goals at 3 months.
Success/Failure Criteria	The study success criterion is to simultaneously demonstrate that the malalignment rate is less than or equal to 0.16 (effectiveness endpoint) and that the composite safety event rate is less than 0.136 (safety endpoint) based on one-sided exact binomial tests with type 1 error rate equal to 0.05. A p-value ≤ 0.05 for both tests will indicate study success.

Hypotheses	IDE Study Arm The **primary effectiveness hypothesis** for this study is that the probability of malalignment for patients undergoing TCAT-assisted implantation using the TSolution One System for TKA is 50% smaller than the reference rate of 32%, that is, less than or equal to 16%. **H_0: $\pi_I \geq 0.16$ (50% of reference rate = 32%)** **H_A: $\pi_I < 0.16$** In this formulation, π_I is the true malalignment probability for the investigational device. A one-sided type 1 error of α=0.05 was assumed. Using industry standard software (nQuery Advisor 7.0, Module POT0x-1), it was determined that statistical power to reject the null hypothesis in favor of the alternative hypothesis is equal to 89.3% with a sample size of N=103 patients if the true malalignment rate is 0.07. The **primary safety hypothesis** for this study is that the probability of experiencing the composite safety endpoint for patients undergoing TCAT-assisted implantation using the TSolution One System for TKA is not clinically significantly elevated relative to the historic control value of 7.6% for manual TKA. Symbolically, the primary safety hypotheses regarding non-inferiority relative to historical control may be represented as follows: **H_0: $\pi_I \geq \pi_C + \delta$ (clinically inferior safety)** **H_A: $\pi_I < \pi_C + \delta$ (not clinically inferior safety)** In this formulation, π_I and π_C are the true event rates when using the investigational device and manual TKA, respectively. As noted above, based on a literature review, π_c = 0.076. A non-inferiority margin of 0.06 was selected. Therefore, these hypotheses reduce to: **H_0: $\pi_{composite} \geq 0.076 + 0.06 = 0.136$** **$H_A$: $\pi_{composite} < 0.076 + 0.06 = 0.136$** A one-sided type 1 error of α=0.05 was assumed. Using industry standard software (nQuery Advisor 7.0, Module POT0x-1), it was determined that statistical power to reject the non-inferiority hypothesis was equal to 82.5% with a sample size of N=103 patients. Continued Access Study Arm There will be no formal hypothesis testing with the Continued Access Arm of the study. Patients will be followed for safety and to gain additional information on device use, therefore, no power analysis has been performed to estimate sample size. The Continued Access Arm will enroll up to 50 patients.

Statistical Methodology	Demographic, baseline, peri-operative and postoperative characteristics for all recruited cases will be assessed from data which is collected on the relevant case report forms. Continuous variables included in demographic, baseline, peri-operative and postoperative summaries, will be evaluated using descriptive statistics (N, mean, median, standard deviation, minimum, and maximum). Dichotomous and polychotomous variables included in demographic, baseline, peri-operative and postoperative summaries, will be described as frequencies and percentages at each level of the categorical variable. The primary effectiveness and safety hypotheses will be tested using exact tests for a single proportion with one-sided type 1 error rate set to α=0.05. The study success criterion requires rejection of both the effectiveness and safety null hypotheses. The primary effectiveness endpoint, the safety endpoint and all secondary endpoints including bleeding and the individual components of the composite safety endpoint, will each be summarized by counts, percentages, and the upper bounds of one-sided 95% exact binomial confidence intervals (CI). Patient function and health related quality-of-life will be described by summarizing baseline, 3-month, 6 month, 12 month (if available) and change scores at each time point in the Knee Society Scores and SF-12 Health Survey Physical and Mental Health Composite Scores (PCS & MCS), using descriptive statistics including mean, standard deviation, median, minimum, and maximum. The ITT analysis set will be used in primary analyses. Specific analyses may be repeated in a Per Protocol analysis set that requires completion of the index procedure and no clinically significant protocol violations. <u>Continued Access Study Arm</u> The continued access study arm will not include any hypothesis testing and will not be part of the primary or secondary endpoint analysis. Data from the continued access arm will be provided as descriptive statistics, which can include counts, percentages, mean, standard deviation, median, minimum, and maximum and the upper bounds of one-sided 95% exact binomial confidence intervals (CI). This will include an analysis of safety, patient function, and health related quality-of-life data described by summarizing baseline, 6 week, 3-month, 6 month, 12 month (if available) and change scores at each time point, as applicable.

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2. INTRODUCTION

2.1. Background

End-stage osteoarthritis of the knee is typically treated with total knee arthroplasty (TKA) in which the articulating surfaces of the distal femur and proximal tibia are replaced with prosthetic components. It is very successful in terms of relieving patients' pain and restoring joint function (1), (2), (3). However, the mechanical alignment of the knee after TKA and the ability to balance soft tissue play a major role in the longevity and success of the implant (4), (5), (6). It has been suggested that errors in surgical technique may be the most common reason for failure of TKAs (7), (1), (8). Thus, one of a surgeon's goals is to achieve accurate alignment of the tibial and femoral components in the frontal, sagittal, and transverse planes (9).

Manufacturers have traditionally recommended positioning the knee implant such that the "ideal" mechanical axis of the knee is restored. This mechanical axis is defined as a straight line passing through the center of the femoral head, the center of the knee joint, and the midpoint of the ankle (10), (11). Implant manufacturers have developed complex instrumentation sets to help achieve this ideal implant placement. However, every mechanical instrumentation system relies on visual inspection and the feel of a surgeon to confirm the accuracy of limb and implant alignment, and implant misalignment is still a problem. Despite a surgeon's best intentions, this results in anywhere from 15-72% of conventional TKA's having an error in mechanical axis alignment of greater than 3° (12), (13). A misalignment of greater than 3° varus-valgus has traditionally been considered the threshold past which implant longevity decreases. Several studies have suggested that if the error in varus-valgus alignment exceeds 3° after TKA, the patients are more likely to experience increased pain, poor biomechanics, reduced function, and a decreased longevity of the implants (14), (10), (15), (5). Jeffery et al. (10) has reported that the rate of loosening was 24% when mechanical axis alignment error exceeded 3° compared to only 3% when mechanical axis alignment was less than 3°. Loosening is the second leading cause for revision surgery with 24.1% of revisions being attributed to aseptic loosening (1). Thus, achieving ideal implant alignment with minimal error is essential for long term surgical success.

A variety of computer assisted navigation systems have been developed to improve alignment accuracy, and have resulted in a reduction in alignment errors (16), (17). However, although these navigation systems are successful at aligning the cutting guides, there still exists an inaccuracy that results from the cutting blocks and oscillating jigs used to prepare the bone (18), (19).

To address the issues with imprecise cutting, robotic systems were developed to combine the placement and alignment accuracy of navigation with the precision of computer controlled machining. Several systems have been developed specifically to address the implementation of TKA by accurately executing the preoperative plan (20), (21), (22), (23). The ROBODOC® Surgical System, an earlier, predicate of TSolution One that has been FDA-cleared for Total Hip Arthroplasty also has an application intended for assisted TKA. This system has been approved in

Korea and other countries outside the US for this intended use has been shown to contribute to improved alignment, fewer outliers, and to allow accurate preoperative planning when compared to conventional TKA (24), (25), (26).

2.2. Investigational Device

The TSolution One Surgical System consists of a three-dimensional graphical preoperative planner and an implementation tool for treatment of patients who require a total knee arthroplasty procedure. With application specific tools and software, it provides stereotactic guidance during orthopedic surgical procedures by using patient CT data to assist a surgeon with presurgical planning and bone preparation. Surgical application specific modules such as total knee arthroplasty are added to the base operating platform.

The TSolution One Surgical System platform includes:

- TPLAN®: a Preoperative Planning Workstation
- TCAT™: an electromechanical robotic arm with a display monitor, operating software, tools and accessories (e.g., cutters, drapes, irrigation sets, probes and markers)

TPLAN

TPLAN is a PC-based workstation with proprietary software that enables the surgeon to select appropriate prosthetic implant(s) and preoperatively determine the optimal positioning in or on the patient's bone. Computed Tomography (CT) scan data of the patient's bone/joint provides input to TPLAN. The TPLAN software combines several individual scan slices to create patient specific three-dimensional images from the CT data.

TPLAN allows the surgeon to select an implant model from a library of implant types and sizes. TPLAN displays three-dimensional (3D) views of selected implant models for computerized templating with the patient specific 3D images from the CT data. The surgeon virtually places the implant in the desired position with respect to the patient image data. In the case of a knee or hip arthroplasty, TPLAN also allows surgeons to preoperatively measure and determine plan characteristics such as Femoral and Tibial Mechanical Axis (FMA, TMA), implant size, shape, implant placement, and measure bone cuts for THA and or TKA. The output from a TPLAN planning session provides TCAT with the planned implant type, size, shape, orientation and position (placement) data. The output is saved onto data transfer media, which is loaded onto TCAT prior to surgery.

TCAT

TCAT is comprised of an electromechanical arm, computers and electronic controls within the base, a display monitor, and a surgeon's pendant control. The electromechanical arm has 5 degrees of freedom (5-DOF) and is mounted on top of a base which houses the computers and electronic controls and acts as an elevator for the arm. The system is equipped with two bone motion monitors (BMMs), one on each side of the TCAT arm, and a digitizer. The User Interface consists of a display monitor, a hand-held pendant for controlling the arm, operator controls (switches/buttons), and indicator lights. Additional peripheral devices include a Force Sensor, Cutter Drive Assembly and Irrigation Pump. The function of the TCAT is to precisely execute the preoperative plan developed by the surgeon using TPLAN.

2.3. Investigational Procedure

Preoperative CT for TCAT Planning

A preoperative CT scan is required to create a 3D model of the patient's anatomy in TPLAN for accurate implant planning, bone resection, and implant placement. A motion rod is scanned with the joint to ensure that the patient did not move during the CT scan.

Preoperative Implant Planning Using TPLAN

Using CT data as an input, the surgeon uses TPLAN to determine the implant sizing, bone resection, and implant placement. TPLAN allows the surgeon to produce a 3D surface model of the bones from the CT data. The surgeon can then select an implant model from the library of 510(k) cleared joint replacement implants available in TPLAN and manipulate the 3D representations of the implant together with the bone to optimally place the implant within the bone. Once the surgeon is satisfied with the implant size and location, the data is written to transfer media for use with the TCAT during surgery. The transfer media created by TPLAN contains the patient scan data, implant data, positioning information, and images to aid in registration point collection during the surgery.

TCAT Setup & Start-Up Diagnostics

Prior to each TCAT surgery, various startup diagnostics must be performed to ensure that the TCAT system is in proper working order.

- TCAT kinematics - The kinematic accuracy of the electromechanical arm is verified using a fixture with previously measured reference points upon which TCAT locates points and compares them with the measured values. This test will verify that the electromechanical arm is positioning to specifications and has not been damaged.

- Digitizer kinematics – the digitizer is used to locate the 3D locations of points within the workspace of the electromechanical arm. The accuracy of the digitizer is verified prior to every procedure. During diagnostics, the digitizer is tested against the same kinematic fixture in the arm verification above to ensure that the ability of the digitizer to locate specific known points on the fixture is within a specified tolerance.

- Base lift accuracy – the accuracy of the base is verified by measuring the known location of a post on a standard kinematic fixture at two different base heights to ensure that the error between the two measurements is within a specified tolerance.

- Tool calibration verification – Prior to making contact with a patient, the TCAT system is covered with a sterile drape to protect both the patient and system during bone preparation. The system performs a test after sterile draping that verifies that the sterile tools have been correctly installed and calibrated.

- Arm to digitizer registration verification – The accuracy of the transformation between the electromechanical arm and the digitizer is verified during sterile diagnostics to ensure that the error is within specification.

- Digitizer calibration verification – The accuracy of the digitizer with a sterile tip is verified to be within the calibrated tolerances required to ensure that the digitized points collected are precisely identified to the best ability of this device.

- Pendant operation - The monitor prompts the users to verify the proper functioning of each button upon installation of a new pendant. After verification, the system may allow the procedure to continue.

- Force sensor operation – The end-effector of the TCAT electromechanical arm is equipped with a six degree-of-freedom force sensor. The accuracy of the force sensor is verified using a tool of known weight that is reoriented by TCAT while forces and torques are measured.

- Redundant encoder operation – Each joint of the TCAT arm is equipped with dual positional encoders. This redundant position monitoring system serves as a safety mechanism that can continuously monitors the commanded arm position. During diagnostics, this system is tested to ensure its functionality and accuracy.

- Bone motion monitor operation – TCAT is equipped with two bone motion monitors (BMMs) that can detect when bones involved in the surgery move after being fixated. The accuracy of the BMMs is verified by placing the BMM test probe in contact with the electromechanical arm ball probe, moving the probe through prescribed locations and comparing the BMM-determined distances to the electromechanical arm-computed distances.

Start-up diagnostics must be performed prior to anesthetizing the patient. In the event that any of the diagnostics tests fails, TCAT notifies the surgeon and prevents the procedure from continuing.

Surgical Exposure

The surgeon proceeds with surgical exposure for the TCAT surgery in the same manner as a conventional TKA procedure.

Fixation

Although the TCAT system incorporates a BMM system to detect motion of the bone, proper fixation of the femur and tibia reduces this motion and keeps surgical time to a minimum. The surgeon fixes the operative joint using a clamp on the femur and pin on the tibia to ensure that there is no motion during bone cutting. Bone motion recovery markers are placed on the femur and tibia to recover the 3D location and orientation of each bone in the event of bone motion. If bone motion occurs during registration or cutting, the BMMs will immediately pause the procedure and require that the bone be re-registered before the procedure can continue.

Registration

Registration serves as the link between the preoperative plan created in TPLAN and the bone cutting during surgery performed by TCAT. Once the bone is registered in the coordinate system, TCAT can accurately machine the bone according to the predefined surgical plan. TCAT uses an accurate point-to-surface technique for registration. Once the joint has undergone fixation, the surgeon will use the digitizer to collect points on the bone with respect to the electromechanical arm coordinate system. The TCAT software will check to ensure that the registration of the bone is within specifications before allowing the surgeon to proceed.

Bone Preparation

The surgeon will ensure that the soft tissue is properly retracted and the electromechanical arm proceeds with cutting of the bone. During cutting, the OR Display Monitor shows a continuously updated graphical representation of cutting progress superimposed on top of the CT data. Throughout this process, the surgeon remains in control of the process and can pause, stop, or abort the use of TCAT at any point if needed.

Implant Fitting & Insertion

The OR Display Monitor prompts the surgeon to move TCAT away from the operating table once TCAT has finished preparing the bone. The surgeon removes the recovery markers and fixation system and proceeds with implant fitting and insertion in the same manner as conventional TKA.

Joint Closure

Once the implant components are cemented (if applicable), the surgeon reviews the execution of the plan. If satisfactory, the exposed joint is closed per standard of care.

3. RISK ANALYSIS

The TCAT system, presented in this clinical protocol, is based on the ROBODOC® Surgical System. The ROBODOC® Surgical System was cleared under K072629 for use in total hip arthroplasty procedures. The ROBODOC System has had a total knee arthroplasty application that has been used extensively outside the U.S. The TSolution One® system incorporates the same operating principles and basic design as the ROBODOC® Surgical System but includes upgrades to the hardware and software. Thus, it shares, for the most part, similar risks and benefits in its technology and use. For total knee arthroplasty procedures, the ROBODOC® Surgical System has been used extensively in a clinical setting outside the US.

3.1. Risks

The possible adverse effects of the clinical study can be broken down into several groups:

- General Surgical Risks
- TKA Specific Risks
- TSolution One® System Specific Risks

General Surgical Risks	TKA Specific Risks	TSolution One® System Specific Risks
• Infection • Seroma • Renal/Urinary • Arrhythmias • GI • Pulmonary Embolism • Rash • Hyponatremia • Deep vein thrombosis • Delayed Wound Healing	• Reaction to wear debris • Allergy to implants • Loosening/Migration/Fracture of components • Breakage/Cracking/Fracture of implants • Pain; • Poor Range of Motion • Dislocation/Subluxation due to inadequate fixation,	• Surgical Delay • Soft Tissue Damage • Electrical Shock • Overcutting of Bone • Bone Fracture • Additional Radiation Exposure

• General Cardiovascular Disorders • Temporary or permanent neuropathies	malalignment, malposition, excessive use • Fretting and crevice corrosion • Valgus-varus deformity • Laxity of the joint • Leg length discrepancy • Fractures of the femur or tibia	

3.2. Methods to Minimize Risk

The risks and adverse events associated with general surgery and knee arthroplasty are well understood. These risk are generally well mitigated through typical clinical practices. The risk associated with a TKA have also improved over time with advances in technology and surgical techniques.

The risks from implantation using the TSolution One® System are described below. In addition to the risk mitigation described in the table, subject selection criteria, study methods, evaluations, follow-up periods, facilities and investigator selection are intended to minimize risk to subjects participating. In this study, subjects will be monitored throughout the study (Day 0 to a maximum of 12 months following the procedure) for the detection of adverse events. Finally, all subjects will be informed of the potential risks through a detailed informed consent.

TSolution One® System Specific Risks	**Risk Mitigation**
Surgical Delay	Navigation systems are known to have an increased operative time of anywhere from 10 to 20 minutes (27) (28) but are not associated with an increased risk of infection. No studies have shown that an increase in time of only 20 to 30 minutes is associated with an increased risk of infection. The ROBODOC system has been shown to have an increased surgical time of approximately 25 minutes per case. As the TCAT system has similar workflow to the ROBODOC system, we expect that there may be an increase in time for these cases, but in all of the previous studies, this has not resulted in adverse patient risk.

TSolution One® System Specific Risks	Risk Mitigation
Soft Tissue Damage	The risk of soft tissue damage is quite similar to a traditional TKA procedure. Labeling and training specifically focus on ensuring retraction of ligaments and soft tissue is adequate to provide clear access for the cutter. During cutting, the surgeon monitors the cutter and can determine if additional soft-tissue retractions is necessary.
Electrical Shock	The TSolution One® system was tested for electrical safety appropriate for an electromedical system and all tests past in accordance with IEC 60601-1: 2005 + CORR. 1 (2006) + CORR. 2 (2007).
Overcutting of Bone	The TSolution One® system reduces the risk of overcutting when compared to a manual sawing technique. During manual sawing, the surgeon is placing the saw through a guide and has nothing to limit how far the cuts are made. TSolution One® is designed prepare the bone according to the specific implant that is selected. The cutter follows a predetermined cut path that only cuts according to the implant shape and preclinical testing (PV/TR 16-070) has verified that the system cuts within the specified tolerance.
Bone Fracture	Intraoperative bone fracture during TKA typically occurs during impaction of the implants. The TSolution One® procedure only assists with preparation of the bony surfaces and not during impaction. Impaction is handled in the same manner as a manual case. Postoperative fractures can occur at pin sites especially in the diaphysis. The TSolution One® system has minimized the risk of postoperative bone fracture by fixating the femur with a clamp that does not result in a hole in the bone and reducing the size of the pin required for tibial fixation to 3mm, which greatly reduces the risk of postoperative fracture, Furthermore, patients with poor bone quality are contraindicated as adequate bone quality is necessary to support fixation.

TSolution One® System Specific Risks	Risk Mitigation
Additional Radiation Exposure	The TSolution One® System does require a preoperative CT scan upon which the surgical plan is based. This does expose the patient to additional radiation. However, these types of CT scans are common to other surgical robotic systems including the MAKO system (Stryker, Mahwah, NJ) and patient specific cutting guide systems (Trumatch, Depuy Synthes, Warsaw, IN). The potential benefits in terms of accuracy and precision can outweigh the risks associated with additional radiation. Without a preoperative CT, conventional alignment jigs and navigation systems rely on the surgeon's ability to locate bony landmarks, which has been known to show large variability (8).

3.3. Potential Benefits

There are clear potential benefits to using the TSolution One® system for assistance during TKA. With current instrumentation, technical errors frequently occur in the implantation of TKA's. These include errors in implant placement, sizing, alignment of the femoral and tibial implants, bone cutting, and issues with implant to bone fixation. The current system has the potential to minimize such errors. Based on preclinical testing and older versions of the system, the TSolution One® system excels in terms of both precision and accuracy when it comes to correctly placing the implant. The TSolution One® system improves the surgeon's ability to align the knee through accurate preoperative planning. During surface registration of the bone in surgery, the surgeon is not asked to identify specific landmarks, but rather select a set of points which are collected in specified regions of the bony surface. The TSolution One® System makes cuts accurately in all planes. These accurate cuts result in an elimination of misaligned implants clinically as stated in the previous section. The method of fixing the implant to the bone is not affected by the TSolution One® system. Bone cement can still be used after the bone has been machined. In the case of cementless implants, because TSolution One® machines such precise cuts, the implants are likely to be more stable and achieve greater bone-implant fixation since there are minimal gaps at the interface.

3.4. Justification of the Clinical Investigation

Based on the potential benefits listed above, and the anticipated risks, Think Surgical believes this study is justified for the following reasons:

- The TSolution One® System has undergone extensive non-clinical testing.
    - Software validation has shown the software to be reliable and safe for use.

  - A Full System Run-Through demonstrates a functional process that can be performed by the surgeon.
  - Registration Accuracy demonstrates the accuracy of the system.
  - Registration Recovery Accuracy demonstrates the ability of the system to recover during the procedure.
  - Implant cutting testing show the ability of the system to make accurate cuts.
  - TKA Usability testing validate the ability of the system to be used in a simulated operation with real world user.
  - Electrical Safety Testing demonstrate testing and compliance with international standards.
  - Sterility and cleaning validation demonstrate the patient contacting instruments can be properly cleaned and sterilized according to a recommended protocol.
  - Biocompatibility evaluations show the materials to be safe for use.
- The risks identified above have been minimized to the furthest extent possible, through pre-clinical bench testing, training, and proper labeling. In addition, all patients will be informed of the potential risks during the informed consent.
- The principles of operation are the same as the ROBODOC system which has been used successfully in a clinical setting outside the US for thousands of cases.
- The clinical protocol is designed to yield valid scientific evidence to support a 510(k) submission.
- Study subjects are selected according to specific inclusion/exclusion criteria and evaluated frequently.
- Think Surgical will closely monitor the study, and adverse events will be recorded and reported promptly to Think Surgical.

Therefore, given the information provided throughout this submission, Think Surgical has adequately evaluated the safety of the device and put into place adequate clinical controls to initiate the start of an IDE study.

4. STUDY OBJECTIVES

The goal of this prospective, non-randomized, multicenter clinical trial is to evaluate the safety and effectiveness of robotic-assisted total knee arthroplasty, and to document the clinical and radiographic outcomes for TCAT-assisted implantation using the TSolution One System for TKA, and to compare these outcomes to those reported in the literature.

4.1. Primary Objectives

The primary objective of this study is to demonstrate that the TSolution One System is safe and effective for use as an alternative to manual planning and sawing/cutting techniques. The primary effectiveness objective of this study is to demonstrate that the TSolution One System is effective for use as an alternative to conventional manual techniques by comparing the rate of

malalignment for mechanical axis greater than 3° at 3 months to the rate reported in the literature (i.e. 32%) and to demonstrate significant clinical benefit by reducing the number of malaligned patients by at least 50% (i.e. from 32% to ≤16%). The safety objective of this study will be based on the rate of intra-operative and postoperative TKA complications, and will compare this rate to the rate reported in the literature.

4.2. Secondary Objective

The secondary objective of this study is to summarize the distribution of improvements in patients' self-reported assessment of postoperative function and quality-of-life from baseline to a maximum of 12 months. Additionally, other pre-operative planning alignment goals (e.g. Knee V-V Alignment; Femoral Joint Line Alignment Angle; Tibial Joint Line Alignment Angle; Tibial Slope Angle) will be compared to the post-operative alignment.

5. STUDY DESIGN

This clinical investigation will be conducted as a prospective, non-randomized, multicenter study. Investigators will recruit patients from patients in their practice who require unilateral total knee arthroplasty. Patients will be screened to identify eligible candidates based on the inclusion and exclusion criteria described in Sections 6.1 and 6.2. A total of one hundred fifteen (115) patients will be enrolled in the study across the participating sites. All patients will sign an informed consent form prior to participating in the study. Prior to the investigational procedure, they will complete baseline surveys of function and quality of life and have baseline radiographs. Each patient will undergo robotic-assisted total knee arthroplasty with the TSolution One System. The Investigator will evaluate intra- and postoperative complications. Postoperative radiographs will be used to measure limb alignment using a standardized radiographic evaluation protocol for the IDE Study Arm (Attachment K of the IDE application). Each patient will complete a postoperative Knee Society Score survey and the SF-12 Health Survey to assess functional outcomes and quality-of-life following the investigational procedure.

The clinical study will have two arms: the IDE Study Arm, and the Continued Access Arm. Once enrollment is complete in the IDE Study Arm, subjects will be enrolled into the Continued Access Arm. Up to an additional 50 patients will be enrolled in this arm.

The TSolution One™ Total Knee Arthroplasty Clinical Trial will be conducted in compliance with this protocol, Good Clinical Practice (GCP) guidelines, and applicable US regulatory requirements.

5.1. Primary Effectiveness Endpoint

The primary effectiveness endpoint is alignment of coronal mechanical axis at 3 months defined as achieving varus-valgus alignment less than or equal to ±3°in the frontal plane after TKA compared to the pre-operative plan. A review of 1,376 patients undergoing conventional TKA with manual instrumentation showed a 32% malalignment for mechanical axis greater than 3° (Mason). This

study is designed to demonstrate that the investigational device is capable of reducing the malalignment rate by 50%, i.e. to 16%.

Note: The primary effectiveness endpoint will be evaluated utilizing only the IDE Study Arm.

5.2. Primary Safety Endpoint

The primary endpoint is a composite endpoint that includes a number of relevant adverse events associated with manual TKA that were defined and published by the Knee Society (Healy et al. 2011), each having an expected incidence $\leq$2.7% based on a literature search summarized in Table 1. The sum of these relatively rare complications is equal to 7.6%. The percentage of patients with TCAT-assisted implantation experiencing the composite safety event will be compared to 7.6% plus a non-inferiority margin of 7.0%.

Note: The primary safety endpoint will be evaluated utilizing only the IDE Study Arm.

5.3. Secondary Endpoints

Bleeding complications have an expected incidence of 36% for unilateral TKA (Bierbaum et al. 1999), and are not rare. These will be assessed separately as a secondary safety endpoint at discharge based on the incidence of transfusions required (autologous or allogenic) as a result of bleeding.

Descriptive safety analyses for the incidence of the individual adverse events comprising the composite will also be performed.

The secondary endpoints also include a comparison of post-operative alignment outcomes other than coronal mechanical axis to the pre-operative alignment goals, and assessment of improvements in Knee Society Scores and SF-12 Health Survey scores.

Table 1: Summary of Primary TKA Complications Assessed in the Primary Safety Endpoint

Complications of Primary TKA (29)	**Knee Society Definition** (29)	**Literature-Based Incidence Rate for Primary TKA**	**Method for Assessing Complications**
1. Medial Collateral Ligament Injury	Intraoperative or early postoperative medial collateral ligament injury requiring repair, reconstruction, a change in prosthetic constraint, revision surgery, or TKA protocol	2.7% (30)	Incidence of intraoperative or postoperative MCL transection or avulsion leading to repair, reconstruction, change in prosthetic constraint, or revision TKA.
2. Extensor Mechanism Disruption	Disruption of the extensor mechanism (surgical repair and/or extensor lag should be recorded)	2.1% (31)	Incidence of iatrogenic extensor mechanism disruption.
3. Neural Deficit	Postoperative neural deficit (sensory or motor) related to the index TKA	1.3% (32)	Incidence of sensory or motor neural deficit (complete or incomplete) related to the TKA procedure.
4. Periprosthetic Fracture	Periprosthetic fracture of the distal femur, proximal tibia or patella (operative or nonoperative treatment should be recorded)	0.68% (32)	Incidence of periprosthetic fracture of the distal femur, proximal tibia or patella. Operative and nonoperative treatment for the fracture will also be recorded.
5. Patellofemoral Dislocation	Dislocation of the patella from the femoral trochlea (direction of instability should be recorded)	0.5% (33)	Incidence of patella dislocation from the femoral trochlea due to postoperative instability. The direction of instability will also be recorded.

Complications of Primary TKA (29)	**Knee Society Definition** (29)	**Literature-Based Incidence Rate for Primary TKA**	**Method for Assessing Complications**
6. Tibiofemoral Dislocation	Dislocation of the tibiofemoral joint (direction of instability should be recorded)	0.2% (34)	Incidence of iatrogenic tibiofemoral joint dislocation. The direction of instability will also be recorded.
7. Vascular Injury	Intraoperative vascular injury requiring surgical repair, bypass grafting, or stenting (compartment syndrome or amputation should be reported)	0.15% (32)	Incidence of iatrogenic vascular injury requiring surgical repair, bypass, grafting, or stenting. Incidents of compartment syndrome or amputation will also be recorded.

6. SELECTION OF STUDY POPULATION

6.1. Inclusion Criteria

In order to be eligible for the study, candidates must meet the following criteria:

a) Is at least 21 years of age.

b) Is skeletally mature, as evidenced by closed epiphyses.

c) Is eligible for primary unilateral TKA due to osteoarthritis defined radiographically by a Kellgren-Lawrence Grade of 3 or higher.

d) Is able to understand and willing to comply with the requirements of the study.

e) Is able to give voluntary, written informed consent to participate and has signed an Informed Consent Form specific to this study.

6.2. Exclusion Criteria

Candidates will be excluded if they meet any of the following criteria:

a) Has undergone previous open knee surgery in the operative knee.

b) Has a body mass index (BMI) > 40 kg/m^2.

c) Is a candidate for bilateral TKA.*

**In the opinion of the Investigator, simultaneous bilateral TKA or staged bilateral TKA (where the second surgical procedure is to be scheduled within 6 months of the first procedure) is determined to be either: (i) clinically necessary or (ii) advised as the treatment plan to address acute symptoms and/or quality of life.*

d) Has a coronal deformity greater than 20° or a sagittal flexion contracture greater than 15°.

e) Has an active systemic infection or an active local infection in or near the operative knee joint, or has a previous history of joint infection.

f) Has a pathological skeletal condition or skeletal immaturity which would significantly compromise the ability of the bone to withstand the stress required for preparation of the bones and proper implantation of the prostheses (e.g., severe osteoporosis, Paget's disease, renal osteodystrophy, AVN, sickle cell disease, etc.).

g) Has femoral or tibial bone stock that is of poor quality or inadequate to provide stability for femoral or tibial fixation.

h) Has any type of metallic implant in the operative leg.

i) Has a known or suspected sensitivity to any of the materials in the investigational device or implant components (i.e. cobalt, chromium, titanium, stainless steel, titanium nitride, aluminum, polyethylene, PVC plastic)

j) Has a systemic illness or a neuromuscular, neurosensory, or musculoskeletal deficiency that would render the patient unable to perform appropriate postoperative rehabilitation.

k) Has a neuromuscular disorder that would create an unacceptable risk of prosthesis instability or fixation failure.

l) Has significant comorbidities or conditions associated with high risk for surgical or anesthetic survival (e.g. peripheral vascular disease, unstable cardiac disease, poorly controlled diabetes, immunosuppression, etc.).

m) Is pregnant or intends to become pregnant during the course of the study.

n) Has previously experienced a stroke.

o) Is participating concurrently in another clinical trial, or has participated in a clinical trial within the last 90 days, or intends to during the course of the study.

p) Has a medical or psychiatric condition which, in the opinion of the investigator, poses a risk of the patient being unable to complete the study or presents risks associated with study participation.

6.3. Screening

The study population will be recruited from patients in the Investigators' practice who need unilateral total knee arthroplasty. Patients in this group will be screened for eligibility based on the inclusion and exclusion criteria described in Sections 6.1 and 6.2. All patient eligibility assessments will be initiated after completing the informed consent process. The screening process may include but will not be limited to a review of the patient's demographics, medical history, physical exam, standing long-leg AP x-rays, standard lateral x-rays, and current medications and therapies.

6.4. Informed Consent

Eligible patients will be recruited for the study by the Investigator and/or approved site staff. The Investigator or designee will provide eligible patients with a verbal overview of the study procedures and requirements, including all follow-up visit requirements. If the patient is willing to participate in the study, they will be asked to review the Informed Consent Form before they are officially enrolled in the study and asked to undergo any screening procedures or assessments. Each patient will be allowed sufficient time to decide whether they wish to participate in the study. If they agree to participate, they must sign and date the IRB-approved Informed Consent Form at or prior to the Baseline Visit. A copy of the signed Informed Consent Form will be given to the patient to take home for their records, and the original copy will be filed in the patient's study records.

Patients will be informed that they may decide to withdraw consent and discontinue their participation in the study for any reason at any time without facing any impact to their regular course of treatment at the study center.

6.5. Study Enrollment

Each Investigator shall maintain a Screening & Enrollment Log for all primary TKA patients that are recruited for the clinical trial and screened for eligibility. This log will be used to document all patients who agree to be screened, including the ones that withdraw consent during the screening process or are determined not to meet the eligibility criteria. If a patient is excluded from the study, the reason for exclusion will be recorded on the log. Patients who meet the eligibility criteria and consent to participate shall be assigned a unique Subject Identification Number that will be captured on the Screening & Enrollment Log and used to identify them on all source documents and Case Report Forms thereafter. Patients will be considered to be enrolled once they have signed the Informed Consent Form and been assigned a Subject Identification Number. Enrolled patients that elect to withdraw consent prior to treatment with the investigational device will be considered screen failures under inclusion criteria (e).

Patients who do not meet eligibility criteria will have the primary reason for ineligibility captured in the study database on the Eligibility Criteria eCRF. No other CRFs will be completed for these patients.

Once enrollment is complete in the IDE Study Arm, subjects will be enrolled into the Continued Access Arm.

7. STUDY PROCEDURES

Unless otherwise noted, the procedures below apply to both the IDE Study and the Continued Access arms of the study.

7.1. Baseline Visit (≤90 days prior to Date of Surgery)

A preoperative baseline clinical visit will be performed within 90 days prior to the patient's surgery, and will serve as a Standard of Care evaluation by the Investigator to confirm patient eligibility. Baseline Visit procedures may be completed in multiple clinic visits if required, but must be completed within 90 days prior to the date of surgery and the preoperative CT scan for surgical planning must be taken within 30 days prior to the date of surgery. Visit procedures will be recorded in the subject's study records and on the Baseline Visit eCRF.

Informed Consent

Prior to initiating any study-related procedures, the Investigator will ensure that the patient has signed a copy of the IRB-approved informed consent form.

Clinical Evaluation

Patient eligibility will be confirmed by reviewing the patient's demographics, medical history, physical exam, and current medications and therapies.

Preoperative Radiographs
Each patient must have preoperative standing long-leg AP x-rays and standard lateral x-rays of the investigational knee per the TSolution One IDE Study Radiographic Evaluation Protocol.

Preoperative CT for TCAT Planning
A preoperative CT scan will be taken of the investigational knee for preoperative planning in TPLAN per the TSolution One IDE Study Radiographic Evaluation Protocol. A motion rod will be scanned with the joint to ensure that the patient did not move during the CT scan. If motion is detected during the scan, the scan will be repeated. This scan must be performed within 30 days prior to the date of surgery.

Surveys
The following surveys will also be completed at this visit to capture baseline data related to function and quality of life:

- Knee Society Score (KSS) – completed by the Investigator and patient
- SF-12 Health Survey – completed by the patient
- Forgotten Joint Score (FJS) Survey – completed by the patient *(Continued Access Arm only)*

Preoperative Implant Planning Using TPLAN
Following the Baseline Visit, the Investigator (or designee) will upload the CT data in TPLAN to determine (i) the desired model and size for the femoral implant, model and size for the tibial base plate and initial trial thickness of the tibial liner insert, (ii) femoral and tibial resection plan, and (iii) implant positioning. The Investigator (or designee) will select an implant model from the library of implants available in TPLAN and will manipulate the 3D representations of the implant together with the bone to optimally place the implant within the bone. Once the Investigator is satisfied with the implant size and location, the data will be written to a transfer media for use with the TCAT during surgery.

7.2. Surgical Visit

Surgical Visit procedures will be recorded in the subject's study records and on the Operative Summary & Discharge eCRF.

Preoperative Labwork
Standard of care tests will be conducted to prepare the patient for surgery, including bloodwork to assess their preoperative hemoglobin and hematocrit levels. This labwork can be collected any time within 30 days prior to the day of surgery.

TCAT Setup & Start-Up Diagnostics
Non-sterile and sterile start-up diagnostics will be performed prior to anesthetizing the patient. The surgeon will also confirm that a full back-up of manual instruments is available in the OR. If any of the diagnostics tests fail, the Investigator will restart the TCAT diagnostics procedure.

Anesthesia and Surgical Exposure

Once the diagnostic procedures have been successfully completed, the patient will be anesthetized. The Investigator will proceed with surgical exposure for the TCAT surgery in the same manner as a conventional TKA procedure.

Fixation

The Investigator will fix the operative joint to ensure that there is no motion during bone cutting. Once fixation has been established, bone motion recovery markers will be placed on the femur and tibia. If a bone motion occurs during registration or cutting, the procedure will be paused to allow the Investigator to re-register the bone before proceeding.

Registration

Once the joint has undergone fixation, the Investigator will use the digitizer to collect reference points on the bone as guided by the TCAT software to assure that the points being collected are properly located and will wait for the system to confirm that the registration of the bone is within specifications. If the registration meets the specifications, he/she will accept the registration and proceed to cutting.

Bone Preparation

The Investigator will ensure that the soft tissue is properly retracted and provide confirmation that the electromechanical arm may proceed with cutting the femur and tibia. During cutting, the OR Display Monitor will show a continuously updated graphical representation of cutting progress superimposed on top of the CT data. The Investigator will remain in control of the process and will pause, stop, or abort the use of TCAT at any point if needed. If the patella is to be resurfaced, the Investigator will prepare the patella using conventional tools and techniques.

Implant Fitting & Insertion

Once TCAT has finished preparing the bone, the Investigator will move TCAT away from the operating table, remove the recovery markers and fixation system and proceed with implant fitting and insertion in the same manner as conventional TKA. Once the Investigator is satisfied with the placement of the implants and stability of the knee, the implants are impacted or cemented as needed.

Joint Closure

Once the implant components are cemented (if applicable), the Investigator will review the execution of the plan. If satisfactory, the exposed joint will be closed per standard of care.

Operative Summary

During the immediate postoperative period, the Investigator's standard postoperative care procedures should be followed. Once the investigational procedure and all post-operative care has been completed, the Investigator will document procedure details in the source documents, including but not limited to the following:

- Surgery duration: measured via the surgery start time (start of anesthesia) and surgery stop time (dressing complete)
- Skin-to-skin time: measured via the time of first incision and time of completion of closure
- TCAT procedural time: measured via the time of insertion of bone motion recovery markers and time of removal of the TCAT system from the operating table
- Use of tourniquet, and estimated time of use

- Use of cement, and specific components that were cemented, if applicable
- Implant details (individual component size, manufacturer, model and implant lot number)
- Use of anesthesia
- Confirmation that the procedure was successfully archived within TCAT and on a transfer media after each procedure
- Documentation of intra- and immediate post-operative complications, if applicable
- Documentation of device malfunctions, if applicable
- Documentation of any instances where the Investigator switched to manual instrumentation
- Archival of the completed case data

7.3. Hospital Discharge

Following discharge, information regarding the patient's hospital stay will be recorded in the subject's study records and on the Operative Summary & Discharge eCRF.

Safety Evaluation & Concomitant Medications/Therapies
All postoperative complications and adverse events will be recorded and assessed as specified under Section 10.0 (Safety Reporting). Concomitant medications and therapies will also be documented during this visit. For the Continued Access Arm, any medications that are administered prophylactically for the surgical procedure (e.g., anesthesia, antibiotics, anti-emetics) are not required to be captured in the Concomitant Medication Log in the study database, with the exception of any medications that are administered post-operatively for pain management.

Postoperative Labwork & Transfusion Summary
Patients will undergo venipuncture to assess their postoperative hemoglobin and hematocrit levels within 3 days after the procedure. The use of autologous or allogeneic blood transfusions and the total number of units that were transfused will also be recorded.

NOTE: Patients who are discharged on the date of surgery will have their hemoglobin and hematocrit levels measured and their transfusion summary documented prior to leaving the hospital.

Additional Assessment
When available the following data will be recorded for patients in the Continued Access Arm of the study:

- Pain Scores on Days 0-3 Post-op - measured with a Pain Numerical Rating Scale (NRS) 0 to 10
- Range of Motion at Discharge for the operative knee

7.4. 6 Week Follow Up Visit (± 2 weeks)

A postoperative clinical visit will be scheduled 6 weeks after the surgery to allow the Investigator to assess the patient's progress. Visit data will be recorded in the subject's study records and on the 6 Week Follow Up Visit eCRF.

Surveys
The following surveys will also be completed at this visit to capture postoperative data related to function and quality of life:

- Knee Society Score (KSS) – completed by the Investigator and patient
- SF-12 Health Survey – completed by the patient
- Forgotten Joint Score (FJS) Survey – completed by the patient *(Continued Access Arm only)*

These surveys should be administered prior to any other study visit assessments or procedures being performed to prevent information from the examination biasing the patient's responses.

Radiographs
Standard AP and lateral x-rays of the knee will be collected at this visit per the TSolution One IDE Study Radiographic Evaluation Protocol.

Safety Evaluation & Concomitant Medications/Therapies
All postoperative adverse events and complications will be recorded and assessed as specified under Section 10.0 (Safety Reporting). Concomitant medications and therapies will also be documented during this visit.

7.5. 3 Month Follow Up Visit (± 2 weeks)

A second postoperative clinical visit will be scheduled 3 months after the surgery to allow the Investigator to assess the patient's progress. Visit data will be recorded in the subject's study records and on the 3 Month Follow Up Visit eCRF.

Surveys
The following surveys will be completed at this visit to capture postoperative data related to function and quality of life:

- Knee Society Score (KSS) – completed by the Investigator and patient
- SF-12 Health Survey – completed by the patient
- Forgotten Joint Score (FJS) Survey – completed by the patient *(Continued Access Arm only)*

These surveys should be administered prior to any other study visit assessments or procedures being performed to prevent information from the examination biasing the patient's responses.

Radiographs
Standing long-leg AP x-rays and standard lateral x-rays of the knee will be collected at this visit per the TSolution One IDE Study Radiographic Evaluation Protocol.

CT Imaging
Patients will have 3D CT images at this visit to collect supplemental outcomes regarding postoperative implant positioning. CT imaging will be collected per the TSolution One IDE Study Radiographic Evaluation Protocol.

Safety Evaluation & Concomitant Medications/Therapies
All postoperative complications and adverse events will be recorded and assessed as specified under Section 10.0 (Safety Reporting). Concomitant medications and therapies will also be documented during this visit.

7.6. 6 Month Follow Up Visit (± 2 weeks)

A third postoperative clinical visit will be scheduled 6 months after the surgery to allow the Investigator to assess the patient's progress. Visit data will be recorded in the subject's study records and on the 6 Month Follow Up Visit eCRF.

Surveys
The following surveys will be completed at this visit to capture postoperative data related to function and quality of life:

- Knee Society Score (KSS) – completed by the Investigator and patient
- SF-12 Health Survey – completed by the patient
- Forgotten Joint Score (FJS) Survey – completed by the patient *(Continued Access Arm only)*

These surveys should be administered prior to any other study visit assessments or procedures being performed to prevent information from the examination biasing the patient's responses.

Radiographs
Standing long-leg AP and standard lateral x-rays of the knee will be collected at this visit per the TSolution One IDE Study Radiographic Evaluation Protocol.

Safety Evaluation & Concomitant Medications/Therapies
All postoperative complications and adverse events will be recorded and assessed as specified under Section 10.0 (Safety Reporting). Concomitant medications and therapies will also be documented during this visit.

7.7. 12 Month Follow Up Visit (± 2 weeks)

Subjects that remain enrolled at the 12 month study timepoint before the last patient completes their 6 month visit will undergo a final postoperative clinical visit 12 months after the surgery to allow the Investigator to assess the patient's progress. Visit data will be recorded in the subject's study records and on the 12 Month Follow Up Visit eCRF.

Surveys
The following surveys will be completed at this visit to capture postoperative data related to function and quality of life:

- Knee Society Score (KSS) – completed by the Investigator and patient
- SF-12 Health Survey – completed by the patient
- Forgotten Joint Score (FJS) Survey – completed by the patient *(Continued Access Arm only)*

These surveys should be administered prior to any other study visit assessments or procedures being performed to prevent information from the examination biasing the patient's responses.

Radiographs
Standard AP and lateral x-rays of the knee will be collected at this visit per the TSolution One IDE Study Radiographic Evaluation Protocol.

Safety Evaluation & Concomitant Medications/Therapies

All postoperative complications and adverse events will be recorded and assessed as specified under Section 10.0 (Safety Reporting). Concomitant medications and therapies will also be documented during this visit.

7.8. Unscheduled Visits

Patients may be seen by the investigator or delegated staff for unscheduled postoperative visits as needed or SOC. These visits should be documented in the study records and the Unscheduled Visit eCRF. Any adverse events and concomitant medication changes that are reported at these unscheduled visits should be documented in the study records and entered on the Adverse Event and Medication Log eCRFs. Adverse event follow up should be completed as per Section 10.0 (Safety Reporting).

Table 2 – Schedule of Procedures (IDE Study Arm)

	Baseline Visit[a]	Surgical Visit	Hospital Discharge	6 Weeks (± 2 weeks)	3 Months (± 2 weeks) Primary Endpoint	6 Months (± 2 weeks)	12 Months (± 2 weeks)
Informed Consent	X						
Inclusion/Exclusion Criteria	X						
Demographics	X						
Medical History & Physical Exam	X						
TPLAN Operative Planning	X						
TCAT-Assisted TKA (Investigational Procedure)		X					
Hemoglobin and Hematocrit Assessment		X[b]	X[b]				
Transfusion Summary			X[b]				
Standing long-leg X-rays	X[AP, WB]				X[AP, WB]	X[AP, WB]	
Standard X-ray	X[L,NWB]	X[AP/L, NWB*]		X[AP,WB & L,NWB]	X[L,NWB]	X[L,NWB]	X[AP,WB & L,NWB]
3D CT Imaging	X[a]				X		
Knee Society Score (KSS) Survey	X			X	X	X	X
SF-12 Health Survey	X			X	X	X	X
Concomitant Medications/Therapies	X	X	X	X	X	X	X
Safety Evaluation[c]		X	X	X	X	X	X
Study Completion[d]						X[d]	X[d]

AP = Anteroposterior View, L = Lateral View, WB = weight bearing, NWB = non-weight bearing

a. Baseline Visit procedures may be completed in >1 clinic visit if required, but must be completed within 90 days prior to the date of surgery. The preoperative CT scan for surgical planning must be taken within 30 days prior to the date of surgery.
b. Patients will have their hemoglobin and hematocrit levels measured preoperatively no earlier than 30 days prior to the surgical procedure and postoperatively no more than 3 days after the procedure. Patients who are discharged on the date of surgery will have their postoperative hemoglobin and hematocrit levels measured and their transfusion summary documented on Day 0 prior to discharge.
c. Patients with ongoing adverse events at their last study visit will be followed until the adverse event is resolved, no further improvement is expected, or the patient has completed study participation and is exited from the study
d. Once the last patient of this study arm completes their 6M visit, the study arm will be terminated. Once this last patient is enrolled, all other active patients who are not expected to reach 12M prior to this patient's 6M visit will be exited at their 6M visits.

* Postoperative x-rays may be collected if required per standard of care but are not required for this investigation.

Table 3 – Schedule of Procedures (Continued Access Arm)								
	Baseline Visit[a]	**Surgical Visit**	**Hospital Discharge**	**6 Weeks** (± 2 weeks)	**3 Months** (± 2 weeks)	**6 Months** (± 2 weeks)	**12 Months** (± 2 weeks)	**Unscheduled Visits**
Informed Consent	X							
Inclusion/Exclusion Criteria	X							
Demographics	X							
Medical History & Physical Exam	X							
TPLAN Operative Planning	X							
TCAT-Assisted TKA (Investigational Procedure)		X						
Hemoglobin and Hematocrit Assessment		X[b]	X[b]					
Transfusion Summary			X[b]					
Pain Score (NRS)[c]			X					
Range of Motion[c]			X					
Standing long-leg X-ray	X				X	X		
Standard AP X-ray		X[d]		X			X	
Standard Lateral X-ray	X	X[d]		X	X	X	X	
3D CT Imaging	X[a]				X			
Knee Society Score (KSS) Survey	X			X	X	X	X	
SF-12 Health Survey	X			X	X	X	X	
Forgotten Joint Score (FJS) Survey	X			X	X	X	X	
Concomitant Medications/Therapies	X	X	X	X	X	X	X	X
Safety Evaluation[e]		X	X	X	X	X	X	X
Study Completion[f]						X	X	

KEY

a. Baseline Visit procedures may be completed in >1 clinic visit if required, but must be completed within 90 days prior to the date of surgery. The preoperative CT scan for surgical planning must be taken within 30 days prior to the date of surgery.

b. Patients will have their hemoglobin and hematocrit levels measured preoperatively no earlier than 30 days prior to the surgical procedure and postoperatively no more than 3 days after the procedure. Patients who are discharged on the date of surgery will have their postoperative hemoglobin and hematocrit levels measured and their transfusion summary documented on Day 0 prior to discharge.

c. Pain Scores and range of motion data may not be available and are not required for this investigation.

d. Postoperative x-rays may be collected if required per standard of care but are not required for this investigation.

e. Patients with ongoing adverse events at their last study visit will be followed until the adverse event is resolved, no further improvement is expected, or the patient has completed study participation and is exited from the study.

f. Once the last patient in the Continued Access study arm completes their 6M visit, the study arm will be terminated. Once this last patient is enrolled, all other active patients who are not expected to reach 12M prior to this patient's 6M visit will start being exited at their 6M visits.

8. STUDY COMPLETION & EARLY DISCONTINUATION

8.1. Criteria for Study Completion & Early Discontinuation

For each study arm (IDE and Continued Access), patients are expected to remain in the study for 6-12 months after undergoing the investigational procedure. Each study arm will be complete once the last enrolled patient in that arm of the study reaches 6 months. Patients who complete their 12 month follow up visit will be considered to have completed study participation and will have their study completion recorded on the End of Study eCRF. Those patients not expected to reach their 12 month visit prior to study termination will be exited at 6 months and will have their study completion recorded on the End of Study eCRF.

All patients with ongoing adverse events must be followed until the adverse event is resolved, no further improvement is expected, or the patient completes study participation and is exited from the study. The Investigator may discontinue a patient from the study in the event of:

- Any medical event/condition that presents a health or safety risk and prevents the patient from continuing in the study
- Patient's failure to comply with protocol requirements
- Patient withdrawing their consent
- Administrative reasons (e.g. Sponsor's decision to stop the study)

8.2. Documentation of Early Discontinuation

In every instance where a patient is treated with the investigational device and does not complete the study, the Investigator will document the primary reason for discontinuation in the patient's records and on the End of Study eCRF.

- All patients are free to withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice. However, if a patient expresses a desire to withdraw their consent for the study, the site should attempt to obtain written documentation for their study records.
- For patients that are discontinued by the Investigator, the Investigator must notify them of their discontinuation from the study in writing.
- For patients that are lost to follow up, the site staff should document a minimum of three attempts to contact them via phone and one attempt to reach them via certified mail to bring them in for a study visit prior to considering them lost to follow up.

8.3. Use of Data from Early Discontinuation Cases

Study data collected previously for patients who are discontinued from the study by the Investigator or lost to follow-up may still be included and used for the study unless the patient presents written notification of withdrawal of consent to the Investigator. In the event that a

patient withdraws consent to participate in the study, data previously collected for the patient may not be included or used for the study.

8.4. Treatment for Early Discontinuation Cases

Patients who withdraw voluntarily or are discontinued by the Investigator will remain eligible for Standard of Care treatment by the Investigator and study staff.

8.5. Stopping Rules

The Sponsor reserves the right to stop the study at any time in the event that there is a device-related serious adverse event or unanticipated adverse device effect which the Sponsor believes signals a safety concern for study participants. The Sponsor also reserves the right to stop the study for non-safety related issues, including but not limited to usability failures.

Refer to Section 10.7 (Study Termination) for additional details regarding study termination procedures for any event that leads the sponsor to believe the investigational device presents an unreasonable risk to study patients.

9. STATISTICAL PLAN

9.1. Determination of Sample Size for Safety Endpoint

IDE Study Arm

The primary safety hypothes**is** for this study is that the probability of experiencing the composite safety endpoint for patients undergoing TCAT-assisted implantation using the TSolution One System for TKA is not clinically significantly elevated relative to the historic control value of 7.6% for manual TKA. Symbolically, the primary safety hypotheses regarding non-inferiority relative to historical control may be represented as follows:

H_0: $\pi_I \geq \pi_C + \delta$ (clinically inferior safety)
H_A: $\pi_I < \pi_C + \delta$ (not clinically inferior safety)

In this formulation, π_I and π_C are the true event rates when using the investigational device and manual TKA, respectively. As noted above, based on a literature review, $\pi_c = 0.076$. A non-inferiority margin of 0.06 was selected. Therefore, these hypotheses reduce to:

H_0: $\pi_{composite} \geq 0.076 + 0.06 = 0.136$
H_A: $\pi_{composite} < 0.076 + 0.06 = 0.136$

A one-sided Fisher's exact test will be used to test the primary safety hypothesis that the composite safety event rate is larger than historical control (0.076) plus the non-inferiority margin of δ=0.06. That is, the null hypothesis is that the investigational device event rate is 0.136 or larger and the alternative hypothesis is that this event is less than 0.136. Based on the Sponsor's expectation that the technology is associated with improved outcomes, it was assumed for the purpose of sample size determination that that composite safety event rate for patients undergoing primary TKA with femoral and tibial preparation by the TSolution One™ Surgical System is 20% smaller than control, or equal to 0.0608. A one-sided type 1 error of α=0.05 was

assumed. Using industry standard software (nQuery Advisor 7.0, Module POT0x-1), it was determined that statistical power to reject the non-inferiority hypothesis was equal to 82.5% with a sample size of N=103. Because of the discreteness of the exact binomial distribution, the power curve is not monotonic. Power for sample sizes of N=102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121 and 122 are 71.9%, 82.5%, 81.8%, 81.1%, 80.3%, 79.6%, 78.9%, 78.1%, 77.3%, 76.6%, 75.8%, 84.9%, 84.3%, 83.7%, 83.1%, 82.5%, 81.8%, 81.1%, 80.5%, 79.8%, and 87.6%. The smallest sample size with power ≥80% is 103. For sample sizes of N=103 and above, power never falls below 75.8%. The minimum sample size for which power remains at least equal to 80% at that value for all larger values is N=113.

The total sample size to be enrolled is equal to 115 (103 plus 10% for possible loss-to-follow-up).

It can be noted that with N=103, the number (%) of patients experiencing the primary composite safety event must be no larger than 8 (7.8%) in order to achieve the primary study success criterion. With 8 of 103 patients experiencing the event, the upper bound of the one-sided 95% exact binomial confidence interval will be 0.1358 which is less than 0.136, thereby permitting rejection of the inferiority hypothesis and a conclusion of no clinically significant increase in the incidence of the composite safety endpoint.

Continued Access Arm

There will be no formal hypothesis testing for the Continued Access Arm of the study. Patients will be followed for safety and to gain additional information on device use, therefore, no power analysis has been performed to estimate sample size. The Continued Access Arm will enroll up to 50 patients.

9.2. Determination of Sample Size for Effectiveness Endpoint

IDE Study Arm

A review of 1,376 patients undergoing conventional TKA showed a 32% malalignment for mechanical axis greater than 3° (13). This proportion will be used as the comparative constant proportion for 3-month follow-up for conventional TKA in this study.

The primary effectiveness hypothesis for this study is that the probability of malalignment for patients undergoing TCAT-assisted implantation using the TSolution One System for TKA is 50% smaller than the reference rate of 32%, that is, 16%.

H_0: $\pi_I \geq 0.16$ (50% of reference rate = 32%)
H_A: $\pi_I < 0.16$

In this formulation, π_I is the true malalignment probability for the investigational device.

A one-sided type 1 error of α=0.05 was assumed. Using industry standard software (nQuery Advisor 7.0, Module POT0x-1), it was determined that statistical power to reject the null hypothesis in favor of the alternative hypothesis is equal to 89.3% with a sample size of N=103

patients if the true malalignment rate is 0.07. The power for this test remains above 80% as long as the sample size is 95 patients or larger.

Continued Access Arm

There will be no formal hypothesis testing with the Continued Access Arm of the study. Patients will mainly be followed for safety and to gain additional information on device use, therefore, no power analysis has been performed to estimate sample size. The Continued Access Arm will enroll up to 50 patients.

9.3. Analysis Plan

Demographic, baseline, peri-operative and postoperative characteristics for all recruited cases (both study arms) will be assessed from data which is collected on the relevant case report forms. Continuous variables included in demographic, baseline, peri-operative and postoperative summaries, will be evaluated using descriptive statistics (N, mean, median, standard deviation, minimum, and maximum). Dichotomous and polychotomous variables included in demographic, baseline, peri-operative and postoperative summaries, will be described as frequencies and percentages at each level of the categorical variable.

IDE Study Arm

The primary effectiveness endpoint, the safety endpoint and all secondary endpoints including bleeding and the individual components of the composite safety endpoint, will each be summarized by counts, percentages, and the upper bounds of one-sided 95% exact binomial confidence intervals (CI).

Patient function and health-related quality-of-life will be similarly addressed by summarizing baseline, 6-week, 3-month, 6-month, and 12-month (if available) reported outcomes and change at each time point in the Knee Society Scores and SF-12 Health Survey Physical and Mental Health Composite Scores (PCS & MCS), using descriptive statistics including mean, standard deviation, median, minimum, and maximum. The ITT analysis set will be used in all safety analysis. Specific analyses may be repeated in a Per Protocol analysis set that requires completion of the index procedure and no clinically significant protocol violations.

Intraoperative and immediate postoperative complication rates will be similarly summarized using descriptive statistics.

In addition to the above analyses, key safety and effectiveness results will be stratified by certain baseline characteristics (investigational site, age, gender, and median value of Knee Society Score) to confirm that the safety and efficacy of the TSolution One™ Surgical System is consistent among different subgroups.

Continued Access Study Arm

The continued access study arm will not include any hypothesis testing and will not be part of the primary or secondary endpoint analysis. Data from the continued access arm will be provided as

descriptive statistics, which can include counts, percentages, mean, standard deviation, median, minimum, and maximum and the upper bounds of one-sided 95% exact binomial confidence intervals (CI). This analysis will included safety, patient function, and health related quality-of-life described by summarizing baseline, 6 week, 3-month, 6-month, and 12-month (if available) scores, and change in scores from baseline at each time point, as applicable.

10. SAFETY REPORTING

10.1. Definitions

Adverse Event – An adverse event (AE) is any untoward medical occurrence, disease, injury, or untoward clinical signs (including abnormal laboratory findings, surgical complications, etc.), whether related or unrelated to the investigational device or its use.

Adverse Device Effect – This is an adverse event related to the use of an investigational device.

Serious Adverse Event – A Serious Adverse Event (SAE) is an adverse event which:

1. Led to a death,
2. Resulted in life threatening illness or injury*
3. Resulted in patient hospitalization or prolongation of existing hospitalization,
4. Resulted in patient disability or permanent damage or required intervention to prevent permanent impairment/damage
5. Led to a congenital abnormality or birth defect

** NOTE: the term "life-threatening" refers to an event in which the patient was at a risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.*

Unanticipated A*dverse *Device Effect (UADE) – An Unanticipated Adverse Device Effect is:

1. Any serious adverse effect on health or safety or any life threatening problem or death caused by, or associated with, a device, if that effect, problem, or death is not identified in nature, severity, or degree of incidence in this protocol; or
2. Any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of the patients.

10.2. Adverse Event Documentation

Adverse event collection will begin from the time of first incision. All medical events and conditions prior to this time point are to be captured as medical history.

Observed and reported adverse events shall be recorded in the patient's study records and on the Adverse Event eCRF within 72 hours of the site becoming aware of each event, and must include the following information at minimum:

- Event Description
- Date of Onset
- Date of Resolution
- Severity
- Seriousness
- Relationship to Study Device/Procedure
- Outcome

Significant new information and updates should continue to be captured in the patient's records and on the Adverse Event eCRF as they become available and the adverse event should be followed until it is resolved, no further improvement is expected, or the patient completes study participation and is exited from the study.

10.3. Assessment of Severity

Investigators will assess the severity of the adverse event and classify it according to the following definitions.

- **Mild**: Event/symptom is transient and well tolerated by the patient.
- **Moderate**: Event/symptom causes discomfort and interferes with routine activities of the patient.
- **Severe**: Event/symptom interferes considerably with the routine activities of the patient or causes inability to work.

10.4. Assessment of Relationship to Use of the Investigational Device

Investigators will assess the potential relationship of the adverse event to the use of the investigational device and classify the causality of the event according to the following definitions.

- **Definitely Related**: An adverse event that has a strong causal relationship. An adverse event that follows a strong temporal relationship to the use of the investigational device, follows a known response pattern, and cannot reasonably be explained by known characteristics of the patient's clinical state or other therapies.
- **Probably Related**: An adverse event that potentially has a causal relationship. The adverse event has a reasonable temporal relationship to the use of the investigational device and alternative etiology is less likely compared to the potential relationship to the use of the investigational device.
- **Possibly Related:** An adverse event that potentially has a causal relationship. The adverse event has a reasonable temporal relationship to the use of the investigational device but alternative

etiology is equally likely compared to the potential relationship to the use of the investigational device.

- **Not Related**: An adverse event without any apparent causal relationship. The adverse event is due to the underlying disease state or is due to concomitant medication or therapy not related to the use of the investigational device.
- **Unknown Relationship**: If the adverse event cannot be determined to have a causal relationship, it will be classified as unknown.

10.5. Serious Adverse Event Reporting

Adverse events shall be recorded in the patient's study records and in the EDC on the Adverse Event eCRF within 72 hours of the site becoming aware of the event. The study database will be configured to notify the Sponsor of all adverse events that are indicated to be 'serious'. Serious Adverse Events (SAEs) will trigger the database to send an email notification to the Sponsor using the contact information provided below.

Sponsor Contact: Valentina Campanelli
E-mail: vcampanelli@thinksurgical.com

The Investigator should provide additional information on the SAE by updating the information on the Adverse Event eCRF as updates become available. The Sponsor may also ask for additional clinical reports including redacted source documents to be provided by the Investigator to assist in the assessment of the event. Significant new information and updates should continue to be submitted promptly to the Sponsor and entered on the Adverse Event eCRF as they become available, and the Investigator should follow the SAE until it is resolved or no further improvement is expected.

The Sponsor shall ensure that the Investigator submits safety event notifications to the governing Investigational Review Board (IRB) within the timeframe specified by the IRB, when applicable. Acceptable means of confirming that the IRB requirements have been met include forwarding a copy of the written, signed report that was sent to the IRB to the Sponsor. Copies of this report should be filed in the Investigator's site files and the Sponsor's clinical investigation files.

10.6. Determination and Reporting of Unanticipated Adverse Device Effects

The Sponsor shall review all reported SAEs to evaluate whether they meet the criteria for an Unanticipated Adverse Device Effect. For adverse events that are determined to be UADEs, the Sponsor will submit an expedited safety report to the FDA's Center for Devices and Radiological Health (CDRH). The expedited safety report will consist of a completed Form FDA 3500A and a cover letter analyzing the significance of the event. The expedited safety report will be submitted

to the FDA as soon as possible and, in no event, later than 10 working days after the Sponsor first receives notice of the UADE. A copy of this safety report will be provided to all participating study investigators.

If, following receipt and investigation of follow-up information regarding an adverse event that was previously determined not to be a UADE, the Sponsor determines that the event does meet the requirements for expedited reporting, the Sponsor will submit a completed Form FDA 3500A and cover letter as soon as possible, but in no event later than 10 working days after this is determined.

10.7. Study Termination for Safety Concerns

The Sponsor, in consultation with the Investigators, shall determine if any reported event presents an unreasonable risk to study patients. If an event is determined to pose an unreasonable risk, the Sponsor shall develop procedures to terminate the study within 5 working days.

10.8. Treatment of Adverse Events

Adverse events that occur during the study shall be handled by established standards of care to protect the health and safety of the patient. Necessary care shall be provided by the Investigator or designee. All patients with ongoing adverse events must be followed until the adverse event is resolved, no further improvement is expected, or the patient completes their study participation and is exited from the study.

11. PROTOCOL DEVIATIONS

All protocol deviations (i.e. any change, divergence or departure from the procedures specified in this protocol, including procedures described in the appendices) must be documented with an explanation for the deviation on the Protocol Deviation eCRF.

Minor Deviations: A minor deviation does not impact the subjects' rights, safety, or well-being, or the completeness, accuracy or reliability of the study data. Minor deviations shall be documented in the study database along with a full description of the event and outcome. The Sponsor will analyze these deviations and assess their significance. Minor deviations should be reported to the reviewing IRB if required by the IRB's deviation reporting guidelines.

Major deviations: A major deviation is a deviation from the protocol that impacts the subjects' rights, safety, or well-being, or the completeness, accuracy or reliability of the study data, or a deviation from FDA regulations or IRB guidelines. Major deviations should be reported to the Sponsor within 24 hours of site awareness of the event and must be documented in the study database along with a full description of the event and outcome. The Sponsor will analyze these deviations and assess their significance. Major deviations should be reported to the reviewing IRB per the IRB's deviation reporting guidelines.

12. DEVICE LABELING

In accordance with federal regulations set forth in 21 CFR 812.5, the TSolution One™ Surgical System and User Manual will be labeled with the following statement:

'CAUTION – Investigational Device. Limited by Federal (or United States) law to investigational use.'

13. ETHICAL REVIEW, REGULATORY CONSIDERATIONS, AND CONFIDENTIALITY

13.1. Ethical Review

Prior to the start of the study the Investigator will provide the Sponsor or its designee with documentation that the IRB has reviewed and approved the protocol and the Informed Consent Form. Additional documentation may be submitted pending applicable local requirements. Each Investigator must provide at least the following documentation:

- IRB approval of the protocol
- IRB approval of the Informed Consent Form
- IRB annual renewed approval of the protocol
- The IRB approval of any revisions to the Informed Consent Form or amendments to the protocol

13.2. Regulatory Considerations

This study will be conducted in accordance with the Good Clinical Practice (GCP) guidelines and other applicable regulatory requirements including but not limited to:

- Food and Drug Administration (FDA) Regulations on Investigational Device Exemption (21 CFR 812)
- FDA Regulations on research with human beings (21 CFR 50, 54 and 56)
- Health and Human Services (DHHS) Regulations on research with human beings
- (45 CFR 46 Subparts A, B, C, and D)
- International Conference on Harmonization (ICH) Guidance for Industry-E6 Good Clinical Practice: Consolidated Guideline
- International Organization for Standards (ISO 14155-1 and 2)

The Investigator will ensure that this study is conducted in full conformity with the 1989 or 1996 revisions of the Declaration of Helsinki.

13.3. Confidentiality

All data and records generated during this study will be kept confidential in accordance with the Privacy Rule (45 CFR Parts 160 and 164) of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). In order to maintain subject confidentiality, Subjects will be identified by a site number, subject number and subject initials on CRFs and other documentation submitted to the Sponsor or designee. All attempts will be taken to maintain subject confidentiality. However, the following individuals or organizations may require access to protected health information in order to monitor and analyze the trial:

- THINK Surgical and designees
- Institutional Review Board
- Office of Human Research Protections (OHRP) or the Food and Drug Administration (FDA)
- Contract Research Organization responsible monitoring the clinical trial

14. DATA HANDLING & RECORD KEEPING

14.1. Data Management

Source documents and electronic Case Report Forms (eCRFs) will be completed in a 21 CFR Part 11 compliant electronic data capture (EDC) system for each patient enrolled into the clinical study. The Study Coordinator will review and sign off on completed eCRFs to attest that all data entered on the eCRFs are complete and accurate after the monitor finishes the source document verification process. The Investigator will sign off on the Eligibility Criteria, all Adverse Event, and Protocol Deviation and Study Completion eCRFs and will sign each patient's casebook once the patient completes the study to attest that all data entered on the eCRFs are complete and accurate. All of the above signatures will be completed digitally within the EDC system using the system's Part 11 compliant digital signature system function.

Any required data clarifications will be handled within the EDC system's query management system. The EDC will be programmed to automatically place data clarification queries on missing values and values out of acceptable ranges. Study monitors and data managers will also be able to add data clarification queries to data points within the system. Study coordinators will have the opportunity to correct data and/or respond to the query for review by monitors and data managers.

14.2. Record Keeping

The Investigator and Sponsor will maintain records in accordance with 21 CFR 812, Subpart G, to include:

- Current and past versions of the IRB-approved clinical protocol and corresponding IRB-approved consent form(s) and, if applicable, patient recruitment advertisements
- FDA correspondence related to the IDE application; including supplemental IDE applications, current investigator lists, progress reports
- IRB correspondence (including approval notifications)including safety and protocol deviation reports, and annual or interim reports
- Signed Investigator Agreements and financial disclosure forms for participating investigators
- Curriculum vitae (Investigator and Sub-Investigators)
- Certificates of required training for Investigators and Sub-Investigators, including human subject protection and Good Clinical Practice
- Instructions for handling the investigational device and other study-related materials
- Signed informed consent forms
- Source Documents
- Monitoring visit reports
- Copies of relevant Sponsor-Investigator correspondence, including notifications of adverse event information
- Screening and Enrollment Log
- Final clinical study report

15. RADIOGRAPHIC ENDPOINT ASSESSMENT

Radiographic assessment of the efficacy endpoints (i.e. coronal alignment relative to the mechanical axis, and post-operative alignment outcomes) will be performed by protocol-trained radiologists at an independent core imaging lab per the TSolution One IDE Radiographic Evaluation Protocol.

Medical Metrics, Inc.
2121 Sage Road, Suite 300
Houston, Texas 77056
Phone: 713-850-7500, x202

www.medicalmetrics.com

This analysis will only be performed for the IDE Study Arm. The Continued Access Arm will continue to collect imaging to monitor safety by the Investigator. Images will be transferred and stored with Medical Metrics, Inc., but no formal analysis will be performed for this arm.

16. STUDY MONITORING

Study monitoring functions will be performed by an independent clinical research organization (CRO) in compliance with recognized Good Clinical Practices, FDA's IDE guidance documents, and federal regulations outlined in 21 CFR 812.43(d) and 21 CFR 812.46.

Musculoskeletal Clinical Regulatory Advisers, LLC (MCRA)
1050 K St NW, Suite 1000
Washington, DC 20001

In addition to ensuring adequate communication between the Investigators and the Sponsor, the CRO's duties include on-site visits and review of study documents and reported data. The CRO study representatives will be provided with appropriate device training prior to the study and will follow a Monitoring Plan for all study-related monitoring activities.

16.1. Monitoring Activities

On-site monitoring visits include a pre-study Site Initiation Visit, periodic Interim Monitoring Visits, and a Close-Out Visit at the end of the site's participation in the study.

Each site's Investigator will allocate adequate time for monitoring activities. The Investigator will also ensure that the monitor or other compliance or quality assurance reviewer is given access to the study-related documents and study related facilities, and has adequate space to conduct the monitoring visit.

Monitoring visits will be documented on monitoring visit reports, and will aim to verify that:

- Compliance with the clinical protocol and applicable regulations is being maintained
- Only authorized individuals are participating in the study
- The investigational device is being used according to the protocol and instructions for use
- Adequacy of staffing and facilities
- Adequate access to eligible patients
- Signed and dated informed consent forms have been obtained from each patient
- eCRFs and queries are complete
- Source data is verified and signed-off upon as accurate
- Patient files are accurate and complete
- All adverse events are reported to the Sponsor

- All serious and unanticipated adverse device events are reported to the Sponsor and the IRB/EC
- All other required reports, notifications, applications, submissions, and correspondence are maintained in the Investigator's files and are accurate
- Maintenance and calibration of equipment relevant to clinical assessments is appropriately performed and documented
- Laboratory certifications/validations are current
- Patient withdrawal has been documented (if applicable)
- Patient non-compliance has been documented (if applicable)
- The Investigator and site staff are informed and knowledgeable of all relevant document updates concerning the clinical investigation
- Corrective and preventive actions have been implemented (if applicable)

16.2. Frequency of Visits

To ensure that the study is conducted in accordance with the terms of the clinical protocol, study monitors must visit each study site at routine intervals throughout the duration of the study. The exact frequency of visits shall be determined on an individual site basis as detailed in the Monitoring Plan, and shall depend upon the following factors:

- Rate of patient enrollment
- Experience of the Investigator in conducting clinical studies
- Record of previous site compliance

17. AUDITS AND INSPECTIONS

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities. The Investigator must also be prepared to permit study-related audits and inspections by the Sponsor, CRO, IRB/EC and the site's institutional compliance and quality assurance groups. The Investigator will ensure the capability for inspections of applicable study-related facilities, records and reports.

18. RECORD RETENTION

The sponsor-investigator will retain the specified records and reports for up to two years after the marketing application is approved for the investigational device; or, if a marketing application is not submitted or approved for the investigational device, until two years after investigations under the IDE have been discontinued and the FDA so notified.

19. PUBLICATION PLAN

Any Investigator involved with this study is obligated to provide the Sponsor with complete test results and all data derived from the study. Investigators are not permitted to publish or share the results or any part of the results of this study, nor any of the information provided by the

Sponsor for the purposes of performing the study, to any third party without the consent of THINK Surgical, Inc.

The study will be registered on Clinicaltrials.gov in compliance with 42 CFR Part 11. Results of the study, including an unanticipated early termination of the trial, will be posted to the Clinicaltrials.gov database at the conclusion of the study. In the event that the study is terminated early, the posting of these results will be completed within 30 days of completion of data analysis.

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APPENDIX: Patient Survey Instruments

Knee Society Score (KSS) Survey
SF-12 Patient Satisfaction Survey
Forgotten Joint Score