

# ***I.M.P.R.E.S.S***

**Intramedullary Nails versus Plate Fixation Re-Evaluation Study in Proximal Tibial Fractures:  
A Multicenter Randomized Trial Comparing IM Nails and Plate Fixation**

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**Statistical Plan pages 10-11**

## **Summary of Study Design**

We propose a multicenter randomized controlled trial in which individuals sustaining a fracture of the proximal metaphysis of the tibia will be operatively managed by one of two strategies. The first strategy involves fixation of the fracture with a reamed, interlocking intramedullary nail (Nail Group). The second treatment strategy involves open reduction and internal fixation of the fracture with a locking periarticular plate (Plate Group). The null hypothesis of the study is that there will be no difference in the two groups with respect to the primary and secondary outcome measures. To the degree possible, patients in the two groups will receive post-operative care according to the same standards and protocols. We will monitor critical aspects of pre-operative and post-operative care and provide immediate feedback to the participating surgeons when any important deviation from the following protocol occurs.

The primary outcome: General outcome will be determined by both the SF-12v2 and EuroQol 5D, disease-specific outcomes will be assessed by the Short Musculoskeletal Functional Assessment measure (SMFA) and a knee score.

The secondary outcomes: Re-operation (secondary procedures), nonunion\*, superficial infection\*\* rates (wound only), deep infection\*\* (bone implant interface), incidence of compartment syndrome\*\*, malunion\*\* ( $>5$  degrees varus/valgus,  $>5$  degrees anterior or posterior angulation,  $>10$  malrotation degrees, and  $>1$  cm shortening) and knee range of motion. The treatment provided will be obvious because of differences in surgical incisions and radiographic appearance of the injured limbs; therefore it will not be possible to blind all the patients, surgeons, and some evaluators to treatment allocation. When possible, outcome assessment will be done by independent, blinded parties. We will follow and monitor primary outcome as described on the ***Intervention Design Grid*** (attached), as well as, secondary outcomes, complications and adverse events continually.

## **Background**

Proximal tibia fractures are unstable injuries that are generally treated with surgical fixation to maintain alignment of the extremity during the healing process. The two most common methods of fixation are intramedullary nailing and plate fixation. Both techniques are considered the standard of care. Each method has risks associated with it and some surgeons prefer one over the other. However, no comparison between the outcomes of the two techniques has been performed. We plan a randomized trial comparing these two fixation methods using standardized validated general and disease specific measures as well as standard radiographic and clinical evaluations.

## **Patient Recruitment**

For this study, we anticipate recruiting 160 patients with closed or open tibial shaft fractures. For our primary outcome, we consider an important difference in SR-12 to correspond to a moderate effect as reported by Cohen as well as a minimally important difference in the SF-12 as reported by Ware. In both cases, the value is at least  $\frac{1}{2}$  the standard deviation, equivalent to a 6-point difference in score. Specifying an alpha-level=0.05, a beta=0.20 (study power=80), we require a sample of least 126 patients (63 per group) to ensure detection of a  $\frac{1}{2}$  standard deviation improvement. We will enroll 160 patients to account for loss to follow-up and errors in randomization.

### **Inclusion Criteria: (see *Proximal Tibia Screening Form*)**

1. Skeletally mature,

2. Extra-articular fracture of the proximal tibia extending into the metaphyseal with or without intra-articular extension not requiring open reduction with complete AP and lateral radiographs,
3. Major fracture line not closer than 4cm from the proximal tibial articular surface,
4. Fracture requiring operative treatment amenable to either IM nail or plate,
5. Surgeon agreed to randomize patient,
6. Informed consent obtained,
7. Patient is English speaking.

Patients may have undergone previous surgical interventions either for placement of a spanning external fixator and/or debridement of open fracture wounds. This may have been done at the eventual treating institution or not. That is, the patient could represent a referral of a proximal tibia fracture, which had undergone previous debridement and / or spanning external fixator placement elsewhere.

**Exclusion Criteria: (see *Proximal Tibia Screening Form*)**

We exclude individuals from the study if they have the following characteristics:

1. Tibial shaft fracture not amenable to intramedullary nailing (i.e. fracture is less than 4 cm from joint surface)
2. Fracture of the proximal tibia with intraarticular extension requiring open reduction
3. Known metabolic bone disease
4. Separate displaced tibial tubercle fragment
5. Soft tissue injuries compromising treatment method with nail, plate, or both
6. Fractures with vascular injury (Gustillo Type IIIC injury) requiring repair
7. Compartment syndrome of the leg diagnosed preoperatively
8. Pathological fracture
9. Retained hardware or existing deformity in the affected limb that would complicate IM nailing, plating, or both
10. Symptomatic knee arthritis
11. Surgical delay greater than 3 weeks for closed fractures or 24 hours for open fractures
12. Contralateral proximal tibia fractures (bilateral injury) or ipsilateral lower extremity injury that would compromise function of the knee
13. Immunocompromised
14. Unable to comply with postoperative rehabilitation protocols or instructions (i.e. head injured or mentally impaired)
15. Current or impending incarceration
16. Unlikely to follow-up in surgeon's estimation

**Inclusion of Children, Women, and Members of Minority Groups**

We include all individuals who are skeletally mature. Skeletal maturity is typically achieved by age 18 in males and age 16 in females but will be based on appearance of growth plate. We are not including individuals with open growth plates (i.e. skeletally immature patients) for two reasons: 1) these individuals are most often treated by non-operative means due to their better healing potential and 2) the insertion of rigid intramedullary nails has the potential to damage the growth plate resulting in growth arrest and deformity. We are also collecting information on gender and race/ethnicity in our baseline evaluation forms. Reports will detail patients' (males, females, unknown) enrolled in the study by the following categories: American Indian, Asian or

Asian American, Native Hawaiian or Pacific Islander, Hispanic or Latino, Black or African American, White or Caucasian, Other or unknown.

### **Eligibility Review and Central Adjudication Committee**

We will register all patients who meet the inclusion criteria and document reasons for failure to randomize. An independent Central Adjudication Committee (CAC) blinded to allocation, will review the initial radiographs and eligibility forms from all randomized patients to ensure that they met eligibility criteria. Patients will only be ruled ineligible if the grounds for ineligibility were known at the time of randomization. The CAC will include the Study Biostatistician, the Principal Investigator, the Co-Principal Investigator, and two orthopaedic surgeons.

### **Patient Enrollment**

When a patient presents with a proximal tibial metaphyseal fracture he or she will be evaluated for possible enrollment in the study. The inclusion /exclusion criteria on the ***Proximal Tibia Inclusion /Exclusion Criteria Form*** will be reviewed by the treating surgeon. He or she will decide if the patient is appropriate for the study. If the patient is deemed appropriate, meaning that they meet all the inclusion criteria and do not meet any exclusion criteria, the patient will be given the consent form to read and it will be reviewed with the patient with time allowed to answer all questions. If the patient agrees to enter the study he or she will sign the consent form. After consent is signed the surgeon or designee will open a randomized envelope to obtain the procedure (see Patient Randomization for more details). The surgeon or his designee will complete the ***Patient Information Form*** in its entirety. Of great importance will be to obtain two alternate contacts to aid in maintaining access to the patient throughout the course of the study. All other data points on the study form will be completed including specifics regarding the site of injury, the mechanism of injury, the Abbreviated Injury Scores (AIS) and the Injury Study Score (ISS). Additionally, information will be gathered on the patient's prior social history, medication history, and surgical history. Finally, the current medications that the patient is taking will be reviewed and confirmed. Upon completion of this data, the fracture itself will be evaluated.

### **Fracture Evaluation**

The patient's fracture will be evaluated as per the ***Fracture Characteristics Form***. Information to be taken includes whether or not the fracture is open, the size of the wound if it is open, or the Tscherne grade if it is closed and the location of the fracture with respect to specific measurements as outlined on the form. The classification of the fracture, using the Orthopaedic Trauma Association (OTA), classification will be collected. A complete physical exam will be done looking for signs of compartment syndrome as well as the sensation of the superficial and deep peroneal nerve, and the posterior tibia nerve. This will all be documented on the ***Fracture Characteristics Form***. These forms can be completed before or after the patient enters the operating room, but the physical examination of sensation will be done prior to surgery.

### **Patient Randomization**

We have chosen the patient as the unit of randomization. . All participants will be assigned individual study numbers in consecutive order. Participants who agree to be randomized will be randomized in consecutive order through a secure, web-based, randomization system. Each site will be trained and given a unique login and password for randomization. Patients who do not meet study criteria will be saved as a "screen failure". Once logged in, the PI or designee will fill out the inclusion/exclusion form electronically. If the patient is eligible, the PI or designee will be asked for the patients initials, medical record number, and date of consent. **NOTE: patient**

**initials and MR number can only be viewed by the site PI for purposes of identifying this patient in the system. This information will be kept in a secure database and will not be available to the coordinating site (Boston Medical Center) or any of the co-investigator sites. All Patient identifying information will be kept in confidence following HIPAA guidelines and no patient identifying information will appear on any reports. Once this information is entered, the treatment allocation is revealed. Randomization should lead to approximately the same number of such patients in the two groups**

Clinical centers receive complete sets of all data forms prior to joining the study. Each randomization package contains the following data forms: ***Inclusion / Exclusion Criteria Form, Patient Information Form, Fracture Characteristics Form, SF-12v2 Form, EQ-5D Form, Short Musculoskeletal Assessment Form, Surgical Summary Form, Adverse Event Form, Follow-up Clinical Assessment Form*** (for each visit), ***Knee Society Form***. The research coordinator for each participating center ensures that all forms are completed and faxed to Boston Medical Center. The data gathered and the time frame is demonstrated in the attached ***Intervention Design Grid***.

## **Interventions**

### Previous Provisional Stabilization in Splint or with External Fixation

Not all fractures will be internally fixed acutely. In the setting of an open fracture, the fracture may undergo irrigation and debridement and placement of a splint or spanning external fixation for later definitive fixation. This may also be the case in a closed fracture with swelling. In both cases, various factors may influence the timing of definitive fixation including the stability of the patient, the condition of the soft tissue, contamination of any open wounds, availability of the surgeon, etc. We will define the “Fixation Procedure” as that surgery in which definitive fixation of the proximal tibia fracture is performed. The number of previous surgeries (and their purpose) prior to the “Fixation Procedure” will be noted. Details of the “Fixation Procedure” ensue.

### Debridement of Open Wounds:

Open wound size and location will be recorded. After appropriate preparation and draping, the open fracture wound will be treated with debridement of the skin, subcutaneous tissue, and bone. The traumatic wound will be extended, with the extent of the wound also recorded. After debridement, the open wound will be irrigated with at least 6 liters of fluid. A new preparation and draping will be performed prior to the fixation procedure. All personnel will put on new gowns and gloves and new instruments will be used.

### Patient Positioning:

The patient will be positioned supine on a conventional operating table with a radiolucent extension, or on a fracture table adapted for fixation of the tibia. Patients with open fractures should not have their leg placed in traction until after adequate debridement has been accomplished with the leg free. A tourniquet may be used during surgical exposure but should not be used during nailing or reaming of the tibia if a nail is used. If a fracture table is used, then a calcaneal pin and an appropriate table attachment that controls rotation and angulation may be used to ensure exposure for distal locking of the tibia. There must be adequate fluoroscopic visualization in the AP and lateral planes from the tibial plateau to the ankle.

### **Tibial Nailing**

#### Starting Portal:

The osseous starting point for insertion of the nail should be a superolateral portal. Whether a medial arthrotomy, a paratendinous or trans-patellar tendon incision is used will depend on the anatomy of the fracture and the surgeon's preference. If there is flexion deformity at the fracture that corrects with extension of the leg, the nailing may be performed via a partial-medial arthrotomy with the knee in the semi-extended position. The specific approach used will be documented. The desired entry is just medial to the lateral tibial spine on the AP view, and at the anterior margin of the articular surface on the lateral view. This position should be confirmed fluoroscopically with an awl, pin, or k-wire. The length of the skin incision, its location, and the entry portal must all be documented on the ***Surgical Summary Form***.

Intra-articular fracture extension:

If present, nondisplaced intra-articular fracture may be held with reduction clamps, provisionally stabilized with k-wires, and fixed with 2 -3 screws not interfering with the planned position of the nail. This should be done under fluoroscopic control. If any such screws are used, their size and number are recorded on the ***Surgical Summary Form***.

Fracture reduction:

Traction, a femur distractor, bumps/towels, leg positioning, and/or the use of blocking screws may accomplish fracture reduction. If blocking screws are used, their position and whether they were inserted before or after the nail are recorded on the ***Surgical Summary Form***.

Reamed Nail Insertion:

Reaming should be conducted over the guide wire with cannulated power reamers. The choice of reamer is left to the operating surgeon. To avoid inconsistencies in the degree of reaming, surgeons are to adhere to the following protocol: 1) Surgeons will ream the intramedullary canal until the first detection of "cortical chatter" (i.e. the reamer just begins to contact the cortical bone of the tibia), 2) The size of the nail (diameter) will correspond to the point of "cortical chatter" (if chatter occurs with a 9mm reamer, then the nail size will be 9mm). Following the appearance of "cortical chatter", surgeons will ream 1-1.5 mm larger than the chosen nail's diameter to facilitate its insertion. If the canal is capacious, a size 10mm or 11mm nail will be used with reaming 1mm larger than the nail. The chosen nail, which will be as long as possible without distracting the fracture by impinging on dense distal metaphyseal bone or protruding above the cortex at the insertion site, is inserted with the appropriate instruments. The position of the knee during nailing (i.e. flexed or extended) is recorded on the ***Surgical Summary Form***.

Distraction of a tibial shaft fracture interferes with healing, so it must be avoided and all attempts at achieving cortical contact will be employed (up to 10 mm shortening acceptable to achieve contact of fracture ends). The choice of intramedullary nail (i.e. company) and material (titanium or stainless steel) is at the discretion of the operating surgeon. Details regarding the manufacturer, length, diameter, and material of the nail used are recorded on the ***Surgical Summary Form***.

Interlocking Screws:

All fractures should be statically interlocked, both proximally and distally, with a minimum of two screws at both ends of the nail. Proximal locking must have at least two (2) screws that are not parallel. The number of transverse and off-axis proximal and distal screws, as well as whether any screws are locked, are recorded on the ***Surgical Summary Form***. Locked screws are those that pass through threaded holes or are stabilized within the nail by some other method. The duration of surgery and total fluoroscopy time are recorded on the ***Surgical Summary Form***.

## **Tibial Plating**

### Incision:

Plates may be inserted with open or percutaneous methods; the technique, incision length, and type are recorded on the ***Surgical Summary Form***.

### Intra-articular fracture extension:

If present, nondisplaced intra-articular fracture may be used with reduction clamps, provisionally stabilized with k-wires, and repaired with 2 –3 screws. This should be done under fluoroscopic control and their size and number documented on the ***Surgical Summary Form***.

### Fracture reduction:

After any nondisplaced intra-articular fractures are addressed (as above), reduction of the metaphyseal fracture should be accomplished by means of traction or femoral distractor, use of appropriately positioned “bumps” beneath the leg, and judicious use of reduction clamps. The reduction should be evaluated with AP and lateral fluoroscopic views. If acceptable percutaneous reduction cannot be achieved, and open reduction of the fracture becomes necessary, this must be specifically documented on the ***Surgical Summary Form***.

### Plate insertion:

Once provisional fracture reduction is accomplished, a plate of correct length is selected. The specific design of plate used is left to the discretion of the surgeon, but the plate must have angular stable (locking) screws in its upper end. The plate should be long enough to extend at least 4 screw holes beyond the most distal extent of the fracture although longer plates are encouraged.

Through the chosen incision the proximal origins of the anterior tibial musculature is released from the tibia, and a blunt elevator is used to separate the muscle from the lateral face of the tibia distally. The plate is affixed to insertion jig (if one exists) and inserted in a sub-muscular fashion. The fracture should be provisionally reduced during this step.

Fluoroscopy and, at the surgeon’s discretion, a small distal incision are used to center the distal tip of the plate on the bone. Correct cranial – caudal position of the plate on the tibia is assured, and the plate is provisionally fixed to the tibia at both ends. Final reduction of the fracture must be done at this point. If necessary, non-locking reduction screws or temporary pins can be used to “pull” the plate to the bone or to correct minor deviations in alignment. Once this is done, multiple locking screws are inserted into the proximal tibia and locking or non-locking screws into the tibial shaft. Not all of the distal screw holes should be used; every other screw hole filled is the desired configuration of diaphyseal screws. Details of the plate (manufacturer, material, length, number of holes), as well as the number, location, and function (locking or non-locking) of all screws used is recorded on the ***Surgical Summary Form***. The duration of surgery and total fluoroscopy time are also recorded on the ***Surgical Summary Form***. The preoperative and postoperative radiographs will be downloaded to the server and stored for independent evaluation if needed see ***Intervention Design Grid***.

## **Ensuring Standardization of Surgical Techniques**

To ensure that all participating surgeons perform both procedures in a similar manner, a practical technique-oriented session is conducted prior to the commencement of each new center’s enrollment. Experts in both techniques will prepare a video highlighting the critical aspects of

both procedures. The principle investigator at every site is responsible for the educational process as they are experts in both techniques.

### **Bone Grafting**

No primary bone grafting will be performed. Bone grafting may be performed within the first six months of the primary fixation surgery in the setting of an open fracture and bone loss.

Antibiotic beads or spacers may be provisionally placed in such cases. In general, bone grafting in the first six months should be reserved for severe bone loss (which is considered a critical defect), if planned at the time of the initial procedure and recorded on the *Surgical Summary Form*.

### **Fasciotomy**

If fasciotomies are necessary (at the discretion of the surgeon), their location is recorded on the *Surgical Summary Form*.

### **Other surgery**

Including fixation of additional fractures, abdominal procedures or any other surgery is recorded on the *Surgical Summary Form*.

### **Planned secondary re-operations**

Any anticipated secondary procedure(s), such as bone grafting, flap coverage, wound V.A.C. changes, etc. is recorded on the *Surgical Summary Form*.

### **Radiographic Alignment**

Radiographic Evaluation will be done on AP radiograph of the knee and tibia and lateral radiograph of the knee and tibia. A centered line drawn in the middle of the shaft of the tibia will determine varus and valgus and it is intersected with a line parallel with the joint surface of the tibia. Neutral will be considered 0° of angulation. For the lateral view, angulation will be judged based on comparison with the normal side or on angulation visualized at the fracture site based on the cortices that are intact. The amount of varus, valgus, anterior, posterior angulation are recorded. Rotation and leg length discrepancy is determined by clinical examination and also recorded on the *Surgical Summary Form*.

### **Rotational Alignment**

The physical exam will include rotational alignment as compared with the normal leg, by determining the position of the foot to the tubercle in the flexed position, or the thigh-foot angle in the prone position.

### **Peri-operative Treatment Common to Both Groups**

To ensure similar peri-operative regimens, key aspects of pre- and post-operative care have been standardized among participating centers.

### **Postoperative Rehabilitation**

There will be two (2) optional postoperative protocol arms, one with Continuous Passive Motion (CPM) and one without CPM. If CPM is used, it will begin on post-operative day number one and will be initiated with a range of motion of 0-30° and advanced as tolerated, generally 5°-10° shift reaching 90° within the first two weeks. CPM may be discontinued when 90° of flexion is sustained. In the second arm, patients will not receive CPM but will initiate range of motion exercises with a physical therapist while in the hospital. Both groups will be seen by physical therapy as inpatients and will be instructed regarding range of motion exercises. Cold therapy

(ice) will be used as long as the patient has a knee effusion. Patients will not be sent to a physical therapist unless they are unable to achieve 90° of passive flexion and full extension at the time of their six two (2) week follow-up. Isometric exercises will begin immediately and minimal weight (3-5 pounds) resistance exercises may be initiated six (6) weeks following surgery if callus is present on radiographs. Increased resistance exercises may be initiated when full weight bearing is started.

### **Weight Bearing**

All patients will be treated with the same postoperative protocol for mobilization. Immediately after surgery, patients will be allowed foot flat weight bearing. Once callus is seen on x-rays, partial weight bearing will be allowed. Patients will be allowed full weight bearing once bridging callus is seen on two orthogonal radiographic views.

### **Antibiotics**

**In Closed Fractures:** 1) Peri-operative antibiotic administration is continued for 24 hours post-operatively (specific antibiotic regimens at the discretion of the operating surgeon: gram-positive coverage).

**In Open Fractures:** 1) Peri-operative intravenous antibiotic administration will be continued for 72 hours post-operatively (specific antibiotics used at the discretion of the attending surgeon). The recommended guidelines include: intravenous (iv) ancef (or other GM(+) coverage) for Grade I-II injuries, iv Zosyn (or other GM(+) and GM(-) coverage) for Grade III injuries, and iv Zosyn plus penicillin for grossly contaminated injuries. 2) Primary wound closure versus wound V.A.C. at the discretion of the surgeon, 3) For wounds left open, repeat irrigation and debridement of soft tissues and contaminated bone repeated as necessary: usually every 48-72 hours until tissues are clean and all non-viable tissue has been removed. 4) Definitive wound closure by delayed primary closure, split thickness skin grafting, or flaps (for grade IIIB only) should ideally occur by 7 days following the initial surgery. The time from injury to debridement (in hours) and time from injury to definitive fixation (in days), as well as the method of provisional stabilization (if any) is recorded on the ***Surgical Summary Form***.

### **Follow-up Evaluation**

Surgical follow-up visits are outlined on the attached ***Intervention Design Grid***. All outcome forms will be completed at the time indicated on the grid. Radiographs will be obtained as displayed on the ***Intervention Design Grid*** and taken according to standard of care.

### **History:**

The surgeon, at the time of each follow-up visit, will make sure that at some point questions one through three (1-3) on the form are completed. These include the times of definitive surgery, definitive closure, and the type of closure. During each visit the surgeon or designee will enter additional information regarding whether CPM is in use, any further surgical procedures performed and if any complications have occurred. If any complication is recognized an ***Adverse Event Form*** (AE) must be completed. The local Institutional Review Board (IRB) at the patient's medical institution must be made aware of any Serious Adverse Event (SAE).

### **Physical Exam:**

The physical exam will include rotational alignment as compared with the normal leg, by determining the position of the foot to the tubercle in the flexed position, or the thigh-foot angle in the prone position. A clinical leg length evaluation will be measured from the top of the tibial

plateau to the medial malleolus or by block testing. Knee flexion and extension and ankle dorsiflexion and plantar flexion will be measured for active and passive range of motion using a large goniometer and not by subjective evaluation. Sensation will be documented as normal, diminished or absent in the superficial and deep peroneal nerve distributions as well as the tibial nerve distribution. Manual muscle testing of the quadriceps and ankle dorsiflexors will be made using standard muscle strength grading (0-5). Other questions regarding the patient's weight bearing status will be answered as they appear on the form including the amount of weight the patient has been bearing the two weeks prior to the visit and what the recommended weight bearing status and ambulatory support are immediately following the visit. Two pain scales will be completed. These are visual and numerical scales for both the fracture site and for generalized pain. The frequency of pain medication and the type of medication will be documented. The workers compensation status and litigation status will be documented.

### **Assurance of Protocol Adherence**

Given the inherent variability in practice patterns among orthopaedic surgeons, it will be important to ensure that surgeons adhere as closely as possible to the surgical management protocol. The Research Coordinator (RC) reviews all surgical reports and makes periodic checks of charts during the rehabilitation process. If the RC finds apparent protocol violations, the site investigators and the methods center receive photocopies of the relevant information from the charts and, if they confirm the problem, take appropriate action. The site investigator receives a random sample of chart documentation from the RC to review for protocol adherence and take appropriate action if problems are detected. In addition, study forms include documentation of fundamental technical aspects that the study coordinator reviews on all patients and inform the Principal Investigator and site investigator if problems are noted.

### **Contamination and Co-intervention**

In general, crossovers (switching treatment groups) should not occur. However, if this occurs (for example due to unrecognized displacement of an intraarticular fracture, lack of availability of a needed implant) patients will be analyzed in an *intention to treat* manner.

Co-intervention with drugs that alter bone turnover (bisphosphonates, estrogens, and steroids) during the course of the study may act as potential confounders to fracture healing. Moreover, surgical co-intervention, such as a general, neurosurgical or other orthopaedic procedures, may confound outcomes. Standardization of management protocols should limit co-intervention, and we will document the use of drugs that affect the bone, as well as major additional procedures that patients undergo. Additionally, no form of bone stimulator may be used prior to six (6) months after the "fixation procedure".

### **Measurement of Outcome**

Follow up will continue for a period of two (2) years following randomization. Clinical and radiologic assessments will occur at the time of admission to hospital (baseline), postoperatively, 3, 6, 12, and 24months (see grid). Follow up assessment forms will include complications (see ***Adverse Event Form***), subsequent operative procedures and functional status.

### **Outcomes**

#### **Primary Outcome: Functional Outcome**

Patient functional outcome will be assessed by a self-administered questionnaire, which the research coordinator supervises at the preoperative, 3, 6, 12, and 24 month visits. Functional assessment includes a generic health status measurement instrument, the SF-12v2, a generic

utility measure EQ-5D, a disease-specific functional measure targeted to patients with lower extremity fractures (Short Musculoskeletal Functional Assessment, SMFA), and a knee score. All measures have been extensively used and validated.

#### Secondary Outcomes:

The secondary outcomes: Re-operation (secondary procedures), nonunion, superficial infection rates (wound only), deep infection (bone implant interface), compartment syndrome, malunion (>5 degrees varus/valgus, >5 degrees anterior or posterior angulation, >10 malrotation degrees, and >1cm shortening), and knee range of motion.

#### **Statistical Plan**

All continuous variables will be evaluated using a standard two tailed t-test with significance set at 0.05. Dichotomous variables will be evaluated using a chi squared statistic, also set at 0.05. Other evaluations, such as regression analysis of the objective measures in predicting patient based outcome will be performed on the group in total and the comparison group.

#### **Ethics, Safety and Confidentiality**

The patient's physician and the study investigators will share responsibility for patient safety. We will ensure patient confidentiality throughout trial management. The CAC comprised of two orthopaedic surgeons, a statistician and an epidemiologist will have primary responsibility for the monitoring and accumulating of study data for adverse events following treatment. Both surgical techniques (nailing and plating) are currently being used in different centers worldwide. Orthopaedic surgeons, each with their own preference, will generally acknowledge the other technique as a treatment option.

#### **Data Management**

##### Patient Classification and Randomization

We document all patients presenting to participating surgeons with a diagnosed proximal tibial fracture amenable to intramedullary nailing or plating. Such patients are classified as 1) excluded (if they subsequently do not meet the eligibility criteria), 2) missed (due to error), or 3) eligible and randomized. Participating surgeons who identify an eligible patient who consents to randomization will open a randomization envelope in consecutive order.

##### Data Entry

Data collection forms will be collected by a trained research associate from the patient at the clinic or before the patient reaches the clinic as part of hospital admission. Upon completion, the research associate will send the forms to the research coordinator at Boston Medical Center. A report of missing data, implausible data, and inconsistencies will be generated and the research coordinators from each clinical center are contacted by phone to ensure problems are corrected.

##### Completeness of Data Collection

Each center will receive a monthly study status report, showing, for each center, the number of: 1) subjects entered into the trial, 2) completed follow ups, 3) outstanding data clarification requests, and 4) overdue assessments. Centers are identified by numbers to preserve their anonymity. The Data Safety Monitoring Board (DSMB) will meet twice a year to ensure the validity of the data.

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