Clinical Protocol - Device

A Prospective, Multi-Center, Post-Market Clinical Study to Evaluate the Performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System in Total Knee Arthroplasty Procedures.

Sponsor and funding source:	Smith & Nephew Inc, 1450 E. Brooks Road Memphis, Tennessee 38116, USA
Investigational and Comparator Product(s)	CORI™ KNEE TENSIONER
Single Identification Number of Clinical Investigation	CORI TENSIONER.2020.04
Protocol Author(s):	Leann Speering, MS, CCRP, Lead – Clinical Study Management Yueming Shi, Statistician, Global Biostatistics Samantha Oneill, Senior Specialist, Global Clinical Strategy
Summary of Revision History	Version 1.0, 29 Jan 2021 Version 2.0, 22 Apr 2022 Version 3.0, 16 Feb 2023

1 SIGNATURES

1.1 Principal Investigator Signature Page

This page will be returned to Smith+Nephew Inc and a copy retained at the investigational site.

I have read the attached protocol entitled "A Prospective, Multi-Center, Post-Market Clinical Study to Evaluate the Performance of CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System in Total Knee Arthroplasty Procedures", version 4.0, dated 05Mar2025, and agree to abide by all provisions set forth herein.

I agree to comply with the Investigator's Obligations stipulated in Section 22.10 of the protocol,

I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the conduct of the described clinical investigation without the prior written consent of Smith+Nephew Inc.

Name, Address, Professional Position	**Signature and Date / DocuSign Stamp**

1.2 Coordinating Investigator Approval

I have read the attached protocol entitled "A Prospective, Multi-Center, Post-Market Clinical Study to Evaluate the Performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System in Total Knee Arthroplasty Procedures", version 4.0, dated 05Mar2025, and agree to abide by all provisions set forth therein.

Name, Address, Professional Position	**Signature and Date / DocuSign Stamp**
Ken Urish, University of Pittsburgh Medical Center (UPMC) 300 Halkett, Pittsburgh, PA 15213	Signed by: Dr Ken Urish Signer Name: Dr Ken Urish Signing Reason: I approve this document Signing Time: 06-Mar-2025 | 03:10:45 PST 28A6FF0A301C486CB98F55C1A07ECAD3

1.3 Sponsor Approval

Name and Title	Signature and Date / DocuSign Stamp
Rachael Jahnke VP, Global Clinical Research Organization (Head of Global Clinical Operations)	Signed by: Signer Name: Rachel Jahnke Signing Reason: I approve this document Signing Time: 07-Mar-2025 | 16:58:53 GMT 98517B5EF45A456CBE7102BF1B8CCDA5
Amir Kamali Sr Director Global Clinical Strategy (Global Clinical Strategy Franchise Head or Representative)	Signed by: Amir Kamali Signer Name: Amir Kamali Signing Reason: I approve this document Signing Time: 07-Mar-2025 | 16:46:18 GMT EC3CA19074E446478F070292FA2D4130
Jay Jantz Director, Clinical Data Analytics (Head of Global Data Analytics)	Signed by: Jay Jantz Signer Name: Jay Jantz Signing Reason: I approve this document Signing Time: 11-Mar-2025 | 23:02:52 GMT B7D37248838E4CACAE11E7E55198A88D
Gion Fessel Lead – Global Medical Affairs (Medical Affairs Representative)	Signed by: Signer Name: Gion Fessel Signing Reason: I have reviewed this document Signing Time: 07-Mar-2025 | 15:28:00 GMT C75697920685412C90F62F0ADC672075
Corrine Herlinger Senior Principal Regulatory Affairs Specialist (Regulatory Representative)	Signed by: Signer Name: Corrine Herlinger Signing Reason: I approve this document Signing Time: 11-Mar-2025 | 15:13:02 GMT EE1E8CD478B846F190E2058F0AF1EE86
Madison Cracknell Specialist - Clinical Compliance (Clinical Compliance and Training)	Signed by: Madison Cracknell Signer Name: Madison Cracknell Signing Reason: I approve this document Signing Time: 06-Mar-2025 | 14:22:24 GMT 3AB419874F3545B2B66A3EDDE7DC1FC9
Karlie Morgan Director, Clinical Study Management (Regional Operations Director)	Signed by: Karlie Morgan Signer Name: Karlie Morgan Signing Reason: I approve this document Signing Time: 06-Mar-2025 | 00:04:43 GMT F420CE2095794AFD8CD1DC3D32055809

2 SYNOPSIS

Title of Study:	A Prospective, Multi-Center, Post-Market Clinical Study to Evaluate the Performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System in Total Knee Arthroplasty (TKA) Procedures.
Sponsor and Funding Source	Smith + Nephew Inc, 1450 E. Brooks Road, Memphis, Tennessee 38116, USA
Study Design:	This is a post-market, prospective, multi-center, open-label study evaluating the performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System at approximately 4 centers across the United States. Patients who are eligible for a robotic assisted TKA procedure with the CORI™ Surgical System will be enrolled and followed for approximately 12 months.
Study Type:	Interventional
Study Product:	The CORI™ KNEE TENSIONER is an accessory to REAL INTELLIGENCE™ CORI™ Surgical System. The TENSIONER may be used to assist the surgeon in providing consistent varus and valgus stress during gap assessment before making any bony resections. The TENSIONER communicates directly with CORI software, providing automated data collection.
Comparison Group(s)*: (*if applicable)	Not Applicable (NA).
Study Purpose:	To evaluate the performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System.
Primary Objective:	To evaluate the performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System by assessing patient satisfaction with the EQ-5D-5L VAS.
Secondary Objective(s):	To further evaluate patient satisfaction using additional scoring tools (i.e., the EQ-5D-5L Index score and the 2011 Knee Society Score (KSS) Objective, Function, and Satisfaction).
Other Objective(s):	To evaluate the repeatability of the gap balancing workflow with the TENSIONER when compared to the surgeon's current, manual gap balancing technique.

	To generate data to support the creation of an optimized workflow for gap balancing with the TENSIONER. To correlate soft tissue balance with subsequent implant placement changes.
Sample Size:	To achieve 80% power, 20 evaluable subjects are required. To allow for up to 25% attrition due to loss to follow-up, a minimum of 27 subjects will need to be enrolled, with a maximum of 83, based on those consented under frequentist sample size calculations in Protocol Version 3.0.
Number of Study Sites:	Approximately 4 sites
Targeted Global Regions:	United States
Inclusion Criteria:	1. Subject agrees to consent to the study by signing the Independent Review Board (IRB) approved ICF. 2. Subject is eighteen (18) years old or older. 3. Subject is willing and able to attend all study follow-up visits for up to one (1) year postoperatively (as defined in the study protocol and ICF). 4. Subject can read, understand, and communicate responses to Patient Reported Outcome Measures (PROMs). 5. Subject is suitable for the CORI™ Surgical System. 6. Subject requires a cemented TKA as a primary indication due to any of the following condition: • Degenerative joint disease, including osteoarthritis • Rheumatoid arthritis. • Avascular necrosis. • Requires correction of functional deformity • Requires treatment of fractures that were unmanageable using other techniques.
Exclusion Criteria:	1. Contraindications or hypersensitivity to the use of the CORI™ Surgical System per the IFU. 2. Participation in the treatment period of another clinical trial within thirty (30) days of the Pre-Operative Visit, or during the study. 3. Women who are pregnant, nursing, or of child-bearing potential who are not utilizing birth control measures. 4. Subjects who are non-English speaking.

5. Any subject that meets the definition of a Vulnerable Subject per ISO 14155.
6. Subjects who have participated previously in this clinical trial
7. Subjects with a history of poor compliance with medical treatment.
8. Subject needs a CORI™ Surgical System TKA on the index joint as a revision for a previously failed surgery, or need for complex implants, or any other implant than a standard TKA (e.g., stems, augments, or custom-made devices).
9. Subject has been diagnosed with post-traumatic arthritis
10. Subject needs a bilateral TKA.
11. Subject has active infection or sepsis (treated or untreated)
12. Subject is morbidly obese with a body mass index (BMI) greater than 40.
13. Subjects with a medical or physical condition that, in the opinion of the Investigator, would preclude safe subject participation in the study. This includes:
    - Advanced osteoarthritis
    - Joint disease
    - Paget's or Charcot's disease
    - Vascular insufficiency
    - Muscular atrophy
    - Uncontrolled diabetes
    - Moderate to severe renal insufficiency
    - Neuromuscular disease
    - Mental illness or mental retardation
    - Drug or alcohol abuse

Study Duration:	Duration of study: estimated 27 months. Enrollment period: estimated 15 months. Follow-Up period: 12 months.
Primary endpoint:	The change from the pre-operative to 12-month follow-up in EQ-5D-5L VAS score.
Secondary endpoint(s):	• The change from the pre-operative to 12-month follow-up in EQ-5D-5L Index score. • The change from the pre-operative to 12-month follow-up in KSS Objective, Function and Satisfaction scores. • Mean of the KSS Expectation scores at pre-operative and at 12-month follow-up.

Other exploratory endpoint(s):	• Evaluate the repeatability, within the same deformity profile, of gap planning with the TENSIONER when compared to the surgeon's manual gap balancing technique. • Medial-to-lateral gap balance measurements at 0/10°, 30°, 60°, and 90° flexion. • Implant position alignment and resection depths. • Incidence and details of soft tissue release. • Analysis of force and deformity data (i.e., deformities outside the given range).
Safety Data	• All adverse events and complications occurring from the time of subject enrollment until study termination or study completion including intra-operative AEs and complications • Device related re-intervention • Device Deficiencies

STUDY SCHEDULE

Visit Type/name	Frequency/Time point
Screening / Pre-Operative	Up to Day -180
Operative	Day 0 - Surgery Day
Follow-up	6 weeks (42 ± 14 days) post-surgery 6 months* (180 ± 30 days) post-surgery 12 months (365 ± 30 days) post-surgery * The 6-month visit may be conducted remotely

3 CONTENTS
3.1 Table of Contents

3.2 List of Tables

3.3 List of Figures

3.4 List of Abbreviations/Acronyms and Definitions

Abbreviation	Definition
ABHI	Association of British Healthcare Industries
ADE	Adverse Device Effect(s)
AE	Adverse Event(s)
ASADE	Anticipated Serious Adverse Device Effect(s)
AVN	Avascular necrosis
BMI	Body Mass Index
(e)CRF	(electronic) Case Report Form(s)
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DD	Device Deficiency(ies)
DMP	Data Management Plan
FAS	Full Analysis Set Population
FDA	Food and Drug Administration
FJS	Forgotten Joint Score
GCP	Good Clinical Practice
CTG	ClinicalTrials.gov
HIPAA	Health Information Portability Accountability Act
IB	Investigator's Brochure
ICC	Intra-Class Correlation Coefficients
ICF	Informed Consent Form
ICMJE	International Committee of Medical Journal Editors

IFU	Instructions for Use
Interventional study	A type of clinical study in which participants are assigned to groups that receive one or more intervention/treatment so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes.
IP	Investigational Product
IRB	Institutional Review Board
ISF	Investigator Site File
KSS	Knee Society Score
KSCR	Knee Society Clinical Rating
NA	Not Applicable
N (or n)	Total Sample Size (or subgroup sample size)
OA	Osteoarthritis
PI	Principal Investigator
PP	Per-protocol Population
RA	Rheumatoid arthritis
S+N	Smith+Nephew Inc
SADE	Serious Adverse Device Effect(s)
SAE	Serious Adverse Event(s)
SAF	Safety population
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOP	Standard Operating Procedures
TKA	Total Knee Arthroplasty
USADE	Unanticipated Serious Adverse Device Effect(s)
VAS	Visual Analogue Score
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

4 INTRODUCTION

4.1 Background

Total knee arthroplasty (TKA) is a highly successful and frequently performed surgical treatment to reduce disability caused by conditions such as osteoarthritis (OA), rheumatoid arthritis (RA), avascular necrosis (AVN), and other joint diseases or deformities.

OA is characterized by loss of cartilage, remodelling of adjacent bone, and inflammation in the affected joint [1, 2], while RA is a progressive inflammatory disease that eventually causes systemic joint damage and disability [3]. As of 2010, there were approximately 250 million people globally with OA of the knee joint (3.6% of the global population) [4]. The prevalence was higher in females than in males [4]. Initial treatment of arthritis may include physical therapy, nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and corticosteroids which can be taken orally or by injection.

AVN has several etiologies but fundamentally results from a decrease in blood flow to the affected bone, leading to cellular death [5]. Studies have reported a 3.4% and 9.4% incidence of spontaneous osteonecrosis in persons older than 50 and 65 years of age, respectively [6]. Initial treatment of AVN may include medication, stretching, not walking on the affected leg.

When the damage to the joint is advanced or available conservative treatment options are exhausted, such as pain medication and physical therapy, advanced treatment such as a TKA procedures are considered.

Technical outcomes for TKA are excellent, with favorable postoperative health-related quality of life [7] and reported survivorship of 82.3% at 25 years [8]. In the United States, it is estimated that 600,000 primary TKAs performed each year, and the number of procedures is expected to annually increase by 10% [9, 10]. The escalating prevalence of end-stage OA places an increased burden on healthcare providers, especially on less experienced surgeons and facilities that perform low numbers of arthroplasties [11, 12]. Lower volume hospitals (200 procedures/years) [12, 13]. Therefore, technology or techniques that could improve outcomes and reduce the risk of revision are becoming increasingly important.

TKAs often involve resection of the medial and lateral menisci as well as the anterior cruciate ligament and, at times, the posterior cruciate ligament. This means that correct balancing of the remaining ligamentous structures is crucial to knee stability. Gap balancing, also called tensioning, or soft tissue balancing, allows the surgeon to evaluate the tension of the ligaments to determine proper placement of a knee implant. During TKA, a surgeon attempts to achieve balanced tension within the knee throughout range of motion to provide implant stability and longevity. Even with good bone cuts, trapezoidal flexion and extension gaps may occur due to soft tissue imbalance. A

trapezoid gap results in uneven tension (tight on one side, loose on the other) which may cause asymmetric wear on the knee.

Soft tissue balancing contributes to short- and long-term success of TKA surgery because a well-balanced knee is shown to decrease postoperative instability and stiffness leading to revision and an improvement in patient reported outcome scores. Surgeons rely on experience and subjective feel to assess joint laxity. Balance is achieved by adjusting implant sizing, implant alignment and soft tissue release; however, this is often very subjective.

The CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System aims to help standardize gap balancing techniques by providing a quantifiable force to distract the knee joint and tension the ligaments. This study is being conducted to show that the TENSIONER can provide a consistent and repeatable force during gap balancing and that improved patient reported outcomes can be achieve using this tool.

4.2 Literature Summary

4.2.1 Search Methodology

A pragmatic review was carried out to identify publications discussing soft tissue balancing with a particular focus on the techniques employed to achieve satisfactory soft tissue balance. Searches were carried out in November 2020 in Embase, PubMed and Google Scholar.

4.2.2 Results

<u>Importance of soft tissue alignment in total knee arthroplasty:</u>

The correct alignment and balancing of soft tissue surrounding the knee is considered to be a key predictor to a successful TKA [14,15]. However, achieving optimal alignment and balancing of soft tissues can often be more challenging than achieving good bony alignment [14]. When a patient has a malaligned and imbalanced knee post-operatively, the likelihood of TKA failure increases, particularly for instability, implant loosening and polyethylene wear [16]. In addition, soft tissue balance is important for maintaining joint alignment during flexion and extension of the joint, thereby allowing the patient to experience the full range of motion required for many activities of daily living [15]. Indeed, there is evidence to demonstrate that patients with well-balanced knees have better post-operative outcomes (including the Knee Society Score (KSS), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), mean activity scores, and the Forgotten Joint Score (FJS)) compared to an unbalanced control group [17,18].

Correct soft tissue balance can be broadly defined by equal, symmetrical flexion and extension gaps [14,19,20]. However, despite its potential importance to post-operative outcomes, definitive values for the laxity of surrounding soft tissue are lacking and there are multiple differing

definitions of what exactly constitutes a well-balanced knee [21,22]. This is compounded by challenges in being able to accurately assess laxity intra-operatively; during surgery, the patient's soft tissues are in a relaxed, non-loaded paralysed state, from which the surgeon has to extrapolate subsequently loaded weight-bearing performance [21,23,24]. Traditionally, soft tissue balancing was often based on the subjective feel of the joint gained from the surgeon's experience, but various techniques have been developed to help with assessment of appropriate knee balancing during TKA [20,25,26].

Traditional methods of soft tissue balancing:

There are two main techniques employed: measured resection and gap balancing [27-29]. The measured resection technique involves using bony landmarks to resect bone. The amount of bone resected depends on the thickness of the prosthetic implant to be inserted. These bone cuts are made independently of soft tissue tension, with soft tissue releases only being carried out if the flexion and extension gaps need equalizing [27-29]. However, evidence has been presented to suggest that there is wide variability in femoral component rotation when using bony landmarks, which can lead to condylar lift off in flexion and asymmetry of the flexion space [29]. This has led some researchers to advocate gap balancing instead [29].

The gap balancing technique involves using ligament tension to determine the amount of bone to resect. In this technique, the joint space is distracted during flexion and a rectangular gap is created which is equal both in extension and flexion of the knee [27-29]. It relies on symmetric tension placed on the ligaments in flexion to set femoral component rotation [30].

There are a number of tools available that can help guide a surgeon's decision-making when assessing flexion-extension gap balance, including spacers, distractors and TENSIONERS [21]. The use of spacers or blocks (or even the implant itself) can be used to perform stress tests. This technique is based on the insertion of a series of fixed thickness spacers into the knee joint and tested during full extension and 90° flexion to measure the resulting gap [31]. Although this technique is relatively simple and fast, it comes at the cost of inaccuracies that can be particularly apparent in flexion [14]. Distractors can be used in the medial and lateral compartments to assess soft tissue laxity. However, due to the possibility of different forces being applied to each compartment, coupled with inherit differences in the visco-elastic properties of the tissues, even an apparently well-balanced knee may in fact be suboptimal for soft tissue balance [14]. Lastly, the use of TENSIONERS allows the flexion and extension gaps to be assessed by the tensioning of the medial and lateral compartments [32-34]. In contrast to spacer blocks, the use of a TENSIONERS allows the surgeon to detect and correct angular or mediolateral soft tissue asymmetry [32].

More recently, the use of sensor-guided knee balancing has appeared allowing for the intraoperative use of a pressure sensor to help guide knee soft tissue balancing. One such example is Verasense™ (OrthoSensor, Dania, Florida), with proponents suggesting that sensor-guided knee balance should improve surgical accuracy compared to conventional gap balancing

techniques [19]. However, electronic sensors are limited in their ability to predict ligament balance and tension before bone resection and lack the ability to predict balance through the full range of motion [19].

Regardless of whether gap balancing, or measured resection is used, or a combination of the two, the surgeon achieves only a partial projection of the knee's final performance [35]. Furthermore, soft tissue balancing remains both subjective and operator-dependent, which is particularly problematic given the high proportion of early TKA revisions that can be attributable to soft tissue balance problems [16].

Integration of gap balancing into navigation/robotic workflows:

Computer-assisted navigation systems, as part of their role in helping to facilitate component alignment, have been designed to improve the reproducibility of conventional techniques for obtaining appropriate gap balancing [36]. It has been suggested that computer navigation may assist the surgeon in measuring laxity more accurately intraoperatively, particularly with its ability to provide the surgeon with real-time numerical feedback [21]. It has been shown that navigation-assisted soft tissue balancing can achieve better gap balancing and less inadvertent medial soft tissue release compared to conventional techniques [37].

Most recently, the use of robotic-assisted TKA systems have been supplemented with robotic-assisted tensioning tools. An example of one such device is BalanceBot™ (Corin, Raynham, MA), which allows surgeons to see intra-operative data on ligament tension, predict post-operative gap balance, and then execute the plan by interacting with the associated robotic-assisted TKA system (OMNIBotics™; Corin, Raynham, MA). Clinical studies have demonstrated that the combination of a robotic-assisted system with ligament tensioning and balancing tools can help with the accurate prediction of TKA postoperative joint gaps, with over 90% of cases having a flexion-to-extension and mediolateral balance within 2mm [21]. This suggests that the use of robotic tensioning systems can help make accurate predictions of gaps throughout the arc of motion, thereby warranting further consideration by surgeons striving to improve outcomes post-TKA.

4.3 Study Purpose

This is a prospective, multi-center, post-market study to evaluate the performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System.

4.4 Safety Considerations

The CORI™ KNEE TENSIONER is an optional accessory to the CORI™ Surgical System. It is a tool used during the gap planning stage of the CORI™ Surgical System workflow to aid in the collection

of consistent gap measurements. Please refer to Section 6 of this protocol and the Instructions for Use (IFU) for a detailed description of the study product and reprocessing instructions.

Risk information is taken from the initial hazard assessment for the TENSIONER [38]. The initial hazard assessment is assessed prior to any mitigations being in place. All potentially hazardous situations with high initial risk levels will be mitigated through risk controls, with some having special considerations just for this clinical study.

Verification and validation testing relating to subject safety of the product throughout the product's life cycle for this specific study is complete.

5 OBJECTIVE(S)

5.1 Primary Objective

The primary objective of this study is to evaluate the performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System by assessing patient satisfaction with the EQ-5D-5L Visual Analogue Scale (VAS).

5.2 Secondary Objective(s)

The secondary objective is to further evaluate patient satisfaction using additional scoring tools (i.e., the EQ-5D-5L Index score and the 2011 KSS Objective, Function and Satisfaction scores).

5.3 Other Objective(s)

Other objectives include evaluating the repeatability of the gap balancing workflow with the TENSIONER when compared to the surgeon's current, manual gap balancing technique. Additional objectives include generating data to support the creation of an optimized workflow for gap balancing with the TENSIONER as well as correlating soft tissue balance with subsequent implant placement changes.

5.4 Claims

No claims to be confirmed by this study.

6 INVESTIGATIONAL PRODUCT

6.1 Identification

6.1.1 Investigational Product

The following CORI™ Surgical System components have 510(k) clearance number (K221224) and are considered post-market products but will be provided to the site as Investigational Products.

- CORI™ KNEE TENSIONER
- CORI™ KNEE TENSIONER Cartridge
- CORI™ KNEE TENSIONER Tray Insert

The following CORI™ Surgical System components, apart from the Case Archive USBs (not considered a medical device), have 510(k) clearance, but are not surgeon-facing products; instead, a Smith + Nephew (S+N) representative will be responsible for handling these Investigational Products and installing it on the CORI™ Surgical System.

- REAL INTELLIGENCE™ Application Software
- Implant Database
- Case Archive USBs

The Investigational Product is manufactured by Smith+Nephew, Blue Belt Technologies, 2905 Northwest Blvd. Suite 40, Plymouth, MN 55441, USA.

Table 6.1.1-1 Investigational Product

	Investigational Product 1	**Investigational Product 2**	**Investigational Product 3**	**Investigational Products 4**
Product	CORI™ KNEE TENSIONER	CORI™ KNEE TENSIONER Cartridge	CORI™ KNEE TENSIONER Tray Insert	REAL INTELLIGENCE™ Application Software, Implant Database, and Case Archive USBs
Catalogue Number	ROB10100	ROB10101	ROB10102	NA
Manufacturer / License Holder	Blue Belt Technologies, Inc.	Blue Belt Technologies, Inc.	Blue Belt Technologies, Inc.	Blue Belt Technologies, Inc.
Regulatory Status	510(k) Cleared	510(k) Cleared	510(k) Cleared	510(k) Cleared
Supplier	S+N Endoscopy, Inc.	S+N Endoscopy, Inc.	S+N Endoscopy, Inc.	S+N Endoscopy, Inc.

TENSIONER Accessory

The CORI™ KNEE TENSIONER is an optional accessory to the CORI™ Surgical System. The TENSIONER is an electromechanical instrument designed to interact with and provide feedback to CORI with respect to the force that the user applies to the joint. Through the CORI software user interface, the surgeon specifies the target force value (50N, 100N, 150N) for optimum ligament tension. CORI collects gap data when the TENSIONER reading is within the specified force range (± 10N of target value).

The surgeon uses the TENSIONER to apply a force to the knee joint and stretch the ligaments throughout the range of motion of the knee during gap balancing. The curved fork and tongue design of the TENSIONER allows the surgeon to distract the joint while maintaining a consistent application of tension on the ligaments throughout the range of motion per the specified force range set by the surgeon.

The addition of the TENSIONER does not change the CORI planning workflow. When the TENSIONER is connected, the surgeon can switch between using the TENSIONER or manual technique by selecting the corresponding button on the touch screen.

Knee TENSIONER Design

The TENSIONER is a retractor with an integrated strain gauge for measuring the applied distraction force from the user. It is a wired surgical instrument that connects to CORI through a USB.

The handheld instrument, CORI™ KNEE TENSIONER is the reusable component of TENSIONER. Reverse action pliers with a fork and tongue design distract the joint as the surgeon takes the leg through a full range of motion. The strain gauge measures the applied distraction force. Plastic housing protects the PCB and USB connection. Reprocessing instructions will be provided with the reusable component. The intended lifetime of the reusable component is 75 reprocessing cycles. The CORI™ Surgical System will track usage count and display a warning to the user when it reaches and exceeds its intended lifetime. The CORI™ KNEE TENSIONER Tray Insert is used for reprocessing of the TENSIONER reusable.

The disposable sterile CORI™ KNEE TENSIONER Cartridge houses embedded software and electronics (PCB and USB Connectors/Cable) and connects to the CORI™ Surgical System. The Cartridge is intended for single use and is sterilized through EtO sterilization.

The TENSIONER is designed to fit in the knee joint and distract the joint when the user squeezes the handle. The thickness and width of the fork allow the surgeon to insert the instrument into the joint prior to bony resection.

6.1.2 Comparator Arm

NA

6.1.3 Ancillary Product

The site will use the REAL INTELLIGENCE™ CORI™ Surgical System (Catalogue Number ROB10024), a commercial product. This product will be provided to the site as ancillary product (AP) unless there is a REAL INTELLIGENCE™ CORI™ Surgical System already on-site.

The CORI™ Surgical System is manufactured by S+N, Blue Belt Technologies, 2905 Northwest Blvd. Suite 40, Plymouth, MN 55441, USA.

6.2 Product Use

The CORI™ Surgical System has a user manual (Document ID: 1000026852, REAL INTELLIGENCE™ CORI™ for Knee Arthroplasty). The purpose of this user's manual is to serve as the master reference document for properly trained users in the function and operation of the CORI™ Surgical System and its accessories.

Gap Planning Technique

Gap balancing in CORI occurs during the planning stage after cuts are planned, but before actual cuts are made, allowing the surgeon to adjust cuts on both the femur and tibia based on ligament tension. This stage allows the surgeon to tension the collateral ligaments to evaluate the joint space and ligament tension, referencing the initial placement of the implants.

For this study, the IFU (CORI™ KNEE TENSIONER Document ID: 1000020561 and CORI™ KNEE TENSIONER Cartridge Document ID: 1000020561) were created and should be used in conjunction with the REAL INTELLIGENCE™ CORI™ user manual.

In addition, the following devices are packaged with an IFU to ensure that the device is used properly and for the intended purposes:

- REAL INTELLIGENCE™ Burs (Document ID: 500172)
- NAVIO™ Flat Markers (Document ID: 500043)
- REAL INTELLIGENCE™ Tubing Set (Document ID: 500173)
- REAL INTELLIGENCE™ Robotics Instruments Tray (Document ID: 500229)

The most current IFU should be referenced at https://ifu.smith-nephew.com/

All Investigators will be familiar with the CORI™ Surgical System and TENSIONER prior to enrollment.

The investigational and ancillary products have storage and handling conditions noted on the label. Data loggers will be supplied to the site to monitor the storage conditions. Additionally, sites will be instructed to store the study products separately from other stock and use only for the purposes of this study. The sites will receive the IP/AP/Supplies: Management Instructions detailing how to manage the investigational and ancillary products while stored onsite.

6.3 Packaging and Labelling

Packaging and labeling will be prepared to meet regulatory requirements. Package integrity and labelling should be verified prior to use of the product.

6.3.1 Labelling of Investigational Product

All product components of the CORI™ Surgical System will be commercially available as post-market products in the US and used as cleared/licensed products. If any component of the CORI™ Surgical System has not been cleared/licensed in the US, that component will not be permitted for use until 510(k) clearance is obtained.

6.3.2 Ancillary Product

The CORI™ Surgical System is a commercial product and will be provided to the sites as AP containing the standard manufacturing label.

6.4 Product Accountability Procedures

The investigational site will maintain an inventory of the IP/AP and Study Supplies.

The Sponsor or its designee will provide a log(s) to facilitate IP/AP Products and Study Supplies inventory control. All IP/AP and Study Supplies accountability logs must be retained in the Investigator Site File (ISF). These records must be available for inspection by the Sponsor, its designees, or by regulatory agencies at any time.

Overall accountability is the responsibility of the Investigator or designated individual maintaining an inventory, which will include details of receipt, use, waste, returns, etc. of IP and product supplies. Accountability records must document which products (identification number, expiry, quantity) were used by which subjects.

The Study Monitor will ensure that the procedures and records are in place for the appropriate reconciliation of all IP/AP and Study Supplies. As part of monitoring, the Study Monitor will check that site personnel are following the proper procedures for accountability and completing all necessary documentation.

6.5 Surgical Technique

All study related procedures with the CORI™ Surgical System must be performed according to the user manual (Document ID: 1000026852, REAL INTELLIGENCE™ CORI™ for Knee Arthroplasty) and according to the recommended surgical technique described in the labelling and IFU of the specific S+N Implant System. The TENSIONER IFU should be followed during the gap collection steps when the subject device is used.

Surgeons selected to participate in this study will be familiar with the CORI™ Surgical System and TENSIONER and have written evidence of training and expertise in the study procedure.

6.7 Medical Procedure Technique

The REAL INTELLIGENCE™ CORI™ for Knee Arthroplasty User Manual should be referenced for the full total knee arthroplasty procedure. The information below, along with the TENSIONER clinical study IFU, are meant to supplement the "Performing Gap Assessment" and "Assessing Postoperative Stressed Gap" sections in the manual.

Performing Gap Assessment

In this stage, the surgeon views a live bone model, showing the interaction of the virtual implants in real time. On the live model, the surgeon sees the femur and tibia bones, the implant components, and orange (medial) and purple (lateral) markers in the joint space indicating the points from which the gaps are being calculated.

The objective is to collect ligament tensioning data by applying varus and valgus stresses to the knee to assist with gap planning. The surgeon is expected to tension both the medial and lateral collateral ligaments consistently throughout the range of motion, or at discrete locations (user-specified flexion angles). Joint space information is used by CORI to predict gaps based on the planned component positions.

Gap assessment data is used in gap planning to inform the user of the predicted joint space based on the implant position. The surgeon can also use (the data) to make fine adjustments to the implant components to achieve the best joint space and ligament tension for the patient.

While it is easier for surgeons to collect data at two reference points, the goal is to stabilize the knee through full range of motion for optimal post-operative flexion and stability.

Surgeons currently perform gap balancing with different techniques and varying results. To perform manual gap balancing, the surgeon lifts the patient's leg and applies varus and valgus pressure while moving the leg through the full range of motion, relying on the "feel" of the tension.

Some surgeons use retractors to provide leverage in gap measurement. While these instruments are not designed for tensioning, surgeons have noted that using an instrument on the joint provides the surgeon a better feel for the tension. Nevertheless, it can be difficult to ensure consistent force on the soft tissue throughout the full range of motion.

Using the TENSIONER in Gap Assessment

The TENSIONER is designed much like a retractor with a bending fork. However, the TENSIONER acts as a sensor, reading in real time the force that the surgeon applies to the knee and communicating that force to CORI.

The user applies force to the knee with the TENSIONER. The TENSIONER communicates with CORI (relays the applied force) which provides feedback to the user in the form of a dynamic bar graph which displays the relative applied force. CORI only collects the gap assessment data when the user specified force is applied.

The CORI workflow stages follow the same path with the TENSIONER. However, the surgeon has the option to choose to use the TENSIONER in gap assessment. Note: The connection, surgeon preferences, planning, and gap assessment (with and without TENSIONER) states will be modified to allow for the addition of the TENSIONER to CORI software.

The surgeon specifies a desired tensioning force range and CORI collects data during intra-operative gap planning. This occurs after bone cut planning but before bony resection, thereby allowing the surgeon to refine cuts based on ligament tension. The available force targets are 50N, 100N, and 150N with the clinically relevant applied force range = 0 to 200N. The allowed range of the measurement is the target value ±10N.

The TENSIONER detects the applied force throughout range of motion and displays the specified force range in a bar graph. The user specified force range displays as a bar across a column. The reading is green, and the readout remains inside the bar when the surgeon is within the user specified range. The reading is red, and the readout displays outside of the bar when the surgeon is outside of the user specified range. The readout allows the surgeon to see when too much force or too little force is applied. The surgeon is able to rely on the readings rather than the "feel" of the tension to maintain constant force.

CORI collects placement data only when the surgeon applies force within the user specified range. This provides consistency during the gap collection/balancing process. Though the force that the surgeon applies may vary throughout ROM, data is collected at a consistent force, tied to the specification previously defined by the surgeon. This provides consistency during the gap collection/balancing process. The surgeon is able see whether the applied force is within the specified range and adjust accordingly if necessary.

The TENSIONER is intended to bring objectivity to gap balancing by providing a quantitative solution rather than the current subjective qualitative method as the gap is measured under consistent applied force.

Using the Tensioner as part of study protocol

Repeatability should be measured as the variation between measurements taken by the same surgeon using the same technique (TENSIONER and current/manual technique). Refer to protocol section 9.2.4 (Repeatability).

7 SUBJECT ENROLLMENT AND WITHDRAWAL

7.1 Subject Population

A minimum of 27 and a maximum total of 83 subjects, 18 years or older, undergoing primary TKA with the CORI™ Surgical System will be enrolled in the study at approximately 4 sites in the United States.

Ethnic minorities are classed as vulnerable subjects according to ISO 14155 however they will be included providing they meet other inclusion criteria and there are informed consent documents and personnel to lead the consent process in a language that is fully understood by the potential subject.

7.1.1 Vulnerable subjects

Subjects who meet the definition of a Vulnerable Subject per ISO14155 will not be enrolled in the study.

7.2 Inclusion Criteria

Subjects will be considered qualified for enrollment if they meet the following criteria:

1. Subject agrees to consent to the study by signing the Independent Review Board (IRB) approved ICF.

2.	Subject is eighteen (18) years or older.
3.	Subject is willing and able to attend all study follow-up visits for up to one (1) year postoperatively (as defined in the study protocol and ICF).
4.	Subject can read, understand, and communicate responses to Patient Reported Outcome Measures (PROMs).
5.	Subject is suitable for the CORI™ Surgical System.
6.	Subject requires a cemented TKA as a primary indication due to any of the following condition: • Degenerative joint disease, including osteoarthritis • Rheumatoid arthritis • Avascular necrosis • Requires correction of functional deformity • Requires treatment of fractures that were unmanageable using other techniques

7.3 Exclusion Criteria

Any one (1) of the following criteria will disqualify a potential subject from participation in the study:

1.	Contraindications or hypersensitivity to the use of the CORI™ Surgical System per the IFU.
2.	Participation in the treatment period of another clinical trial within thirty (30) days of the Pre-Operative Visit, or during the study.
3.	Women who are pregnant, nursing, or of child-bearing potential who are not utilizing birth control measures.
4.	Subjects who are non-English speaking.
5.	Any subject that meets the definition of a Vulnerable Subject per ISO 14155 Section 3.55.[1]
6.	Subjects who have participated previously in this clinical trial.
7.	Subjects with a history of poor compliance with medical treatment.
8.	Subject needs a CORI™ Surgical System TKA on the index joint as a revision for a previously failed surgery, or need for complex implants, or any other implant than a standard TKA (e.g., stems, augments, or custom-made devices).

1. ISO 14155 Section 3.55 States: Vulnerable subject – Individuals who are unable to fully understand all aspects of the investigation that are relevant to the decision to participated, or who could be manipulated or unduly influenced as a result of compromised position, expectation of benefits or fear of retaliatory response…

9.	Subject has been diagnosed with post-traumatic arthritis.
10.	Subject needs a bilateral TKA.
11.	Subject has active infection or sepsis (treated or untreated).
12.	Subject is morbidly obese with a body mass index (BMI) greater than 40
13.	Subjects with a medical or physical condition that, in the opinion of the Investigator, would preclude safe subject participation in the study. This includes: • Advanced osteoarthritis • Joint disease • Paget's or Charcot's disease • Vascular insufficiency • Muscular atrophy • Uncontrolled diabetes • Moderate to severe renal insufficiency • Neuromuscular disease • Mental illness or mental retardation • Drug or alcohol abuse

7.4 Screening

To eliminate the potential for selection bias, Investigators should consecutively screen all subjects presenting with degenerative joint disease of the knee, requiring correction of functional deformity, or treatment of fractures that were unmanageable using other techniques to determine whether they meet all inclusion and none of the exclusion criteria.

Participating study sites are required to document all screened subjects considered for inclusion in this study. If a subject is excluded from the study, the reasons for exclusion will be documented in the subject's source documents and noted on the Screening and Enrollment Log. All screening activities that occur prior to consent shall be referred to as pre-screening.

Part of the screening process will include documentation of women's childbearing potential. If the woman is not of childbearing potential this should be documented in the medical history (e.g., surgically postmenopausal, postmenopausal [i.e., at least one year without menses]). For women of childbearing potential, their method of birth control should be documented in the source.

Effective birth control methods should be determined by the Investigator.

7.5 Informed Consent

Before conducting any study procedures or examinations, the purpose and nature of the study should be explained to the subject in their native language. The subject, or their legally authorized representative, will then **read**, **sign**, and **personally date** the Institutional Review Board (IRB)-approved informed consent document(s) (see below for difficulties with reading and writing). Additionally, the individual who obtains consent from the subject will sign and date the informed consent document. A copy of the signed informed consent document will be provided to the subject, a copy will be placed in the subject's medical record, with the original filed in the ISF.

If the subject is unable to read, the informed consent document and associated study information may be read aloud to the subject in the presence of an impartial witness. If possible, the subject shall sign and personally date the Informed Consent Form (ICF). Where this is not possible, due to difficulties in writing, the subject shall provide verbal consent to participate in the study. The witness shall then personally sign and date the informed consent form, attesting that the information was accurately explained and that the informed consent was freely given.

Informed consents will be obtained in compliance with Health Information Portability Accountability Act (HIPAA) regulations.

If new information becomes available during the course of the study that can significantly affect a subject's future health and medical care, S+N will ensure that information shall be provided to the subject(s) affected in written form and if relevant, all affected subjects shall be asked to confirm their continuing consent in writing.

7.6 Enrollment

Subjects for whom the consent process has been completed, have met all eligibility criteria, and have been treated with the study product are considered enrolled. Treatment with the study product will be defined as the execution of the plan created using the TENSIONER.

Subjects will be assigned a Subject Identification (ID) at the time of consent. Subject IDs will be allocated using the following format: XX.NNN, where XX is the site number composed of a 2-digit site code (XX) and a 3-digit (NNN), the consecutive subject ID number, starting at 001.

Example: 01.001 = Subject 001 at Site 01

7.7 Lost to Follow-up

A subject will be considered lost to follow-up if he/she does not appear for the scheduled study visit for 2 consecutive visits and does not return for a final visit, and study personnel are unable to contact the subject.

Some actively enrolled subjects will not return for follow-up exams on time. Study personnel must make a reasonable effort to contact the subject and document the following contact attempts before declaring a subject to be lost to follow-up: the subject has been contacted according to the site's policies, but no fewer than two documented phone contacts and one certified letter without response. Copies of all attempts to reach the subjects by mail or email and/or the attempts to contact the subject via other means should be documented, and that documentation should be kept with the subject's source documents.

7.8 Withdrawal

7.8.1 Withdrawal from Treatment

Subjects may be withdrawn during the operative visit with the TENSIONER at the discretion of the Investigator due to:

- A change in treatment is clinically warranted
- An AE
- Any other significant reason identified by the Investigator

The withdrawal of a subject during the operative visit requires the subject to be discontinued from the study. If more than 5% of planned subjects to be enrolled are withdrawn prior to treatment an additional 5% subjects will be enrolled into the study as replacement after fulfilment of the eligibility criteria.

7.8.2 Withdrawal from Study

The Investigator may withdraw subjects from the study for many reasons, including but not limited to the following:

- subject noncompliance (e.g., did not follow instructions, took disallowed medications)
- subject lost to follow-up
- if the Investigator or the Sponsor stops the study for any reason and decides to withdraw subject(s) from the study
- concurrent illness
- AEs/Adverse Device Effects (ADEs)
- any other significant reason identified by the Investigator

For each case, information will be obtained in the source document and the Case Report Form (CRF), detailing circumstances leading to the withdrawal.

Subjects who drop out or are withdrawn will not be re-entered into the study at a later date.

7.8.3 Subject's Withdrawal of Consent to Participate in Study

Study participation is voluntary, and subjects may withdraw at any point during the study without giving their reason for doing so. Where subjects withdraw consent, the Investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's privacy. The reason for withdrawal will be recorded in the CRF and source documents.

Subjects who withdraw consent after completing operative visit will be considered terminated from the study and will not be replaced.

7.8.4 Use of Data Following Withdrawal

In cases where the subject withdraws consent, the data collected up to the point of withdrawal may be used, but no additional data for that subject may be collected.

7.9 Subject Reimbursement and Incentives

Subjects will be reimbursed for the costs of taking part in the study if agreed to by the study site as documented within the Clinical Trial Agreement. These costs will only cover study-specific activities or visits including time, travel, parking, and inconvenience and will not cover activities or visits associated with the subject's standard clinical care. Payments to the subject will be proportionate to the time and expense involved in study participation and not so large as to unduly encourage the subjects to participate or affect the subject's ability to withdraw prematurely form the study. All arrangements for reimbursement payments to subjects will be approved by the IRB and/or local site authority as required.

8 STUDY DESIGN

8.1 Study Design

This is a post-market, prospective, multi-center, non-randomized, open-label study evaluating the performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System. A minimum of 27 subjects having consented and underwent cemented primary TKA will be included. Approximately 4 sites will participate in the United States. The study is expected to enroll all subjects within a 15-month timeframe. Subject follow-up visits will be conducted at 6 weeks, 6 months and 12 months post-operatively.

NOTE: This study was initially registered on Clinicaltrials.gov (CTG) as a pre-market, interventional study in Apr2021. The product was FDA approved 19Aug2022. A protocol revision in Feb2023 (Ver3.0 16Feb2023) was done in part, to change from a pre-market study to a post-market study. No change to CTG classification is warranted since some subjects were enrolled under the pre-market, interventional study (i.e. the more stringent of the CTG definitions).

8.2 Data Management

This study utilizes a validated, 21 CFR Part 11 compliant, electronic data capture system. Access to the electronic data capture system is controlled through S+N procedures.

A Data Management Plan (DMP) is written according to S+N procedures containing details of the data management process. The following is a brief description of the key points detailed in this plan.

8.2.1 Data Review and Quality Assurance

Data will be transcribed from the data source to an electronic Case Report Form (eCRF). All data requested on the eCRFs are considered required. Data points not collected and/or recorded will be considered deviations unless otherwise specified.

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the Principal Investigator (PI). The PI is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. The PI must provide his/her electronic signature on the appropriate eCRFs to be documented in compliance with local regulations. Changes to data previously submitted to the sponsor will require a new signature by the Investigator to acknowledge/approve the changes.

Visual and computer data review will be performed in line with S+N procedures to identify possible data discrepancies. Manual and automatic queries will be created within the electronic data capture system and will be issued by S+N to the site for appropriate response. Site staff are responsible for resolving all queries in the electronic data capture system.

8.2.2 Retention Period

All eCRFs will be archived once the study is completed and will be kept for a period of no less than five years after the later of the following dates: the date of which the study is terminated or completed or the date that the records are no longer required supporting marketing applications.

8.3 Study Endpoints

8.3.1 Primary Endpoint

The primary endpoint of this study is the change from the preoperative to 12-month follow-up in EQ-5D-5L VAS.

8.3.2 Secondary Endpoints

The following are the secondary endpoints defined for this study:

- The change from the preoperative to 12-month follow-up in EQ-5D-5L Index score
- The change from the preoperative to 12-month follow-up in 2011 KSS Objective, Function, and Satisfaction scores
- Mean of the KSS Expectation scores at pre-operative and at 12- month follow-up

8.3.3 Other Endpoints

To evaluate the repeatability, within the same deformity profile, of gap planning with the TENSIONER when compared to the surgeon's manual gap balancing technique.

The following endpoints have been defined for this study in order to support the creation of an optimized gap balancing workflow.

- Medial-to-lateral balance measurements at 0/10°, 30°, 60°, and 90° flexion
- Implant position alignment and resection depths
- Incidence and details of soft tissue release
- Analysis of force and deformity data (i.e., deformities outside the given range)

8.3.4 Safety Endpoints

Safety endpoints include the collection of the following:

- All AEs and complications occurring from the time of subject enrollment until study termination or study completion including intra-operative AEs and complications.
- Device related re-intervention.
- Device Deficiencies (DD).

8.4 Methods Used to Minimize Bias and Maximize Validity

8.4.1 Subject Attrition

Subjects will be enrolled at multiple sites. This will reduce the effect of observer bias that might arise at any one investigational site as well as maximize the diversity of subjects in the study.

8.4.2 Prospective and Consecutive Enrollment

Consecutive enrollment will be utilized to enroll subjects who meet the inclusion/exclusion criteria.

8.4.3 Pre-Specification of Statistical Analysis

The primary outcome measure has been pre-specified as well as the type of statistical analysis to be performed in order to evaluate this outcome. The details of the analysis will further be pre-specified in the Statistical Analysis Plan (SAP) so as minimize any threats to external validity and yield clinically relevant estimates of effects and precision.

9 STUDY PROCEDURES

9.1 Visits and Examinations

9.1.1 Summary

Table 9.1.1-9-1: Study Procedures by Visit

Schedule of events	**Screening/Pre-Operative Data** (Up to Day -180)	**Operative / Discharge Data** (Day 0)	**6-week Follow-Up** (Day 42 ± 14 days)	**6-month[C] Follow-Up** (Day 180 ± 30 days)	**12-month Follow-Up** (Day 365 ± 30 days)
Informed Consent	X				
Inclusion/Exclusion	X	X			
Demographics/ Medical History	X				
Urine Pregnancy[A]	X[A]				
Operative Data Collection		X			
Concomitant Medications[B]	X[B]	X[B]	X[B]	X[B,C]	X[B]
KSS and EQ-5D-5L Questionnaires	X		X	X[C]	X

Details of Deformity	X			
CORI Robotics Case Report	X			
Incidence of soft tissue release and rationale	X			
Adverse Event Assessment	X	X	X[C]	X
Discharge Data Collection	X			
End of Study/Exit	*	*	*	X

*As needed (i.e., patient withdrawal)
[A] For females of childbearing potential, only.
[B] Only medications related to the study treatment and medications used to treat an AE related to the study device will be recorded in the eCRF. Please reference the eCRF Completion Guidelines for how medications are recorded.
[C] The 6-month visit may be conducted remotely.

9.1.2 Screening/Preoperative Visit (Up to Day -180)

NOTE: Any subject who signs an informed consent/assent but fails to meet the required entry criteria is considered to be a Screen Failure. Demographic information for Screen Failures must be captured in the appropriate CRF with the reason for screen failure specified.

1.	Obtain written informed consent from the subject as detailed in Section 7.5 ----- **Do not proceed until consent has been obtained** -----
2.	Obtain demographic information and medical history, including information on concomitant medications/therapies.
3.	Obtain urine pregnancy test for females of childbearing potential.
4.	Screen the subject for protocol inclusion/exclusion criteria.
5.	Assign the subject a study number and instruct the subject on treatment procedures.
6.	Have subject complete the Pre-Op KSS and EQ-5D-5L questionnaires.
7.	Collect the Pre-Op KSS score objective measures (joint alignment, instability, motions & symptoms).
8.	Subjects will be instructed to return to the treatment facility for their scheduled Operative Visit (conducted within 28 days of Screening Visit)

9.1.3 Operative Visit (Day 0)

1. Query subject regarding any changes in general health and the use of concomitant medications.
2. Confirm subject still meets eligibility criteria. If the subject is no longer eligible, document as a screen failure.
3. Perform surgery and collect operative data as outlined in the applicable CRF.

   Note: For the initial gap assessment workflow, complete the stressed range of motion three (3) times using the TENSIONER and then three (3) times using the manual technique. Clear each of the first 6 collections using the "go back" button. A seventh (7) and final stressed range of motion will be completed using the TENSIONER and the surgeon will proceed to the next step in the CORI workflow. See section 9.2.4 for additional information.
4. Collect the Subject's CORI Robotics Case Report, generated by CORI Robotics Software and will include the following:
   - Knee tension force selection
   - Medial-to-lateral gap balance measurements at 0/10°, 30°, 60°, and 90° flexion
   - Implant position and size measurements
   - Analysis of force and deformity data (i.e., deformities outside the given range)

   The reports will be extracted post-operatively from the system by a S+N representative via download to a USB drive. See sections 9.2.3 through 9.2.8 for additional information.
5. If any AEs or DDs are observed or reported, they must be recorded as instructed in Section 12, adverse events and device deficiencies.
6. Instruct the subject on proper postoperative care/procedures, including any contraindicated treatments/medication(s).
7. Instruct the subject on follow-up procedures, including returning to the office for the 6-week Follow-Up Visit in 42 (± 7) days.

9.1.4 6-Week Follow-Up Visit (Day 42 ± 14 days)

1. Query subject regarding any changes in general health and the use of concomitant medications.
2. Have subject complete the Post-Op KSS and EQ-5D-5L questionnaires.
3. Collect the Post-Op KSS score objective measures (joint alignment, instability, motions & symptoms).

4. If any AEs or DDs are observed or reported, they must be recorded as instructed in Section 12, adverse events and device deficiencies.
5. Instruct the subject on follow-up procedures, including returning to the office for the 6-month Follow-Up Visit. If the month 6 visit is to be completed remotely, make courier arrangements to deliver the 6-month PROMs to the subject to be completed remotely during the month 6 remote visit.

9.1.5 6-Month Follow-Up Visit (Day 180 ± 30 days [Phone Call if Remote])

1. Query subject regarding any changes in general health and the use of concomitant medications.
2. Have subject complete the Post-Op KSS and EQ-5D-5L questionnaires. Collect the KSS score objective measures (joint alignment, instability, motions & symptoms) (if it is an onsite visit)
3. Collect the KSS score objective measures (joint alignment, instability, motions & symptoms) (if it is an on-site visit).
4. If any AEs or DDs are observed or reported, they must be recorded as instructed in Section 12, adverse events and device deficiencies.
5. If the visit was remote, arrange for a courier to return the completed PROMs to the site.
6. Instruct the subject on follow-up procedures, including returning to the office for the 12-month Follow-Up Visit.

9.1.6 12 Month Follow-Up Visit and Exit Visit (Day 365 ± 30 days)

1. Query subject regarding any changes in general health and the use of concomitant medications.
2. Have subject complete the Post-Op KSS and EQ-5D-5L questionnaires.
3. Collect the Post-Op KSS score objective measures (joint alignment, instability, motions & symptoms).
4. If any AEs or DDs are observed or reported, they must be recorded as instructed in Section 12, adverse events and device deficiencies.
5. Complete Exit Visit CRF

9.1.7 Unscheduled Visits

An Unscheduled Visit is defined as a visit in which a subject may return to the office/treatment facility for study-related reasons; however, this visit is not a part of the pre-determined study visit schedule. This may be warranted as a result of an AE or DD.

All information obtained during an unscheduled visit should be recorded in the source documents and on the appropriate CRF.

9.1.8 Concomitant Medications and Therapies

Concomitant medications and concomitant therapies (e.g., physical therapy, pain medications) are recorded at any time from enrollment into the study through the subject's last study visit.

Concomitant Medications

Excluded Concomitant Medications

There are no restrictions on concomitant medications for this study.

Recording Concomitant Medications in CRF

Only medications related to the study treatment and medications used to treat an AE related to the study device will be recorded in the eCRF. Please reference the eCRF Completion Guidelines for how medications are recorded.

Concomitant Therapies

Therapies Prohibited During the Study

There are no restrictions on concomitant therapies for this study.

Recording Concomitant Therapies in the CRF

Only therapies related to the study treatment and therapies used to treat an AE related to the study device will be recorded in the eCRF. Please reference the eCRF Completion Guidelines for how therapies are recorded

9.1.9 Discontinued Subjects

Discontinued subjects are those who voluntarily discontinue participation, who are withdrawn for reasons of safety, who are lost to follow-up, or who have missed 2 consecutive study visits. Where possible, a full Exit Visit should be completed for all subjects who discontinue the study early. Where consent is withdrawn, the date and any reason given for discontinuation should be captured, at a minimum (see Section 7.8.2).

All females of childbearing potential must also undergo a urine pregnancy test upon exiting the study. If appropriate, the Investigator will also advise the subject of subsequent therapy and/or procedures necessary for their medical condition.

9.1.10 Subject Pregnancy

Women of child-bearing potential are not excluded from the study as long as adequate birth control methods are being used by the subject as outlined in the protocol's exclusion criteria. However, if a woman becomes pregnant during the study, S+N must be contacted immediately once the investigator is made aware of the pregnancy and a decision will be made regarding the continuation in the study of the pregnant woman. Pregnancy is not an AE; however, complications related to the pregnancy may be reportable as determined on a case-by-case basis. Pregnancy-related information will be collected until the end of the pregnancy.

9.2 Study Methods and Measurements

9.2.1 Knee Society Score (KSS)

The 2011 KSS will be collected at the pre-operative visit and at the 6-week, 6-month, and 12-month Follow-Up Visits.

This is a validated tool that combines an objective physician-derived component with a subjective subject-derived component. The objective section rates alignment, instability, joint motion and symptoms. Patient reported expectations and satisfaction questions evaluate pain relief, functional abilities, satisfaction and fulfilment of expectations using a subjective perspective. A functional score is derived from assessments of walking and standing, standard activities, advanced activities and discretionary activities.
A paper questionnaire will be provided by the Sponsor to be completed by the subject. Responses for the KSS Score will then be recorded in the eCRF.

9.2.2 EQ-5D-5L

The EQ-5D-5L will be collected at the pre-operative visit and at the 6-week, 6-month, and 12-month Follow-Up Visits.

The EQ-5D-5L essentially consists of 2 pages: the descriptive system and the VAS.

The descriptive system is used to describe the subject's state of health and consists of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels to choose the most appropriate answer: no problems, slight problems, moderate problems, severe problems, and extreme problems. The subject is asked to indicate his/her state of health by marking the most appropriate statement in each of the five areas.

The EQ VAS records the subject's self-rated health on a vertical visual analogue scale. The endpoints on the scale are labelled "The best health you can imagine" and "The worst health you can imagine". The VAS can be used as a quantitative measure of health outcome as judged by the individual respondents.

A paper questionnaire will be provided by the Sponsor to be completed by the subject. Responses for the EQ-5D-5L Score will then be recorded in the eCRF.

9.2.3 Implant Position and Sizing Plan Measurements

Implant position measurements will be captured by the CORI™ Surgical System and will be exported in the CORI Robotics Case Report. The reports will be extracted post-operatively from the system by a S+N representative via download to a USB drive. Two implant position plans will be captured. The first plan is created by the CORI™ Surgical System utilizing the mesh and digitized bone collected during the registration stage. The second will be following the initial gap assessment.

Implant position and sizing measurements will be made up of the following:

- Implant Size
  - Femoral Component Size
  - Tibia Component Size
  - Insert Thickness
- Implant Orientation
  - Alignment
  - Rotation
- Resection Depth for Femoral and Tibia Components
- Leg alignment

9.2.4 Repeatability

Repeatability should be measured as the variation between measurements taken by the same surgeon using the same technique (TENSIONER and current/manual technique).

1. TENSIONER Gap Assessment: Complete CORI gap assessment workflow using the TENSIONER 3 times. Before starting the first collection with the TENSIONER, select the desired form applied to the joint space (Low, Medium or High). This selection will be the same for all 3 collections with the TENSIONER.
2. After each collection, do not select the "Continue" button. Use the "Go Back" button to clear the collection. Repeat the process 2 more times with the TENSIONER.
3. Manual Gap Assessment: Once you are back at a new TENSIONER gap assessment screen, select the manual collection button on the left side of the screen. Complete the manual gap assessment workflow 3 times using the same steps to clear the collected data.
4. After all 6 gap assessments are completed (3x tension, 3x manual), **a 7th gap assessment will be completed with the TENSIONER.**
5. The CORI workflow will continue based on the 7th gap assessment collection.

The CORI™ Surgical System will log each of the stressed range of motion measurements and they will be exported in the CORI Robotics Case Report. The reports will be extracted post-operatively from the system by a S+N representative via download to a USB drive.

9.2.5 Gap Planning Measurements

Gap planning measurements will be defined as the medial-to-lateral balance measurements at 0/10°, 30°, 60°, and 90° flexion. Gap planning measurements are collected 2 times during the CORI workflow. The first is at the implant planning stage and the second is when final trial components are in place. Gap planning measurements should be collected per the TENSIONER IFU.

If soft tissue release is required per the surgeon following the post-operative gap assessment, another gap assessment will be required for the study. This is to measure the gap changes resulting from the soft tissue release.

Gap planning measurements will be captured by the CORI™ Surgical System and included in the CORI Robotics Case Report. The reports will be extracted post-operatively from the system by a S+N representative via download to a USB drive.

9.2.6 Soft Tissue Release

Incidence and details of soft tissue release will be collected during or immediately following the procedure. Each soft tissue release and the details regarding the rationale for the release will be recorded in the corresponding CRF.

9.2.7 Deformity Profile

The deformity profiles are varus, valgus and neutral. Varus deformity is defined as greater than (>) five (5) degrees Varus. Valgus deformity is defined as greater than (>) five (5) degrees valgus. Neutral is defined as those knees whose pre-op alignment falls between the varus and valgus deformity. The deformity profile will be recorded in the corresponding CRF.

9.2.8 Force Selection

Prior to starting a gap assessment, the surgeon selects the desired force level they want to apply to the joint with the TENSIONER. There are three force levels that surgeon can select by taping the touch screen: Low (50N), Medium (100N) and High (150N). The selected force will be captured by the CORI™ Surgical System and included in the CORI Robotics Case Report. The reports will be extracted post-operatively from the system by a S+N representative via download to a USB drive.

9.3 Health Economics/Quality of Life

NA.

10 STATISTICAL DESIGN

A SAP will be written and finalized prior to database lock. The following is a brief description of the analyses to be described in this plan.

10.1 General

The SAP will exclusively detail all statistical analyses to be performed. The methods that will be used to handle missing or incomplete data and for the derivation of all pertinent endpoints will also be detailed in the SAP.

S+N Global Biostatistics Department will conduct statistical analysis. All significance tests and/or hypothesis testing will be two-sided and performed at the 5% significance level unless otherwise specified.

Where data summaries are specified, categorical and ordinal variables will be summarized using frequency distributions which will detail the number and percentage of subjects which fall into each category. Continuous variables will be summarized using the following summary statistics: mean, median, standard deviation, minimum and maximum values, and number of observations.

10.2 Analysis Populations

- Safety Population (SAF), including all subjects who have received IP.
- Full analysis set population (FAS), all subjects who were enrolled into the study and had at least one post-baseline effectiveness assessment
- Per-Protocol Population (PP), including all subjects in the full analysis set who have no significant protocol deviations and met all inclusion/exclusion criteria.

10.3 Baseline Data

Baseline data summarized will include, but not be limited to, all collected demographic variable such as age, gender, primary diagnosis, height, weight, BMI and medical history.

10.4 Efficacy Analysis

10.4.1 Analysis of Primary Endpoint

The EQ-5D-5L VAS score will be summarized at the pre-operative, 6-week, 6-month and 12-month follow-up visits. The change from the preoperative visit to follow-up visits will also be summarized. The significance of the change from preoperative to 12- month follow-up EQ-5D-5L VAS scores are statistically significantly greater than 0 (i.e., $\mu_1-\mu_0 > 0$) will be tested with Bayesian modeling.

A literature review[45] was performed and produced 24 sets of data from 20 TKA studies with reported EQ-5D VAS scores at baseline and one year. A meta-analysis was performed to amalgamate this data.

For the Bayesian modeling, prior information was obtained from this comprehensive meta-analysis. Lower limit of the 95% confidence interval of the studies was used to derive the meta-analysis summary result for conservativeness. The meta-analysis summary result presented a mean change of EQ-5D VAS score at 12 months against baseline of 11.977 and standard deviation (SD) of 17.743. The 95% CI was 4.879 and 19.076.

A conservative normal prior will be used as the mean prior distribution from the meta-analysis result of the lower CI limit of mean change, i.e. Normal (4.879, 17.743). A Cauchy prior (0, 17.743) will be used as the prior for the standard deviation to account for variability. Significance against 0 will be concluded if the lower limit of the two-sided 95% Highest Density Credible Interval (HDI) for the posterior distribution is > 0.

10.4.2 Analysis of Secondary Endpoints

The EQ-5D-5L index score will be summarized at the pre-operative, 6-week, 6-month and 12-month follow-up visits. The change from the preoperative visit to follow-up visits will also be summarized. A paired t-test will be used to assess if change from pre-operative to the 12-month follow-up EQ-5D-5L index scores are significantly greater than 0 (i.e., μ_1-μ_0> 0). If the lower limit of the two-sided 95% CI for (μ_1-μ_0) from the t-statistic is > 0, then it will be concluded that the change is significantly different from 0.

The 2011 KSS (Satisfaction, Objective, and Function) will be summarized at the pre-operative, 6-week, 6-month and 12-month follow-up visits. The change in the 2011 Satisfaction, Objective and Function scores from preoperative to the follow-up visits will also be summarized. The analyses for these scores will be analogous to that specified for the EQ-5D index score.

The KSS Expectation score will be summarized descriptively at the preoperative and follow-up visits using summary characteristic for continuous variables.

10.4.3 Analysis of Other Endpoints

Within each deformity profile for the 3 assessments of the TENSIONER (Yi) and the 3 assessments of the Comparator group (Xi) on each of the N subjects enrolled, the difference in assessments between both groups (i.e., Yi-Xi) and the average of the results for both groups (i.e. {Yi+Xi}/2) for each subject will be estimated. Scatter plots of the difference versus the average scores known as the Bland-Altman plots will be plotted to visually assess the extent of agreement between the two groups (i.e., degree of bias).

The average of the observed differences in assessments between both groups (i.e. Σ(Yi-Xi)/N) and its corresponding two-sided 95% CI, i.e. the limit of agreement will be estimated. If >95% of the data displayed within the scatter plot are within the limits of agreement, then it will be concluded that TENSIONER results within the given deformity profile are agreeable with the comparator method.

To assess the degree of concordance in the repeated assessments within each deformity profile of the TENSIONER group, additional analyses will be performed to determine the inter- and intra-measurement reliability coefficients through the use of intra-class correlation coefficients (ICCs).

ICCs range between 0 and 1 and will quantify the magnitude of strength of agreement between the measurements. For each of the measurements on the N subjects in the TENSIONER group, ICCs will be calculated according to a model assuming that each of the three repeated measurements has a measurement each on each subject. The appropriate ICC based on these assumptions is based on the Shrout-Fleiss method [39]. The ICC coefficients obtained from this method will be categorized as follows: 0-0.3; Poor, 0.4 – 0.6; Moderate, ≥ 0.7 - <1-; High, and 1.

10.5 Safety Analyses

All safety analyses will be conducted using the SAF population. The number of incidences and number of subjects reporting all adverse events will be summarized both overall and by seriousness, severity, relationship to study device and outcome. Incidences and number of subjects reporting device deficiencies will also be summarized. Further summaries of safety data will be elaborately described in the SAP.

10.6 Interim Analyses

NA.

11 SAMPLE SIZE JUSTIFICATION

The primary outcome is a statistically significant EQ-5D VAS change from preoperative (μ_0) to postoperative follow-up (μ_1) i.e., $\mu_1-\mu_0>0$. A Bayesian approach has been selected to allow for greater flexibility, efficiency and the integration of prior knowledge. To perform a sample size calculation, anticipated effect size and variability were obtained from systematic literature review[45] (Section 11.1), and used as prior information in Bayesian sample size determination (Section 11.2).

11.1 Systematic Literature Review and Meta-analysis

Studies that used robotic assisted techniques were prioritized; however, due to a lack of robotic assisted TKA studies reporting EQ-5D VAS scores at 12 months, conventional techniques were also eligible for inclusion. Improvements between pre and postoperative EQ-5D VAS scores between robotic and conventional techniques have been shown to be similar[41-44]. Indeed, in a randomized clinical trial (RCT) by Clement et al, 2024 the study investigators compared EQ-5D VAS improvement at 12 months postoperatively between MAKO® (Stryker) and conventional TKA and found no statistical difference between change in EQ-5D VAS (change from pre to post op as follows: MAKO 3.1, conventional 8.1, p=0.27)[41]. EQ-5D VAS at 2 years has also been reported to show similar postoperative scores between NAVIO™ (Smith & Nephew) and conventional patient groups (p=0.37)[42], as well as between an unknown robotic system and conventional in a

conference abstract at weeks 2, 6 and 3 months ($p \geq 0.05$)[43]. This is also backed up by the lack of statistically meaningful difference in EQ-5D between robotic and conventional TKA ($p=0.31$)[44].

This literature review[45] provided 24 sets of data from 20 studies with reported EQ-5D VAS scores at baseline and one year. A multilevel (within study and between studies) random effects meta-analysis was performed to amalgamate this data.

11.2 Bayesian sample size determination

As stated above, prior information for Bayesian sample size determination was obtained from a systematic literature review and meta-analysis. Lower limit of the 95% confidence interval of the studies was used to derive the meta-analysis summary result for conservativeness. The meta-analysis summary result presented a mean change of EQ-5D VAS score at 12 months against baseline of 11.977 (4.879 - 19.076, 95% confidence interval), and a SD of 17.743.

To determine sample size, a simulation approach was used. Change scores were generated from multiple random samples from the normal distribution with mean and SD from the meta-analysis result, i.e. Normal (11.977, 17.743). A Bayesian model was then fitted to these scores, using a conservative normal prior based on the lower 95% CI limit of change in EQ-5D from the meta-analysis result, i.e. Normal (4.879, 17.743). A Cauchy prior (0, 17.743) was used as the prior for the standard deviation to account for variability. Significance against 0 will be concluded if the lower limit of the two-sided 95% Highest Density Credible Interval (HDI) for the posterior distribution is > 0. This simulation process was repeated across 50 iterations to estimate statistical power.

To achieve 80% power, 20 evaluable subjects are required. To allow for up to 25% attrition due to loss to follow-up, a minimum of 27 subjects will need to be enrolled with a maximum of 83 based on those consented under frequentist sample size calculations in Protocol Version 3.0.

12 ADVERSE EVENTS AND DEVICE DEFICIENCIES

12.1 Definitions

The categories of adverse events are shown in table 12.1-1. The definitions for each of these categories are given in the subsequent sections.

Table 12.1-1: Categories of Adverse Event

	NOT DEVICE-RELATED	DEVICE- OR PROCEDURE- RELATED	
Non-Serious	**Adverse Event (AE)**	**Adverse Device Effect (ADE)**	
Serious	**Serious Adverse Event (SAE)**	**Serious Adverse Device Effect (SADE) (See 12.1.3)**	
		Anticipated	**Unanticipated**
		Anticipated Serious Adverse Device Effect (ASADE)	**Unanticipated Serious Adverse Device Effect (USADE)**

12.1.1 Adverse Event

An Adverse Event (AE) is any untoward medical occurrence, unintended disease or injury or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated.

Note 1: This definition includes events related to the investigational medical device or the comparator.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.

AE is used both to refer to AE which do not meet the definitions of Adverse Device Effects or Serious Adverse Events and as an umbrella term referring to adverse events of all classifications.

An AE can be any unfavorable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease. For reporting purposes, emphasis is placed first and foremost on whether or not the event constitutes an untoward medical occurrence.

12.1.2 Adverse Device Effect

An Adverse Device Effect (ADE) is an adverse event related to the use of an investigational medical device.

Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation or operation, or any malfunction of the investigational medical device.

Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

Note 3: This includes "comparator" if the comparator is a medical device.

Not Related - An AE is considered to be not related to the use of an IP or the procedure when the effect is DEFINITELY UNRELATED to have any relationship to the use of the IP or the procedure.

Related – An AE is considered to be related to the use of an IP or the procedure when there is a POSSIBLE, or DEFINITE relationship between the AE and the use of the IP or the procedure.

An ADE is further categorized depending on whether the criteria in section 12.1.3 and 12.1.4 are met.

12.1.3 Serious Adverse Events and Serious Adverse Device Effects

An AE or ADE is considered a **Serious** Adverse Event (SAE) or **Serious** Adverse Device Effects (SADE) if, it led to any of the following:

a) death,
b) serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:
    1) a life-threatening illness or injury, or
    2) a permanent impairment of a body structure or a body function including chronic diseases, or
    3) in-patient or prolonged hospitalization, or
    4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
c) fetal distress, fetal death or a congenital abnormality or birth defect including physical or mental impairment

Note 1: Planned hospitalization for a pre-existing condition, or a procedure required by the study protocol, without serious deterioration in health, is not considered a serious adverse event.

Provide relevant examples of SAE/SADE for the study if wished.

12.1.4 Anticipated/Unanticipated Serious Adverse Device Effect

An Unanticipated Serious Adverse Device Effect (USADE) is a serious ADE which by its nature, incidence, severity or outcome has not been identified in the current version of the risk assessment.

Note 1: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity, or outcome has been identified in the risk assessment.

12.1.5 Severity

The severity of every AE will be assessed by the PI or medically qualified site staff to whom the responsibility has been delegated and documented on the delegation of authority log. AE should be classified as mild, moderate, or severe, regardless of whether or not the AE are considered to be serious or non-serious. The classification should be based on the following definitions:

Mild - An event is mild if the subject is aware of but can easily tolerate the sign or symptom.

Moderate - An event is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities.

Severe - An event is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities.

12.1.6 Device Deficiency

A Device Deficiency (DD) is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance.

Note 1: DD includes malfunctions, use errors and inadequacy in the information supplied by the manufacturer including labelling.

Note 2: This definition includes device deficiencies related to the investigational medical device or the comparator.

Device deficiencies that did not lead to an adverse event but could have led to a medical occurrence if suitable action had not been taken, intervention had not been made, or circumstances had been less fortunate are considered Device Deficiencies with potential to cause SADE and shall be reported as specified in section 12.3.

12.2 AE Coding Dictionary

Coding for this study will be done per International Medical Device Regulators Forum AE Terminology Annex E – Clinical signs, symptoms, and conditions.

12.3 Reporting procedures

AE of any kind and DD will be recorded in the applicable CRF and source notes to include the date of occurrence, treatment, and the details resolution. The Investigator will evaluate all AE for relationship to the device and procedure, seriousness, and severity (if applicable). DD will be evaluated for potential to cause SADE. The following timescales should be followed for the AE/DD information to be submitted/entered into the CRF and reported to the Sponsor or designee (see figure 12.2-1):

- ADE and DD – without unreasonable delay
- SAE, SADE, and DD with potential to cause SADE – immediately (i.e., within 24 hours of the investigator being informed about the event)
- All other events – according to usual timescales

In addition to inputting SAE and SADE information within 24 hours of being aware of the event, the investigator should email Clinical.safety@Smith-nephew.com to alert the safety representative of the events existence and to clarify details if necessary.

For ADE and DD, date of occurrence, and details of the product/procedure related to the event will be included and where applicable, pictures taken of the device. The deficient product should be retained for return to S+N unless it is contaminated (e.g., used dressings must not be retained). Updates to submitted information will be recorded in the CRF according to the timescales above.

All adverse events will be reviewed by a medically qualified person appointed by the Sponsor to determine which, if any, meet criteria for expedited reporting to the regulatory authorities.

The investigator will inform the regulatory agency and IRB of adverse events according to the IRB requirements.

Unanticipated SADE's and DD's that could have led to SADE will be reported to IRB and regulatory authorities within 10 working days.

All other events will be reported on a periodic/annual basis.

Depending on the nature of the adverse event, S+N may request copies of the subject's medical records, imaging, operative notes, as well as results of any relevant laboratory tests performed, or other documentation related to the AE. If the subject was hospitalized, a copy of the discharge

summary may be requested by S+N and should be forwarded as soon as it becomes available. In certain cases, S+N also may request a letter from the Investigator that summarizes the events related to the case. Refer to the ISF Sponsor Contact Information Sheet to report SAE, unanticipated SADE, anticipated SADE, and DD.

Figure 12.3-12-1: Evaluation and Reporting of AE

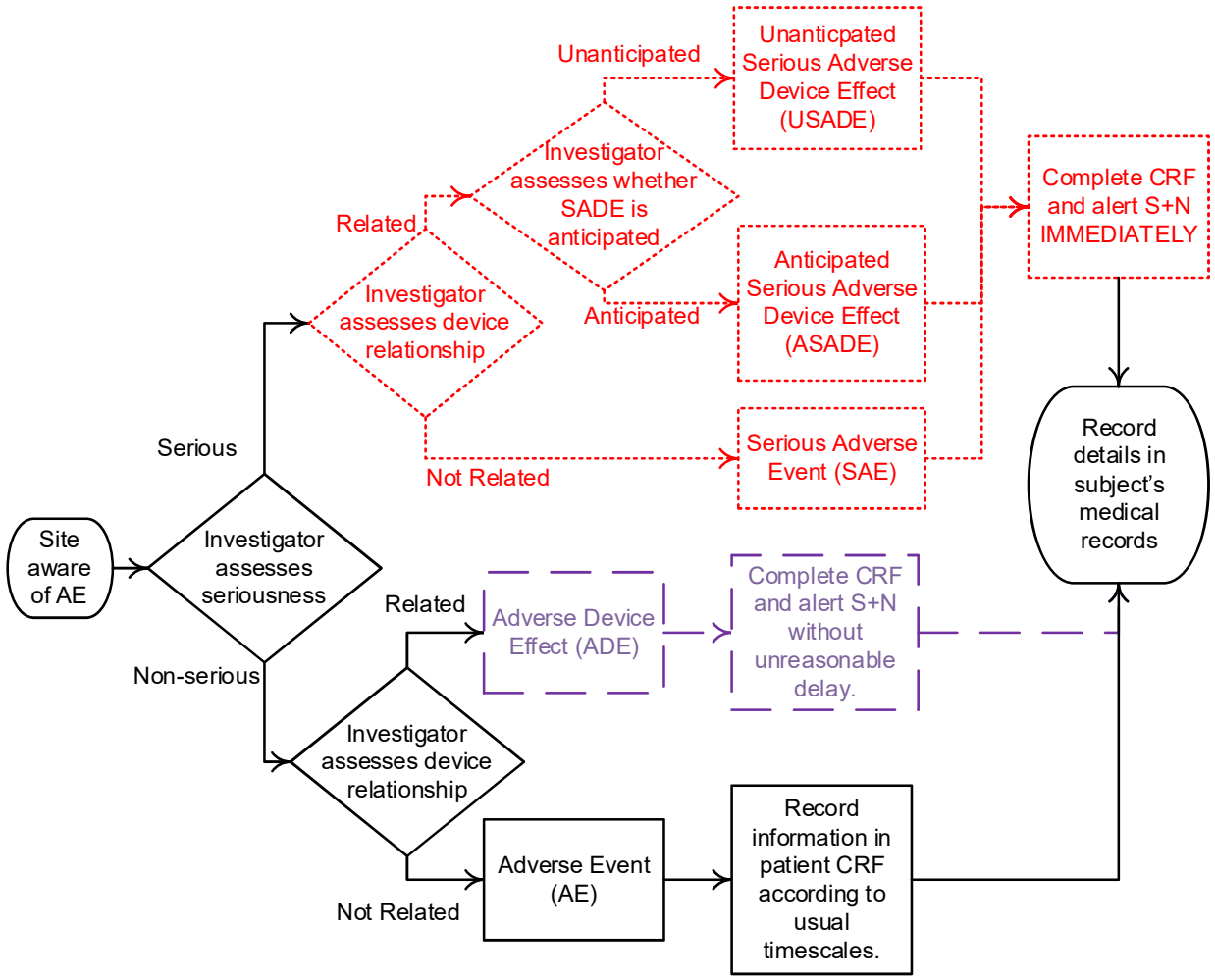
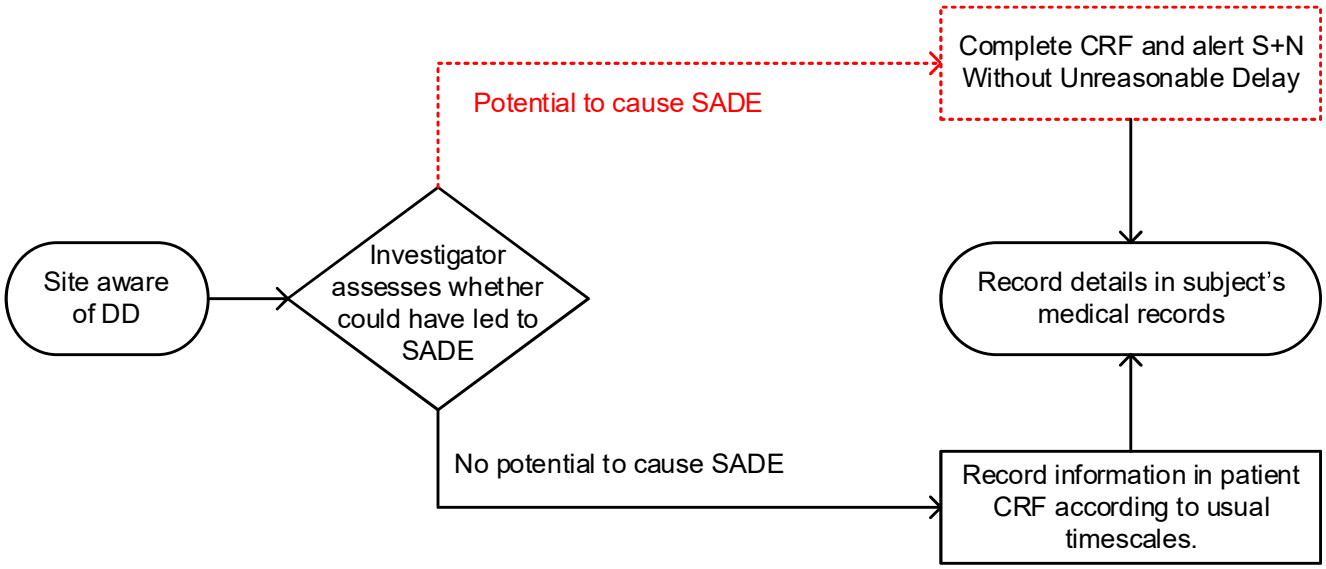


Figure 12-2: Evaluation and Reporting of DD



12.4 Unblinding of Investigational Product

NA.

12.5 Follow-up of Subjects with Adverse Events

For subjects who are experiencing ongoing unresolved AE at the time of their study completion or early discontinuation from the study, it is recommended that the Investigator schedule an appropriate follow-up visit to determine the outcome of the event.

Any additional data must be documented and available to the Sponsor who will determine whether the data need to be documented in the CRF/Clinical Study Report.

12.5.1 Ongoing Adverse Events at Study Discontinuation

Adverse events which are **related** to a study procedure or S+N IP and are ongoing at the end of subject's participation: The event should be followed until it is either resolved or until the event has become chronic and is not expected to further improve based on Investigator's review of the event.

Adverse events which are **not related** to a study procedure or S+N IP and are ongoing at the end of subject's participation should be followed for 30 days after discontinuation or if the AE is resolved, whichever is sooner.

At the time of data analysis (e.g., interim or final), an evaluation of ongoing events should take place and be listed as ongoing in the safety table.

13 INVESTIGATOR OBLIGATIONS

The Principal Investigator will comply with the commitments outlined in the in the Statement of Investigator, provided by the Sponsor/within the Clinical Trial Agreement, and with Good Clinical Practice (GCP), and all applicable regulatory requirements as outlined in Appendix 22.9 of this protocol. Sub-Investigators, who are individual member of the investigation site team designated and supervised by the Principal Investigator at an investigation site to perform clinical investigation-related procedures or to make important clinical investigation-related and medical treatment decisions, may have responsibilities delegated to them by the Principal Investigator. However, the Principal Investigator retains overall responsibility for the clinical investigation at the site.

In addition, the PI will ensure that the Financial Disclosure Statements will be completed by the PI and the Sub-Investigator upon entry into the study and as any changes that affect their financial disclosure status occur during the course of the study and up to one year after study completion.

The Coordinating Investigator appointed by the Sponsor will assist in coordinating the work in the multicentre clinical investigation.

14 SPONSOR AND MONITOR RESPONSIBILITIES

The Sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals. The clinical investigation will be monitored to ensure that: the rights and wellbeing of the subjects are protected; the reported data are accurate, complete, and verifiable from the source documents; and the study is conducted in compliance with the currently approved protocol and amendment(s), if applicable, with GCP regulations, and with applicable regulatory requirements.

Detailed monitoring requirements will be documented in the Clinical Monitoring Plan for this study.

14.1 Site Qualification Visit

A site qualification visit may be performed by the Sponsor prior to the execution of a clinical agreement to ensure that all Investigators have the appropriate training, staff, facilities, and resources to adequately conduct the study.

14.2 Site Initiation Visit

A site initiation visit to provide training on the specifics of the study, site obligations and expectations of study conduct will be performed by the Sponsor or qualified person designated by the Sponsor following the execution of the Clinical Trial Agreement and documented IRB approval.

14.3 Interim Monitoring Visit

Regular interim monitoring visits will be performed by the Sponsor or qualified person designated by the Sponsor.

14.4 Close-Out Visit

A study close-out visit will be performed by the Sponsor or designee to retrieve and account for all remaining clinical data and to resolve outstanding queries. During study close-out, the monitor will review investigator files to ensure required documents and records are on file, confirm the disposition of any other ancillary items used for the study, and review regulatory requirements regarding records retention and IRB reporting requirements. When no subjects have been included, a remote close-out visit may be conducted.

14.5 Sponsor Audits and Regulatory Inspection

Quality Assurance auditors, whether an employee of the Sponsor or its designee, may evaluate study conduct at the study sites. These parties must have access to any and all study reports and source documentation, regardless of location and format.

15 PROTOCOL DEVIATIONS

An Investigator must not make any changes or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency. Protocol deviations reported by the Investigator or discovered during monitoring visits will be compiled in a Protocol/GCP Deviation Log (FRM-402046 Protocol/GCP Deviation Log). Significant and/or recurrent protocol/GCP deviations will be documented on a protocol deviation form (FRM-400347 Protocol/GCP Deviation) including

identified root cause and, as necessary, appropriate corrective and preventive actions will be put in place and signed off by the study personnel. If it is deemed necessary full clinical Corrective and Preventive Action (CAPA) will be initiated.

It is not allowed to use waivers to allow planned deviation of the study protocol.

An investigator may be early terminated from the study upon identification of serious protocol deviations whereby there are concerns for patient safety or data quality (especially those not reported to the sponsor by the site). Early termination may also occur if there are repeated protocol deviations which have previously been addressed via corrective and preventative actions thereby suggesting an issue with site compliance.

The site staff must promptly report any deviations from the protocol that affect the rights, safety or well-being of the subject or the scientific integrity of the clinical investigation, including those which occur under emergency circumstances, if required by the IRB, protocol or national regulations. The site must report protocol deviations to the IRB per the IRB requirements.

16 PROTOCOL AMENDMENTS

Amendments should be made only in necessary cases once the study has started. Protocol amendments must be approved by the protocol signatories prior to submission to the IRB. Protocol amendments need to be approved by the IRB, according to the applicable requirements prior to implementation at the site.

17 CONFIDENTIALITY OF THE STUDY

The confidentiality of this study and associated documents is governed by the terms of the Clinical Trial Agreement (CTA).

18 STATEMENTS OF COMPLIANCE

The investigation was conducted in compliance with applicable requirements in the protection of human subjects' regulations in 21 CFR part 50, Good Clinical Practice's, the institutional review boards regulations in 21 CFR part 56.

This clinical study will be performed in compliance with the ethical principles of the Declaration of Helsinki; and ISO 14155: Clinical investigation of medical devices – Good Clinical Practice.

This clinical study will not commence until the required approval/favorable opinion from the IRB or regulatory authority has been obtained. Any additional requirements imposed by the IRB or regulatory authority will be followed.

Public/Products Liability Insurance has been purchased by Smith & Nephew plc. Worldwide and incorporates coverage for personal injury in respect of clinical studies. The Sponsor agrees to operate in good faith and in accordance with ABHI (Association of British Healthcare Industries) guidelines regarding compensation for injury arising in the course of clinical studies.

The clinical study is financed by the sponsor. All financial arrangements between the sponsor and investigation sites/investigators are documented separate clinical trial agreements.

19 END OF STUDY

The end of the study is defined as the last visit of the last subject in the study.

Should circumstances arise which require the termination of the entire study prior to its planned completion (e.g., safety concerns) or circumstances arise which mean the end of the participation of an individual site (e.g., departure of Investigator, non-compliance), then this will be undertaken according to the SOPs of the Sponsor. The requirement for subject follow-up in these instances will be considered as part of these processes.

The sponsor may decide to discontinue a specific study site under the following conditions:

- Non-compliance to GCP or study protocol
- Failure to enroll subjects
- Unsafe or unethical practices

20 PUBLICATION POLICY

20.1 Publication of Study Data

The study is registered as an Interventional study in www.clinicaltrials.gov (NCT04749884) and the results will be made available within that database as applicable, based on CTG study classification.

It is intended that the results of this study will be submitted for publication within a manuscript.

The preparation and submission for publication of manuscripts containing the study results shall be in accordance with a process determined by the Clinical Trial Agreements between the study sponsor and participating institutions. The publication or presentation of any study results shall comply with all applicable privacy laws, including, but not limited to the Health Insurance Portability and Accountability Act of 1996.

20.2 Data Sharing

S+N is committed to upholding the highest ethical and legal standards involved in conducting clinical trials. S+N, therefore, supports the data sharing requirements of The International Committee of Medical Journal Editors (ICMJE) published on the 6th June 2017. In accordance, S+N will consider requests to share individual (de-identified) participant data that underlie the results of any interventional clinical trial, as presented from the 1st July 2018 within an ICMJE associated journal. Requests made by researchers who provide a methodologically sound proposal will be considered. Requests may include data that underlie results presented in text, tables, figures, and appendices, together with data dictionaries. Availability of these data will begin nine months and end 36 months after article publication. Data supplied may only be used by the researcher(s) named in the approved research proposal for the purposes of achieving the aims of the analyses specified therein. All proposals should be directed to datasharing.gcs@smith-nephew.com. To gain access, data requestors will need to sign a data access agreement.

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22 APPENDICES

22.1 Protocol Amendment (1)

22.1.1 General Purpose (of amendment 1)

Version 1.0 of this protocol was amended to clarify statements regarding safety considerations of the product, to remove language regarding the need for pre-study cases, and to update the AP information. Additionally, minor administrative edits have been made throughout the document.

22.1.2 Rationale (of amendment 1)

Rationale for the changes in amendment 1 are as follows:

1. To clarify statements regarding verification of the study product
2. To update labelling information regarding IP
3. To update language regarding pre-study cases
4. To update ancillary product information
5. Other minor administrative items

22.1.3 Effect on Study Status (of amendment 1)

NA: this amendment is to be in effect and implemented prior to subject enrollment.

22.1.4 Details (of amendment 1)

Section	Current Text 29Jan2021 Version #1.0	Revised Text 22Apr2021 Version #2.0
Safety Considerations	All verification and validation relating to safety and efficacy of the product throughout its life cycle for this specific study will be completed before enrollment begins.	Verification relating to subject safety of the product throughout the product's life cycle for this specific study will be completed before enrollment begins.
Ancillary Product	No ancillary products are to be provided.	The REAL INTELLIGENCE™ CORI™ Surgical System will be provided to the site as ancillary product (AP). The CORI™ Surgical System is manufactured by S+N, Blue Belt

		Technologies, 2905 Northwest Blvd. Suite 40, Plymouth, MN 55441, USA.
Labelling of Investigational Product	**6.3.1 Labelling of Investigational Product** Labels on the primary packaging of the Tensioner will contain the following information: • Study number • Identification number • Quantity • Expiry Date • Site number and address • Caution: New Device - Limited by Federal Law to Investigational use • Sponsor: S+N, Inc. • Manufacturer Information: Blue Belt Technologies, Inc • All required symbols for hazard warnings.	**6.3.1 Labelling of Investigational Product** In addition to standard packaging, labels will state "Caution: Investigational Device - Limited by Federal Law to Investigational use." When the TENSIONER workflow is loaded, the screen will notify the user that the software is unapproved and for clinical use only. Additionally, the CORI™ Surgical System itself will be labelled as having unapproved software for clinical use only. **6.3.2 Ancillary Product** The CORI™ Surgical System is a commercial product. Standard device procurement and management will be used per site processes.
Surgical Technique	Surgeons selected to participate in this study will be familiar with the CORI Surgical System and have written evidence of training and expertise in the study procedure. Pre-study cases shall be performed until the surgeon feels comfortable with the system in order to prevent any learning curve during the study. The number of pre-study cases depends on the level of the individual experience of the surgeon. Anonymized CORI Robotics Case Reports will be collected for this pre-study cases as proof of experience.	Surgeons selected to participate in this study will be familiar with the CORI™ Surgical System and have written evidence of training and expertise in the study procedure.

Additionally, minor updates have been made throughout the protocol. This includes updates to the Schedule of Events for clarity purposes and the fixing of typographical errors.Approval/Notification (of amendment 1)

This amendment was submitted to the IRB for approval prior to subject screening and enrollment.

22.2 Protocol Amendment (2)

22.2.1 General Purpose (of amendment 2)

This amendment is to update the study title from pre-market to post-market following 510(k) clearance, update the IP name, the sample size, the number of sites, and the study purpose. Additional reasons include clarification regarding the secondary endpoints, other exploratory endpoints, the Investigational and Ancillary Products, collection of data from the CORI Robotics Case Report, updating the month-6 follow-up visit to optional in-person or remote visit, and analysis populations. Additionally, minor administrative edits have been made throughout the document.

22.2.2 Rationale (of amendment 2)

Rationale for the changes in this amendment are as follows:

1. Up version to comply with TMP-800052 Rev 4 of the template.
2. To update the study title from pre-market to post-market following 510(k) clearance.
3. To update the IP name from following 510 (k) clearance.
4. To update:-
    a. the sample size from n=80 TKAs to n=90 TKAs
    b. study duration, and the
    c. Increase number of sites from 2 to approximately 4sites
5. To update the study purpose.
6. To clarify the secondary endpoints and other exploratory endpoints.
7. To clarify the Investigational and Ancillary Products.
8. To clarify collection of data from the CORI Robotics Case Report.
9. To extend the Week 6 follow-up visit window.
10. To clarify analysis populations.
11. To update sample size justification.
12. Other minor administrative items.
13. To update the month 6 follow-up visit making it an option for a remote visit to boost enrollment. The KSS would not have the "Objective Knee Indicators " (clinician-generated) questionnaire component completed if the visit is remote. However, per the 2011 Knee

Society Knee Scoring System Licensed User Manual [40], outcomes are only scored using patient-reported responses. Data derived from items on the "objective" (clinician-generated) component of the questionnaire is collected for background information and to facilitate comparing patient outcomes with the old knee society clinical rating score (KSCR).

14. Used the new protocol template (TMP)800052. Section 7.9 is part of the new template.

22.2.3 Effect on Study Status (of amendment 2)

None. The study status remains unchanged once protocol version 3.0 is approved. Most changes described above are clarifications to wording and updates to minor protocol sections and are unlikely to impact the study significantly. When this amendment was submitted for internal approval, one site was active, with six patients enrolled.

22.2.4 Details (of amendment 2)

Section	Current Text 22Apr2021 Version #2.0	Revised Text 31Jan2023 Version #3.0
Section 2 Synopsis		
Title of Study	A Prospective, Multi-Center, Pre-Market Clinical Study to Evaluate the Performance of the REAL INTELLIGENCE™ Tensioner as an accessory to the CORI™ Surgical System in Robotic Total Knee Arthroplasty Procedures	A Prospective, Multi-Center, Post-Market Clinical Study to Evaluate the Performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System in Total Knee Arthroplasty Procedures
Study Design	This is a prospective, multi-center, open-label study evaluating the performance of the REAL INTELLIGENCE™ Tensioner as an accessory to the CORI™ Surgical System at approximately 2 centers across the United States. Eighty patients …	This is a post-market, prospective, multi-center, open-label study evaluating the performance of CORI™ KNEE TENSIONER…CORI™ Surgical System at approximately 4 centers across the United States. Ninety 90 patients …

Study Purpose	To support R&D validation of the surgical workflow for gap balancing using the Tensioner and to produce product marketing material and publication to support product launch and commercialization.	To evaluate the performance of the TENSIONER as an accessory to the CORI™ Surgical System.
Secondary Objectives	To further evaluate patient satisfaction using additional scoring tools (i.e., the EQ-5D-5L Index score and the 2011 KSS Objective, Function, Satisfaction and Expectation).	To further evaluate patient satisfaction using additional scoring tools (i.e., the EQ-5D-5L Index score and the 2011 KSS Objective, Function, and Satisfaction).
Sample Size	80 TKAs *Not present in v2.0	90 Subjects A sample size of 72 evaluable are required. To allow for up to 25% attrition due to loss to follow-up, a total sample of n = 90 subjects will be enrolled under competitive enrollment.
Number of Study Sites	Approximately 2 sites	Approximately 4 sites
Inclusion Criteria	3. Subject is willing to attend all study follow-up visits for up to one (1) year postoperatively (as defined in the study protocol and ICF).	4. Subject is willing **and able** to attend all study follow-up visits for up to one (1) year postoperatively (as defined in the study protocol and ICF).
Exclusion Criteria	3. Women who are pregnant, nursing, or of child-bearing potential who are not utilizing **highly effective** birth control measures. 5. Any subject that meets the definition of a Vulnerable Subject	3. Women who are pregnant, nursing, or of child-bearing potential who are not utilizing birth control measures. 5. Any subject that meets the definition of a Vulnerable Subject per ISO 14155

	per ISO 14155 :2011 Section 3.44.	
Study Duration	Duration of study: estimated 18 months Enrollment period: estimated 16 weeks Follow-Up period: 1 year	Duration of study: estimated 27 months Enrollment period: estimated 15 months Follow-Up period: 12 months
Secondary endpoint(s)	The change from the pre-operative to 12-month follow-up EQ-5D-5L Index score. The change from the pre-operative to 12-month follow-up KSS Objective, Function, Satisfaction and Expectation scores.	The change from the pre-operative to 12-month follow-up in EQ-5D-5L Index score. The change from the pre-operative to 12-month follow-up in KSS Objective, Function, and Satisfaction scores. Mean of the KSS Expectation scores at pre-operative and at 12-month follow-up.
Other exploratory endpoint(s)	Evaluate the repeatability, within the same deformity profile, of gap planning with the ….	Included: Analysis of force and deformity data (i.e., deformities outside the given range)
Safety Data	• All adverse events and complications	• All adverse events and complications occurring from the time of subject enrollment until study termination or study completion including intra-operative AEs and complications …
Study Schedule Follow-up	6 weeks (42 ± 7 days) 6 months (180 ± 30 days)	6 weeks (42 ± 14 days) 6 months* (180 ± 30 days) * The 6-month visit may be conducted remotely

4.3 Study Purpose	This is a prospective, multi-center, pre-market study to support R&D validation of the surgical workflow for gap balancing using the Tensioner. The main objective …	This is a prospective, multi-center, post-market study to evaluate the performance of the TENSIONER as an accessory to the CORI™ Surgical System.
4.3 Safety Consideration	All potentially hazardous situations with high initial risk levels will be mitigated through risk controls, **with some having special considerations just for this clinical study.**	Deleted: with some having special considerations just for this clinical study**.**
	Verification relating to subject safety of the product throughout the product's life cycle for this specific study will be completed before enrolment begins.	Verification and validation testing relating to subject safety of the product throughout the product's life cycle for this specific study is complete.
5.2 Secondary Objective (s)	The secondary objective is to further evaluate patient satisfaction using additional scoring tools (i.e., the EQ-5D-5L Index score and the 2011 KSS Objective, Function, Satisfaction and Expectation).	The secondary objective is to further evaluate patient satisfaction using additional scoring tools (i.e., the EQ-5D-5L Index score and the 2011 KSS Objective, Function and Satisfaction scores).
5.3 Other Objective (s)	…Additional objectives include generating data to support the creation of an optimized workflow for gap balancing with the Tensioner, as well as correlating soft tissue balance with subsequent implant placement changes.	…Additional objectives include generating data to support the creation of an optimized workflow for gap balancing with the TENSIONER as well as correlating soft tissue balance with subsequent implant placement changes.

6.1.1 Investigational Product	Tensioner Accessory… Knee Tensioner Design… The handheld instrument is the reusable component of Tensioner. Reverse action pliers with a fork and tongue design distract the joint as the surgeon takes the leg through a full range of motion. The strain gauge measures the applied distraction force. Plastic housing protects the PCB and USB connection. Reprocessing instructions will be provided with the reusable component. The intended lifetime of the reusable component is 100 reprocessing cycles. The CORI system will track usage count and display a warning to the user when it reaches and exceeds its intended lifetime. The disposable sterile cartridge houses embedded software and electronics (PCB and USB Connectors/Cable) and connects to CORI. The cartridge is intended for single use and will be sterilized through EtO sterilization.	Included Investigational Products: The following CORI™ Surgical System components have 510(k) clearance number (K221224) and are considered post-market products but will be provided to the site as Investigational Products. Added: The following CORI™ Surgical System components, apart from the Case Archive USBs (not considered a medical device), have 510(k) clearance but are not surgeon-facing products; instead, a Smith + Nephew (S+N) representative will be responsible for handling these Investigational Products and installing it on the CORI™ Surgical System. • REAL INTELLIGENCE™ Application Software • Implant Database • Case Archive USBs The Investigational Product is … Northwest Blvd. Suite 40, Plymouth, MN 55441, USA. Included table **6.1.1-1** for investigational products TENSIONER Accessory… Knee TENSIONER Design…The handheld instrument, CORI™ KNEE TENSIONER is the reusable component of TENSIONER…The intended lifetime of the reusable component is 75 reprocessing

		cycles. The CORI™ Surgical System … the TENSIONER reusable. The disposable sterile CORI™ KNEE TENSIONER Cartridge houses embedded software and electronics (PCB and USB Connectors/Cable) and connects to the CORI™ Surgical System. The Cartridge is intended for single use and will be sterilized through EtO sterilization…
6.1.3 Ancillary Product	The REAL INTELLIGENCE™ CORI™ Surgical System will be provided to the site as ancillary product (AP).	The site will use the REAL INTELLIGENCE™ CORI™ Surgical System (Catalogue Number ROB10024), a commercial product. This product will be provided to the site as ancillary product (AP) unless there is a REAL INTELLIGENCE™ CORI™ Surgical System already on-site.
6.2 Product Use	Gap Planning Technique For this study, the IFU for the Tensioner were created and should be used in conjunction with the CORI Surgical System user manual. All Investigators will be familiar with the CORI Surgical System prior to enrollment.	The CORI™ Surgical System has a user manual (Document ID: 1000026852, REAL INTELLIGENCE™ CORI™ for Knee Arthroplasty). Gap Planning Technique For this study, the IFU (CORI™ KNEE TENSIONERDocument ID: 1000020561 and CORI™ KNEE TENSIONER Cartridge Document ID: 1000020561) were created and should be used in conjunction with the REAL INTELLIGENCE™ CORI™ user manual. All Investigators will be familiar with the CORI™ Surgical System and TENSIONER prior to enrollment. Included: The investigational and ancillary products have storage and handling conditions noted on the label.

		Data loggers will be supplied to the site to monitor the storage conditions…
6.3.1 labelling of Investigational Product	In addition to standard packaging, labels will state "Caution: Investigational Device - Limited by Federal Law to Investigational use." When the Tensioner workflow is loaded, the screen will notify the user that the software …	All product components of the CORI™ Surgical System will be commercially available as post-market products in the US and used as cleared/licensed products. If any component of the CORI™ Surgical System has not been cleared/licensed in the US, that component will not be permitted for use until 510(k) clearance is obtained.
6.3.2 Ancillary Product	The CORI Surgical System is a commercial product. Standard device procurement and management will be used per site processes.	The CORI™ Surgical System is a commercial product and will be provided to the sites as AP containing the standard manufacturing label with an additional "CAUTION: Investigational Device – Limited by…
6.5 Surgical Technique	…Surgeons selected to participate in this study will be familiar with the CORI Surgical System and have written evidence of training and expertise in the study procedure.	…Surgeons selected to participate in this study will be familiar with the CORI™ Surgical System and TENSIONER and have written evidence of training and expertise in the study procedure.
6.7 Medical Procedure Technique	*Not present in v2.0	*Using the Tensioner as part of study protocol* Repeatability should be measured as the variation between measurements taken by the same surgeon using the same technique (TENSIONER and current/manual technique). Refer to protocol section 9.2.4 (Repeatability).
7.1 Subject Population	A total of 80 subjects, 18 years or older, undergoing primary TKA with CORI Robotics will be enrolled in the study at	A total of 90 subjects, 18 years or older, undergoing primary TKA with the CORI™ Surgical System will be enrolled in the

	approximately 2 sites in the United States. Ethnic minorities are classed as vulnerable subjects according to ISO 14155:2011 however…	study at approximately 4 sites in the United States. Ethnic minorities are classed as vulnerable subjects according to ISO 14155 however…
7.2 Inclusion Criteria	*Not present in v2.0	The subject or parent/legal guardian must provide written informed consent (reference section 7.5).
7.3 Exclusion Criteria	3. Women who are pregnant, nursing, or of child-bearing potential who are not utilizing **highly effective** birth control measures. 5. Any subject that meets the definition of a Vulnerable Subject per ISO 14155:2011 Section 3.44 1. ISO 14155:2011 Section 3.44 States: Vulnerable subject – individual whose willingness to volunteer in a clinical investigation could be unduly influenced by the expectation…	3. Women who are pregnant, nursing, or of child-bearing potential who are not utilizing birth control measures 5. Any subject that meets the definition of a Vulnerable Subject per ISO 14155 1. ISO 14155 states: Vulnerable subject – individuals who are unable to fully understand all aspects of the investigation that are relevant to the decision to participate…
7.8.1 withdrawal from Treatment	The withdrawal of a subject during the operative visit requires the subject to be discontinued from the study. Withdrawn subjects during the operative visit will not be replaced…	The withdrawal of a subject during the operative visit requires the subject to be discontinued from the study. If more than 5% of planned 5% of planned subjects to be enrolled are withdrawn prior to treatment an additional 5% subjects will be enrolled into the study as replacement after fulfilment of the eligibility criteria.

7.9 Subject Reimbursement and Incentives	*Not present in v2.0	Added: Subjects will be reimbursed for the costs of taking part in the study if agreed to by the study site as documented within the Clinical Trial Agreement. These costs will only cover study-specific activities or visits including time, travel, parking, and inconvenience and will not cover activities or visits associated with the subject's standard clinical care. Payments to the subject will be proportionate to the time and expense involved in study participation and not so large as to unduly encourage the subjects to participate or affect the subject's ability to withdraw prematurely form the study. All arrangements for reimbursement payments to subjects will be approved by the IRB and/or local site authority as required.
8.1 Study Design	This is a prospective, multi-center, non-randomized, open-label study designed to evaluate the performance of the Tensioner by assessing patient satisfaction…	This is a post-market, prospective, multi-center, non-randomized, open-label study evaluating the performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System. One Hundred Twenty-Five subjects undergoing cemented primary TKA will be included...
8.3.2 Secondary Endpoints	…The change from the preoperative to 12-month …	• …The change from the preoperative to 12-month follow-up in 2011 KSS Objective, Function, and Satisfaction scores Mean of the KSS Expectation scores at pre-operative and at 12-month follow-up
8.3.3 other Endpoints	… The following endpoints have been defined for this study in order to support the creation of an optimized gap balancing	… The following endpoints have been defined for this study in order to support the creation of an optimized gap balancing workflow…

	workflow with the Tensioner and to understand the relationship between the gap-balancing plan and final alignment with respect to knee deformities.	
9.1.1 Study Procedures – Table 9,1	Study Procedures by Visit table Concomitant Medications under Screening not selected Selected Urine Pregnancy under 12-month Follow-Up 6-Week Follow-Up Visit (Day 42±7 days) *Not present in v2.0	Study Procedures by Visit table Selected Concomitant Medications under Screening Included: B Only medications related to the study treatment and medications used to treat an AE related to the study device will be recorded in the eCRF. Please reference the eCRF Completion Guidelines for how medications are recorded. Deselected Urine Pregnancy under 12-month Follow-Up 6-Week Follow-Up Visit (Day 42±14 days) [C] The 6-month visit may be conducted remotely.
9.1.3 operative Visit Day 0	3. Perform surgery and collect operative data… 4. Collect the Subject's CORI Robotics Case Report…	3. Perform surgery and collect… workflow. See section 9.2.4 for additional information. 4. Collect the … • Analysis of force and deformity data (i.e., deformities outside the given range) The reports will be extracted post-operatively from the system by a S+N representative via download to a USB

		drive. See sections 9.2.3 through 9.2.8 for additional information.
9.1.5 6-Week Follow-Up Visit (Day 42 ± 14 days)	4. Instruct the subject on follow-up procedures, including returning to the office for the 6-month Follow-Up Visit.	4. Instruct the subject on follow-up procedures, including returning to the office for the 6-month Follow-Up Visit. If the month 6 visit is to be completed remotely, make courier arrangements to deliver the 6-month PROMs to the subject to be completed remotely during the month 6 remote visit.
9.1.5 6-Month Follow-Up Visit (Day 180 ± 30 days [Phone Call if Remote])	9.1.5 6-Month Follow-Up Visit (Day 180 ± 30 days) 4. *Not present in v2.0	9.1.5 6-Month Follow-Up Visit (Day 180 ± 30 days [Phone Call if Remote]) 4. If the visit was remote, arrange for a courier to return the completed PROMs to the site.
9.2.1 2011 Knee Society Score (KSS)	The 2011 KSS will be collected at the pre-operative visit and at the 6-week, 6-month, and 12-month Follow-Up Visits…	Included: A paper questionnaire will be provided by the Sponsor to be completed by the subject. Responses for the KSS Score will then be recorded in the eCRF.
9.2.3 Implant Position and Sizing Plan Measurements	Implant position measurements will be captured by the CORI Surgical System and will be included in the case reports…	Implant position measurements will be captured by the CORI™ Surgical System and will be exported in the CORI Robotics Case Report. The reports will be extracted post-operatively from the system by a S+N representative via download to a USB drive…
9.2.4 Repeatability	The CORI Surgical System will log each of the stressed range of motion measurements and they will be exported in the CORI Robotics Case Report. The reports will be extracted post-operatively from the system via download to a USB drive.	The CORI™ Surgical System will log each of the stressed range of motion measurements and they will be exported in the CORI Robotics Case Report. The reports will be extracted post-operatively from the system by a S+N representative via download to a USB drive.

9.2.5 Gap Planning Measurements	…Gap planning measurements will be captured by the CORI Surgical System and included in the CORI Robotics Case Report. The reports will be extracted post-operatively from the system via download to a USB drive.	… Gap planning measurements will be captured by the CORI™ Surgical System and included in the CORI Robotics Case Report. The reports will be extracted post-operatively from the system by a S+N representative via download to a USB drive.
9.2.7 Deformity Profile	The deformity profiles are varus, valgus and neutral. Varus deformity is defined as greater than (>) five (5) degrees Varus…	The deformity profiles are varus, valgus and neutral… The deformity profile will be recorded in the corresponding CRF.
9.2.8 Force Selection	Prior to starting a gap assessment, the surgeon selects the desired force level…	Prior to starting a gap assessment, the surgeon …The reports will be extracted post-operatively from the system by a S+N representative via download to a USB drive.
10.2 Analysis Populations	Intention to Treat population (ITT)… Full analysis set population (FAS)… Safety Population (SAF)… Per-Protocol Population (PP)…	Safety Population (SAF), including all subjects who have received IP. Full analysis set population (FAS), all subjects who were enrolled into the study and had at least one post-baseline effectiveness assessment Per-Protocol Population (PP), including all subjects in the full analysis set who have no significant protocol deviations and met all inclusion/exclusion criteria.
10.4.2 Analysis of Secondary Endpoints	…The 2011 KSS (Satisfaction, Objective, Function, and Expectation)…	…The 2011 KSS (Satisfaction, Objective, and Function)…
11 SAMPLE SIZE JUSTIFICATION	Outcome is EQ-5D VAS change from preoperative (μ_0) to	The primary outcome is a statistically significant EQ-5D VAS change from

	postoperative follow-up (μ_1) i.e. μ_1-μ_0. The minimum clinical important difference is 9.1. H0 (null): μ_1-μ_0 < 9.1 versus Ha (alternate): μ_1-μ_0 ≥ 9.1 Type I error (α) = 0.05 and Type II error (β) = 0.2 (Statistical Power = 80%). Standard error of difference, σ_d = 27.0. Based on these assumptions, N = 72 samples need to be enrolled. Further assumption of an attrition of 10% will require 80 samples will be enrolled.	preoperative (μ_0) to postoperative follow-up (μ_1) i.e., μ_1-μ_0>0. Given an estimated mean difference in preoperative to postoperative EQ-5D VAS of 9.1, Type I error (α) = 0.05, Type II error (β) = 0.2 (Statistical Power = 80%), and standard error of difference, σ_d = 40.0 units. n = 72 evaluable subjects are required. To allow for up to 25% attrition due to loss to follow-up, a total of 90 subjects will be enrolled. If more than 5% (>6) of the planned number of subjects to be enrolled withdraw consent prior to treatment, then an additional 5% subjects will be enrolled into the study as their replacement after satisfactory fulfillment of the study's eligibility criteria.
16 PROTOCOL DEVIATIONS	An Investigator must not make any changes… *Not present in v2.0	Deleted: Give notification requirements and timeframes here for site staff and monitor to report to S+N and PI to report to IRB (which may be conducted by CSM). Added: The site staff must promptly report any deviations from the protocol that affect the rights, safety or well-being of the subject or the scientific integrity of the clinical investigation, including those which occur under emergency circumstances, if required by the IRB, protocol or national regulations. The site must report protocol deviations to the IRB per the IRB requirements.

20.01 Publication of Study Data	*Not present in v2.0	The study will be registered in www.clinicaltrials.gov and the results will be made available within that database.
21 References	40. *Not present in v2.0	40. 2011 Knee Society Knee Scoring System Licensed User Manual - https://www.kneesociety.org/assets/2011KSS%20Support%20Materials.pdf
22.7 Contract Research Organization	M Squared (statistics)	Propharma (statistics).
23.6 Contract Research Organization	Missing section23.6 Contract Research Organization.	Added section23.6 Contract Research Organization. S+N will use the following external organizations in the conduct of this study: • IQVIA (monitoring) • Veranex (data management) • MSquared (statistics).

Additionally, minor updates have been made throughout the protocol. This includes updates to the Schedule of Events for clarity purposes and the fixing of typographical errors.

22.2.5 Approval/Notification (of amendment 2)

This amendment will be submitted to the IRB for approval prior to implementation at the study sites.

22.3 Protocol Amendment (3)

22.3.1 General Purpose (of amendment 3)

The primary reason for this major protocol amendment, from protocol Version 3.0 to Version 4.0, is a reduction in the sample size determination. There were a few minor administrative edits since the protocol was undergoing this revision.

22.3.2 Rationale (of amendment 3)

Rationale for the changes in amendment 3/Version 4.0 is a modification of the sample size. As part of ongoing study management due diligence, study timelines and sample size were revisited to ensure reliable assumptions based on an updated literature review. The updated evidence evaluation revealed that the sample size could be reduced from 90.

22.3.3 Effect on Study Status (of amendment 3)

The effect of this proposed protocol change is 1) reduced sample size, 2) enrollment completion, and 3) decreased overall study timeline.

Site activation and screening commenced in February 2022. Not all subjects were enrolled (see Section 7.6 for definition). Based on the Bayesian model, a minimum of 27 subjects is required. However, to account for all subjects that have been enrolled/treated under the previous protocol versions, the maximum sample size will be 83 subjects. Since the desired sample size has already been reached (minimum of 27 subjects and maximum of 83 subjects), this amendment/Protocol Version 4.0 will effectively satisfy the enrollment milestone.

Therefore, this study will no longer be 'Open to Enrollment' but status will change to 'In Follow-up'.

22.3.4 Details (of amendment 3)

Section	Current Text 16Feb2023 Version 3.0	Revised Text 05Mar2025 Version 4.0
1.3 Sponsor Approval		Updated staff, to reflect current team and updated titles
2 Synopsis, Study Design	Ninety (90) patients who are eligible for a robotic assisted TKA procedure with the CORI™ Surgical System will be followed for approximately 12 months.	Patients who are eligible for a robotic assisted TKA procedure with the CORI™ Surgical System will be enrolled and followed for approximately 12 months.
2 Synopsis, Sample Size	Ninety (90) subjects. A sample size of evaluable subjects is required. To allow for up to 25% attrition due to loss to follow-up,	To achieve 80% power, 20 evaluable subjects are required. To allow for up to 25% attrition due to loss to follow-up, a minimum of 27 subjects will need

	a total sample size n = 90 subjects will be enrolled under competitive enrollment.	to be enrolled with a maximum of 83 based on those consented under frequentist sample size calculations in Protocol Version 3.0.
3.4 Abbreviations	N/A	Updated, added ClinicalTrial.gov (CTG) and Standard Deviation (SD)
6.2 Product Use	N/A	The most current IFU should be referenced at https://ifu.smith-nephew.com/
7.1 Subject Population	A total of 90 subjects, 18 years or older….	A minimum of 27 and a maximum total of 83 subjects, 18 years or older…
8.1 Study Design	This is a post-market, prospective, multi-center, non-randomized, open-label study evaluating the performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System. Ninety subjects undergoing cemented primary TKA will be included.	This is a post-market, prospective, multi-center, non-randomized, open-label study evaluating the performance of the CORI™ KNEE TENSIONER as an accessory to the CORI™ Surgical System. A minimum of 27 subjects having consented and underwent cemented primary TKA will be included. Approximately 4 sites will participate in the United States. The study is expected to enroll all subjects within a 15-month timeframe. Subject follow-up visits will be conducted at 6 weeks, 6 months and 12 months post-operatively. **NOTE:** This study was initially registered on Clinicaltrials.gov (CTG) as a pre-market, interventional study in Apr2021. The product was FDA approved 19Aug2022. A protocol revision in Feb2023 (Ver3.0 16Feb2023) was

		done in part, to change from a pre-market study to a post-market study. No change to CTG classification is warranted since some subjects were enrolled under the pre-market, interventional study (i.e. the more stringent of the CTG definitions).
10.4.1 Analysis of Primary Endpoint	The EQ-5D-5L VAS score will be summarized at the pre-operative, 6-week, 6-month and 12-month follow-up visits. The change from the preoperative visit to follow-up visits will also be summarized. A paired t-test will be used to assess if change from preoperative to 12-month follow-up EQ-5D-5L VAS scores are statistically significantly greater than or equal to 9.1 (i.e. $\mu_1 - \mu_0 \geq 9.1$). If the lower limit of the tw−sided 95% Confidence Interval (CI) for (μ_1-μ_0) from the t-statistic is $\geq$ 9.1 using at a $p<0.05$ (demonstration of a satisfactory change in VAS assessment).	The EQ-5D-5L VAS score will be summarized at the pre-operative, 6-week, 6-month and 12-month follow-up visits. The change from the preoperative visit to follow-up visits will also be summarized. The significance of the change from preoperative to 12- month follow-up EQ-5D-5L VAS scores are statistically significantly greater than 0 (i.e., μ_1-μ_0> 0) will be tested with Bayesian modeling. A literature review[45] was performed and produced 24 sets of data from 20 TKA studies with reported EQ-5D VAS scores at baseline and one year. A meta-analysis was performed to amalgamate this data. For the Bayesian modeling, prior information was obtained from this comprehensive meta-analysis. Lower limit of the 95% confidence interval of the studies was used to derive the meta-analysis summary result for conservativeness. The meta-analysis summary result presented a mean change of EQ-5D VAS score at 12 months

		against baseline of 11.977 and standard deviation (SD) of 17.743. The 95% CI was 4.879 and 19.076. A conservative normal prior will be used as the mean prior distribution from the meta-analysis result of the lower CI limit of mean change, i.e. Normal (4.879, 17.743). A Cauchy prior (0, 17.743) will be used as the prior for the standard deviation to account for variability. Significance against 0 will be concluded if the lower limit of the two-sided 95% Highest Density Credible Interval (HDI) for the posterior distribution is > 0.
11 Sample Size Justification	The primary outcome is a statistically significant EQ-5D VAS change from preoperative (μ_0) to postoperative follow-up (μ_1) i.e., $\mu_1-\mu_0>0$. Given an estimated mean difference in preoperative to postoperative EQ-5D VAS of 9.1, Type I error (α) = 0.05, Type II error (β) = 0.2 (Statistical Power = 80%), and standard error of difference, σ_d = 40.0 units. N = 72 evaluable subjects are required. To allow for up to 25% attrition due to loss to follow-up, a total of 90 subjects will be enrolled. If more that 5% (>6) of the planned number of	The primary outcome is a statistically significant EQ-5D VAS change from preoperative (μ_0) to postoperative follow-up (μ_1) i.e., $\mu_1-\mu_0>0$. A Bayesian approach has been selected to allow for greater flexibility, efficiency and the integration of prior knowledge. To perform a sample size calculation, anticipated effect size and variability were obtained from systematic literature review[45] (Section 11.1), and used as prior information in Bayesian sample size determination (Section 11.2).

	subjects to be enrolled withdraw consent prior to treatment, then an additional 5% subject will be enrolled into the study as their replacement after satisfactory fulfillment of the study's eligibility criteria.	
11.1 Systematic Literature Review and Meta-Analysis	N/A	Studies that used robotic assisted techniques were prioritized; however, due to a lack of robotic assisted TKA studies reporting EQ-5D VAS scores at 12 months, conventional techniques were also eligible for inclusion. Improvements between pre and postoperative EQ-5D VAS scores between robotic and conventional techniques have been shown to be similar[41-44]. Indeed, in a randomized clinical trial (RCT) by Clement et al, 2024 the study investigators compared EQ-5D VAS improvement at 12 months postoperatively between MAKO® (Stryker) and conventional TKA and found no statistical difference between change in EQ-5D VAS (change from pre to post op as follows: MAKO 3.1, conventional 8.1, p=0.27)[41]. EQ-5D VAS at 2 years has also been reported to show similar postoperative scores between NAVIO™ (Smith & Nephew) and conventional patient groups (p=0.37)[42], as well as between an unknown robotic system and conventional in a conference abstract at weeks 2, 6 and 3 months (p≥0.05)[43]. This is also backed up by the lack of statistically meaningful difference

		in EQ-5D between robotic and conventional TKA (p=0.31)[44]. This literature review[45] provided 24 sets of data from 20 studies with reported EQ-5D VAS scores at baseline and one year. A multilevel (within study and between studies) random effects meta-analysis is performed to amalgamate this data.
11.2 Bayesian Sample Size Determination	N/A	As stated above, prior information for Bayesian sample size determination was obtained from a systematic literature review and meta-analysis. Lower limit of the 95% confidence interval of the studies was used to derive the meta-analysis summary result for conservativeness. The meta-analysis summary result presented a mean change of EQ-5D VAS score at 12 months against baseline of 11.977 (4.879 – 19.076, 95% confidence interval), and a SD of 17.743. To determine sample size, a simulation approach was used. Change scores were generated from multiple random samples from the normal distribution with mean and SD from the meta-analysis result, i.e. Normal (11.977, 17.743). A Bayesian model was then fitted to these scores, using a conservative normal prior based on the lower 95% CI limit of change in EQ-5D from the meta-analysis result, i.e. Normal (4.879, 17.743). A

		Cauchy prior (0, 17.743) was used as the prior for the standard deviation to account for variability. Significance against 0 will be concluded if the lower limit of the two-sided 95% Highest Density Credible Interval (HDI) for the posterior distribution is > 0. This simulation process was repeated across 50 iterations to estimate statistical power. To achieve 80% power, 20 evaluable subjects are required. To allow for up to 25% attrition due to loss to follow-up, a minimum of 27 subjects will need to be enrolled with a maximum of 83 based on those consented under frequentist sample size calculations in Protocol Version 3.0.
20.1 Publication of Study Data	The study will be registered in www.clinicaltrials.gov and the results will be made available within that database.	The study is registered in www.clinicaltrials.gov (NCT04849884) and the results will be made available within that database as applicable, based on CTG study classification.
21 References		• Reordered based on chronology rather than alphabetically • Addition of references #41-45
All Sections from 22.3 through end of document		All sections after 22.3 have had a numbering change due to this addition of Protocol Amendment (3) details
22.4 Instructions for Use (originally Section 22.3)	N/A	The most current IFU should be referenced at https://ifu.smith-nephew.com/.

22.8 Contract Research Organization (originally Section 22.7)	S+N will use the following external organizations in the conduct of this study: • IQVIA (monitoring) • Veranex (data management) • Propharma (statistics).	S+N will maintain a list of names and addresses of external organizations involved in the study which may be provided upon request. External organizations will be used in the conduct of the following activities: • monitoring services

22.3.5 Approval/Notification (of amendment 3)

This amendment/Version 4.0 will be submitted to the IRB for approval prior to implementation at the study sites. Upon IRB approval, study enrollment will be officially closed. CTG registration will be updated as appropriate.

22.4 Instructions for Use

Always refer to the IFU and user manual supplied with this protocol. The most current IFU should be referenced at https://ifu.smith-nephew.com/.

22.5 Equipment and Special Instructions

The investigational and ancillary products have storage and handling conditions noted on the label. Additionally, Data loggers will be supplied to the site to monitor storage conditions. Data loggers will require periodic calibration, which will be managed by S+N.

22.6 Health Economic Outcome Measures/Quality of Life measures

NA.

22.7 Clinical Study Sites

S+N will maintain a list of the name and address of involved sites in the Trial Master File. This list is available upon request.

22.8 Contract Research Organization

S+N will maintain a list of names and addresses of external organizations involved in the study which may be provided upon request. External organizations will be used in the conduct of the following activities:

- monitoring services

22.9 Additional Information

NA.

22.10 Principal Investigator Obligations (ISO 14155)

1. General:
   a. The role of the PI is to implement and manage the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety, and well-being of the subjects involved in the clinical investigation.
   b. The PI is responsible for ensuring adequate training and qualification of the investigation site team and for maintaining oversight of their activities. The principal investigator may delegate tasks to qualified members of the investigation site team but retains responsibility for the clinical investigation (see also 7.6). This also applies when activities are outsourced to an external organization by the principal investigator in which case, he/she shall implement procedures to ensure the integrity of all tasks performed and any data generated by this external organization.
2. Qualification of the PI. The PI shall:
   a. be qualified by education, training, and experience to assume responsibility for the proper conduct of the clinical investigation in accordance with this International Standard; evidence of such qualifications of the PI and key members of the investigation site team shall be provided to the Sponsor through up-to-date Curriculum Vitae (CV) or other relevant documentation,
   b. be experienced in the field of application and trained in the use of the investigational device under consideration,
   c. disclose potential conflicts of interest, including financial, that interfere with the conduct of the clinical investigation or interpretation of results, and
   d. be knowledgeable with the method of obtaining informed consent.
3. Qualification of investigation site. The PI shall be able to demonstrate that the proposed investigation site:
   a. has the required number of eligible subjects needed within the agreed recruitment period, and;

b. has an investigation site team that is: qualified by education, training, and experience to assume responsibility for the proper conduct of the clinical investigation in accordance with this document; evidence of such qualifications for members of the investigation site team shall be documented through up-to-date CVs or other relevant documentation;
c. has adequate facilities.

4. Communication with the IEC. The PI shall:
   a. provide the Sponsor with copies of any clinical-investigation-related communications between the PI and the IEC,
   b. comply with the requirements described in 4.5 of ISO 14155.
      i. Submit to the IEC the following information, any amendments and any additional documentation required by the IEC: The Protocol; IB or equivalent; informed consent form and any other written information provided to subjects; procedures for recruiting subjects and advertising materials, if any; a copy of the CV of the PI(s) for with the IEC has oversight.
      ii. Provide documentation of the IECs approval/favorable opinion, identifying the documents and amendments on which the opinion was based, to the Sponsor, prior to commencing the clinical investigation.
      iii. Submit the following to the IEC if required by national regulations, the protocol or IEC, whichever is more stringent:
         1. SAEs
         2. Requests for deviations, and reports of deviations, if the deviation affects subject's rights, safety, and well-being, or the scientific integrity of the clinical investigation. Document and report to the Sponsor and IEC a report of deviations made to protect the rights, safety, and well-being of human subjects under emergency circumstances.
         3. Progress reports, including safety summary and deviations
         4. Amendments to any documents already approved by the IEC.
         5. If applicable, notifications of suspension or premature termination
         6. If applicable, justification and request for resuming the clinical investigation after suspension.
         7. Clinical investigation report or summary.
      iv. As a minimum, during the clinical investigation, the following information shall be obtained in writing from the IEC prior to implementation:
         1. Approval/favorable opinion of amendments
         2. Approval of the request for deviations that can affect the subject's rights, safety, and well-being or scientific integrity of the clinical investigation
         3. Approval for resumption of a suspended clinical investigation if applicable.
   c. obtain the written and dated approval/favorable opinion of the IEC for the clinical investigation before recruiting subjects and implementing all subsequent amendments, if required,
   d. promptly report any deviations from the protocol that affect the rights, safety or well-being of the subject or the scientific integrity of the clinical investigation, including those which

occur under emergency circumstances, if required by the IEC, protocol or national regulations. In particular circumstances, the communication with the IEC can be performed by the Sponsor, partly or in full, in which case the Sponsor shall keep the Principal Investigator informed.

5. Informed consent process. The PI shall:
   a. General:
      i. Informed consent shall be obtained in writing from the subject and the process shall be documented before any procedure specific to the clinical investigation is applied to the subject; except when special circumstances for emergency treatments apply (see below)
   b. Process of obtaining informed consent. The general process for obtaining informed consent shall be documented in the protocol and shall comply with the following. These requirements also apply with respect to informed consent obtained from a subject's legally authorized representative:
      i. Ensure that the PI or their authorized designee conducts the informed consent process
      ii. Include all aspects of the clinical investigation that are relevant to the subject's decision to participate throughout the clinical investigation
      iii. Avoid any coercion or undue improper influence on, or inducement of, the subject to participate
      iv. Not waive or appear to waive the subject's legal rights
      v. Use native non-technical language that is understandable to the subject
      vi. Provide ample time for the subject to read and understand the informed consent form and to consider participation in the clinical investigation
      vii. Include personally dated signatures and the PI or an authorized designee responsible for conducting the informed consent process
      viii. Show how informed consent will be obtained in special circumstances (see below) where the subject is unable to provide him or herself, and
      ix. Ensure important new information is provided to new and existing subjects throughout the clinical investigation.
   c. Special circumstances for informed consent (the following provisions are subject to national regulations):
      i. Subject needing legally authorized representatives: informed consent may be given by the legally authorized representative only if a subject is unable to make the decision to participate in a clinical investigation (e.g., infant, child, or juvenile, seriously ill or unconscious subject, mentally ill person, mentally handicapped person). In such cases, the subject shall also be informed about the clinical investigation within their ability to understand.
      ii. Subject unable to read or write: informed consent shall be obtained through a supervised oral process if a subject or legally authorized representative is unable to read or write. An independent witness shall be present throughout the process. The written informed consent form and any other information shall be read aloud and explained to the prospective subject or their legally authorized representative and,

whenever possible, either shall sign and personally date the informed consent form. The witness also signs and personally dates the informed consent for attesting that the information was accurately explained and that the informed consent was freely given.

iii. Emergency treatments:
   1. For clinical investigations involving emergency treatments, when prior informed consent of the subject is not possible because of the subject's medical condition, the informed consent of the subject's legally authorized representative, if present, shall be requested.
   2. When it is not possible to obtain prior informed consent from the subject, and the subject's legally authorized representative, is not available, the subject may still be enrolled if a specific process has been described in the protocol.
   3. Arrangements shall be made to inform the subject or legally authorized representative, as soon as possible, about the subject's inclusion in the clinical investigation and about all aspects of the clinical investigation.
   4. The subject shall be asked to provide informed consent for continued participation as soon as their medical condition allows.

d. The Principal Investigator may not enroll a subject without obtaining informed consent of the subject or their legally authorized representative only when the following conditions are fulfilled: the prospective subject fulfils the emergency conditions and is obviously in a life-threatening situation; no sufficient clinical benefits are anticipated from the currently available treatment; there is a fair possibility that the life-threatening risk to the prospective subject can be avoided if the investigational device is used; anticipated risks are outweighed by the potential benefits of applying the investigational device ; the legally authorized representative cannot be promptly reached and informed.

e. Information provided to the subject. All information pertinent to the clinical investigation, including at least the following, shall be provided in writing and in native, non-technical language that is understandable to the subject (or the subject's legally authorized representative):
   i. Description and purpose
   ii. Potential benefits
   iii. Risks and inconveniences or the subject and, when applicable, for any embryo, fetus or nursing infant
   iv. Alternative procedures
   v. Confidentiality
   vi. Compensation
   vii. Anticipated expenses, if any, to be borne by the subject for participating in the clinical investigation
   viii. Information on the role of Sponsor's representative in the clinical investigation
   ix. Contact persons
   x. Statement declaring that new findings or the reasons for any amendment to the protocol that affect the subject's continued participation shall be made available to the subject

xi. Statement indicating that, upon the subject's approval, the subject's personal physician will be informed of the subject's participation in the clinical investigation
xii. Statement indicating that a description of the clinical investigation has or shall be registered in a publicly accessible database
xiii. Termination procedures

f. Informed consent signature shall contain the following:
i. The voluntary agreement to participate in the clinical investigation and follow the investigator's instructions
ii. A statement declaring that refusal of participation incurs no penalty for the subject and no loss of benefits to which the subject is otherwise entitled;
iii. A statement declaring that discontinuation/withdrawal and thereby revoking the informed consent at any time incurs no penalty for the subject;
iv. A statement with regard to the possible consequences of withdrawal
v. An acknowledgment of the information provided and confirmation that all the subject's questions were answered that the subject acknowledges the information provided during the informed consent process and that (s)he had ample time to consider participation
vi. A statement confirming that the subject or their legally authorized representative agrees to the use of the subject's relevant personal data for the purpose of the clinical investigation
vii. A statement confirming that the subject or their legally authorized representative agrees that Sponsor's representatives, regulatory authorities and IEC representatives will be granted direct access to the subject's medical records.

g. New information: if new information becomes available that can significantly affect a subject's future health and medical care, that information shall be provided to the subject(s) affected in written form. If relevant, all affected subjects shall be asked to confirm their continuing consent in writing.
h. ensure compliance with the applicable regulatory requirements and ethical principles for the process of obtaining informed consent, and
i. ensure and document appropriate training if an authorized designee is appointed to conduct the informed consent process.

6. Compliance with the protocol. The Principal Investigator shall:
a. indicate their acceptance of the protocol in writing,
b. conduct the clinical investigation in compliance with the protocol,
c. create and maintain source documents throughout the clinical investigation and make them available as requested during monitoring visits or audits as well as maintain documentation of the type and location of these source documents,
d. ensure that the investigational device is used solely by authorized users as specified in 6.2, and in accordance with the protocol and instructions for use,
e. propose to the Sponsor any appropriate modification(s) of the protocol or investigational device or of the use of the investigational device,

f. refrain from implementing any modifications to the protocol without agreement from the Sponsor, IEC and regulatory authorities, if required,
g. document and explain any deviation from the approved protocol that occurred during the course of the clinical investigation,
h. ensure that an adequate investigation site team and facilities exist and are maintained and documented during the clinical investigation,
i. ensure that maintenance and calibration of the equipment relevant for the assessment of the clinical investigation is appropriately performed and documented, where applicable,
j. ensure the accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor in the CRF and in all required reports,
k. maintain the device accountability records,
l. Comply with the procedure for the safe return of investigational devices including potentially hazardous devices and, in the case of reported device deficiencies, collaborate with the sponsor to provide the necessary information allowing an accurate analysis where appropriate. requirements and provide any information need to analyze device deficiencies, if applicable.
m. allow and support the Sponsor to perform monitoring and auditing activities,
n. be accessible to the monitor and respond to questions during monitoring visits,
o. determine the cause and implement appropriate corrective and preventative actions to address significant noncompliance,
p. allow and support regulatory authorities and the IEC when performing auditing activities,
q. ensure that all clinical-investigation-related records are retained as required taking measures to prevent accidental or premature destruction, and
r. review and sign the clinical investigation report, as applicable.

7. Medical care of subjects. The Principal Investigator shall
   a. provide adequate medical care to a subject during and after a subject's participation in a clinical investigation in the case of adverse events,
   b. inform the subject of the nature and possible cause of any adverse events experienced,
   c. provide the subject with the necessary instructions on proper use, handling, storage, and return of the investigational device, when it is used or operated by the subject,
   d. inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required,
   e. provide the subject with well-defined procedures for possible emergency situations related to the clinical investigation, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded/masked clinical investigations, as needed,
   f. ensure that clinical records are clearly marked to indicate that the subject is enrolled in a particular clinical investigation,
   g. if appropriate, subjects enrolled in the clinical investigation shall be provided with some means of showing their participation in the clinical investigation, together with identification and compliance information for concomitant treatment measures (contact address and telephone numbers shall be provided),

h. inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation, and
i. make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from the clinical investigation while fully respecting the subject's rights.

8. Safety reporting. The Principal Investigator shall:
   a. record every adverse event and observed device deficiency, together with an assessment,
   b. report to the Sponsor, without unjustified delay, all serious adverse events and device deficiencies that could have led to a serious adverse device effect; this information shall be promptly followed by detailed written reports, as specified in the protocol,
   c. report to the IEC serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by the national regulations or protocol or by the IEC,
   d. report to regulatory authorities, serious adverse events and device deficiencies that could have led to a serious adverse device effect, as required by the national regulations, and
   e. supply the Sponsor, upon Sponsor's request, with any additional information related to the safety reporting of a particular event.

An investigator shall prepare and submit the following complete, accurate, and timely reports:

9. Unanticipated Adverse Device Effects. An investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.
10. Withdrawal of IRB approval. An investigator shall report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
11. Progress. An investigator shall submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
12. Deviations from the investigational plan. An investigator shall notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB also is required.
13. Informed consent. If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.
14. Final report. An investigator shall, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.
15. Other. An investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.