Randomized controlled study comparing Vanguard with KneeAlign2 navigational system versus Vanguard conventional

PROTOCOL NUMBER:	**ORTHO.CR.GK53**
PROTOCOL VERSION:	**V 1.1 (20.JAN.2016)**
BRIEF TITLE:	**Vanguard TKA With KneeAlign 2 and Without KneeAlign 2**
SPONSOR:	**ZIMMER BIOMET Japan**
PRINCIPLE INVESTIGATOR:	**Dr. Minoda**
NCT NUMBER:	**NCT02695329**

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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

AE	Adverse Event
AKS	American Knee Society Score
CA	Competent Authority
CRF	Case report form
EQ5D	EuroQol questionnaire for quality of life assessment
EC	Ethical committee
FU	Follow up
FAS	Full Analysis Set
FTA	Femorotibial angle
IC	Informed Consent
ITT	Intention to treat
IQR	Interquartile range
OA	Osteoarthritis
OKS	Oxford Knee Score
PROMs	Patient Reported Outcome Measures
SD	Standard Deviation
(S)AE	(Serious) Adverse Event
(S)ADE	(Serious) Adverse Device Event
Sponsor	The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.
TKA	Total Knee Arthroplasty
USADE	Unanticipated Serious Adverse Device Event

SUMMARY

TITLE	Randomized controlled study comparing Vanguard with KneeAlign navigational system versus Vanguard conventional
DESIGN	Prospective, two arm, randomized, controlled, multi center
PURPOSE	Determine the effectiveness of the KneeAlign2 system in terms of precise implant alignment by demonstrating that KneeAlign2 provides better tibial alignment compared to conventional instruments
OUTCOME MEASURES	Patient demographics, Operative Data, Patient Reported Outcome Measures (PROMs), Radiographic Assessment, Adverse Events, and Survivorship
POPULATION	100 knees (2 groups of 50 patients) in Japanese patient population at maximum 5 sites
ELIGIBILITY	Patients will be included according to locally approved labeling of device in accordance with indications and contraindications for use.
DURATION	Follow-up will take place at 3 months and 6 months postoperatively. Assuming the enrolment will be completed in one year total study duration will be 24 months including central radiographic assessment.

1. INTRODUCTION

1.1 BACKGROUND

Total Knee Arthroplasty (TKA) is well established surgical intervention to patients, who suffer from pain and dysfunction due to joint deformation by degenerative disease, such as Osteoarthritis and Rheumatoid Arthritis. Although TKA has been showing excellent clinical results, some early complications have been reported, one of causes is implant mal-positioning. To overcome such alignment issues, implant manufacturers have invested their resources to improve reproducibility of precise osteotomy and other companies invented Computer Technology based system, like Navigation system. Navigation System improved accuracy of implant alignment; however the initial and running costs are high. Also hospital needs to prepare sufficient storage space due to size of the equipment.

The company called, OrthAlign, has developed portable Navigation system “KneeAlign2” to overcome the cost issue as well as storage issue while maintaining the advantage of Navigation system. Accelerometer based KneeAlign2 does not require many steps of pre-operative and intra-operative registration process.

1.2 DEVICE DESIGN AND DESCRIPTION

The Vanguard Complete Knee system is available in cruciate retaining (CR), posterior stabilized (PS) and rotating-platform (RP) variant. All femoral components are made of cast cobalt chromium alloy. Different bearing options are available: a CR, CR-lipped and anterior stabilized one (AS), PS made as well as high-flex RP from ArCom or stabilized by vitamin E. The tibial component for CR and PS type is made from titanium or cobalt chrom alloy and tibial component for RP is made from cobalt chrom alloy. The femoral and the tibial parts are available cemented as well as cementless. In the case of patella being resurfaced, all polyethylene cemented patella component can be used.

1.3 RATIONALE AND PURPOSE FOR CURRENT STUDY

The purpose of current study is to compare accuracy of implant alignment between patients operated with KneeAlign2 (investigational group) and patients operated without KneeAlign2 (Control group) using same implant system (Vanguard system, Zimmer Biomet).

2. STUDY DESIGN

The study is a prospective, non-blinded, randomized multi-center study, comparing the clinical outcomes Vanguard with the use of KneeAlign2 accelerometer based navigational device versus Vanguard with conventional instrumentation in hand of experienced Vanguard surgeons. A total of 100 subjects will be recruited prospectively and randomized according to a 1:1 scheme.

2.1 STUDY GROUPS/TREATMENTS

There will be two study groups with each 50 patients. Patients will be assigned to the investigational or the control group using 1:1 randomization. In the investigational group, patients will be treated with Vanguard and the acceloremeter based navigational device Knee Align2. Patients in the control group will have Vanguard total knee replacement with conventional instrumentation.

Group 1 "Investigational": Patients receiving a Vanguard Total Knee using KneeAlign2.

Group 2 "Conventional Signature": Patients receiving a Vanguard Total Knee using Conventional Instruments

2.2 NUMBER OF SITES AND SUBJECTS/PROCEDURES

100 cases will be enrolled and randomly assigned to either the investigational or the control group. This study will be conducted at 5 Japanese hospitals.

2.3 PRIMARY AND SECONDARY ENDPOINTS

Primary Endpoint

The primary study endpoint is the accuracy of tibial alignment at 6 months for the study group compared to the control group, measured as the proportion of subjects that have alignment within 2 degrees from neutral.

Secondary Endpoints

- Surgery time,
- Tibial posterior slope alignment (comparing to planned angle)
- Femoral varus/valgus angle (comparing to planned angle)
- Less chance to perform re-osteotomy for angle correction with KneeAlign2,

2.4 ASSESSMENT PROCEDURE

The study assessment period will be 18 months, 1 year recruitment and 6 months follow-up. The follow-up for all patients will be at the following time points: baseline (preoperative), surgery, 3 months and 6 months.

A. Preoperative:
    a. Informed Consent
    b. Randomization
    c. Enrollment Form
    d. Historical Record
    e. AKS
    f. PROMs: OKS, EQ5D

B. Operative
    a. Operative Form
        i. Surgery time 1 (from skin incision to trial component usage)
        ii. Surgery time 2 (Total duration of surgery, from skin incision to closure)
        iii. Patella resurfacing (Yes / No)
        iv. Targeted femoral varus/valgus angle
        v. Targeted tibial posterior slope
        vi. Implanted component information
        vii. Surgical approach

C. 3 month
    a. Long leg & Tibial long lateral x-rays

D. 6 month
    a. Long leg & Tibial long lateral x-rays
    b. Complications (if applicable)
    c. AKS
    d. PROMs: OKS, EQ5D

2.5 ASSESSMENT PARAMETERS AND METHODS

Preoperative Data

After the patient has been consented he/she will be assigned randomly to either the investigational or control group. Demographic information will be collected, a detailed medical history will be obtained and a physical examination will be performed (including height and weight). Current medications and smoking history, if applicable, will also be recorded. A baseline AKS and patient questionnaires will be collected.

Clinical Assessments

AKS will be used to assess the difference between investigational and control group. This assessment will be completed preoperatively.

Patient Questionnaires

The Oxford Knee Score[5,6] (OKS), and the EQ5D[7] will be taken preoperatively and at 6 months post-operatively

EQ5D: Descriptive system of health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).

The OKS consists of twelve questions covering function and pain associated with the knee.

Radiographic Assessments

At 3 month and 6 month follow-up visits, standardized weight-bearing long leg anteroposterior x-ray and weight bearing Tibial long lateral x-ray will be taken. Tibial varus/valgus angle, Tibial Posterior slope angle as well as Femoral varus/valgus angle will be measured by independent reviewer.

Independent reviewer: Dr. Kentaro Iwakiri (Shiraniwa Hospital, Ikoma City, Nara, Japan)

2.6 ASSESSMENT TIMELINES/SCHEDULE

Each follow-up visit time point will be determined based on the date of surgery. Each follow-up visit has a specific allowed time window:

- Preoperative (within 3 months prior to surgery)
- Admission period

- 3 month and 6 months (+/- 2 weeks)

In the table below the retrieved information is per follow-up visit is found.

Assessment	Preop	Operative	3 Months	6 Months
Enrollment Form	*			
Informed Consent	*			
Randomization	*			
Historical Record	*			
Operative Record		*		
Knee Society Score	*			*
Oxford Knee Score	*			*
EQ5D Patient Questionnaire	*			*
Long leg, standing x-ray			*	*
Tibial long lateral x-ray			*	*
Independent Radiographic Review		*		*
Complications		As needed	As needed	As needed

2.7 ALLOWED WINDOW OF EACH SCHEDULE -SEE 2.6

3. SELECTION AND WITHDRAWAL OF SUBJECTS

3.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, a subject must meet all of the following criteria.

- Knee (either unilateral or bilateral) Osteoarthritis (varus deformity only)

Additional inclusion criteria include:

- Male or female
- > 20 years of age
- Subjects willing to return for follow-up evaluations.

Study Specific Requirements for Investigator/Site

- Investigator/site must have experience of 10+ cases of KneeAlign2 with Vanguard Knee and Vanguard Conventional instrument system before any study specific activities.

- Site has sufficient resources to take long leg x-ray and Tibial long lateral x-ray at both 3 month and 6 month follow-up visit.

3.2 EXCLUSION CRITERIA

A potential subject who meets any of the following criteria will be excluded from participation in this study.

Absolute contraindications include:

- Knee degenerative diseases other than Knee Osteoarthritis (such as necrosis / Rheumatoid Arthritis)
- Too severe OA deformation (FTA: > 185 degrees / < 175 degrees)
- Active Infection (or within 6 weeks after infection)
- Sepsis
- Osteomyelitis
- Any type of implant is inserted in the affected side of lower extremity
- Hip disease on the affected side

Additional contraindications include:

- Uncooperative patient or patient with neurologic disorders who are incapable of following directions
- diagnosed Osteoporosis or Osteomalacia
- Metabolic disorders which may impair bone formation
- Distant foci of infections which may spread to the implant site
- Rapid joint destruction, marked bone loss or bone resorption apparent on roentgenogram
- Vascular insufficiency, muscular atrophy or neuromuscular disease.

3.3 SUBJECT WITHDRAWAL

It is recognized that the subject's participation in this trial is entirely voluntary, and that she/he may refuse to participate and may withdraw from participation at any time without jeopardy to any future medical care. It is also recognized that the investigator, at his/her discretion, may withdraw a subject from this study based upon his/her professional judgment. In event of subject withdrawal, applicable local procedures should be followed.

If a patient is withdrawn or rescinds their consent, a "Lost to Follow-up" case report form should be completed detailing the reason for the patient withdrawal. The site should also notify their Ethical Committee (EC) if applicable. If a patient is withdrawn from the study by the investigator, the patient should be notified of their removal by a letter from the site or according to the local EC.

It is required that patients return within the defined follow-up period to complete all study assessment forms and radiographs. Patients that miss or will not return for follow-up are not considered "protocol deviations" or "lost to follow-up."

Specific criteria for withdrawal (if applicable)

If patients meet any of the following criteria, a subject withdrawal form should be completed, and below data documented on the form:

1. Patient rescinds consent in writing: Date of occurrence
2. Patient Death: Reason and date of death should be documented.
3. Implant Removal: Date of revision, all component part numbers removed, and reason for revision
4. Revision of Metal Components (Femur or Tibia)*: date of revision, all component part numbers removed, and reason for revision

**Bearing revisions in which only the polyethylene is replaced will not be withdrawn from the study.*

Replacement of individual subjects after withdrawal

Subjects will not be replaced, unless they do not have surgery or intraoperatively it has been recognized the patient is not eligible for a treatment with Vanguard.

Follow-up of subjects withdrawn from treatment

Subject withdrawn from the study will obtain standard medical treatment as foreseen at the investigational site.

4. PROTOCOL DEVIATION MANAGEMENT AND REPORTING

Any deviation from the protocol should be documented on the "Protocol Deviation" case report form.

5. ADVERSE EVENT MANAGEMENT AND REPORTING

Any adverse event should be documented on the Adverse Event case report form. A record of all adverse events, including details of the nature, onset, duration, severity, relationship to the device, relationship to the operative procedure and outcome, will be made on the relevant section(s) of the subject's CRF. The subject will be questioned about any adverse event(s) at each subsequent follow-up assessment visit.

Any serious adverse events (SAE/SADE/USADE) must be reported to head of institution and must be notified to other institutions participating in this study in accordance with Ethical Committee and Ethical Guidance for clinical study including human subject.

Adverse Event (AE):

An adverse event is any untoward medical occurrence in a patient receiving an investigational medical device that does not necessarily have to have a causal relationship with the device under investigation. An AE can therefore be any unfavorable and unintended sign (including abnormal laboratory finding), symptom, or condition temporally associated with the use of a medical device whether or not considered related to the medical device.

Serious Adverse Event (SAE):

A serious adverse event is an adverse event that

a) led to death,

b) led to a serious deterioration in the health of the patient that

c) led to fetal distress, fetal death or a congenital abnormality or birth defect.

1) resulted in a life-threatening illness or injury,

2) resulted in a permanent impairment of a body structure or a body function,

3) resulted in medical or surgical intervention to prevent permanent impairment to body structure or body function,

4) required in-patient hospitalization or prolongation of existing hospitalization,

A planned hospitalization for a pre-existing condition, or a procedure required by this protocol, without serious deterioration in health, is not considered a serious adverse event

Adverse Device Effect (ADE):

An ADE is any untoward and unintended response to an investigational medical device.

Serious Adverse Device Effect (SADE):

A SADE is any untoward and unintended response investigational medical device that has resulted in any of the consequences characteristic of a serious adverse event or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less opportune.

Unanticipated serious adverse device effect (USADE)

Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report (see section 10).

6. IMPLANT RETRIEVAL AND ANALYSIS OF REMOVED IMPLANTS

Should any implant failures occur, please contact the Study Manager or any other Zimmer Biomet personnel to coordinate the implant retrieval process.

7. STATISTICAL ANALYSIS PLAN

7.1 SAMPLE SIZE CALCULATION

The primary analysis for the study will compare the proportion of Tibial varus/valgus alignment ranging 2 degrees from neutral on the 6 month postoperative x-ray for KneeAlign2 vs. Control. Sample size calculations for this study are done using data found in a paper by Nam et al[1]. In this study, 95.7% of the tibial components in the accelerometer-based navigation cohort were within 2 degrees of neutral, as compared to 68.1% in the conventional cohort. Our sample size calculation assumes the results in this study will be similar to what is reported in Nam et al.

The primary analysis will test the null hypothesis that the proportion of Tibial alignment within 2 degrees of neutral for the Investigational group (KneeAlign2) is equal to that of the patients operated without KneeAlign2. The alternative hypothesis is that the proportion of Tibial alignment within 2 degrees of neutral for the KneeAlign2 group is not equal to that of the patients operated without KneeAlign2.

Null Hypothesis: Ho: $\pi A - \pi B = 0$

Alternative Hypothesis: HA: $\pi A - \pi B \neq 0$

where πA represents the proportion of Tibial alignment within 2 degrees from neutral in investigational group on the immediate postoperative x-ray and πB represents the proportion of Tibial alignment within 2 degrees from neutral in control group on the 6 month postoperative x-ray.

If we reject the null hypothesis, we can conclude that KneeAlign2 instruments are more accurate than conventional instruments in TKA surgery with regards to tibial alignment.

This sample size calculation was conducted anticipating the use of a Fisher's exact test.

Alpha level: 5% (two sided)

Power: 90%

Investigational group proportion within 2 degrees from neutral: 95.7%

Control group proportion within 2 degrees from neutral: 68.1%

The resulting calculation gives n=41 per group. 50 patients per group will allow for up to 20% attrition.

Overall population per protocol: 100

7.2 DETAILED DESCRIPTION OF RANDOMIZATION

In this study, patients will be randomized in one of the two treatment arms: Vanguard with KneeAlign2 (Investigational group) or Vanguard with conventional instrumentation (Control group). The randomization scheme is based on equal numbers per group. The randomization will occur via a random number generator (computer) using blocked randomization procedure. The doctor or other health care professional does not have influence on the randomization scheme. Sealed opaque envelopes, which will be prepared based on predetermined randomization assignment, will be provided to each study site before study initiation.

7.3 HANDLING OF MISSING AND INCOMPLETE DATA

Data will be considered "missing" for the primary endpoint if this outcome cannot be determined or is unavailable for a subject. Every effort will be made to collect the data necessary to evaluate the primary endpoint. In the event that the tibial alignment cannot be determined at 6 month postoperative visit, then

the x-ray taken at 3 month visit will be used. Subjects who have been lost to follow-up and do not have tibial alignment at 3 or 6 months will not be included in the primary study analysis.

Sensitivity analyses will be performed to assess the impact of missing data on the primary study analysis. These analyses may include a best-case and worst-case imputation as well as a tipping point analysis.

7.4 DATA ANALYSES

Data will be analysed using SAS 9.0 or higher. The Type I error rate for the primary study analysis will be 0.05. Comparisons for secondary, exploratory, and safety analyses will be two-sided comparisons using $\alpha = 0.05$, with no adjustment for multiple comparisons.

Primary Analysis: The primary analysis will be presented as both intention-to-treat (ITT) and Full Analysis set (FAS). In the ITT analysis for the primary endpoint, missing data will be treated as described in Section 7.3. A two-tailed Fisher's Exact Chi-Square test at $\alpha = 0.05$ will be used to assess the study hypotheses and determine whether there is a statistically significant difference between investigational and control groups with regard to the proportion of patients with tibial alignment within 2 degrees of neutral.

Secondary Analysis: Analyses for secondary endpoints will be FAS, and will only use those cases with complete data for the endpoint being analysed.

Continuous data (e.g. age, BMI, VAS pain) will be reported using mean, standard deviation, median, and range. Comparisons of Investigational vs Control with regard to continuous baseline and secondary outcomes will be performed using standard statistical tests and will be chosen as appropriate for the scale and distribution of the measures being analyzed. For example, a t-test, Wilcoxon test, or one-way ANOVA (as appropriate) may be performed to assess differences.

Categorical data (e.g. gender, ASA) will be reported using frequency and percentage. Comparisons of Investigational vs Control with regard to categorical baseline, secondary and safety outcomes will be performed using standard statistical tests and will be chosen as appropriate for the scale and distribution of the measures being analyzed. For example, categorical outcomes may be compared for investigational and control groups using the Fisher's Exact test (for 2x2 tables) or the Likelihood Ratio chi-square test (for tables larger than 2x2).

Knee prosthesis survivorship will be assessed using a Kaplan-Meier analysis. Comparison of survivorship for Investigational vs Control will be done using the Log-Rank test.

7.5 STUDY REPORT

The primary analysis will be performed after all patients reach the 6 months follow up time point. Data will be analysed using the methods described in Section 7.4.

8. DATA COLLECTION, HANDLING AND RETENTION

8.1 SOURCE DOCUMENTATION REQUIREMENTS

No source data will be available to the Sponsor of the study according to local law.

8.2 CASE REPORT FORMS

Data for this clinical trial will be collected and documented on the subject Case Report Forms (CRFs) provided in an electronic form. Authorized study site personnel will complete the digital CRFs only. CRFs must be reviewed by the investigator or his/her designees.

8.3 STUDY DOCUMENT RETENTION

Study documents should be retained for 5 years after the study is complete.

9. DATA REPORTING

Within 6 months of the study close the sponsor will present a final study report to summarize all data collected throughout the study duration, complications throughout the course of the data collection, and general findings.

The report will contain the results of all primary and secondary endpoints. Also, patient follow-up will be analyzed throughout the data collection according to the following definition and equations:

Lost To Follow-Up:
1. Death
2. Implant Removal: Date of revision, all component part numbers removed, reason for revision, and any relation to study device.
3. Revision of Metal* Components (Femur or Tibia): date of revision, all component part numbers removed, and reason for revision Consent Rescinded

**Bearing revisions in which only the polyethylene is replaced will not be withdrawn from the study.*

$$\text{Percentage Follow-up} = \frac{\text{\# Patients with Follow-Up}}{\text{(Theoretically due – Lost To Follow-Up)}} \times 100$$

$$\text{Percentage Accounted for} = \frac{\text{(\# with Follow-Up + Lost To Follow-Up)}}{\text{Theoretically due}} \times 100$$

Both the sponsor and investigators will make reasonable efforts to publish the results of this trial.

10. RISK ANALYSIS

The site and investigator is responsible for following all directions and labeling associated with the product device and its use in total knee arthroplasty. It is expected that all use of the product will be according to the label with full knowledge of all Warnings, Precautions, and Possible Adverse Events associated with the device.
In accordance with the risk management file of the sponsor the following risk may occur:

- Higher wear rates may be caused by cement or metal particles or other debris that can cause abrasion of articulating surfaces. A high level of wear can shorten the service life of the prosthesis and lead to early revision for the replacement of worn prosthetic components.
- In all cases of joint replacement, asymptomatic localized progressive bone resorption (osteolysis) may be noted around prosthetic components as a result of foreign body reactions triggered by particles. These particles are generated by the interaction between the various components, as well as between the components and bone, mainly through mechanisms of wear, adhesion and fatigue. Other particles may also be produced by the wearing of another body. Osteolysis may lead to successive complications requiring the removal and replacement of prosthetic components.

- Calcification or periarticular ossification, peroneal nerve palsy and hematoma can result from improper handling of implants and associated instrumentation. The risk of embolism, pain and postoperative infections associated with any surgical procedure also applies to the implementation of this prosthesis.
- Although rare, cases of metal intolerance following joint replacement have been observed. Implantation of foreign material in tissues may result in histological reactions involving the formation of macrophages and fibroblasts.
- Dislocation or subluxation of prosthetic components due to improper positioning and/or migration of components can occur. Muscle and fibrous tissue laxity can also contribute to these conditions.
- Prosthetic components can come loose or migrate following trauma.

11. MONITORING PLAN

Zimmer Biomet, as the sponsor of this study, will monitor the data collection to ensure that the investigation is being conducted consistent with the protocol. The following describes the monitoring activities, which may take place during the course of the study.

11.1 FREQUENCY

Pre-Investigational Visit/Conference:

Prior to initiation of the study, the study manager will provide the investigator with all the necessary information to enable him to carry out his responsibilities. This prepares the site with an in-depth training on the protocol, case report forms, and data collection process for the length of the study. The study manager will also train the site on using the Zimmer Biomet Joint Assist database.

Monitoring of the Data

Monitoring of the data will occur at least annually, and as often as monthly.

11.2 SAMPLING PLAN

All data will be monitored for completeness and accuracy on at least an annual basis.

11.3 MONITORING TASKS

Zimmer Biomet will continually monitor the progress of the clinical trial. These activities include:

- Tracking of patient enrollment

- Review of all electronic patient data forms received by Zimmer Biomet for completeness
- Tracking of patients to ensure follow-ups are being completed at appropriate intervals
- Review of all adverse events
- Maintaining open communication with all investigational sites in order to ensure the quality of the clinical trial.
- In-house audits as needed

Upon completion of any type of monitoring, the site is responsible for resolving all discrepancies found in a timely manner. These will be sent to the site with an audit report by the study manager. All discrepancies found within the Joint Assist database will be queried and sent directly to the site. Delays in resolving queries are to be avoided at all costs; this provides the study with the most accurate data, prevents delay in reporting procedures & publication.

11.4 STUDY CLOSE-OUT

When a site has completed their data collection, a visit may be necessary by a Zimmer Biomet monitor to ensure all data has been obtained. Data will be reviewed for completeness, and monitored to ensure that all discrepancies have been resolved.

12. LABELING

The devices and products will be used in accordance with their instructions for use and/or approved labeling. The package insert for the device(s) in this study is included in the Investigator Binder.

13. ETHICAL AND REGULATORY REQUIREMENTS

13.1 CODE OF CONDUCT

The investigator will ensure that the clinical study is conducted in accordance with

1. Protocol
2. Ethical Guidance for clinical study including human subject (MHLW, Dec. 22, 2014)

13.2 INSTITUTIONAL REVIEW BOARDS/ETHICS COMMITTEE

The investigator must obtain appropriate Ethics Committee approval before the study can be initiated.

13.3 INFORMED CONSENT

Subjects (or the subject's legally authorized representative) will be provided with an informed consent and patient information sheet in order to give ample opportunity to review the consent and ask questions. The signed informed consent will be obtained before any study procedures begin. If the subject agrees to participate in the study, the subject/representative must sign the informed consent form. The witness and the investigator must also sign the informed consent form. A copy of the informed consent form should be given to the subject/representative. All subjects who meet all of the entry criteria will be considered for inclusion in this trial. Any subject meeting any of the exclusion criteria will be excluded from the trial.

The informed consent form must be approved by the institution's EC.
Subjects will be informed of new information learned during the study, which may affect the subject's decision to continue participation in the study.

An Informed Consent Log should be completed to document the existence of the signed informed consent form. The log will contain: Subject ID, date informed consent form signed, and the version signed.

13.4 SUBJECT CONFIDENTIALITY

The case report forms do not include any patient identifying information. Therefore, once the data is entered in the online database a patient can no longer be identified.

By assigning patients a unique ID number, their identity is protected in Joint Assist, the online database. The database is restricted, allowing a doctor to only view and enter data from his own patients. User authentication is required to view research data. The data is transmitted to a centralized database through a secured (SSL) channel on the Internet. Data in transit is in 128-bit encryption. The access to the centralized database is limited to those who are responsible for maintaining the database.

14. PUBLICATION PLAN

Upon completion of all x-ray measurements and statistical analyses, manuscript will be written in English to meet peer-reviewed journal requirements. Manuscript then will be submitted to one of below or other suitable journal.

- KSSTA (Knee Surgery, Sports Traumatology, Arthroscopy)

- CORR (Clinical Orthopaedics and Related Research)
- JOA (Journal of Arthroplasty)
- Acta Orthopaedica
- The Knee

15. REFERENCES

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16.APPENDICES

Appendix 1 Instruction for Use