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FastFrame™ External Fixation System Post-Market Clinical Follow-Up Study

Knee Spanning Kit and Damage Control Kit

Post-Market Clinical Follow-Up Study

CMU2017-95T

Rev 1

16 Sep 2020

United States

STUDY SPONSOR

Zimmer Biomet
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United States
800-613-6131

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I. Contact Information

Title	FastFrame™ External Fixation System Post-Market Clinical Follow-Up Study
Protocol Number	CMU2017-95T
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Monitoring Contact Information	Madison Murphy, Zimmer Biomet (or Designee) 1800 W. Center Street, MS4020 Warsaw, IN 46580 USA (574) 373-2265

II. Abbreviations

A/P	Anterior/Posterior
ADE	Adverse Device Effect
AE	Adverse Event
CFR	Code of Federal Regulations
CI	Confidence Interval
CRF	Case Report Form
CTA	Clinical Trial Agreement
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EEA	European Economic Area
EU MDD	European Medical Device Directive MDD/93/42/EEC
EU MDR	European Regulation (EU) 2017/745
FastFrame	FastFrame External Fixation Kit
FDA	Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ID	Identification
IRB	Institutional Review Board
ISO	International Standards Organization
LAR	Legally Authorized Representative
OR	Operating Room
PMCF	Post-Market Clinical Follow-Up
SAE	Serious Adverse Event

III. Study Synopsis

Title	FastFrame™ External Fixation System Post-Market Clinical Follow-Up Study
Protocol Number	CMU2017-95T
Sponsor	Zimmer Biomet
Legal Manufacturer	Zimmer, Inc.
Study Device(s)	• FastFrame External Fixation System – Knee Spanning Kit • FastFrame External Fixation System – Damage Control Kit
Study Objectives/Endpoints	The objective of this observational, prospective study is to confirm safety and performance of the FastFrame External Fixation System and corresponding instrumentation. • Primary Endpoint Frequency and incidence of device-related adverse events and device deficiencies before the FastFrame

	External Fixation System is exchanged by another device (i.e. plates, screws, etc.). • Secondary Endpoint Adverse events that occur between application of the FastFrame External Fixation System and exchange with another device that do not fall within the primary endpoint.
Indications/Target population	66 patients in the United States who have undergone fracture stabilization using the FastFrame External Fixation System - Knee Spanning Kit or Damage Control Kit
Inclusion/Exclusion criteria	Inclusion Criteria: • Patient must be 18 years of age or older • Patient must have been treated with either Knee Spanning or Damage Control FastFrame External Fixation System according to the indications stated in this protocol* Exclusion Criteria: • Patient has an active or suspected infection • Conditions that limit the patient's ability and/or willingness to follow instructions during the healing process • Inadequate skin, bone, or neurovascular status • Patient is a prisoner • Patient is pregnant and/or breastfeeding • Patient is a known current alcohol and/or drug abuser in the opinion of the Investigator • Patient has a mental or neurologic condition that will not allow for proper informed consent and/or participation in follow-up program in the opinion of the Investigator *EEA Indications (a subset of the cleared US indications): The FastFrame External Fixation System – Knee Spanning Kit is indicated for use in treatment of long bone (distal femur, proximal tibia) fractures. Specifically, the system is intended for temporary stabilization of open or closed fractures about the knee, typically in the context of polytrauma or where open or alternative closed treatment is undesirable or otherwise contraindicated. The FastFrame External Fixation System – Damage Control Kit is indicated for use in treatment of mid-shaft long bone (femur, tibia) fractures. Specifically, the system is intended for temporary stabilization of open or closed fractures of the femur and tibia, typically in the context of polytrauma or where open or alternative closed treatment is undesirable or otherwise contraindicated.

Study Design	Prospective enrollment, prospective follow-up, single cohort study
Clinical Phase	Postmarket
Sample Size	Considering a 95% device success rate (5% device related complications) and a 10% non-inferiority margin, 60 subjects with a follow-up are required. With an estimated lost to follow-up/subject withdrawal rate of 10%, 66 subjects will have to be enrolled.
Length of Study	3 years (2 years of enrollment plus follow-up until exchange with another device) A follow-up visit will be completed at the time of exchange from FastFrame System to another device. Typically, this exchange occurs 2 to 4 weeks after injury.
Materials and Methods	Device-related complications and device deficiencies will be reported at the baseline/operative and follow-up visits, if applicable. If required, photographs of the study device will be taken to document any loss of stability requiring unplanned adjustment of the study device.
Data Collection	eCRF
Statistical Reporting	Data collected will be summarized and reported to each participating Investigator. Statistical analysis will be conducted by Zimmer Biomet (or Designee).
Scores/Performance Assessments	Device-related complication and device deficiency rates will be recorded
Standards	The PMCF is compliant with the below: • ISO 14155:2020 - Clinical investigation of medical devices for human subjects - Good clinical practice. • The Declaration of Helsinki (DoH) - Ethical principles for medical research involving human subjects. • European Regulation (EU) 2017/745 • MDCG 2020-10/1 • Safety reporting in clinical investigations of medical devices under the Regulation (EU) 2017/745

IV. Data Collection Overview

The following table indicates the necessary CRFs to be completed at each given time point throughout the study. The person responsible for completing each CRF is also listed. Please note the **Site Delegation Log** may list designees for the investigator who are also allowed to complete specific CRFs.

CRF	Baseline/Operative (Day 1)	Follow-Up (Day 14-28)
Informed Consent (ICF)	Patient	
Inclusion/Exclusion Criteria	Investigator	
Demographic Evaluation	Investigator	
Operative Record	Investigator	
Surgical Device	Investigator	
Physician Imaging Assessment	Investigator	Investigator (as applicable)
Physician Follow-Up Assessment		Investigator
Study Completion		Investigator
Adverse Event Report*	Investigator (as applicable)	Investigator (as applicable)
Protocol Deviation	Investigator (as applicable)	Investigator (as applicable)

* If a device-related Adverse Event occurs, supporting documents must be sent to the Sponsor and include the operative report and any relevant imaging

Required for Patient to be considered enrolled in the study

V. Introduction and Purpose

The management of orthopaedic polytrauma patients has developed greatly since the 1970s, when patients were deemed incapable of undergoing surgery[3]. In recent years, the use of temporary stabilization of fractures has been used with the goal to decrease operative time[3], blood loss[3], and the “second hit” inflammatory response from definitive surgical fixation[2]. External fixators, a type of device intended for temporary stabilization, are typically made up of a combination of a frame, clamps, pins, and bars that properly stabilize and support the injured limb[1]. In order for this stabilization to occur, the fractured bones are adjusted to reduce the fracture and the bars are connected to maintain the reduction[1]. Unlike typical external fixators, the FastFrame External Fixation frames are pre-assembled and are designed for simplicity in the operating room. Each kit includes clamp bodies, pins, and telescoping bars that allow for proper reduction and rigid external fixation. This study will document the clinical outcomes of

trauma patients who require the use of the FastFrame External Fixation System - Knee Spanning and Damage Control kits legally manufactured by Zimmer, Inc.

VI. Study Objectives

The objective of this observational, prospective study is to confirm safety and performance of the FastFrame External Fixation System and corresponding instrumentation. The endpoints are defined to include the following:

Primary Endpoints

- Frequency and incidence of device-related adverse events and device deficiencies before the FastFrame External Fixation System is exchanged by another device (i.e. plates, screws, etc.). Refer to Section XII for additional details related to adverse event classification and device deficiencies.

  Examples of device-related adverse events and device deficiencies include:
  - Pin breakage and/or loosening requiring surgical intervention (i.e. pin removal or exchange) before planned exchange of the complete frame by another device
  - Frame component failure (i.e. loosening, breakage, etc.) leading to clinically unacceptable loss of stability requiring unplanned readjustment or replacement of the frame

Secondary Endpoints

- Adverse events that occur between application of the FastFrame External Fixation System and exchange with another device that do not fall within the primary endpoint. Refer to Section XII for additional details related to adverse event classification.

VII. Study Design and Endpoints

This is a PMCF study designed to collect and evaluate outcome measures and adverse event data. A maximum of three sites will contribute to this study. Each Investigator will be skilled in external fracture stabilization and experienced in implanting the devices included in this study, as determined by the Sponsor.

Each Investigator will be responsible for obtaining IRB approval as required prior

to conducting the study. In order to avoid potential selection bias, each Investigator will offer study participation to each consecutive eligible patient presenting need for temporary stabilization with the FastFrame External Fixation System - Knee Spanning or Damage Control Kits. Eligible candidates who express interest in study participation will be offered **Informed Consent**. All potential study subjects will be required to participate in the Informed Consent process and will not be considered enrolled in the study until the candidate has signed and dated the IRB approved **Informed Consent** and the study device has been implanted.

VIII. Study Population

A maximum of three (3) sites in the United States will contribute to this study. No randomization will take place, as all subjects must receive the study device that best treats their clinical need.

The study population for primary statistical analysis will be comprised of all enrolled subjects who satisfy the Inclusion/Exclusion Criteria outlined in 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 **Informed Consent** has been completed.

Inclusion Criteria

- Patient must be 18 years of age or older
- Patient must be treated with either the Knee Spanning or Damage Control FastFrame External Fixation System according to the indications stated in this protocol*

*EEA Indications (a subset of the cleared US indications):

The FastFrame External Fixation System – Knee Spanning Kit is indicated for use in treatment of long bone (distal femur, proximal tibia) fractures. Specifically, the system is intended for temporary stabilization of open or closed fractures about the knee, typically in the context of polytrauma or where open or alternative closed treatment is undesirable or otherwise contraindicated.

The FastFrame External Fixation System – Damage Control Kit is indicated for use in treatment of mid-shaft long bone (femur, tibia) fractures. Specifically, the system is intended for temporary stabilization of open or closed fractures of the femur and tibia, typically in the context of polytrauma or where open or alternative closed treatment is undesirable or otherwise contraindicated.

Exclusion Criteria

- Patient has an active or suspected infection
- Patient has conditions that limit their ability and/or willingness to follow instructions during the healing process
- Patient has inadequate skin, bone, or neurovascular status
- Patient is a prisoner
- Patient is pregnant and/or breastfeeding
- Patient is a known current alcohol and/or drug abuser in the opinion of the Investigator
- Patient has a mental or neurologic condition that will not allow for proper Informed Consent and/or participation in follow-up program in the opinion of the Investigator

IX. Study Device Information

The FastFrame External Fixation System Knee Spanning and Damage Control Kits are single-use external fixators that are sterile packed with all the required components (i.e., frame, pins, driver, tissue sleeve, and lockout tab). The device indications and contraindications for use can be found on the applicable package inserts. Surgical procedures involved in the use of FastFrame are located on the Zimmer Biomet website.

The following components and materials, used in both FastFrame Kits, have direct human tissue contact during the surgical procedure:

- 5mm Pin – 316L Stainless Steel
- Tissue Trocar – ULTEM® (Black)
- Tissue Sleeve Shaft – 304 Stainless Steel

These materials were tested for cytotoxicity, sensitization, intracutaneous reactivity, and acute systemic toxicity. The test results concluded that these materials are biocompatible and toxicologically safe for use as materials in orthopaedic surgery.

X. Study Procedures

All procedures are to be conducted in accordance with the current surgical techniques supplied to all Investigators in the clinical study and found on the Zimmer Biomet website.

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**.

Informed Consent Process

Informed Consent will be completed by patients who are able to consent themselves or if unable, have a proxy available. The patient will be given an adequate amount of time to read the consent and ask questions to the investigator and/or research staff. If the patient agrees to participate in the study, he/she will sign the consent form. If a patient is unable to consent for him/herself due to the need for immediate surgical intervention, a proxy signature may be used to consent on the patient's behalf. The following individuals may serve as a proxy on behalf of the patient during the Informed Consent process: legal guardian, proxy health care agent, or a close family member of the patient. The relationship of the proxy to the patient must be documented on the **Informed Consent Log**. If the patient becomes able to consent himself or herself at any point in time, a re-consent must occur with the patient’s signature. Due to the immediate surgical intervention regarding the study operation, Informed Consent can be obtained after surgery, but no later than the follow-up visit defined in this protocol.

Informed Consent/Enrollment Log

An **Informed Consent/Enrollment Log** 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 and/or proxies as defined in the Informed Consent Process section of this protocol underwent the Informed Consent process, signed and dated the IRB 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 (i.e., due to a protocol amendment, protocol revisions, re-consent after surgery, etc.), subsequent signings will also be recorded in the log. If a proxy signature is used, the relationship of the proxy to the patient must be documented. The **Informed Consent/Enrollment Log** will be filed in the site Regulatory Binder for the study.

Subject Enrollment

Once the **Informed Consent** has been signed and dated by the subject (or proxy as defined in the Informed Consent Process section of this protocol) and a FastFrame System has been implanted, the subject will be considered enrolled in the study. A unique case identification number (Case ID) will be assigned to each participating subject (bilateral subjects will be assigned a unique case ID number for each temporary stabilization procedure). 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.

Monitoring Log

The **Site Monitoring Visit Log** 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 closeout, etc.). The **Site Monitoring Visit Log** will be filed in the site Regulatory Binder for the study.

Delegation of Authority/Site Signature Log

A **Delegation of Authority/Site Signature Log** will be maintained throughout the study and will contain the names, initials, signatures, and study responsibilities of all site personnel and designees involved in the study procedures and data collection. The Investigator is responsible to sign and date the log after any updates to the log to acknowledge the change(s). The **Delegation of Authority/Site Signature Log** will be filed in the site Regulatory Binder for the study.

Baseline Procedure

Subjects will be enrolled prior to undergoing a procedure using the FastFrame External Fixation System, therefore allowing for the capture of baseline data to be

collected on the following CRFs:

- **Inclusion/Exclusion Criteria**
- **Demographic Evaluation**
- **Protocol Deviation, if applicable**

Operative/Immediate Post-Operative Procedure

All surgeries will take place following the standard, approved surgical technique. During the course of the surgery, a **Surgical Device** CRF must be completed documenting the part and lot numbers of the implants. The FDA cleared or other local government regulatory body approved instructions for use and surgical technique must be followed for this product. Please refer to the latest versions of these documents on the Zimmer Biomet website, contact your local Clinical Study Manager, or contact a Zimmer Biomet sales associate for additional details. The following operative data will be collected on the following CRFs:

- **Operative Record**
- **Surgical Device**
- **Protocol Deviation, if applicable**
- **Adverse Event Report, if applicable**
- **Physician Imaging Assessment**
- **Photographs of study device in two (2) planes (A/P and lateral)**

Photographs will be stored in the Subject Binder as part of their casebook. Please write the Subject Case ID Number, Subject Initials, and Date (YYYY-MM-DD) on the photographs. If an adverse event occurs, an **Adverse Event Report** CRF will also be completed. See Management of Incurrent Events for additional details. Reason(s) for study completion must be documented on the **Study Completion** CRF.

Post-Operative Follow-Up Procedure

Post-operative clinical assessment will be conducted at the device exchange follow-up visit after the procedure. The device exchange of a FastFrame External Fixation Kit typically occurs 2-4 weeks after surgery. The following

CRFs will be collected at the follow-up visit when the study device is removed from the subject:

- **Physician Follow-Up Assessment**
- **Protocol Deviation, if applicable**
- **Adverse Event Report, if applicable**
- **Physician Imaging Assessment, if required**
- **Photographs of study device in two (2) planes (A/P and lateral), if required**
- **Study Completion**

Subjects will be followed post-operatively until the FastFrame External Fixation Kit is exchanged with another device or unless the primary endpoint is reached prior. 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 (does not include device removal as part of standard treatment), or expires.

If the surgeon anticipates a loss of stability that will require unplanned device adjustment, photographs of the study device will be taken to document any loss of stability that occurs. It is up to the Investigator or Designee to take the appropriate amount and type of photographs to clearly show the stability issue(s) with the study device. Please write the Subject Case ID Number, Subject Initials, and Date (YYYY-MM-DD) on the photographs. Photographs (baseline and post-operative) will be sent to the Study Manager via e-mail within 14 days of the occurrence and stored in the Subject Binder as part of their casebook. If an adverse event occurs, an **Adverse Event Report** CRF will also be completed. See Management of Incurrent Events for additional details. Reason(s) for study completion must be documented on the **Study Completion** CRF.

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, subjects should be counseled on the importance of completing the future study follow-up visit.

XI. Reporting

The management of all study data received by the Sponsor will be the responsibility of the Sponsor (or Designee). The use or disclosure of all protected health information will comply with the 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. 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 or year of birth.

Activities Required Prior to Initiation of the Study

Clinical Trial Agreement (CTA) and Financial Arrangements

A fully executed (signed by all required parties) CTA must be on file with the Sponsor prior to any Investigator participating in this study. This agreement must explain the financial arrangement with the investigative site.

Institutional Review Board Protocol Approval

This study protocol must be submitted to and approved by the Investigator's Institutional Review Board (IRB). A copy of the IRB approval letter must be submitted to the Sponsor. The letter should identify the following:

- Protocol name and/or number
- Date of IRB meeting (if available)
- Date of approval
- Date of expiration
- Signature of IRB

ClinicalTrials.gov Registration

The Sponsor will be responsible for registering this study on www.ClinicalTrials.gov if required by local and national regulations.

Clinical Data Collection/Submission

Summary of Case Report Form Data Collection

Study data will be collected on source documents, which may include study-specific worksheets provided by the Sponsor. For subjects undergoing temporary stabilization using multiple FastFrame External Fixation Kits, separate case report forms must be completed for each operative device.

The following source document/CRF completion guidelines should be followed:

- Complete carefully and accurately
- Complete header information consistently across all case report forms for each individual study subject
- Be sure that data on the source documents match that which is entered through the EDC system
- Use the study subject's unique Case ID number assigned as instructed
- Do not provide information that is not requested on the CRFs
- 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.

Data Submission

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.

Quality Assurance of Data

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. The Sponsor will maintain quality control systems, in accordance with the Sponsor's policies and procedures.

Reporting Requirements

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 as required to maintain IRB approval throughout the study, and will provide any required final reporting to the IRB upon study completion/termination. A copy of all IRB re-approval letters must be submitted to the Sponsor. If the IRB 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 regarding any changes significantly affecting the conduct of the study, and/or increasing risk to the subjects.

Retention of Records

For this study, study records must be retained by the Investigator or Designee for a minimum of 15 years from the Investigator's study termination date, or per applicable regulatory and/or IRB requirements (whichever time period is greater). Measures shall be taken to prevent accidental or premature destruction.

Study records are defined as the all information in original records, certified copies of original records of clinical findings, observations or other activities in a clinical study, including source data initially recorded in an electronic format, necessary for the reconstruction and evaluation of the clinical study. This may include but is not limited to: hospital records, clinic records, laboratory notes, device accountability records, photographs, radiographs, subject casebooks, regulatory records, signed informed consents, and all other study-related documents.

Management of Incurrent Events

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 ICF), data for that candidate will not be collected for this study.

Adverse Events

See Safety Management – Medical Events/Adverse Events Section of this protocol for additional information regarding adverse event classifications.

Reporting and Documentation of Adverse Events and Adverse Device Effects

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

Reporting and Documentation of Serious Adverse Events, Serious Adverse Device Effects, and Device Deficiencies

Serious Adverse Events and **Serious Adverse Device Effects** have to be **reported to the Sponsor as soon as possible**. The incidence has to be documented on the Adverse Event Report form over the whole time of the investigation including information on the date of onset, treatment and resolution, as well as assessment of both the seriousness and the relationship to the study device based on the evaluation of the Investigator. The outcome of such complications has to be documented and any changes in outcome have to be updated during the course of the study. In case of early termination of the study, further follow-up of the study subject shall proceed according to the hospital's standard procedure.

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

The **Investigator** is responsible for reporting all SAEs, SADEs and Device Deficiencies that could have led to a SADE to the Institutional Review Board if required by national regulations or by the IRB.

Schedule

In the event that early removal of one or more of the study related components is necessary, 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** CRF as well as a **Study Completion** CRF terminating the subject from the study. Relevant radiographs and/or photographs of the explanted component(s) will be sent to the Sponsor.

All components removed outside of standard of care should be promptly returned to Zimmer Biomet for analysis. The Investigator or Designee must notify the Clinical Study Manager prior to the return of any device. Properly prepared components are to be sent to the following address:

Zimmer Biomet
Attention: Product Services Department
1777 W. Center St.
Warsaw, IN 46580 USA

Investigator Withdrawal

The Investigator can choose to withdraw a subject from the study if it is deemed to be in the subject's best interest or the subject does not consent to continue in the study after being informed of changes in the research that might affect them. The reason for the Investigator's withdrawal of the subject must be documented on the **Study Completion** CRF.

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 whom no longer wishes to participate in the study. The reason for the subject withdrawal must be documented on the **Study Completion** CRF.

Lost to Follow-up

Subjects will be considered lost to follow-up after they have missed their follow-up visit and a reasonable number of attempts to locate and evaluate them have failed. All attempts of contact have to be documented on the **Study Completion** CRF and in particular, the reason should be documented. Patients lost to follow-up will not be replaced within the study.

Protocol Deviations

The Investigator should not deviate from the agreed upon protocol unless it is to eliminate hazard to the patient. However, any deviation from the protocol has to be documented on the **Protocol Deviation** CRF along with an explanation for the

deviation and reported to the Sponsor. Each significant deviation will be reported to the IRB, if applicable, within the appropriate deadlines stipulated by the appropriate regulatory authorities. Significant deviations are defined as those impacting or potentially impacting patient safety.

Investigator disqualification criteria leading to exclusion from the clinical study include fraud, misconduct, and serial non-compliance.

Study Termination

Study subject participation is expected to end upon completion of the subject's device exchange 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 an unplanned revision to remove a study device, or expires. Reason(s) for study completion must be documented on the **Study Completion** CRF.

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 as applicable according to local and national laws/regulations.

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 must be obtained prior to implementation, if required according to the local and/or national laws/regulations.

XII. Safety Management – Medical Events/Adverse Events

Adverse events are required to be reported on the **Adverse Event Report** CRF. The completed **Adverse Event Report** CRF 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.

The following definitions are from ISO 14155:2020 and Regulation (EU) 2017/745: Safety reporting in clinical investigations of medical devices.

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 and whether anticipated or unanticipated.

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

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

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

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

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

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

Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the 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):
A Serious Adverse Device Effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Unanticipated Adverse Device Effect (UADE)
An unanticipated adverse device effect is a serious adverse device effect which nature, incidence, severity, or outcome has not been identified in the current risk assessment.

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

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

Note 1: Device Deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labeling.

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

It is important to document in the study also all device deficiencies that could have led to a medical occurrence, but did not lead to an adverse event.

Causality Assessment (Relation to Device)

The relationship between the use of the medical device (including the medical - surgical procedure) and the occurrence of each adverse event shall be assessed and categorized.

During causality assessment activity, clinical judgement shall be used and the relevant documents, such as the Investigator's Brochure, the Clinical Investigation Plan, or the Risk Analysis Report shall be consulted, as all the foreseeable serious adverse events and the potential risks are listed and assessed there. The presence of confounding factors, such as concomitant medication/treatment, the natural history of the underlying disease, other concurrent illness or risk factors shall also be considered.

Each adverse event will be classified according to four different levels of causality:

- Not Related
- Possible
- Probable
- Causal Relationship (Definitely Related)

The sponsor and the investigators will use the following definitions to assess the relationship of the adverse event to the investigational device, the comparator or the investigation procedure.

Not Related:
Relationship to the device, comparator or procedures can be excluded when: the event has no temporal relationship with the use of the investigational device, or the procedures related to application of the investigational device.

Possible:
The relationship with the use of the investigational device or comparator, or the relationship with procedures, is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.

Probable:
The relationship with the use of the investigational device or comparator, or the relationship with procedures, seems relevant and/or the event cannot be reasonably explained by another cause.

Causal Relationship (Definitely Related):
The serious adverse event is associated with the investigational device, comparator or with procedures beyond reasonable doubt.

Note: Complications caused by concomitant treatments not imposed by the clinical investigation plan are considered not related. Similarly, several routine diagnostic or patient management procedures are applied to patients regardless of the clinical investigation plan. If routine procedures are not imposed by the clinical investigation plan, complications caused by them are also considered not related.

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 a 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.

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.

XIII. Monitoring

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, IRB 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 visits 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 will be documented using the **Monitoring Visit Log**.

XIV. Risk Analysis

This PMCF 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 the FastFrame External Fixation System are similar to those of the historical standard, the XtraFix® External Fixation System by Zimmer, Inc., when used for the same clinical indication or purpose. These risks are either general surgical risks or risks associated with the subject procedure/study device; however, unanticipated adverse events can occur.

XV. Statistical Methods

General Statistical Methods

Statistical methodology will consist of summarizing collected data descriptively. Categorical data (i.e., gender or race) will be summarized using counts and percentages, and 95% 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 will be summarized using a Kaplan-Meier method and presented with rates (as percentages) and confidence intervals.

Sample Size

Calculation of sample size is based on previously published literature involving longitudinal data collection on temporary external fixation. Assuming a power level of 80% and an alpha level of significance of 0.05 ($\alpha = 0.05$), calculations were performed in order to determine the sample size needed for study significance using the following hypothesis test:

The hypothesis will be tested by the exact binomial test:

$H0: E1 - E0 \leq -\delta E$

$Ha: E1 - E0 > -\delta E$

where:

$E0 = 95\%$, the expected success rate

$E1$ = the success rate in the FastFrame System treatment group

$\delta E = 0.10$, non-inferiority margin

In addition, one-sided 95% exact confidence Interval (CI), lower limit of the success rate, will be calculated.

Based on the hypothesis test above, 60 subjects will provide approximately 80% power for the one-sided exact binomial test at 0.05 significant level. The sample size was calculated using SAS for Windows version 9.4.

It was determined that the complication rate of devices comparable to the FastFrame External Fixation System is approximately 5%. Utilizing this figure, the power, and alpha level of significance, a sample size total (without any subjects becoming lost to follow-up) of 60 was obtained. Finally, in order to maintain a sample size large enough for statistical significance an estimated, 90% subject return rate is assumed for the duration of the device exchange follow-up visits. These lost to follow-up patients increase the sample size requirements to 66 subjects (after rounding up).

Visit	Subjects remaining in the study
Baseline	66
Follow-Up	60

XVI. Quality Control & Quality Assurance

The study is conducted in accordance with the Declaration of Helsinki and the ISO 14155:2020 and Regulation (EU) 2017/745.

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 subjects 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.

XVII. Suspension or Premature Termination of the Clinical Investigation

A description of the criteria and arrangements for suspension or premature termination of the whole clinical investigation, of the clinical investigation in one or more investigation sites, or for individual subjects. Include the following, as applicable:

- Criteria for access to and breaking the blinding/masking code in the case of suspension or premature termination of the clinical investigation.
- Requirements for subject follow-up.

XVIII. Vulnerable Populations

Patients that are within one or more vulnerable populations, including children, prisoners, pregnant women, and handicapped or mentally disabled persons, are to be excluded from this study.

XIX. Amendments to the Clinical Investigation Plan

All amendments shall be agreed with the Sponsor and Investigator(s) and be recorded with a justification for the amendment. Approval of the IRB 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 will be documented in the document history.

XX. 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.

XXI. Document History

Revision Number	Date	Description of Change	Person in Charge of Change
0	02 Dec 2019	Initial Release	Madison Murphy
0.1	24 Mar 2020	Corrected typo in table within Section IV. Data Collection Overview	Madison Murphy
1	16 Sep 2020	Replaced radiograph requirements with photographs of the device. Deleted Radiographic Assessment CRF requirement. Rewrote Informed Consent sections. Updated Record Retention and Adverse Event section to Regulation (EU) 2017/745 requirements.	Madison Murphy

XXII. References

[1]Fragomen, Austin T., and S. Robert Rozbruch. “The Mechanics of External

Fixation." HSS Journal, vol. 3, no. 1, 2006, pp. 13–29., doi:10.1007/s11420-006-9025-0.

[2]Giannoudis, Peter V, et al. "Damage Control Orthopaedics: Lessons Learned." Injury, vol. 40, 2009, doi:10.1016/j.injury.2009.10.036.

[3]Halvorson, Jason J., et al. "Orthopaedic Management in the Polytrauma Patient." Frontiers of Medicine, vol. 6, no. 3, 2012, pp. 234–242., doi:10.1007/s11684-012-0218-2.