Clinicaltrials.gov NCT #: NCT03807349

N-Force Screws Augmented With N-Force Blue in Intracapsular Proximal Femur Fracture Treatment

Post Market Clinical Follow-Up Study (PMCF)

Protocol # CMU2017-60T
Region: United States

[20JAN2020] – Version 3.0

Previous Versions: v2 [18JUN2018]; v1 [9MAY2018]

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I. Study Synopsis

Study Title	N-Force Screws augmented with N-Force Blue in Intracapsular Proximal Femur Fracture Treatment
Abbreviated Study Title	N-Force Study
Sponsor	Zimmer Biomet, Warsaw, Indiana
Protocol Number	CMU2017-60T
Anticipated Start Date	Q4 2018
Study Objectives	The objective of this prospective study is to confirm safety and performance of N-Force Screws augmented with N-Force Blue applied in intracapsular proximal femur fracture treatment. Further results will be compared to non-augmented standard cannulated screws (historic control). Primary Endpoint: • Re-operation within 12 months after initial surgery to promote fracture healing, relieve pain, treat infection, or improve function[4]. Secondary Endpoints: • Radiographic and clinical fracture healing of the proximal femur using standard scoring methods and patient satisfaction. • Cost effectiveness
Target Population	Patients with primary Garden I and II intracapsular proximal femur fractures requiring surgical intervention and eligible for fixation by three cannulated screws augmented with N-Force Blue.
Study Design	Multicenter, prospective, non-controlled clinical study
Study Type	Post-market clinical follow-up study (PMCF)
Sample Size	190 Subjects (151 + 20% anticipated lost to follow-up)
Length of Study	3 years (1 year enrollment, 1 year follow-up and 1 year study close-out)
Follow-up Intervals	6 weeks, 3 months, 6 months and 12 months after surgery
Inclusion/Exclusion Criteria	Inclusion Criteria: • Patient has primary Garden I or II intracapsular proximal femur fracture requiring surgical intervention and is eligible for fixation by three cannulated screws augmented with N-Force Blue.

	• Patient receives operative treatment within 7 days of injury. • Patient was ambulatory before injury. • Patient is 50 years of age or older. Exclusion Criteria: • Patient has Garden III or IV intracapsular proximal femur fracture. • Patient has major cognitive impairment (including dementia). • Patient is on dialysis. • Patient is not expected to survive follow-up schedule. • Patient is expected to have problems maintaining follow-up compliance, i.e. patients with no fixed address, patients not mentally competent to give informed consent, etc. (Investigator's discretion). • Patient is a prisoner. • Patient is known to be pregnant and/or breastfeeding. • Patient is a known alcohol or drug abuser. • Patient had previous/has active acute or chronic infections, especially at the site of operation. • Patient has non-viable bone, or has areas where surrounding bone is not viable or capable of supporting and anchoring the implant. • Patient has traumatic injuries with open wounds or close to the proximal femur fracture, which are likely to become infected. • Patient is expected to be non-compliant with recommended post-operative weight-bearing instructions. • Physical conditions, in the opinion of the investigator, that would prohibit adequate implant support or impede healing.
Study Device	N-Force Fixation System 7.3 mm (Non-fenestrated/fenestrated) applied with washers; N-Force Blue (Bone Substitute Material)
Outcome Measures	• RUSH Score • FIX-IT • Avascular necrosis (Steinberg classification) rate at 12 months follow-up • Harris Hip Score • Timed "Up-And-Go" Test • EQ-5D-5L • Adverse Events

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 compliant with ISO 14155 Standard for Clinical Investigation of Medical Devices For Human Subjects – Good Clinical Practice [1] , is in accordance with US Code of Federal Regulations 21 CFR Parts 11, 50 and 56 [2], and The Declaration of Helsinki (DoH) – Ethical principles for medical research involving human subjects.

II. 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 & Discharge	6 weeks Post-op (±- 14 days)	3 months Post-op (± 30 days)	6 months Post-op (± 60 days)	12 months Post-op (± 90 days)	Revision
Informed Consent	X						
Inclusion/Exclusion Criteria	X						
Demographic Evaluation	X						
Operative & Surgical Device Information		X					
Postoperative Discharge Assessment		X					
Timed "Up and Go" Test			X	X	X	X	
X-rays (A/P and Lateral – Operated Side)	X	X	X	X	X	X	X
EQ-5D-5L			•	•	•	•	
Postoperative Follow-Up			X	X	X	X	
FIX-IT Score			X	X	X	X	
Harris Hip Score			X	X	X	X	
Study Completion		*	*	*	*	*	X
**Adverse Event (Complication)	*	*	*	*	*	*	X
Protocol Deviation	*	*	*	*	*	*	*
Physician Radiographic Assessment (including RUSH)			*♦	*♦	*♦	*♦	*♦
Steinberg Classification						*♦	
Explanted Device		*	*	*	*	*	*

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 forwarded to the sponsor within 7 days of occurrence. Supporting documents must be 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

Intracapsular Proximal Femur Fractures are a common injury especially in the elderly population. Optimal treatment remains controversial. Frequently applied operative treatments include three cannulated screws, sliding hip screw, hemi- and total arthroplasty. AAOS Guidelines for femoral neck fractures in the elderly recommend operative fixation for stable non-displaced fractures and arthroplasty for unstable displaced fractures. In a recent landmark randomized trial including more than one thousand patients comparing sliding hip to cannulated screws, every fifth patient had to be repeated to promote fractures

healing [4]. Reoperation rates of 20% for sliding hip screw and 22% for cannulated screw were found; however, the difference was not statistically significant.

Zimmer Biomet offers a Hip Screw technology that is capable of delivering a Bone Substitute Material (BSM) to the fracture-implant interface for fixation of fractures of the femoral neck [5][6]. This device allows hard setting BSM to the precise location, providing a multi-dimensional fixation that is critical to reduce the chance of joint collapse and articular fragment displacement and ultimately could reduce the high reoperation rates reported for this kind of injury.

This study will assess the reoperation rates, including revision, and document the clinical and radiographic outcomes of hip fracture patients, utilizing the N-Force Fixation System. Results will be compared to "standard" non-augmented cannulated screw (historic control).

IV. Study Objectives

The objective of this prospective study is to assess safety and performance of N-Force Screws augmented with N-Force Blue applied in intracapsular proximal femur fracture treatment. Further results will be compared to non-augmented standard cannulated screws (historic control).

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 fracture healing (union) rate at 6 weeks, 3 months, 6 months, and 12 months postoperatively.

The primary endpoint of this study is defined as re-operation within 12 months after initial surgery. Reoperation is defined as a second surgery to correct the previous procedure or the complications of a previous surgery. For this study, reoperation will include second surgeries to promote fracture healing, relieve pain, treat infection, or improve function including:

- Removal of the implant prior to fracture healing
- Internal fixation with another implant during revision surgery
- Revision to total hip arthroplasty
- Incision and drainage or other soft tissue procedure due to deep infection at the bone implant interface.

Secondary endpoints of this study include:

- Clinical (FIX-IT) and radiologic (RUSH) [8][9] fracture healing at 6 weeks, 3, 6 and 12 months post-surgery.
- Length of femoral neck 1.a.[7]
- Proportion of patients with avascular necrosis at one year FUP (Steinberg classification)
- Functional Index for Trauma (FIX-IT) [10]
- Harris Hip Score [11]
- Timed "Up-And-Go" Test [12]
- EQ-5D-5L
- Adverse events (complications)

Additionally, a cost effective analysis comparing N-Force to standard non-augmented cannulated screws will be performed.

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.

V. Study Design

This is a prospective, multicenter, non-controlled clinical study designed to facilitate the collection and evaluation of fracture healing, pain, function, quality of life, radiographic assessment, and adverse event data. A maximum of 16 sites will contribute to this study. Enrollment per site will be approximately 12 implanted devices with a site maximum of 47 (25% of total study population). Each Investigator will be skilled in proximal femur fracture treatment and experienced implanting the devices included in this study, as determined by the Sponsor.

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 proximal femur fracture treatment using the commercially available (FDA cleared) N-Force Screws augmented with N-Force Blue. 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 N-Force Screws augmented with N-Force Blue 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 pre-operative and operative data 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 Ethics Committee approvals and patient consent is obtained. The post-operative clinical and radiographic evaluations will be conducted at 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 the incidence of loss of reduction, implant migration and 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 require intracapsular proximal femur fracture repair and satisfy the inclusion/exclusion criteria outlined in this section of the protocol. In total, one-hundred-and-ninety (190) patients will be enrolled.

In order to avoid potential selection bias, each Investigator will offer study participation to each consecutive eligible patient presenting as a candidate for intracapsular femur fracture repair using the commercially available (FDA cleared) N-Force Screws augmented with N-Force Blue. Eligible candidates who express interest in study participation will be offered Informed Consent. The **Inclusion/Exclusion Criteria** case report form should not be completed until the study-specific consent form has been completed.

1. Inclusion Criteria

- Patient has primary Garden I or II intracapsular proximal femur fracture requiring surgical intervention and is eligible for fixation by three cannulated screws augmented with N-Force Blue.
- Patient receives operative treatment within 7 days of injury.
- Patient was ambulatory before injury.

- Patient is 50 years of age or older.

Note: *Patients who have previously received N-Force Screws augmented with N-Force Blue may be enrolled in the study if informed consent occurs prior to the end of the 6 weeks follow-up visit window.*

1. Exclusion Criteria

- Patient has Garden III or IV intracapsular proximal femur fracture.
- Patient has major cognitive impairment (including dementia).
- Patient is on dialysis.
- Patient is not expected to survive follow-up schedule.
- Patient is expected to have problems maintaining follow-up compliance, i.e. patients with no fixed address, patients not mentally competent to give informed consent, etc. (Investigator's discretion).
- Patient is a prisoner.
- Patient is known to be pregnant and/or breastfeeding.
- Patient is a known alcohol or drug abuser.
- Patient had previous/has active acute or chronic infections, especially at the site of operation.
- Patient has non-viable bone, or has areas where surrounding bone is not viable or capable of supporting and anchoring the implant.
- Patient has traumatic injuries with open wounds or close to the proximal femur fracture, which are likely to become infected.
- Patient is expected to be non-compliant with recommended post-operative weight-bearing instructions.
- Physical conditions, in the opinion of the investigator, that would prohibit adequate implant support or impede healing.

*Inclusion/Exclusion criteria address the N-Force Screw, N-Force Delivery System, and N-Force Blue

VII. Study Device Information

The N-Force Fixation System is designed to provide fracture fixation and stabilization of femoral neck fractures by the use of the N-Force 7.3mm Fenestrated and Non-Fenestrated Screws (Figure 1) (N-Force 4.0mm screws will not be used in this study). N-Force 7.3mm is intended for use in the femoral neck fractures of the proximal femur. Washers are available for use with the 7.3mm Screw design.

Figure 1: left 7.3 mm Non-Fenestrated Screw, right 7.3 mm Fenestrated Screw

The N-Force Fixation System Screws and Washers are fabricated from Titanium alloy (Ti-6AL-4V) and are biocompatible for human implantation.

The N-Force Fixation System is designed to be used with the N-Force Blue Mixing & Delivery System (Figure 2). These components are single use instruments designed to be used for the mixing of bone substitute materials.

Figure 2:

The N-Force Blue Porous Bone Substitute material is a synthetic, biocompatible bone graft substitute material that forms a poorly crystalline hydroxyapatite at body temperature. It is provided in a single patient, single use kits in various volumes appropriate to the surgical site.

VIII. Study Procedures

A. Offer Study Participation

Study participation will be offered to each consecutive eligible patient presenting as a potential candidate for intracapsular proximal femur fracture repair using the commercially available (FDA cleared) N-Force Screws with N-Force Blue. 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. After a subject receives the study device during surgery, the date of surgery will be added to the log. The subject will now be considered an active study subject. In the event that a subject does not receive the study device at the time of surgery, a **Study Completion** case report form must be submitted and this will be documented as a screen failure on the Informed Consent/Enrollment Log.

D. Subject Enrollment

Once the Informed Consent has been signed and dated by the subject or delegated signatory, 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. 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 **the Informed Consent/Enrollment Log** (see above).

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 Assessment

Baseline/pre-operative data will be collected on the following case report forms at the time of enrollment:

1. Informed Consent

2. Inclusion/Exclusion Criteria
3. Demographic Evaluation
4. Adverse Event Report(s) (as applicable)
5. Protocol Deviation(s) (as applicable)

H. Surgical Technique

Standard operative procedures will be followed and all surgical procedures will be performed under aseptic conditions. Investigators will implant all commercially available N-Force Screws with N-Force Blue and any other compatible products in compliance with corresponding labeling requirements and in accordance with appropriate surgical technique(s).

I. Surgical, Immediate Post-surgical Procedures and Discharge (Data Collection)

Surgical and immediate post-surgical data will be collected on the following case report forms:

1. Operative and Surgical Device Information
2. X-rays (AP and Lateral)
3. Postoperative Discharge Assessment
4. Adverse Event Report(s) (as applicable)
5. Protocol Deviation(s) (as applicable)
6. Explanted Device Form (as applicable)
7. Study Completion (as applicable)

J. Post-surgical management

Post-surgical management for study subjects will follow the investigator's standard of care for patients undergoing intracapsular proximal femur fracture. Post-surgical rehabilitative therapy will be as prescribed by the investigator.

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

Post-operative clinical evaluations/assessments will be conducted at 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. X-rays (AP and Lateral)
3. Physician Radiograph Assessment including RUSH

4. Steinberg Classification (12 months Follow-Up only)
5. EQ-5D-5L
6. FIX-IT
7. Timed "Up and Go" Test
8. Harris Hip Score
9. Adverse Event Reports(s) (as applicable)
10. Protocol Deviation(s) (as applicable)
11. Explanted Device Form (as applicable)
12. Study Completion (as applicable)

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), 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.

L. 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.

M. Radiographic Definitions and Methods

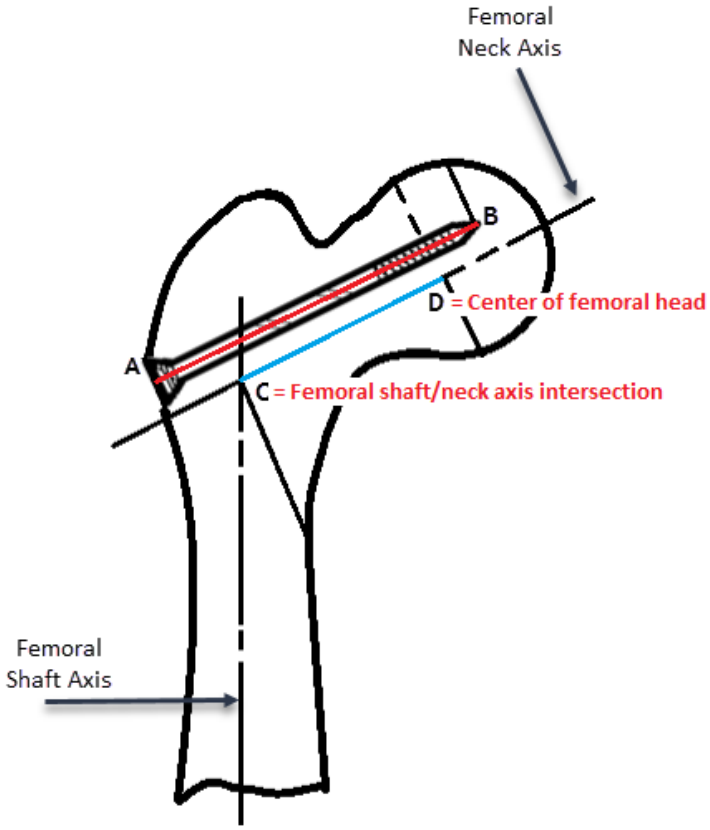
All postoperative radiographic evaluations performed according to the protocol will be reviewed by the Investigator at the time of the evaluation and documented using the **Physician Assessment of Post-op Radiographs** case report form. This includes documentation of any significant radiographic findings. In addition, an **Adverse Event** case report form must be completed for those findings indicated by an asterisk on the **Physicians Assessment of Post-op Radiograph** case report form, or for any other findings identified as an adverse event.

- **Method to derive the length of the femoral neck:**
  1. Draw a line along the femoral shaft axis.
  2. Draw a line along the femoral neck axis.
  3. Measure the distance CD (blue line) in millimeter.
  4. Measure the distance AB (red line) of the **inferior** screw in millimeter.

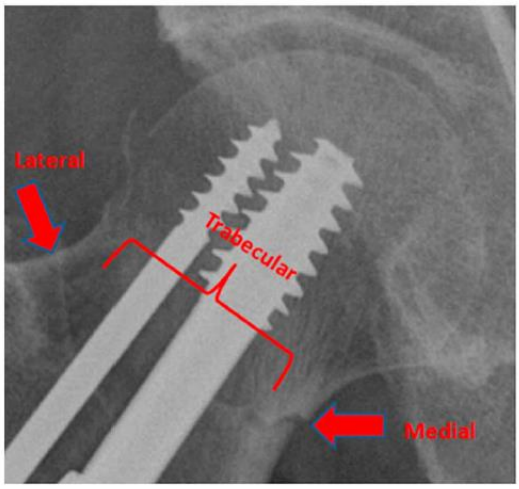
  To adjust for x-ray magnification the actual length of the femoral neck will be calculated using the following formula:

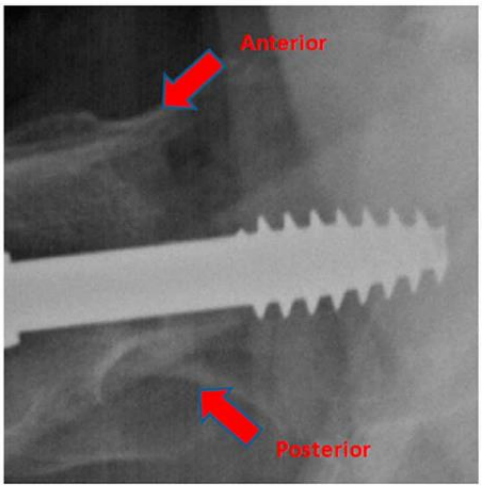
$$Length\ of\ the\ femoral\ neck\ [mm] = CD_{measured} \times \frac{AB_{true}}{AB_{measured}}$$

$AB_{true} = Known\ screw\ length$ [mm].



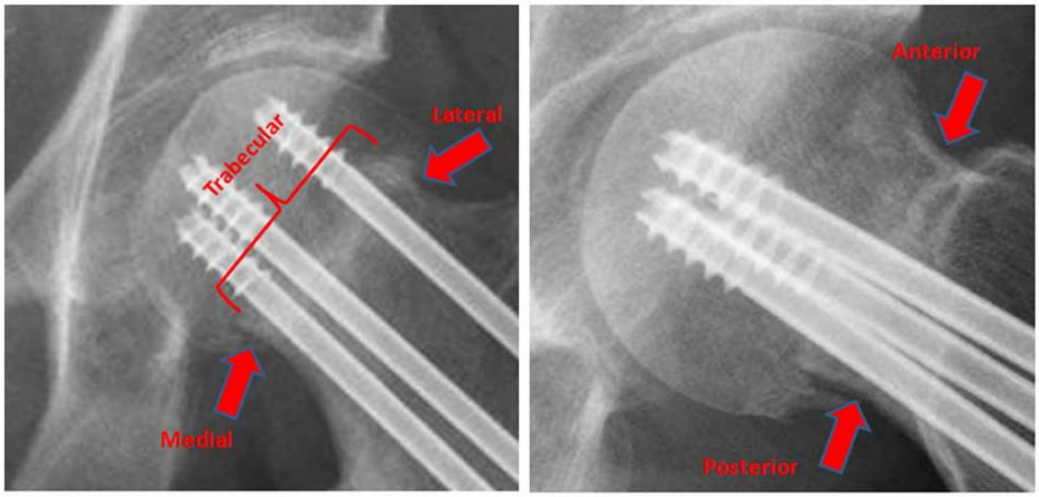
- **Non-union definition:** A total RUSH score below 18 at six month post-surgery is considered a non-union [9].
    - RUSH scoring examples:





	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**

1. Required radiographic views
   Standing anteroposterior (AP) (a supine AP view will be accepted if the patient is unable to stand), and standard lateral radiographs of the operative femur are required to be captured at the pre-op, operative/post-op, 6 weeks, 3 months, 6 months, and 12 months post-surgery.

   Radiographs should have similar exposure and must show the entire study device 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.

N. Recommended Revision Procedure

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

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 (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 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 intracapsular 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[(2)]. 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.

   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 Postop Radiographs** case report form. An **Adverse Event** case report form must be completed for those findings indicated by an asterisk on the **Physicians Assessment of Postop Radiograph** case report form.

   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. For the study completion status, select "Study Device Removed". This procedure also applies to partial revisions e.g. removal of one of the three screws.

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 one 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), 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.

The following definitions are from ISO 14155:2011.

1. Classification of the Event

Adverse Event (AE):

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

Note 1: This definition includes events related to the investigational 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.

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.

Device Deficiency:
A Device Deficiency is defined as an inadequacy of medical device with respect to its identity, quality, durability, reliability, safety or performance.

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 reoperation and removal of a study device.

Reoperation of Affected Hip:
The adverse event resulted in reoperation of the fracture, 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 evaluation 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 **Site Monitoring Visit Log** (Appendix C).

X. Risk Analysis

This post-market clinical study is classified as minimal risk 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 the use of N-Force Screws augmented with N-Force Blue are similar to those of standard intracapsular femur fracture treatment systems used for the same clinical indication or purpose. These risks are categorized below as either general surgical risks or risks associated with the intracapsular femur fracture procedure/study device. 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

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.

B. Sample Size

Using an observed historical control performance reoperation rate of ~15% [4][7],

for intracapsular femur fractures, 151 evaluable subjects will be required at 12 months follow-up to show necessary statistical improvement from the historical revision rate. With an expected lost to follow-up rate of 20%, 190 subjects will be required for this clinical study. The assumed reoperation rate for the N-Force Screws augmented with N-Force Blue is 7.5%.

XII. Quality Control & Quality Assurance

The study is conducted in accordance with the Declaration of Helsinki and the ISO 14155:2011.

The Investigator will be required to permit representative(s) of the Sponsor's monitoring team to inspect all Case Report Forms and corresponding sections of the study patients office records and/or hospital original medical records. These audits will be done for quality assurance purposes, i.e. verifying adherence to the Clinical Investigation Plan and the completeness and accuracy of the data being entered on the Case Report Forms.

The Clinical Investigation Plan will be provided to all participating study centers. The Investigators will be fully trained in the proper reporting and submission of trial data prior to patient enrolment. Completed Case Report Forms will be reviewed before entering the data into a central database by the Sponsor.

The Clinical Study Manager is responsible for generating data queries for missing or unclear data if needed. It is the responsibility of the Clinical Study Manager to ensure data quality.

There are regular meetings between the Investigators and Zimmer Biomet Clinical Affairs staff. Written correspondence to all sites is used to inform the Investigators of routine study details and to update them on study status.

XIII. Suspension or Premature Termination of the Clinical Investigation[1]

Sponsor may suspend or prematurely terminate clinical investigation site(s) or entire clinical investigation for significant and documented reasons. If suspension or premature termination occurs at an individual investigation site, sponsor shall inform the responsible regulatory authority(s) as appropriate and ensure that ethic committee(s) are notified. If the suspension or premature termination was in the interest of safety, the sponsor shall inform all other principal investigators. If suspension or premature termination occurs,

- The sponsor shall remain responsible for providing resources to fulfull the obligations from the clinical investigation plan and existing agreements for following up the subjects enrolled in the clinical investigation, and

- The principal investigator or authorized designee shall promptly inform the enrolled subjects at his/her investigation site, if appropriate.

XIV. Amendments to the Clinical Investigation Plan

All amendments shall be agreed upon with the Sponsor and the Investigator and be recorded with a justification for the amendment. Approval of the Institutional Review Board that reviewed the original protocol must be obtained if required according to the corresponding regulations. In the case of an amendment to the protocol, the revision history shall be documented.

XV. Publication Policy

Both the Clinical Investigator and the Sponsor have the right to publish or allow the results of the clinical trial to be published. The Clinical Investigator recognizes that the Sponsor has a special interest in the results of the clinical study and will submit manuscripts to the Sponsor prior to publication. If the Sponsor desires changes to be made, these are communicated to the Clinical Investigator within 30 days of submission. Pooled data may be used for training and meetings

XVI. Document History

Revision Number	Date	Description of Change	Person in Charge of Change
2.0	18JUN2018	Inclusion/Exclusion Criteria Updated	Ryan Boylan
3.0	20JAN2020	Inclusion Criteria Updated; AE Definitions Updated; Section 12, 13, 14, 15, and 16 added.	Ryan Boylan

References

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

[2] Code of Federal Regulations

- Code of Federal Regulations, Title 21, Part 11: Electronic Records; Electronic Signatures
- Code of Federal Regulations, Title 21, Part 50: Protection of Human Subjects
- Code of Federal Regulations, Title 21, Part 56: Institutional Review Boards

[3] https://www.aaos.org/research/guidelines/hipfxguideline.pdf

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II. Appendices:

Appendix A Sample Informed Consent

Appendix B Case Report Forms

Appendix C Study Logs