Clinicaltrials.gov NCT #: NCT03870477

Intracapsular and Intertrochanteric Fracture Fixation with the THP™ Hip Fracture Plating System

Clinical Outcome Study

Protocol Number: *CSU2017-22T*

Protocol Version: *Version 2.0*
Region: *United States*

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I. Study Synopsis

Study Title	Intracapsular and Intertrochanteric Fracture Fixation with the THP Hip Fracture Plating System Clinical Outcome Study
Abbreviated Study Title	THP Clinical Outcome Study
Sponsor	Zimmer Biomet, Warsaw, Indiana
Protocol Number	CSU2017-22T
Anticipated Start Date	Q3 2018
Study Objectives	The objective of this observational prospective study is to systematically document the clinical outcome of THP Hip Fracture Plating System when used to treat intracapsular and intertrochanteric fractures. Primary Endpoint: • Revision rate due to device related complication(s) or non-union of the femur. Secondary Endpoints: • Radiographic and clinical fracture healing of the proximal femur using standard scoring methods.
Target Population	190 subjects who have undergone one of the following with the THP Hip Fracture Plating System: • Intracapsular fracture repair (101 subjects) • Intertrochanteric fracture repair (89 subjects)
Study Design	Multicenter, prospective, observational study
Study Type	Post-Market Clinical Follow-up Study (PMCF)
Sample Size	190
Length of Study	3 years (2 years of enrollment and 1 year of follow-up)
Follow-up Intervals	1 to 6 weeks, 3 months, 6 months, and 12 months after surgery
Inclusion/Exclusion Criteria	Inclusion Criteria • Patient must be 18 years of age or older. • Patient must be eligible for an open reduction and internal fixation of the proximal femur. • Patient must have an intracapsular or intertrochanteric fracture. • Patient must have need for alignment, stabilization, and reduction of bone fractures. • Patient must have ability and willingness to follow

	postoperative care instructions until healing is complete. • Patient must be in good nutritional state. • Patient must be able and willing to sign the IRB/EC approved informed consent. Exclusion Criteria • Patient is a prisoner. • Patient is a current alcohol or drug abuser. • Patient is known to be pregnant or breastfeeding. • Patient has a psychiatric illness or cognitive deficit that will not allow proper informed consent. • Infection. • Patient conditions including bloody supply limitations, obesity or insufficient quantity or quality of bone. • Patient with mental or neurologic conditions who are unwilling or incapable of following postoperative care instructions. • Patient has foreign body sensitivity. Where material sensitivity is suspected or unknown, testing is to be completed prior to implantation of the device. • Patient is expected to be non-compliant with recommended post-operative weight-bearing instructions.
Study Device	THP™ Hip Fracture Plating System
Outcome Measures	• VAS Pain Scale • EQ-5D-5L • RUSH Score • FIX-IT • Implant Survivorship • Adverse Events • Operative Time • Readmissions • Reoperations
Documentation	Electronic Case Report Forms
Statistical Reporting	Data collected will be summarized and reported to each participating investigator. Statistical analysis will be conducted by Zimmer Biomet or its designee.

This protocol is written based on guidelines from ISO 14155 Standard for Clinical Investigation of

Medical Devices For Human Subjects – Good Clinical Practice [(i)] and is in accordance with US Code of Federal Regulations 21 CFR Parts 11, 50 and 56 [(ii)]

II. Data Collection Overview

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

Form Name	Enrollment	Operative	Discharge Assessment	1 to 6 Weeks Post-op (+14 days)	3 Months Post-op (± 30 days)	6 Months Post-op (± 60 days)	1 Year Post-op (± 90 days)	Revision
Enrollment Form	X							
Demographic Evaluation	X							
Operative Record		X						
Postoperative Discharge Assessment			X					
VAS Pain				•	•	•	•	
EQ-5D-5L				•	•	•	•	
FIX-IT				X	X	X	X	
X-rays	X	X	X	X	X	X	X	X
Postoperative Follow-up Evaluation				X	X	X	X	
Study Completion		*	*	*	*	*	*	X
**Adverse Event (Complication)	*	*	*	*	*	*	*	X
Protocol Deviation	*	*	*	*	*	*	*	*
Physician Radiographic Assessment (Including RUSH)				*♦	*♦	*♦	*♦	*♦
Explant Device			X	X	X	X	X	X

X Completed by Investigator or Designee (required)
• Completed by Patient
* Completed by Investigator or Designee (as applicable)
♦ Independent radiographic review may be performed by Sponsor's designee if requested by the Sponsor.

** If device related Adverse Event occurs, a Product Experience Report (PER) must be completed and sent to the sponsor as well and include the Operative Report (index and revision) and Radiographs (immediate post-op, all follow-up visits, and pre-revision).

III. Introduction and Purpose

Zimmer Biomet has developed a telescoping lag Screw and Hip Fracture Plate for fixation of fractures of the proximal femur, intracapsular and intertrochanteric femoral fractures. The device will compete with traditional devices, including cannulated screws used for

neck fractures and compression hip screws use for intertrochanteric fractures. Hemi-hip arthroplasty is also an alternative for some patients.

Although various techniques have been developed for internal fixation with open or closed reduction of femoral neck fractures, numerous complications such as non-union and femoral head avascular necrosis may require additional interventions.[3] This study will document the clinical and radiographic outcomes of hip fracture patients, utilizing a hip fracture plate construct manufactured by Zimmer Biomet.

IV. Study Objectives

The objective of this observational prospective study is to systematically document the clinical outcome of the THP Hip Fracture Plating System when used infractures of the proximal femur, intracapsular and intertrochanteric fractures, as compared to historical literature data for the same indications when using cannulated or hip screws [1][2]. These objectives will be assessed using standard scoring systems, radiographic evidence, and adverse event records.

Safety: Will be assessed by monitoring the frequency and incidence of adverse events (AE), serious adverse events (SAE), adverse device effects (ADE), serious adverse device effects (SADE), and unanticipated serious adverse device effects (USADE) and device deficiencies.

Performance: Will be determined by analyzing the implant survival, overall pain and functional performances on standard scales, subject quality of life, and radiographic parameters of subjects who received the subject device(s). Operative time and readmissions will also be analyzed. Implant survival will be based on removal or intended removal and determined using the Kaplan-Meier method.

- **Overall pain and functional performance** will be based on Visual Analog Scale (VAS) Pain, Rush Score, EuroQul 5D-5L (ED-5D-5L), and Functional Index for Trauma (FIX-IT).
- **Survivorship** will be based on the rate of revision in the study device due to fixation failure or non-union of the femur.
- **Radiographic parameters** to be analyzed may include, but are not limited to, implant fracture, significant implant migration or subsidence, and implant loosening. Other significant findings may also be observed and reported during the course of this study.

It is planned that once sufficient data has been collected allowing meaningful statistical analysis; contributing investigators can use the data for peer reviewed publications, podium presentations and as a basis for surgeon discussions and learning.

Study Endpoints: The primary endpoint of this study is defined as the rate of revision after 12 months due to device related complication or non-union of the femur. The secondary endpoints of this study are defined as radiographic and clinical fracture healing of the proximal femur using standard scoring methods.

V. Study Design

This is a prospective, multicenter, non-controlled clinical study designed to facilitate the collection and evaluation of pain, function, quality of life, radiographic assessment, and adverse event data. A maximum of 10 sites will contribute to this study to enroll a study maximum of 190 subjects. Enrollment per site will not exceed 57 subjects (30% of the total sample). Each Investigator will be skilled in femur fracture treatment and experienced implanting the devices included in this study, as determined by the Sponsor.

Due to the different historical revision rates for intertrochanteric fractures (~7%)[1] and neck fractures (~20%)[2], study enrollment will be split between the two groups to maintain the integrity of the sample size with an expectant lost to follow-up rate of 15%. Intertrochanteric fractures will be limited to a maximum of 89 enrolled subjects and intracapsular fractures will be limited to a maximum of 101 enrolled subjects. This will provide enough evaluable data for both indications to show the necessary statistical improvement from the historical revision rates[1][2].

Each Principal Investigator will be responsible for obtaining Institutional Review Board (IRB) or Ethics Committee (EC) 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 hip fracture repair using the commercially available (FDA cleared) THP Hip Fracture Plating System. 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/EC approved patient Informed Consent. Study data cannot be collected until the candidate has completed the Informed Consent process and signed and dated the IRB or EC approved Informed Consent.

Once Informed Consent has been obtained, preoperative, operative, and discharge documentation will be collected either via retrospective chart review or direct interview with the subject. Patients who have previously received THP Hip Fracture Plating System may be enrolled in the study if Informed Consent occurs prior to the end of the 6 weeks follow-up visit window. This will include retrospective chart review for patients who meet the inclusion criteria (and do not meet any of the exclusion criteria) and have available surgical data. Patients that meet these requirements will be asked to consent to study

participation postoperatively. The consented patients will be followed prospectively at designated follow-up visits if all appropriate IRB/EC approvals and patient consent is obtained. The post-operative clinical and radiographic evaluations will be conducted at 1 to 6 weeks, 3 months, 6 months, and 12 months post-surgery.

Review of radiographs will be completed by the investigators at each clinical follow-up interval to determine radiographic evidence of fracture healing. In addition, the Investigator will review radiographs at each clinical follow-up interval to ensure radiographic evidence of adverse events is documented and reported to the IRB or EC and the Sponsor as required. At the Sponsor's discretion, the Sponsor may request copies of these radiographs for independent radiologic review. The Sponsor may request one central reviewer for all radiographs independent of the surgeon and institution.

VI. Study Population

The study population for primary statistical analysis will be comprised of males and females who 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. Eligible candidates who express interest in study participation will be offered Informed Consent. Inclusion/Exclusion Criteria should not be evaluated until the study-specific consent form has been completed.

A. Inclusion Criteria

a. Patient must be 18 years of age or older.
b. Patient must be eligible for an open reduction and internal fixation of the proximal femur.
c. Patient must have an intracapsular or intertrochanteric fracture.
d. Patient must have need for alignment, stabilization, and reduction of bone fractures.
e. Patient must have ability and willingness to follow postoperative care instructions until healing is complete.
f. Patient must be in good nutritional state.
g. Patient must be able and willing to sign the IRB/EC approved informed consent.

Note: *Patients who have previously received THP Hip Fracture Plating System may be enrolled in the study if informed consent occurs prior to the end of the 6 weeks follow-up visit window.*

B. Exclusion Criteria

a. Patient is a prisoner.
b. Patient is a current alcohol or drug abuser.
c. Patient is known to be pregnant or breastfeeding.
d. Patient has a psychiatric illness or cognitive deficit that will not allow proper informed consent.
e. Infection.
f. Patient conditions including bloody supply limitations, obesity or insufficient quantity or quality of bone.
g. Patient with mental or neurologic conditions who are unwilling or incapable of following postoperative care instructions.
h. Patient has foreign body sensitivity. Where material sensitivity is suspected or unknown, testing is to be completed prior to implantation of the device.
i. Patient is expected to be non-compliant with recommended post-operative weight-bearing instructions.

VII. Study Device Information

The THP Hip Fracture Plating System are left or right side specific plates designed to provide fracture fixation and stabilization of intracapsular fractures and intertrochanteric fractures by the use of telescoping lag screws. The plates are secured to the lateral aspect of the femoral shaft with either locking or non-locking cortical screws. They are intended for use in intracapsular fractures and intertrochanteric fractures of the proximal femur.

Figure 1 depicts the Hip Fracture Plates and the associated telescoping lag screws.

FIGURE 1: THP Hip Fracture Plate

The fracture plates are contoured plates made of Ti-6Al-4V titanium alloy conforming to ASTM F-136 with aTiMax™ Type II anodized surface finish. There are three (3) proximal threaded screw holes oriented 130 degrees from the plate surface to replicate a 130-degree femoral neck angle. The screw holes are threaded to allow the telescoping lag screws to lock into the plate. There are either two (2) or four (4) holes along the plate body designed for use with cortical bone screws. The screw holes in the plates are threaded, utilizing SphereLock™ Technology, to allow for the use of locking or non-locking cortical screws at the surgeons discretion.

The telescoping lag screws are 7.5mm in diameter with lengths ranging from 70mm to 130mm in 5mm increments. The head of the lag screw barrel is threaded to allow it to lock into the threads of the fracture plate. The telescoping screw portion is free to translate as much as 20mm within the barrel. The telescoping lag screws are made entirely of Ti-6Al-4V titanium alloy conforming to ASTM F-136 with a TiMax Type II anodized surface finish.

Optional limited collapse sleeves are available in 5mm, 10mm, 15mm and 20mm lengths to limit the amount of translation of the screws within the barrel. They are designed to slide into the barrel of the screw and lock into place. The use of a 5mm insert will limit the translation to 15mm whereas the use of a 15mm insert will limit the translation to 5mm. The use of the 20mm insert will make the screw virtually a non-translational (solid body) screw. The limited collapse sleeves are made of Ti-6Al-4V titanium alloy conforming to ASTM F-136 with a Type III color anodized surface finish. Figure 2 represents a 10mm limited collapse sleeve.

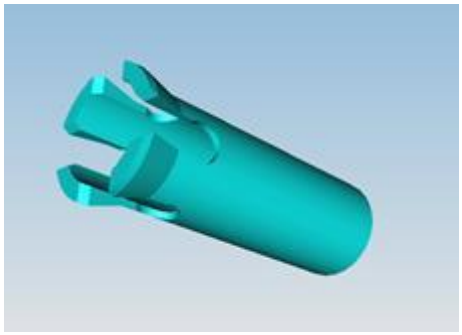


FIGURE 2: Limited Collapse (Sleeve 10mm)

The THP Hip Fracture Plating System plates are secured to the lateral aspect of the proximal femur by the use of 5.0mm diameter cortical screws. The cortical screws come in either a locking design or a non-locking design. The screw heads utilize a hexalobular drive design and the locking design screws have external threads incorporated into the screw head so that the screw can be locked into the threaded holes on the plate body. The head of the non-locking screws do not include the external threads. The cortical screws are made of Ti-6Al-4V ELI and

conforming to ASTM F136 with Type II color anodized surface finish. The cortical screws are available in lengths of 14mm to 60mm in 2mm increments, and from 60mm to 95mm in 5mm increments.

VIII. Study Procedures

A. Offer Study Participation

Study participation will be offered to each consecutive eligible patient presenting as a potential candidate 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 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 for prospective subjects. Subjects enrolled retrospectively may sign and date the Informed Consent after 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 / Enrollment Log

An **Informed Consent / Enrollment 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, signed and dated the IRB or EC approved Informed Consent, and were provided with a copy of the fully executed consent with all required signatures. 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 Informed Consent/Enrollment Log will be filed in the site Regulatory Binder for the study.

D. Subject Enrollment

Once the Informed Consent has been signed and dated by the subject, the subject will be considered enrolled in the study. A unique case identification number (Case ID) will be assigned to each participating subject/femur (bilateral subjects will be assigned a unique case ID number for each femur). 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.

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/Site Signature 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. This log will be filed in the site Regulatory Binder for the study.

G. Baseline/Pre-operative/Operative/Discharge Assessment

Data collection required for baseline, operative, and discharge will be collected preoperatively if the subject signs their informed consent prior to surgery. If the subject meets all inclusion and none of the exclusion criteria and signs an informed consent prior to the end of the 6 weeks follow-up visit window, retrospective chart review will be conducted for preoperative data. At a minimum, this will include physical exam data, demographic data, and operative data. However, it may include additional information related to pain, function, and radiographic evaluation if available. The following case report forms will be collected baseline, operatively, and at discharge:

1. Enrollment Form
2. Demographic Evaluation
3. Operative Record
4. Postoperative Discharge Assessment
5. X-Rays (any available views)
6. Adverse Event(s)
7. Protocol Deviation(s)
8. Study Completion
9. Explanted Device

H. Post-Surgical Management

Post-surgical management for study subjects will follow the investigator's standard of care for patients undergoing femoral neck or intertrochanteric fracture repair. Post-surgical rehabilitative therapy will be as prescribed by the investigator. The FDA cleared instructions for use and surgical technique must be followed for this product. Please refer to the latest versions of these documents on the zimmerbiomet.com website or contact your local clinical study manager or Zimmer Biomet sales associate for additional details.

I. Post-operative Follow-up Procedures (Data Collection)

Post-operative clinical evaluations/assessments will be conducted at 1 to 6 weeks (+ 14 days), 3 months (± 30 days), 6 months (± 60 days), and 12 months (± 90 days) post-surgery. The following case report forms will be collected at

each interval:

1. Postoperative Follow-up
2. VAS Pain
3. EQ-5D-5L
4. RUSH
5. FIX-IT
6. X-rays (A/P and lateral views of the hip or pelvis)
7. Physician Radiographic Assessment
8. Adverse Event(s)
9. Protocol Deviation(s)
10. Study Completion
11. Explanted Device

Subjects will be followed post-operatively for 12 months. 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, (due to complication) including partial removal i.e. screw, or expires. See Management of Incurrent Events for additional details. Reason(s) for study completion must be documented on the Study Completion case report form.

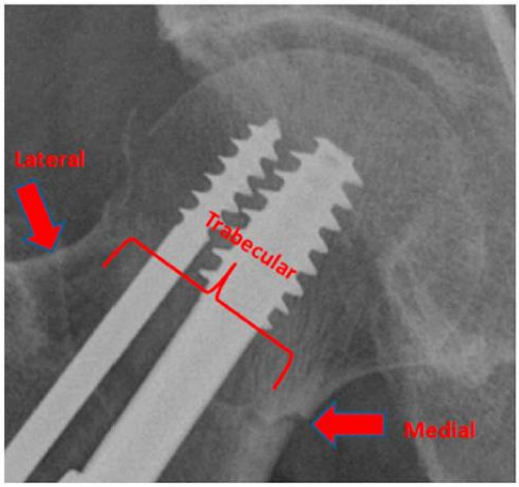
J. Minimization of Subjects Lost to Follow-up

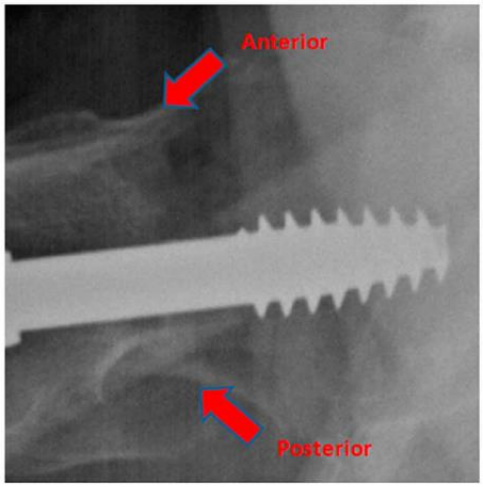
Subject follow-up is extremely important for the conduct of a clinical study, and the expectation is to maintain the highest possible rate of follow-up compliance throughout this study. During the informed consent process and at each follow-up interval, subjects should be counseled on the importance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

K. Radiographic Definitions and Methods

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 Radiographic Assessment** case report form. This includes documentation of any significant radiographic findings. In addition, an **Adverse Event** case report form must be completed for those findings indicated by an asterisk on the **Physician Radiographic Assessment** case report form, or for any other findings identified as an adverse event.

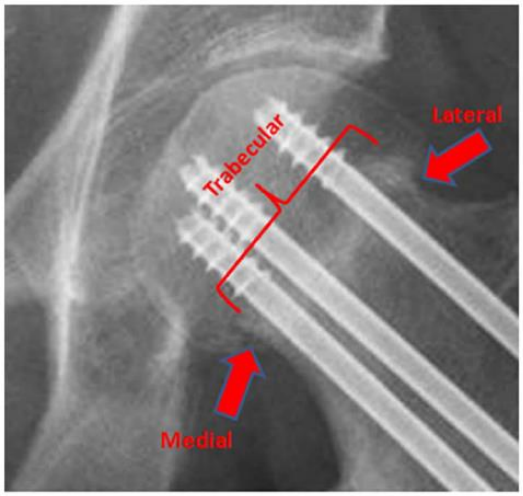
- Non-union definition: A total RUSH score below 18 at six month post-surgery is considered a non-union[4].
    - RUSH scoring examples:

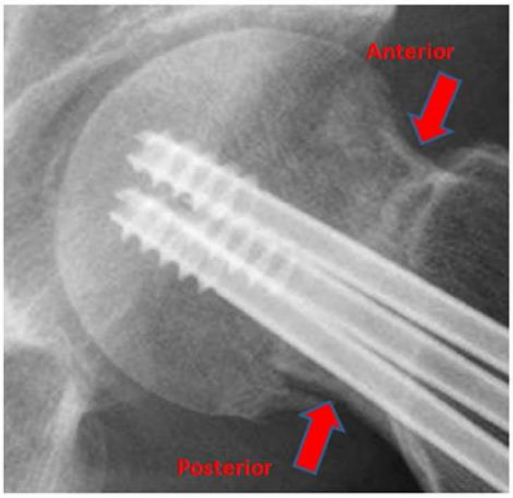




	Cortical Bridging	Cortical Fracture Line Disappearance
Anterior	1	2
Posterior	1	1
Medial	1	1
Lateral	1	1
Total:	**4**	**5**

Trabecular Consolidation	**1**
Trabecular Fracture Line Disappearance	**1**
RUSH Total:	**11**





	Cortical Bridging	Cortical Fracture Line Disappearance
Anterior	3	3
Posterior	2	2
Medial	2	2
Lateral	3	3
Total:	**10**	**10**

Trabecular Consolidation	**3**
Trabecular Fracture Line Disappearance	**3**
RUSH Total:	**26**

Acceptable views include A/P and lateral views of the hip and/or pelvis and must include view of the implanted devices and the treated fracture and/or healing or healed fracture.

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

IX. Reporting

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.

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 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 if required by local and national regulations.

B. Clinical Data Collection/Submission

1. Summary of Case Report Form Data Collection
   a. Study data will be collected on source documents which may include study-specific worksheets provided by the Sponsor. For subjects having bilateral proximal femur facture treatment, separate case report forms must be completed for each operative side.

   b. The following source document/CRF completion guidelines should be followed:
      i. Complete carefully and accurately.
      ii. Complete header information consistently across all case report forms for each individual study subject (when study-specific CRFs are used).
      iii. Be sure that data on the source documents match that which is entered through the electronic data capture (EDC) system
      iv. Use the study subject's unique Case ID number assigned as instructed. Do not provide information that is not requested on the CRFs.
      v. 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.

2. Data Submission
   a. Completed CRFs 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 30 days of the visit completion.

3. Quality Assurance of Data
    a. The Investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor in the CRFs and in all required reports. Data reported on the CRF, which are derived from source documents, should be consistent with the source documents 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. Adverse Events
   An adverse event is any unfavorable or unintended sign, symptom, or disease that impacts the subject. Adverse event is synonymous with complication or medical event.

   See Section IX, Subsection E of this protocol for additional information regarding adverse event classifications. Femur related, serious, and unanticipated events are required to be reported on the **Adverse Event Report** case report form. The completed **Adverse Event Report** case report form must be submitted to the Sponsor in a timely manner. The Investigator or Designee will also promptly provide the Sponsor with any additional requested information required for the Sponsor to comply with regulatory requirements. If applicable per their reporting requirements, the Investigator or Designee will also report applicable adverse event(s) to their IRB or EC.

3. Revision
   In the event that removal of one or more of the study related components is necessary (due to complication), the Investigator will determine the best treatment and/or revision method for the subject. Once the revision surgery has been completed, the Investigator or qualified Designee must complete an **Adverse Event Report** case report form as well as a **Study Completion** case report form terminating the subject from 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** case report 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** case report form.

6. Lost to Follow-up

   A study subject will be considered lost to follow-up after they have missed a visit and a reasonable number of attempts to locate and evaluate them have failed. All attempts to contact the subject are to be documented in the subject's medical record and on the **Study Completion** case report form. In particular, the reason for the Study Completion must be documented. Missed visit(s) also must be documented using the **Protocol Deviation** case report form, unless the visit is retrospective.

7. Protocol Deviations

   Investigators should not deviate from the study protocol. If a protocol deviation does occur, the deviation must be documented on the **Protocol Deviation** case report 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 1 year 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, (due to complication) including partial removal i.e. screw, or expires. Reason(s) for study completion must be documented on the **Study Completion** case report 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

   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 subject. Adverse event is synonymous with complication or medical event.

Adverse events are required to be reported on the **Adverse Event Report** case report form. The completed **Adverse Event Report** case report form must be submitted to the Sponsor in a timely manner. The Investigator or Designee will also promptly provide the Sponsor with any additional requested information required for the Sponsor to comply with regulatory requirements. If applicable per their reporting requirements, the Investigator or Designee will also report applicable adverse event(s) to their IRB or EC.

1. Classification of the Event

Adverse Event (AE):

An adverse event is any unfavorable or unintended sign, symptom, or disease that impacts the subject.

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.

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

If an Unanticipated Serious Adverse Device Effect (USADE) is identified by the Sponsor, 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.

   Pending:
   Treatment or diagnostic studies were prescribed for the adverse event and the outcome of the adverse event is not yet known.

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

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

   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.

   Death:
   The outcome indicates the subject died as a direct result of the

reported adverse event.

F. Monitoring of the Study

Prior to initiating the clinical study, the Sponsor may 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 will 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 inspect all source data/documents, study documents/binders, study subject case report forms, corresponding sections of study subject medical/hospital records, and any other documents relevant to the study. All Sponsor visits (including site initiation) will be documented using the **Monitoring Visit Log**.

X. 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 labelling, the risks associated with the use of the THP System are similar to those of standard femoral neck or intertrochanteric fracture treatment system used for the same clinical indication or purpose. Unanticipated adverse events can also occur.

For general surgical risks, please refer to the FDA cleared instructions for use for this product.

XI. Statistical Considerations

Performance of the commercially available THP System for treatment of femoral neck fractures or intertrochanteric fractures will be evaluated for fracture healing, pain, function, quality of life, and survivorship. 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.

B. Sample Size

Due to the different historical revision rates for intertrochanteric fractures (~7%)[1] and intracapsular fractures (~20%)[2], study enrollment will be split between the two groups to maintain the integrity of the sample size with an expectant lost to follow-up rate of 15%. Intertrochanteric fractures will be limited to a maximum of 89 enrolled subjects and intracapsular fractures will be limited to a maximum of 101 enrolled subjects. This will provide enough evaluable data for both indications to show the necessary statistical improvement from the historical revision rates[1][2]. The assumed revision rate of the THP Hip Fracture Plating System is 15% for intracapsular fractures and 5% for intertrochanteric fractures with a non-inferiority margin of 8%.

XII. References

[1] Matre K, Havelin LI, Gjertsen JE, Vinje T, Espehaug B, Fevang JM. Sliding hip screw versus IM nail in reverse oblique trochanteric and subtrochanteric fractures. A study of 2716 patients in the Norwegian Hip Fracture Register. Injury. 2013 Jun;44(6):735-42.

[2] Fixation using Alternative Implants for the Treatment of Hip fractures (FAITH) Investigators. Fracture fixation in the operative management of hip fractures (FAITH): an international, multicentre, randomised controlled trial. Lancet. 2017 Apr 15; 389(10078):1519-1527.

[3] Stiasny J, Dragan S, Kulej M, et al. Comparison analysis of the operative treatment results of the femoral neck fractures using side-plate and compression screw and cannulated AO screws. Ortop Traumatol Rehabil. 2008 Jul-Aug; 10(4): 350-61.

[4] Frank T, Osterhoff G, Sprague S, Garibaldi A, Bhandari M, Slobogean GP; FAITH Investigators. The Radiographic Union Score for Hip (RUSH) Identifies Radiographic Nonunion of Femoral Neck Fractures. Clin Orthop Relat Res. 2016 Jun;474(6):1396-404.

Guideline Reference:

i. ISO 14155:2011(E). International Standard for Clinical investigation of medical devices for human subjects – Good clinical practice

ii. Code of Federal Regulations
   1. Code of Federal Regulations, Title 21, Part 11: Electronic Records; Electronic Signatures
   2. Code of Federal Regulations, Title 21, Part 50: Protection of Human Subjects
   3. Code of Federal Regulations, Title 21, Part 56: Institutional Review Boards

XIII. Appendices:

Appendix A Sample Informed Consent

Appendix B Case Report Forms

Appendix C Study Logs