ROSA Total Knee
Post Market Study

PROSPECTIVE MULTICENTER U.S. STUDY
OF THE
ROSA KNEE SYSTEM

Protocol # CMU2018-34K

11/08/2018 – Version 1.0
09/05/2019 – Version 2.0
10/14/2019 – Version 3.0
10/02/2020 – Version 3.1

STUDY SPONSOR
Zimmer Biomet Orthopaedics
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Appendices:

I. Document History

Version No.	Date	Description of change	Author
Version 1.0	1 March 2018	Initial Document	Tory Sears
Version 2.0	5 September 2019	Additional CRF added to Section III – Data Collection Overview, and Section IX – Study Procedures	Tory Sears
Version 3.0	14 October 2019	Changes to sections II and VI: -Increase in maximum enrollment per site. -Removal of specific requirements regarding equivalent enrollment into robotic/conventional groups	Tory Sears
Version 3.1	31 Mar 2020	Changes to section II and VI include an increase in maximum number of research sites from 6 to 10; as well as, sites will enroll competitively up to the maximum allowed per site, or until the max study population is achieved. Correction of typographical/grammatical errors throughout document	Tory Sears

II. Study Synopsis

TITLE:	*ROSA Total Knee Post Market Study*
SPONSOR:	Zimmer Biomet Inc., Warsaw, IN
PROTOCOL NUMBER	CMU2018-34K
STUDY OBJECTIVES	The primary objective of this study is to collect and compare clinical outcomes data using the commercially available ROSA Knee System and conventional instrumentation. The assessments will include: 1. Planned vs actual component positioning. 2. Workflow efficiency. 3. Patient safety based on incidence and frequency of adverse events. 4. Clinical performance measured by overall pain and function, quality of life data, and radiographic parameters.
TARGET POPULATION:	Patients qualifying for primary total knee arthroplasty who meet the inclusion/exclusion criteria for study participation
STUDY DESIGN:	Prospective, multicenter study, using Zimmer Biomet commercially available Persona, Vanguard, and NexGen total knee implant systems.
STUDY TYPE:	Post-market
SAMPLE SIZE:	A Maximum study enrollment of 300 subjects competitively enrolled at up to 10 U.S. sites, with participating sites each enrolling up to 45 Robotic knees and up to 30 conventional knees; with a max site enrollment, of up to 75 total knees. Once the maximum study enrollment has been reached, enrollment at all sites will be closed.

LENGTH OF STUDY:	One-year Post-operative study; Post-op follow-up visits include: 6 weeks, 3months, and 1 year. Total Enrollment time: 12-18 Months. Total Study Length: 2 - 2.5 years
INCLUSION/EXCLUSION CRITERIA:	INCLUSION CRITERIA: 1. Patient is a minimum of 18 years of age 2. Independent of study participation, patient is a candidate for commercially available *Persona, NexGen, or Vanguard* knee components implanted in accordance with product labeling 3. Patient has participated in the study-related Informed Consent process 4. Patient is willing and able to provide written Informed Consent by signing and dating the IRB or EC approved Informed Consent form 5. Patient is willing and able to complete scheduled study procedures and follow-up evaluations EXCLUSION CRITERIA: 1. Patient is currently participating in any other surgical intervention studies or pain management studies 2. Patient has undergone contralateral UKA or TKA within the last 18 months 3. Hip pathology with significant bone loss (e.g. avascular necrosis of the femoral head with collapse, severe dysplasia of the femoral head or the acetabulum) 4. Hip pathology severely limiting range of motion (e.g. arthrodesis, severe contracture, chronic severe dislocation) 5. Patient is pregnant or considered a member of a protected population (e.g., prisoner, mentally incompetent, etc.) 6. Patient has previously received partial or total knee arthroplasty for the ipsilateral knee **Note:** During the surgical preparation, if there is presence of strong infrared sources or infrared reflectors in the vicinity of the NavitrackERs, the subject cannot continue with the study. A Study Completion form must be completed. **Note:** The use of Tibial/Fibular Augments and stems, constrained liners, and any use of guidance systems are excluded from this study

TESTING ARTICLE	*The ROSA Knee System*
CLINICAL OUTCOMES MEASURES:	EQ-5D Oxford Knee Score
CLINICAL PERFORMANCE ASSESSMENTS:	Post-Operative Pain & Satisfaction Functionality & Range of Motion Radiographic parameters
STATISTICAL REPORTING:	Performance will be evaluated for pain, function, quality of life, and planned component position vs post-op component position. Data will be summarized descriptively additional to evaluation of data on surgical technique and instrumentation. Categorical data (e.g., gender or race) will be summarized using counts and percentages with 95% Confidence Interval (CI) limit over the time period of interest. Continuous data, such as age, will be summarized by using means, medians, SD, minimum, maximum, and 95% CI over the time period of interest. Implant survival and return to function will be summarized using a Kaplan-Meier method and presented with rates (as percentages) and CI. Routine summaries of complication data is represented by frequencies and percentages. Sample size is based on a longitudinal data collection model and using functional outcomes as the primary endpoint of interest.

This protocol is written based on guidelines from ISO 14155 : 2011Standard for Clinical Investigation of Medical Devices For Human Subjects – Good Clinical Practice [(i)] the ICH Guideline on Good Clinical Practice[(ii)], and the Declaration of Helsinki [(iii)] and is in accordance with US Code of Federal Regulations 21 CFR Parts 11, 50 and 56 [(ii)]. IRB or EC approval for each site will be obtained prior to conducting this study, as applicable.

III. Data Collection Overview

The following table indicates the necessary case report forms to be completed at the given time point:

Form Name	Pre-op	Operative	6 Week	3 Month	1 Year
Informed Consent	●				
Inclusion/Exclusion Criteria	X				
Demographic Evaluation	X				
Pre-op plan for Conventional Instrumentation		X			
Operative Information		X			
Surgical Device Information		X			
Discharge Summary		X			
Physical Exam			X	X	X
Objective Knee Assessment	X		X	X	X
EQ-5D	●		●	●	●
Oxford Knee Score	●		●	●	●
Physician Assessment of Radiographs	X*		X	X*	X
Adverse Event Report		★	★	★	★
Protocol Deviations	★	★	★	★	★
Study Completion	★	★	★	★	★

* Long Leg Radiograph required at this interval

* Central or Independent radiographic review performed by Sponsor's designee, if applicable, at discretion of the Sponsor

The following table indicates the necessary case report forms required to be completed for revision patients:

Form Name	Revision (as applicable)	Comments
Physician Assessment of Post-op Radiographs	★	Mark the "pre-revision" exam period.
Adverse Event Report	★	Document adverse event resulting in the revision
Study Completion	★	Complete indicating "Study Prosthesis Removed" under Study Completion Status.

- ● Completed by Patient
- X Completed by Investigator or Designee
- ★ Completed by Investigator or Designee as applicable
- ♦ Central or Independent radiographic review performed by Sponsor's designee, if applicable, at discretion of the Sponsor

IV. Introduction and Purpose

Total knee arthroplasty (TKA) is a reliable treatment option for knee osteoarthritis. As laid out in the CERs of the subject instrument system's compatible Zimmer Biomet's TKA implant systems, recent systematic reviews[1] and orthopaedic registries[2, 3] have reported 90% or higher implant survival at 10 years for TKA. Over the last two decades, there is a growing interest towards perioperative variables that are controlled by the orthopaedic surgeon[4]. These variables include leg alignment, soft tissues balance, joint line maintenance and the alignment, sizing and fixation of the components; and each of these variables are determinants of arthroplasty outcomes[4]. Along with the return to premorbid function, pain relief is an aim of arthroplasty. Currently, it is estimated that up to 19% of patients undergoing total knee arthroplasty may not be satisfied with the outcome[5]. In a follow-up period ranging from 3 months to 5 years, Beswick et al found that 10-34% of patients experienced unfavorable pain outcomes after total knee arthroplasty[6]. They also noted that even in studies reporting good patient satisfaction from arthroplasty, an unfavorable pain outcome was reported in around 20% of patients after total knee arthroplasty[6].

In addition to patient outcomes, the ultimate shortcoming of an arthroplasty is the need for revision. A major factor affecting the rate of knee arthroplasty failure is tibiofemoral alignment. Although there is a vivid discussion with regard to the ideal positioning of implant component, there is still wide consensus that unintentional component malplacement should be avoided, as this can have an adverse impact on implant function and longevity[7-10]. Revision of joint arthroplasty increases load on the health-care system and also incurs significant costs, with a revision total knee arthroplasty estimated to cost a multiple of primary procedures, depending on complexity and indication[11]. Therefore, there is an economic, as well as clinical, case for maximizing outcomes from primary knee arthroplasties. Further shortcomings of existing strategies are inter-surgeon variability and variation in quality of outcomes. There is a lack of precise reproducibility of surgeon's experience, and most procedures have a relatively steep learning curve.

The primary aim of robotics in arthroplasty is precise reproduction of the surgeon's preoperative plan during surgery. It is hypothesized that more accurate implant placement will translate to better clinical placement, which will translate to better clinical outcomes, although the current data supporting improved patient satisfaction are conflicting. Robotics offers several other potential advantages. The ability to create a preoperative plan and accurately execute it during surgery using intraoperative feedback reduces variation in component placement. This benefit may also be true for less experienced surgeons.

The ROSA Knee System is the natural progression of technology, combining imaging modalities, patient specific guides, navigation, and soft tissue respecting philosophies; all applied to one concise tool which provides reproducible patient outcomes. In addition, it’s coupled with precision-engineered industry-leading products: NexGen, Persona, and Vanguard total knee systems. The ROSA Knee system provides streamlined workflow that is customizable to surgeon’s needs, and keeps the surgeon in control - bridging the patient satisfaction gap through more precise and accurate cuts, and providing a personalized fit and positioning that can be adapted to the patient intraoperatively.

V. Study Objectives

The primary objective of this study is to collect and compare clinical outcomes and surgical data using the commercially available ROSA Knee System instrumentation and conventional instrumentation.
This will be done by analysis of validated outcome measurement tools, radiographs and adverse event data.

The assessments will include:

1. Comparison of planned operative vs. actual operative component position
2. Operative workflow efficiency
3. Patient safety based on incidence and frequency of adverse events.
4. Clinical performance measured by overall pain and function, quality of life data, and radiographic parameters.

VI. Study Design

This is a prospective, multicenter clinical study designed to facilitate the collection and evaluation of workflow efficiency, patient pain and function, and adverse event data. This clinical study will include Persona, NexGen, and Vanguard product families using the ROSA Knee System or conventional instrumentation. The primary objective of this study is to collect and compare clinical and surgical data using the commercially available ROSA Knee System instrumentation and conventional instrumentation.

A maximum of 300 subjects are to be competitively enrolled in this study across all sites; a maximum of 10 U.S sites will contribute, with participating sites each enrolling up to 75 implanted knees. Sites will enroll up to 45 patients using The ROSA Knee System and up to 30 patients using Conventional instrumentation; total study enrollment into these arms are not to exceed 180 subjects and 120 subjects respectively. Once the maximum study enrollment has been reached, enrollment at all sites will be closed.

Investigators will be skilled in total knee arthroplasty and experienced implanting Persona, NexGen, and/or Vanguard knee systems. Each Principal Investigator will be responsible for obtaining Institutional Review Board (IRB) approval as required prior to conducting the study. In order to avoid potential selection bias, each Investigator will offer study participation to each consecutive eligible patient presenting as a candidate for primary total knee arthroplasty using the aforementioned implants. Eligible candidates who express interest in study participation will be offered Informed Consent. All potential study subjects will be required to participate in the Informed Consent process and will not be considered enrolled in the study until the candidate has signed and dated the IRB approved Informed Consent Form. Study data cannot be collected until the candidate has completed the Informed Consent process and signed and dated the IRB approved Informed Consent Form. All study subjects will undergo preoperative clinical evaluations prior to their Robotic-assisted total knee arthroplasty.

At the Sponsor's discretion, the Sponsor may request copies of radiographs for independent radiologic review. The Sponsor may request one central reviewer for all radiographs independent

of the surgeon and institution.

VII. Study Population

The study population for primary statistical analysis will be comprised of males and females who require primary total knee arthroplasty and satisfy the inclusion/exclusion criteria outlined in this section of the protocol. In order to avoid potential selection bias, each Investigator will offer study participation to each consecutive eligible patient presenting as a candidate for primary total knee arthroplasty using the commercially available (FDA cleared) Persona, Vanguard, and NexGen knee systems. Eligible candidates who express interest in study participation will be offered Informed Consent. The inclusion/exclusion CRF should not be completed until the study-specific consent form has been completed.

a. Inclusion Criteria:

1. Patient is a minimum of 18 years of age
2. Independent of study participation, patient is a candidate for commercially available *Persona, NexGen, or Vanguard* knee components implanted in accordance with product labeling
3. Patient has participated in the study-related Informed Consent Process
4. Patient is willing and able to provide written Informed Consent by signing and dating the IRB or EC approved Informed Consent form
5. Patient is willing and able to complete scheduled study procedures and follow-up evaluations

b. Exclusion Criteria

1. Patient is currently participating in any other surgical intervention studies or pain management studies
2. Patient has undergone contralateral UKA or TKA within the last 18 months
3. Hip pathology with significant bone loss (e.g. avascular necrosis of the femoral head with collapse, severe dysplasia of the femoral head or the acetabulum)
4. Hip pathology severely limiting range of motion (e.g. arthrodesis, severe contractures, chronic severe dislocation)
5. Patient is pregnant or considered a member of a protected population (e.g., prisoner, mentally incompetent, etc.)
6. Patient has previously received partial or total knee arthroplasty for the ipsilateral knee

Note: During the surgical preparation, if there is presence of strong infrared sources or infrared reflectors in the vicinity of the NavitrackERs, the subject cannot continue with the study. A Study Completion form must be completed.

Note: The use of Tibial/Fibular Augments and stems, constrained liners, and any use of guidance systems are excluded from this study

VIII. Study Device Information

The ROSA Knee System and all TKA device components included in this study are commercially available (FDA cleared) products. All implantable device components are intended for long-term survivorship in accordance with product labeling. Please refer to the package insert for additional instructions, information, and indications for use. The ROSA Knee System is intended to assist the

surgeon in providing software-defined spatial boundaries for orientation and reference information to anatomical structures during surgery. The ROSA Knee System application will support the following Zimmer Biomet total knee systems in both cement and cementless options:

a. Persona® The Personalized Knee

Persona knee components included in this study are fixed bearing configurations with various component sizes to accommodate anatomical variation. Femoral components replicate native A/P with 21 distinct profiles in 2mm increments.

b. NexGen® Complete Knee Solution

NexGen's Primary TKA components in this study will include both fixed and mobile bearing configurations. NexGen accommodates both Cruciate Retaining (CR) and Posterior Stabilized constraint options. The NexGen Flex knee offers patients a larger range of active flexion, accommodating deep flexion up to 155 degrees.

c. Vanguard® Knee System

The Vanguard Knee System offers an entire spectrum of knee stability, featuring both Cruciate Retaining (CR) and Posterior Stabilized (PS) femoral stabilization options. Component variation includes ten femoral component sizes, nine tibial component sizes, and five levels of bearing constraints.

IX. Study Procedures

a. Offer Study Participation

Study participation will be offered to each consecutive eligible patient presenting as a potential candidate for total knee arthroplasty using the commercially available ROSA Knee System. An **Enrollment/Informed Consent Log** (Appendix C) will be completed to document all individuals screened as potential candidates for the study. Eligible candidates who express interest in study participation will be offered Informed Consent. Prior to patient involvement in the study, the patient must participate in the Informed Consent process and sign and date the IRB or EC approved Informed Consent.

b. Informed Consent Process

For candidates that express interest, the Investigator or Designee will describe relevant study information, including the purpose, procedures, possible risks, and potential benefits associated with study participation. The Investigator or Designee will also review, along with the candidates, the Informed Consent approved by both the governing IRB or EC and the study Sponsor. Candidates should be made aware that any and all data collected electronically within the ROSA Knee System will be made available to the sponsor for research related purposes. Candidates shall have sufficient time to read and understand the IRB or EC approved Informed Consent and discuss whether they wish to participate in the study. Candidates will be asked to acknowledge whether all of their questions and concerns have been addressed to their satisfaction. Any questions that candidates may have will be addressed appropriately by the Investigator or Designee. Candidates will be further instructed that they are free to obtain additional information from the Investigator or Designee at any time, that they are free to decline participation, and that they are free to withdraw their consent and discontinue their participation at any time without prejudice.

After completing the Informed Consent process, candidates who agree to enter the study must sign and date the IRB or EC approved Informed Consent. The Informed Consent must be signed and dated prior to the date of the study surgery.
A copy of the signed Informed Consent must be provided to the study subject. The original signed Informed Consent is to be filed in the subject's medical record, study subject binder, or regulatory binder.

Study data will not be collected until the Informed Consent has been signed and dated. If the candidate does not wish to participate (does not sign and date the Informed Consent), data for that candidate will not be collected for this study.

c. Informed Consent and Subject Identification Log

A **Subject Identification/Informed Consent Log** (Appendix C) will be maintained at the site throughout the course of the study. The purpose of the log is to provide documentation that all enrolled study subjects underwent the Informed Consent process, and signed and dated the IRB or EC approved Informed Consent. All candidates who sign and date the approved Informed Consent for the study must be entered in the log. If a subject signs and dates additional Informed Consent(s) after enrollment (e.g., due to a protocol amendment, protocol revisions, etc.), subsequent signings will also be recorded in the log. The **Subject Identification/Informed Consent** will be filed in the site Regulatory Binder for the study. The proposed date of surgery for each subject will be added to the log. The subject will be considered an active study subject after receiving the study device during surgery. In the event that a subject does not receive the study device at the time of surgery, a **Study Completion** form must be submitted and this will be documented as a screen failure.

d. Subject Enrollment

Once the Informed Consent has been signed and dated by the subject, the subject will be considered enrolled in the study. Robotic and conventional patients should be enrolled using a consecutive and concurrent approach. A unique case identification number (Case ID) will be assigned to each participating subject. This unique case ID number will be used throughout the study for identification. Case ID numbers will be assigned consecutively in ascending order per site, with the starting number for a given site defined by the Sponsor. In the event that the subject does not receive the study device at the time of surgery, the subject will be considered a screen failure and documented on a **Study Completion** form (see above). In the occurrence of a screen failure, the surgeon may have the option to enroll an additional patient as long as the subject did not receive the study device.

e. Monitor Log

The **Site Monitoring Visit Log** (Appendix C) will be maintained throughout the course of the study. The log will contain the visit date, monitor name/signature and the purpose of the visit (i.e. site initiation, onsite interim monitoring (as applicable), site close-out, etc.). The site monitoring visit log will be filed in the site Regulatory Binder for the study.

f. Delegation of Authority (Site Signature Log)

A **Delegation of Authority Log** (Appendix C) will be maintained throughout the study and will contain the names, initials, signatures and study responsibilities of all site personnel/designees involved in study procedures and data collection. The **Delegation of Authority Log** will be filed in the site Regulatory Binder for the study.

g. Baseline / Pre-operative Assessment

Baseline/pre-operative data to be collected on the following source documents at the time of enrollment:

1. Inclusion/Exclusion Criteria
2. Demographic Evaluation
3. Pre-op plan for Conventional Instrumentation (when applicable)
4. Physician Assessment of Radiographs (Long-Leg)
5. Objective Knee Assessment
6. EQ-5D
7. Oxford Knee Score
8. Protocol Deviations (as applicable)
9. Study Completion (as applicable)

h. Surgical Technique

Through the use of either conventional or robotic techniques, standard operating procedures will be followed and all surgical procedures will be performed under aseptic conditions. Investigators will implant all commercially available Persona, NexGen, and Vanguard Total Knee components in compliance with corresponding labeling requirements, and in accordance with appropriate surgical technique(s).

i. Surgical and Immediate Post-Surgical Procedures (Data Collection)

Surgical and immediate post-surgical data to be collected on the following source documents:

1. Operative Workflow
2. Surgical & Operative Information
3. Discharge Summary
4. Adverse Event Report (as applicable)
5. Protocol Deviations (as applicable)
6. Study Completion (as applicable)

Post-surgical management for study subjects will follow the investigator's standard of care for patients undergoing total knee arthroplasty (e.g. prophylactic antibiotic therapy, prevention of deep vein thrombosis, prevention of pulmonary embolism, etc.). Post-surgical rehabilitative therapy will be as prescribed by the investigator.

j. Post-operative Follow-up procedures (Data Collection)

Post-operative clinical evaluations/assessments will be conducted at the following visit intervals:

Clinical Interval	Interval Window in Days Post-op*	Approximate Window in Weeks or Months Post-op*
6 weeks	21 to 63 days	-/+3 weeks
3 months	61 to 120 days	-/+1 month
1 year	300 to 420 days	-/+2 months

*Visit(s) outside of window will be determined based on Days Post-op

Post-operative clinical data will be collected on the following case report forms:

1. Physical Exam
2. EQ-5D
3. Oxford Knee Score
4. Objective Knee Assessment
5. Physician Assessment of all Follow-up Radiographs
6. Adverse Event Report (as applicable)
7. Protocol Deviations (as applicable)
8. Study Completion (as applicable)

Subjects will be followed post-operatively for 1 year. Unless the study is otherwise closed, data will continue to be collected until the subject completes the study per the protocol, voluntarily withdraws from the study, is withdrawn from the study by the investigator, is lost to follow-up, undergoes revision to remove a study device, or expires. See Management of Incurrent Events (Section IX, Subsection D of this protocol) for additional details. Reason(s) for study completion must be documented on the **Study Completion** case report form.

k. Minimization of Subjects Lost to Follow-up

Subject follow-up is extremely important for the conduct of a clinical study, and the expectation is to maintain the highest possible rate of follow-up compliance throughout this study. During the informed consent process and at each follow-up interval, subjects should be counseled on the importance of completing future study follow-up intervals.

l. Radiographic Definitions and Methods

1. Required radiographic views

   Radiographs will be performed at the following intervals:

Clinical Interval	Required Radiograph	Approximate Visit Window
Pre-op	AP and ML long-leg *Optional: Skyline view*	N/A
6 Week	AP and ML short film or long-leg *Optional: Skyline view*	7-63 days post-op
3 Month	AP and ML long-leg *Optional: Skyline view*	-/+1 month
1 year	AP and ML short film or long-leg *Optional: Skyline view*	-/+2 months

Investigators may obtain additional radiographs within their normal standard of care but the Sponsor will not require notification, unless an Adverse Event is identified.

Preoperative Radiographs:
All preoperative radiographic evaluations performed according to the protocol will be reviewed by the Investigator at the time of the evaluation and documented using the **Physician Assessment of Pre-Op Radiographs** form. Preoperative radiographs will be evaluated using Kellgren-Lawrence Osteoarthritis grading for both medial and lateral knee compartments.

Anteroposterior (AP) and mediolateral (ML) long-leg radiographs are required for pre-operative planning of the operative knee. Skyline view radiographs are optional. Sites collecting skyline view as part of their standard of care will be asked to submit these radiographs to the Sponsor.

Postoperative Radiographs:
All postoperative radiographic evaluations performed according to the protocol will be reviewed by the Investigator at the time of the evaluation and documented using the **Physician Assessment of Post-Op Radiographs** form. An **Adverse Event Report** form must be completed for those findings identified as an adverse event.

AP and ML long-leg radiographs are required for the 3 month post-operative radiograph of the operative knee. Skyline view radiographs are optional. Sites collecting skyline view as part of their standard of care will be asked to submit these radiographs to the Sponsor.

** The 3 month post-operative film will be used as the baseline radiograph.*

Radiographs should have similar exposure and must show all TKA components and surrounding bone. For consistency, every effort should be made to capture all radiographic views for a given subject using the same institution throughout the study. However, radiographs captured at a different institution may be used for the study, provided they meet required study specifications and are captured within the required interval window. The investigative site will retain copies (hard copy/CD/digital) of all radiographs referenced for the study.

2. Submission to Sponsor
   At the Sponsor's discretion, study radiographs may be requested from the sites for independent radiographic review and assessment of appropriate parameters.

m. Recommended Revision Procedure

See Management of Incurrent Events (Section IX, Subsection D of this protocol)

X. Reporting

The Sponsor will collect all data in a central database. The management of all study data received by the Sponsor will be the responsibility of the Sponsor or its Designee. The use or

disclosure of all protected health information will comply with the Health Insurance Portability and Accountability Act (HIPAA). All information will be treated with strict adherence to professional standards of confidentiality and will be filed by the Sponsor under adequate security and restricted accessibility by clinical personnel. All electronic systems used to create, modify, maintain, or transmit study records will be validated according to 21 CFR Part 11(ii). Reports and communications relating to study subjects will typically identify each subject only by the subject's initials, assigned study subject Case ID number, date of surgery, operative side, and date of birth. This code must be clearly linked to the patient identity and can only be decoded by the study center.

A. Prior to Initiation of the Study

1. Clinical Trial Agreement (CTA)
   A fully executed (signed by all required parties) CTA must be on file with the Sponsor prior to any investigator participating in this study.

2. Institutional Review Board/Ethics Committee Protocol Approval
   This study protocol must be submitted to and approved by the Investigator's Institutional Review Board (IRB) or Ethics Committee (EC). A copy of the IRB or EC approval letter must be submitted to the Sponsor. The letter should identify the following:
   - Protocol name and/or number
   - Date of IRB or EC meeting (if available)
   - Date of approval
   - Date of expiration
   - Signature of IRB or EC

3. Informed Consent
   A Sponsor-approved **Informed Consent template** (Appendix A Sample) will be provided along with the study protocol for IRB or EC submission and approval. If the IRB or EC requires revisions to the provided Informed Consent, the requested revisions must be submitted by the Investigator to the Sponsor for review and approval. Once the Sponsor has reviewed and approved the revision, the Informed Consent will be re-submitted to the IRB or EC for final review and approval. A copy of the final IRB or EC approved Informed Consent form (ICF) must be submitted to the Sponsor.

4. ClinicalTrials.gov Registration
   The Sponsor will be responsible for registering this study on www.ClinicalTrials.gov.

B. Clinical Data Collection/Submission

1. Summary of Source Document Data Collection
   Study data will be collected on source documents, which may include study-specific documents provided by the Sponsor.

   The following source document completion guidelines should be followed:
   - Complete carefully and accurately.
   - Complete header information consistently across all source documents for each individual study subject (when study-specific forms are used).
   - Be sure that data on the source documents match that which is entered through the electronic data capture (EDC) system

- Use the study subject's unique Case ID number assigned as instructed. Do not provide information that is not requested on the source document.
- Ensure that all fields are completed. For fields completed by the subject, efforts should be made to obtain any missing responses prior to the subject completing their visit.

Pre-operative planning and final post-operative component positioning data will be extracted from The ROSA Knee System at the discretion of the sponsor. This data will be uploaded by the sponsor into the electronic data capture (EDC) system.

2. Data Submission
   Completed source documents will be submitted directly to the Sponsor by electronic data capture and submission via a method approved by the Sponsor. Every effort must be made to ensure data submission to the Sponsor is made within 14 days of the visit completion.

3. Quality Assurance of Data
   The Investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor in the source documents and in all required reports. Data reported on the source documents and clinic records should be consistent, or the discrepancies should be explained. All electronic systems used to create, modify, maintain, or transmit electronic study records will be validated according to 21 CFR Part 11(ii). The Sponsor will maintain quality control systems, in accordance with the Sponsor's policies and procedures.

C. Reporting Requirements

1. Investigator Reporting Responsibilities
   The Investigator should ensure the accuracy, completeness, legibility, and timeliness of data reported to the Sponsor in accordance with this protocol. The Investigator or Designee will provide periodic reports to their IRB or EC as required to maintain IRB or EC approval throughout the study, and will provide any required final reporting to the IRB or EC upon study completion/termination. A copy of all IRB or EC re-approval letters must be submitted to the Sponsor. If the IRB or EC terminates or suspends its approval of the study, the Investigator or Designee will suspend study-related activities and will promptly notify the Sponsor. The Investigator should also promptly provide written reports to the Sponsor and the IRB or EC regarding any changes significantly affecting the conduct of the study, and/or increasing risk to the subjects.

2. Retention of Records
   Study records must be retained by the Investigator or Designee for a minimum of 2 years from the Investigator's study termination date, or per applicable regulatory and/or IRB or EC requirements (whichever time period is greater). Measures shall be taken to prevent accidental or premature destruction.

D. Management of Incurrent Events

1. Failure to Obtain Informed Consent
   Study data will not be collected until the Informed Consent has been signed and dated by the candidate. If a candidate does not wish to participate (does not sign and date the Informed Consent), data for that candidate will not be collected for this study.

2. Reporting and Documentation of Medical Events, Adverse Events, Adverse Device Effects and Device Deficiencies

   Reporting and Documentation of Adverse Events and Adverse Device Effects
   Adverse Events and Adverse Device Effects have to be documented on the Adverse Event Report form over the whole time of the investigation including information on the date of onset, treatment and resolution, as well as assessment of both the seriousness and the relationship to the study device. Further the outcome of complications has to be documented and any changes in outcome are to be updated during the course of the study. In case of early termination of the study, further follow-up of the patient shall proceed according to the hospital's standard procedure.

   Reporting and Documentation of Serious Adverse Events, Serious Adverse Device Effects, and Device Deficiencies
   Serious Adverse Events and **Serious Adverse Device Effects** have to be **reported to the Sponsor as soon as possible**. The incidence has to be documented on the Adverse Event Report form over the whole time of the investigation including information on the date of onset, treatment and resolution, as well as assessment of both the seriousness and the relationship to the study device based on the evaluation of the investigator. The outcome of such complications has to be documented and any changes in outcome have to be updated during the course of the study. In case of early termination of the study, further follow-up of the study subject shall proceed according to the hospital's standard procedure.
   Device Deficiencies that did not lead to an adverse event but **could have led** to a medical occurrence if suitable actions had not been taken, if intervention had not been made or if circumstances had been less fortunate shall be **reported to the Sponsor as soon as possible**, as well.
   The **Investigator** is responsible for reporting all SAEs, SADEs and Device Deficiencies that could have led to a SADE to the **Ethics Committee** if required by **national regulations** or by the Ethics Committee.

   See Section X, Subsection E of this protocol for additional information regarding adverse event classifications. All medical events, regardless of classification, are required to be reported on the **Adverse Event Report** form. The Investigator or Designee will also promptly provide the Sponsor with any additional requested information required for the Sponsor to comply with regulatory requirements.

3. Revision
   In the event that removal of one or more of the study knee components is necessary, the Investigator will determine the best treatment and/or revision method for the subject.

   Prior to revision surgery, the Investigator or qualified Designee must document any significant radiographic findings related to the need for revision on the **Physician Assessment of Post-Op Radiographs** form. An **Adverse Event Report** form must be completed for those findings indicated by an asterisk on the **Physicians Assessment of**

Post-Op Radiograph form.

Once the revision surgery has been completed, the Investigator or qualified Designee must complete an **Adverse Event Report** form as well as a ***Study Completion** form terminating the subject from the study. For the study completion status, select "Study Prosthesis Removed".

**Study completion is only required for subjects with femoral or tibial component revisions. Subjects with articular surface revisions will remain in the study.*

4. Investigator Withdrawal
   The Investigator can choose to withdraw a subject from the study if the subject no longer meets study inclusion/exclusion criteria. The reason for the Investigator's withdrawal of the subject must be documented on the **Study Completion** form.

5. Subject Withdrawal
   Study subjects may choose to withdraw from the study at any time, for any reason. If possible, a final evaluation will be completed for any subject who no longer wishes to participate in the study. The reason for the subject withdrawal must be documented on the **Study Completion** form.

6. Lost to Follow-up
   Subject follow-up is extremely important for the conduct of a clinical study, and the expectation is to maintain the highest possible rate of follow-up compliance throughout this study. During the informed consent process and at each follow-up interval, subjects should be counseled on the importance of completing future study follow-up intervals.
   In an effort to minimize lost-to-follow-up subjects, the following recommendations and/or study requirements are essential to ensure proper patient selection and compliance:
   1. Patient Eligibility: Subjects will be selected according to the study inclusion/exclusion criteria and are expected to return for all follow-up visits.
   2. Patients Counseled: Patients will be counseled during the informed consent process on the importance of returning for follow-up visits.
   3. Patient Exclusion: Patients who are not willing to return for study required follow-up visits and/or are not willing to comply with the follow-up schedule will not be considered for enrollment into the study.
   4. Contact Tracking: Attempts to contact subjects will be documented in the study subject's medical record.

   A study subject will be considered lost to follow-up after they have missed a visit and attempts to locate and evaluate the subject using the procedure outlined below have failed. All attempts to contact the subject are to be documented in the subject's medical record and on the **Study Completion** form. Missed visit(s) also must be documented using the **Protocol Deviations** form, unless the visit is retrospective. The first three contact attempts should be made by telephone, with additional attempts as outlined in the following table:

If	Then
a response is not received after three (3) phone calls,	the Investigator or Designee should send a letter to the subject explaining the follow-up agreement per the Informed Consent, and requesting a response from the subject.
all attempts to contact the subject are unsuccessful or the subject is contacted and chooses to withdraw from the study,	a **Study Completion** form will be completed and will specify the reason the subject is no longer participating in this study.

7. Protocol Deviations
   Investigators should not deviate from the study protocol, unless patient safety is at risk. If a protocol deviation does occur, the deviation must be documented on the **Protocol Deviation** form and submitted to the Sponsor. If applicable per their reporting requirements, the Investigator or Designee will also report applicable protocol deviations to their IRB or EC.

8. Study Termination
   Study subject participation is expected to end upon completion of the subject's last follow-up visit unless the subject voluntarily withdraws from the study, is withdrawn from the study by the Investigator, is lost to follow-up, undergoes revision to remove a study device, or expires. Reason(s) for study completion must be documented on the **Study Completion** form.

   If the Sponsor decides to terminate the study early, the Sponsor will inform the Investigators of the reason for early study termination. It is the responsibility of the Investigators to inform their IRB or EC as applicable according to local and national laws/regulations.
9. Modification of the Protocol/Clinical Investigation Plan
   All amendments to this clinical protocol shall be agreed to by the Sponsor and be recorded with a justification for the amendment prior to implementation. Approval of the applicable IRB or EC must be obtained prior to implementation, if required according to the local and/or national laws/regulations.

E. Medical Events/Adverse Events Definitions and Classifications

An adverse event is any unfavorable or unintended sign, symptom, or disease that impacts the operative knee, such as musculoskeletal. Adverse event is synonymous with complication or medical event.

1. Classification of the Event
   Adverse Event (AE)[(i)]*:*
   An Adverse Event is defined as 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.

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 investigational medical devices.

Serious Adverse Event (SAE)[(i)]:
A Serious Adverse Event is any adverse event that

a. led to death
b. led to serious deterioration in the health of the subject, that either resulted in:
    1. a life-threatening illness or injury, or
    2. a permanent impairment of a body structure or a body function, 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. led to fetal distress, fetal death or a congenital abnormality or birth defect.

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

Adverse Device Effect (ADE)[(i)]:
An Adverse Device Effect is an adverse event related to the use of a 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 medical device.
Note 2: This definition includes any event resulting from use error or from intentional misuse of the medical device.

Serious Adverse Device Effect (SADE)[(i)]*:*
A Serious Adverse Device Effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Device Deficiency [(i)]*:*
A Device Deficiency is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

NOTE: Device Deficiencies include malfunctions, use errors, and inadequate labelling. Device Deficiencies that did not lead to an adverse event but could have led to a medical occurrence if suitable actions had not been taken, if intervention had not been made, or if circumstances had been less fortunate, shall be reported to the Sponsor as soon as possible, as well.

The Sponsor is responsible for determining the final classification of adverse events.

If an Unanticipated Serious Adverse Device Effect (USADE) is identified it will be promptly reported to concerned Investigators and regulatory authorities as required by applicable regulatory requirements. If applicable per their reporting requirements, the Investigator or Designee will report the USADE to their IRB or EC.

2. Intensity of Symptoms

Mild:

The subject is aware of the sign or symptom, but finds it easily tolerated. The event is of little concern to the subject and/or little clinical significance. The event is not expected to have any effect on the subject's overall health or well-being.

Moderate:

The subject has discomfort enough to cause interference with or change in usual activities. The event is of some concern to the subject's health or well-being and may require medical intervention and/or close follow-up.

Severe:

The event interferes considerable with the subject's usual activities. The event is of definite concern to the subject and/or poses substantial risk to the subject's health or well-being. The event is likely to require medical intervention and/or close follow-up and may be incapacitating or life threatening. Hospitalization and treatment may be required.

NOTE: The term "severe" refers to the intensity of the event and can be used with any event, without regard to whether or not it meets the criteria for being classified as "serious" or "unanticipated". For example, a subject can have a severe headache, but it is not a serious event.

3. Outcome Definitions

The outcome is in relationship to the Adverse Event, not the treatment rendered for the event (if any).

Resolved:

The adverse event has been resolved and/or no further treatment is required to treat the reported condition or illness.

Tolerated:

The adverse event will most likely never be resolved. The subject "tolerates" the illness or condition as a matter of life.

Study Withdrawal:

Due to the adverse event, the subject was withdrawn from the study.

Device Revision/Removal:

The adverse event resulted in the removal of a study device.

Death:

The outcome indicates the subject died as a direct result of the reported adverse event.

Reoperation of Affected Joint:
The adverse event resulted in reoperation of the study joint, but the reoperation did not include removal of a study device.

4. Collection Approach
   The type of approach taken to collect adverse event information, whether systematic or non-systematic.

   Systematic:
   Based on checklists, questionnaires, or tests

   Non-Systematic:
   Based on spontaneous reporting and recording

F. Monitoring of the Study

Prior to initiating the clinical study, the Sponsor will conduct a site initiation visit to ensure the Investigator(s) and study staff understands the study protocol and requirements and have adequate time and resources to implement and conduct the study. Prior to study initiation, the Investigator must have a fully executed CTA and IRB or EC approval of the study protocol and the study Informed Consent.

During the course of the study, the Sponsor may conduct periodic central monitoring and maintain contact with the study staff to monitor compliance and evidence of adverse events, in accordance with the Sponsor's policies and procedures. The Sponsor will address any identified non-compliance with the executed CTA, study protocol, and applicable regulatory requirements.

If onsite monitoring visit(s) are deemed appropriate by the Sponsor, the Investigator will permit representatives of the Sponsor's monitoring team to have direct access to all source data/documents, study documents/binders, corresponding sections of study subject medical/hospital records, and any other documents relevant to the study, via printed or electronic. All Sponsor visits (including site initiation) will be documented using the **Site Monitoring Visit Log** (Appendix C).

XI. Risk Analysis

This post-market clinical study is classified as minimal risk(ii) and there are no anticipated risks specific to study participation other than the potential loss of confidentiality. There are no experimental procedures in this study, and participation in this study is not anticipated to affect the medical treatment of enrolled subjects. When used in accordance with product labeling, the risks associated with robotic TKA surgery, using Persona, NexGen, and Vanguard knee systems, are similar to those of the conventional method used for the same clinical indication or purpose. The risks associated with the Robotic Assisted Total Knee Arthroplasty procedure/study device are identified below. Unanticipated adverse events can also occur.

A. General Surgical Risks

General surgical risks and post-operative adverse events can occur with any surgery and will be discussed with the study subject by the surgeon or surgeon designee, prior to informed consent, as part of standard of care.

B. Risks Associated with Total Knee Arthroplasty Procedure/Study Device

Potential adverse events associated with total knee arthroplasty include, but are not limited to:

- Wear of the polyethylene articulating surface
- Progressive bone resorption (osteolysis) as a result of foreign-body reaction to wear debris
- Loosening of the prosthetic knee components
- Fracture/damage of the prosthetic knee components
- Soft tissue impingement or damage
- Dislocation and/or joint instability
- Malalignment of the prosthetic knee components
- Bone fracture
- Nerve damage
- Swelling
- Infection
- Leg length discrepancies
- Poor range of motion
- Delayed wound healing
- Temporary or permanent neuropathies
- Pain related to knee arthroplasty and placement of NavitrackERs
- Cardiovascular disorders including venous thrombosis, pulmonary embolism, or myocardial infarction
- Histological reactions resulting in inflammation
- Metal sensitivity
- Corrosion of metal components (the significance and long-term implications are uncertain and await further clinical evidence and evaluation)

Minimization of Risk

Although the total knee implants being used in this study are not the study device, complications can still occur. Complications and/or failure of prosthetic implants are more likely to occur in patients with unrealistic functional expectations, heavy patients, physically active patients, and/or with patients who fail to follow through with the required rehabilitation program. Physical activity or trauma can result in loosening, wear, and/or fracture of the implant. The patient must be counseled about the capabilities of the implant and the impact it will have on his or her lifestyle. The patient must be instructed about all postoperative restrictions, particularly those related to occupational and sports activities and about the possibility that the implant or its components may wear out, fail or need to be replaced. The implant may not last the rest of the patient's life, or any particular length of time. Because prosthetic implants are not as strong, reliable, or durable as natural, healthy tissues/bones, all such devices may need to be replaced at some point.

XII. Statistical Considerations

Performance of the commercially available ROSA Knee System will be evaluated for pain, function, quality of life, and operative efficiency. Data collected in this study will be summarized descriptively and descriptive summaries will be the basis of any study reports issued. These summaries may be used for interim study reports and may also be used to support regulatory submissions, presentations, and/or publications. Additional surgical technique and instrumentation data may be collected and evaluated.

A. General Statistical Methods

Statistical methodology will consist of summarizing collected data descriptively. Categorical data (e.g., gender or race) will be summarized using counts and percentages, and 95% Confidence Interval (CI), over the time periods of interest. Continuous data, such as age, will be summarized by using means, medians, standard deviation, minimum, maximum, and 95% CI over the time periods of interest. Implant survival and return to function will be summarized using a Kaplan-Meier method and presented with rates (as percentages) and confidence intervals. Routine summaries of complication data is represented by frequencies and percentages. Subgroup analysis per indication will also be performed.

B. Sample Size

This study does not have a set of hypotheses to prove and will openly enroll patients to monitor and analyze safety and efficacy. Sample size is capped by a maximum enrollment ceiling per site.

XIII. References

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Guideline Reference

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ii. Barnett Educational Services. 2011 Code of Federal Regulations Reference Guide for Medical Devices. Revised April 1, 2011.

iii. WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI, World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. 59th WMA General Assembly, Seoul, October 2008.