## ABSTRACT OF RESEARCH PLAN

| INVESTIGATOR NAME/INSTITUTION | PROJECT TITLE |
|---|---|
| **INSTITUTION:**<br>**Western University,**<br>**London Health Sciences Centre, Victoria Hospital** | **A Prospective Randomized Study to Compare Open Reduction, TightRope Fixation and Ligament Repair (AR) versus Open Screw Fixation (OS) of the Tibio - Fibular Syndesmosis.** |

Abstract of research plan: Please provide a 250 word abstract with 5 underlined phrases for project summary, to fit in the box below. Avoid summaries of past accomplishments and the use of the first person. The abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application.

Tibio-fibular syndesmosis injury occurs in a significant proportion of ankle injuries and is assumed to disrupt the syndesmotic ligaments.

The goal of operative treatment is to reduce the ankle mortise to restore normal joint kinematics. Syndesmosis repair can be performed using either open or closed reduction, combined with fixation between the distal tibia and fibula. Closed fixation has demonstrated high rates of non anatomic reductions greater than 40%; therefore, open reduction will be performed in this study. Screw fixation is stable but concerns exist regarding potential excess rigidity.

Recently, flexible fixation techniques combined with anatomic reduction have demonstrated improvements in functional outcomes and reduction quality. Both open reduction and flexible TightRope fixation have considerable support in the literature in cohort studies but have not been compared to open screw fixation in a randomized controlled trial.

Direct repair of the AiTFL may be added to syndesmosis repair. The AiTFL is the initial lateral ligament compromised in syndesmotic injury. Restoration of the AiTFL combined with open reduction provides an anatomic repair and a trend to better functional outcome compared with screw fixation alone in cohort studies.

In this multi centre randomized study, radiographic, economic and functional outcomes are compared between [open reduction, flexible Tightrope syndesmosis fixation and AiTFL repair (AR)] and [open reduction screw fixation (OS)] of the syndesmosis.

We hypothesize that AR will provide improvement in reduction and functional outcome compared to OS. The result of this study will define the future state of the AR in syndesmosis surgery.

## Research Plan

### A) Scientific Aims

The goal of operative treatment is to anatomically reduce the ankle mortise to permit syndesmosis ligament healing and restoration of the normal tibiofibular joint kinematics.

Most current syndesmosis repair techniques include either open or closed reduction, combined with fixation between the distal tibia and fibula. Due to the mechanism of injury, the anterior inferior tibio fibular ligament (AiTFL) is the primary and may be the only lateral ligamentous stabilizing structure compromised in syndesmotic injury (11). We hypothesize that restoration of the AiTFL combined with open reduction and tibio fibular fixation is more likely to provide an anatomic repair and better stabilization, and hence faster return to functioning.

This randomized multi centre study evaluates the quality of reduction reduction and function in patients who have undergone surgical repair of their unstable fracture of the ankle. We will compare radiographic, economic and functional outcomes measures from patients who have had repair of their unstable syndesmosis using either: 1) open anatomic repair with TightRope stabilization of the syndesmosis coupled with AiTFL repair (AR) or 2) open reduction and syndesmosis stabilization by screw only (OS).

The research questions that this study will answer include the following:

1. Does anatomic reduction, AiTFL repair and TightRope syndesmosis stabilization (AR) provide better reduction compared to open reduction and syndesmosis screw stabilization (OS)?

2. Which surgical technique provides better functional outcomes?

3. Are complications and costs associated with repair comparable between surgical techniques?

We hypothesize that AR will provide better reduction and functional outcomes compared to OS. The result of this study will be important to define the future state of syndesmosis surgery.

The scientific aims of this study are to compare:

1. anatomic reduction between the two groups using CT scan and plain radiographs.

2. post-operative pain and functional performance in each group.

3. rates of complication for each method of fixation.

**4.** economic costs for each method of fixation

## B) **BACKGROUND and SIGNIFICANCE**

Syndesmosis injury can occur in isolation or in association with ankle fractures (2). The injury is assumed to disrupt the syndesmotic ligaments, leading to instability (1).

The goal of operative treatment is to anatomically reduce the ankle and to permit syndesmosis ligament healing. Restoration of the normal tibiofibular joint kinematics lessens the risk of posttraumatic arthritis (-7, 14). Even 1 mm of displacement or lateral shift of the talus will alter ankle joint loading, leading to dysfunction and degenerative joint changes (3).

Syndesmosis repair can be performed using either open or closed reduction, combined with fixation between the distal tibia and fibula. Open reduction offers improvements in anatomic reduction rates compared to closed reduction and will be performed in this study. While screw fixation provides stability, concerns exist regarding excessive rigidity (5). More recently, flexible fixation combined with anatomic (open) syndesmosis reduction has demonstrated excellent functional outcomes and rates of anatomic reduction (8, 12, 13, 15, 16).

Clinical studies have shown that anatomic reduction of the posterior inferior tibio fibular ligament (PiTFL) provides a more accurate reduction of the ankle mortise than percutaneous reduction (12), while fixation of the PiTFL has been shown on both biomechanical (9) and clinical studies to provide greater stability than syndesmotic screws alone (11). However, the PiTFL is not always accessible in syndesmosis repair, and PiTFL exposure may lead to greater stiffness.

The anterior inferior tibio fibular ligament (AiTFL) is the first lateral ligamentous stabilizing structure compromised in syndesmotic injury, and is accessible during open reduction. Kinematically, this ligament provides roughly half of the strength of the syndesmosis (11). Most current syndesmosis repair techniques traverse the tibia and fibula but do not anatomically reconstruct the AiTFL.

Recently, we have added direct repair of the AiTFL to open anatomic syndesmosis reduction. We have noted that restoration of the AiTFL combined with open reduction provides an anatomic repair and a trend towards better functional outcome in a cohort study (17, 18).

We believe that this study will enhance the mission of the OTA in promoting excellence in patient care. In light of the existing models of syndesmosis injury, and our understanding of the importance of syndesmosis reduction, this study aims to provide clinical evidence that open reduction, flexible Tightrope fixation and repair of the AiTFL may potentially unlock a higher rate of anatomic reductions and positive outcomes for patients, enhancing their return to function.

## C) Previous work done on project

In this study, determination of syndesmostic stability is determined clinically by use of fluoroscopic external rotation stress examination exam intra operatively. We have completed a study assessing surgeons' ability to diagnose ankle instability in 40 patients (19). In this study, we noted that surgeons were able to diagnose a 1 mm difference in ankle displacement compared to the opposite side uninjured side in all cases using the external rotation stress view. This external rotation stress view will be used to confirm eligibility for enrolment in this study.

Biomechanical studies in our lab using cadaveric ankles compared whether a technique of syndesmosis repair concentrating on open anatomic reduction and restoration of the AiTFL ligament (ART) provides a more anatomic reconstruction of the syndesmosis joint than rigid screw or posterior malleolus fixation (SCREW). The ART and SCREW groups were compared looking for fibular subluxation using pre- and post-operative axial computer tomography. The ART group did not demonstrate a single specimen that was subluxed, while the SCREW group was found to have 33% of specimens tested demonstrating anterior subluxation of the fibula in the post-operative group. A test of the biomechanical strength of each repair technique determined mean torque to failure was higher for the ART group compared to the SCREW group (24.8 ± 5.5Nm (ART) vs. 16.8 ± 5.8Nm (SCREW) p=0.01) (26). These findings have demonstrated that anatomic repair technique (ART) offers a repair which is sufficiently stable compared to screw fixation, with a lower incidence of malreduction as visualized on CT scan.

A cohort study of Weber C ankle fractures with syndesmotic disruption comparing anatomic reduction and repair of the AiTFL with suture anchors (ART) versus closed percutaneous screw only reduction (CS) is currently underway in our facility and will be presented at the 2014 OTA annual meeting in Tampa, Florida. The primary outcome measure was radiographic reduction, as measured on CT scan performed 3 months following the initial surgical procedure. Preliminary results to date indicate that the ART group has shown a reduction in the relative AP distance from 1.09 (+/-0.69) mm to 0.47 (+/- 0.37) mm ($p<0.03$) when compared to standard CS. 73% of CS group had a relative AP difference above 1 mm compared to only 11% of ART group. 9% of CS group had a relative AP difference above 2 mm, compared to none in the ART group (17, 18).

This research suggests that ORIF repair of the AiTFL in addition to the stability provided by syndesmotic screw enhances syndesmosis stability. In other words, fixing the AiTFL may provide a better outcome and faster return to functioning. In addition the anatomic repair technique (ART) lead to a more accurate maintenance of the syndesmosis reduction compared to conventional closed reduction and screw fixation (CS). Because the quality of reduction is known to be an important predictor of functional outcome in longer term analysis, we believe that further study of the ART technique is warranted.

We have extensive experience in randomized controlled trial (RCT) design, participation and conduct. The Principal Investigator (PI) was clinical chair of the FOCUS study, which enrolled over 2000 patients with hip fractures in a RCT comparing thresholds for transfusion. This study was published in the New England Journal of Medicine (23, 24).

The PI was also a co PI in the SPRINT study (25), which enrolled over 1200 patients with tibia fractures. The PI's site had the highest enrolment across all centers.

We have published small RCTs on patient satisfaction after ankle fracture repair (20) and are currently completing a RCT on hip fracture fixation techniques. THE PI won the Bovill award for work on operative versus no operative treatment of ankle fractures, published in Journal of Orthopedic Trauma (22), which also included a formal economic analysis (21).

## C) Method

This study is a multi centre randomized controlled trial comparing clinical, economic and functional outcomes between open reduction, flexible Tightrope syndesmosis fixation coupled with AiTFL repair (AR) to open reduction screw fixation (OS) for syndesmotic injuries in high ankle fractures, involving the fibula 1 cm above the level of the syndesmosis (Weber-C (OTA 44.C)). We anticipate recruiting 50 patients (25 in each arm) from 3 clinical sites across North America. Post operative follow up will occur at 2 and 6 weeks, 3, 6, and 12 months. At each follow up, radiographic and functional outcomes will be assessed as well as documentation of costs associated with treatment and rehab.

**Please note: Protocol has been submitted to our IRB on 25 June 2014 for review scheduled to occur on 08 July 2014. IRB recommendations and investigator notification routinely requires several weeks post review.**

**Patient recruitment**
To be eligible for study inclusion, the patient must meet the following criteria:
1. male or female 18 years of age or greater with a diagnosis of a closed Weber C ankle (OTA 44C) fracture or isolated syndesmotic injury.
2. demonstrates lateral subluxation of the talus on x-ray or stress views (instability)
3. no history of previous severe ankle injury or pathologic fracture, metabolic bone disease or ligamentous laxity .
4. no ipsilateral lower extremity injury.
6. no neuromuscular or sensory deficiency.

At time of fracture diagnosis and prior to surgery, patients meeting the study eligibility above will be approached by a member of their health care team for study participation. The study will be explained to the patient in detail and any questions answered. The patient will be given sufficient time to consider the study until time of surgery. If the patient agrees to participate, the study consent will be signed. A copy will be given to the patient.

**Randomization**
Determination of whether syndesmosis repair is needed, may at times only be made during surgery. Therefore, patients will be consented to the study and randomized to a treatment group prior to surgery (i.e randomize with presumed injury, exclude if stress test indicates syndesmosis is stable.

**Surgical Procedure**
Perform fibular/malleolar fixation as required using standard "AO" techniques. Following fibular and/or malleolar fixation, syndesmosis reduction is performed as per randomization procedure below.

For both operative groups, the following will be performed as necessary:
1) ORIF of the fibula, medial and/or posterior malleolar fracture using standard "AO" techniques.
2) Fluoroscopic stress test of the syndesmosis to determine stability (talar shift of >1 mm or diastasis of > = 5 mm). Those patients that do not demonstrate instability will be withdrawn from the study.
3) If the syndesmosis is unstable, reduction and fixation according to randomization.

**Group 1 (Control- OS group):** Syndesmosis reduction will be by open reduction, clamp stabilization and fixation with at least two 3.5 mm cortical screws applied with tricortical fixation.

**Group 2 (Study: AR Group):** Syndesmosis reduction will be performed under direct visualization allowing for anatomic reduction, AiTFL repair and TightRope stabilization of the syndesmosis.

i) If the AiTFL is repairable, use swivel lock suture anchor (1.5 mm braided suture; 35 mm swivel lock anchor)
ii) If AiTFL unrepairable, use Lateral Brace (Arthrex): 5 mm tibia; 3.5 mm swivel lock anchor, 5 mm labral tape).
iii) Tightrope transyndesmotic repair (knot or knotless as available).

**Post op rehab:** Following surgery, both groups will be treated the same:
1) non weight bearing in plaster slab for 2 weeks.
2) After 2 weeks, non weight bearing in removable boot cast. Low impact range of motion exercises are encouraged.
3) At 6 weeks, weight bearing as tolerated (WBAT) in boot cast. Continue range of motion. Start physio and/or continue with exercises.
4) At 3 months, discontinue boot cast, WBAT, strengthening and range of motion with physiotherapy.

**Assessment of AIM 1 of Study:**
Does anatomic reduction, AiTFL repair with TightRope syndesmosis stabilization (AR) provide better reduction compared to open reduction and syndesmosis screw only stabilization (OS)?

**Clinical outcomes:** At 6 weeks, 3, 6 and 12 months, surgeons will perform a radiographic assessment of fracture reduction. Accuracy of reduction between the two treatment groups will be assessed using bilateral ankle CT scans at 3 months. Axial CT images measured 1 cm above the tibial plafond will be used to compare to contralateral side for each treatment.

**Statistical Analysis**
Two sided T test comparisons will be made between the injured and non injured ankle in both groups. 1 mm of anterior or posterior translation or diastasis of >= 1 mm will be considered a malreduction.

**Assessment of AIM 2 Study:**
Which surgical technique permits better functional outcomes?

**Functional outcomes:** All patients will complete validated self administered functional outcome, pain and quality of life questionnaires at the time of study enrolment and at 6 weeks, 3, 6 and 12 months following enrolment. Questionnaires will include a generic health status measurement instrument (EQ-5D) and a disease specific outcome measure (Foot and Ankle Disability Index (FADI)). The EQ5D is widely used to describe the extent to which patients are having a problem in each of 5 dimensions of health (mobility, ability to self care, usual activities, pain, and anxiety/depression). The FADI is designed to assess functional limitations related to foot and ankle conditions. It captures activities of daily living and more difficult tasks essential to sport activity (FADI Sport).

In addition, the AAOS Hindfoot Score will be completed by the surgeon. This score assesses pain, function, alignment, stability and motion. Patients will be asked if they have returned to work with modified duties etc.

**Statistical Analysis**
Secondary endpoints include the validated patient completed, EQ5D, FADI and the surgeon completed AOFAS Hindfoot Score. Differences in secondary outcome measures will be compared by ANOVA ($P<0.05$) between the two treatment groups.

**Assessment of AIM 3 and 4 of Study:**
Are complications and costs associated with repair comparable between surgical techniques?

**Cost comparison, Work Productivity and Complications**
At each follow up visit (2, 6 weeks, 3, 6 and 12 months), the patient will complete

1) the Work Productivity Impairment Questionnaire: specific Health Problem (WPAI:SHP). This questionnaire captures the patient's ability to perform work duties and activities of daily living.
2) a Cost Diary in which information about costs associated with their treatment/injury( e.g. time off work, medications, equipment, physical therapy) will be recorded.

Complications are secondary outcomes in this study and will be included in the secondary analyses. These include deep infection, superficial wound infection, skin ulceration or breakdown, reflex sympathetic dystrophy or complex regional pain syndromes, cast or brace failure requiring change, loss of reduction not felt to require operative intervention, delayed union (failure of progression of the fracture to heal at 3 months), prominent hardware not requiring removal, and ankle stiffness. The need for reoperation will also be assessed at each visit.

**QALY / Cost utility ratio**
The QALY is a standard measure of health related quality of life in medical cost effectiveness research. The cost of a QALY may be used to compare the cost effectiveness of value of diverse medical treatments. Cost effective treatments have lower costs per QALY. When combined with the cost of providing the intervention, a cost utility ratio can be determined.

Costs will be defined as the sum of facility costs (hospital) plus the surgical professional fee as determined by Ontario Ministry of Health billing guidelines.

QALYs will be determined by multiplying the difference in health related quality of life scores (EQ5D), before and after treatment by life expectancy

**Sample Size:**

Estimated total sample size/number of patients is 60 patients (30 in each treatment arm) calculated using an online calculator:

www.stat.ubc.ca/rollin/stats/ssize/n2.

The primary endpoint is the radiographic measurement of syndesmosis reduction based on CT scans at 3 months postop. This was estimated from:

1) **literature for open reduction** (device group): 0-15% clinical malreduction rate was found (Sagi et al.2012).

Even with an estimated standard deviation of 20 to 25%, the level of confidence ranges from 97 to 100% with the numbers (DSS Research Statistical Power Calculator).

Sagi, H. Claude MD; Shah, Anjan R. MD; Sanders, Roy W. MD. The Functional Consequence of Syndesmotic Joint Malreduction at a Minimum 2-Year Follow-Up. J. Ortho Trauma: 26(7): 439–443. July 2012.

2) **Based on CT scan analysis from a prospective clinical trial comparing open versus closed reduction syndesmotic repair (Haman et al. 2014):**, ""The average difference in ankle translation and diastasis between injured and non-injured ankles was 0.473 +/- 0.38 mm in the AR group (mean +/- stdev), compared with 1.09 +/- 0.69 mm in the CR group ($p<0.03$).

**Secondary outcomes are functional assessments** .

3) **Based on functional outcome measures from a prospective clinical trial comparing open versus closed reduction syndesmotic repair (Haman et al. 2014):** The Maryland Pain subscore showed a statistically significant ($p<0.05$) improvement in the ART group compared to the CR group. Improved outcome scores were noted in the functional outcome measures using the ART technique compared with the CR technique, but did not reach statistical significance with the 29 patients enrolled.

To achieve a statistical significance in the functional outcome assessments, it was determined that 20 patients per group would be required. This was based on the Maryland Total Foot Score at 6 months (Mean ART= 88; Mean CR =79; Combined sigma =10; alpha =0.05; power = 80%, 2 sided test.). Sample sizes per group were adjusted for a 20% loss to follow-up. At 20% loss to follow-up, 25 patients are needed per group for a total of 50 patients. However, given that this study is utilizing open reduction for both arms of the study, we anticipate needing larger patient numbers to show a significance in detection of both functional outcomes and anatomic reduction between the groups. This margin is estimated at an additional 20%. Hence, 60 pateints in total are required (30 in each arm).

Hamam, W., Sanders, D, Tieszer C., Lawendy, A. 2014. A Prospective Study to Compare Open Reduction and Ligament Repair Versus Percutaneous Screw Fixation of the Tibia Fibular Syndesmosis.. (COA Meeting Montreal June 2014).

Each centre participating in the study sees more than 30 patients a year that would meet study eligibility criteria. Therefore, we expect to complete enrollment in 6-12 months. In the event that additional assistance is needed to meet our target deadline, additional sites can be added through the national trauma organization.

Table 1: Chart indicating study procedures at each visit.

| Study Activity | Enrolment (preop) | 6 week | 3 months | 6 months | 12 months |
|---|---|---|---|---|---|
| Inclusion/Exclusion | X | | | | |
| Informed Consent | X | | | | |
| Demographics/Medical History | X | | | | |
| Functional Evaluation Questionnaires/Assessments | X | X | X | X | X |
| Radiography (plain films) as needed | X | X | X | X | X |
| CT scan (bilateral) | | | X | | |

Table 2: Study Timeline.

| Study Milestone | Target Date |
|---|---|
| First patient in | October 2014 |
| Last patient in | April -October 2015 |
| Last patient last visit | April - October 2016 |
| Final data analysis | December 2017 |
| | |

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## APPENDICES

1. Functional Assessments (
    - (Foot and Ankle Disability Index (FADI)
    - AAOS Hindfoot Score
    - Work Productivity Impairment Questionnaire: specific Health Problem (WPAI:SHP).

***Open Tightrope Ligament Repair versus Screw only Syndesmosis Repair for Unstable Ankle Fractures***

Pt Study # _____ Pt Initials: ___ ___ ___

## AOFAS Ankle-Hindfoot Scale

Visit Date: _____/_____/_____ (dd/mmm/yy) □ **6 week** □ **3 month** □ **6 month** □ **12 month**

| | | | | | |
|---|---|---|---|---|---|
| **Pain** (40 points) | None | **40** | **Function Cont'd** | **Gait Abnormality** | |
| | Mild, occasional | **30** | | None, slight | **8** |
| | Moderate, daily | **20** | | Obvious | **4** |
| | Severe, almost always present | **0** | | Marked | **0** |
| **Function** (50 points) | **Activity limitations, support requirement** | | | **Sagittal motion (flexion plus extension)** | |
| | No limitations, no support | **10** | | Normal or mild restriction (30° or more) | **8** |
| | No limitations of daily activities, limitation of recreational activities, cane | **7** | | Moderate restriction (15° -29°) | **4** |
| | Limited daily and recreational activities, cane | **4** | | Severe restriction (< 15°) | **0** |
| | Sever limitation of daily and recreational activities, walker, crutches, wheelchair, brace | **0** | | **Hindfoot motion (inversion plus eversion)** | |
| | **Maximum walking distance, blocks** | | | Normal or mild restriction (75%-100% normal) | **6** |
| | **> 6** | **5** | | Moderate restriction (25%-74% normal) | **3** |
| | **4-6** | **4** | | Marked restriction(<25% normal) | **0** |
| | **1-3** | **2** | | | |
| | **< 1** | **0** | | **Ankle-hindfoot stability (anteroposterior, varus-valgus)** | |
| | | | | Stable | **8** |
| | **Walking surfaces** | | | Definitively unstable | **0** |
| | No difficulty on any surface | **5** | | | |
| | Some difficulty on uneven terrain, stairs, inclines, ladders | **3** | **Alignment** | **Good** (plantigrade foot, ankle-hindfoot well aligned) | **10** |
| | Severe difficulty on uneven terrain, stairs, inclines, ladders | **0** | (10 points) | **Fair** (plantigrade foot, some degree of ankle-hindfoot malalignment observed, no sumptions) | **5** |
| | | | | **Poor** (nonplantigrade foot, severe malalignment, symptoms) | **0** |

**Open Tightrope Ligament Repair versus Screw only Syndesmosis Repair for Unstable Ankle Fractures**

**Work Productivity and Activity Impairment Questionnaire:**
**Specific Health Problem V2.0 (WPAI:SHP)**

**The following questions ask about the effect of your PROBLEM on your ability to work and perform regular activities.** ***Please fill in the blanks or circle a number, as indicated.***

*1.* Are you currently employed (working for pay)? _____ NO ___ YES
*If NO, check "NO" and skip to question 6.*

The next questions are about the **past seven days**, not including today.

*2.* During the past seven days, how many hours did you miss from work because of problems associated with your PROBLEM? *Include hours you missed on sick days, times you went in late, left early, etc., because of your PROBLEM. Do not include time you missed to participate in this study.*

_____ HOURS

During the past seven days, how many hours did you miss from work because of any other reason, such as vacation, holidays, time off to participate in this study?

_____HOURS

During the past seven days, how many hours did you actually work?

_____HOURS *(If "0", skip to question 6.)*

During the past seven days, how much did your PROBLEM affect your productivity while you were working?

*Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If PROBLEM affected your work only a little, choose a low number. Choose a high number if PROBLEM affected your work a great deal.*

Consider only how much PROBLEM affected productivity while you were working.

PROBLEM had _____ PROBLEM

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| no effect on my work | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | completely prevented me from working |

CIRCLE A NUMBER

*6.* During the past seven days, how much did your PROBLEM affect your ability to do your regular daily activities, other than work at a job?

*By regular activities, we mean the usual activities you do, such as work around the house, shopping, childcare, exercising, studying, etc. Think about times you were limited in the amount or kind of activities you could do and times you accomplished less than you would like. If PROBLEM affected your activities only a little, choose a low number. Choose a high number if PROBLEM affected your activities a great deal.*

Consider only how much PROBLEM affected your ability to do your regular daily activities, other than work at a job.

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PROBLEM had no effect on my daily activities | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | PROBLEM completely prevented me from doing my daily activities |

CIRCLE A NUMBER

Open Tightrope Ligament Repair versus Screw only Syndesmosis Repair for Unstable Ankle Fractures:
Pt Study # _____ Pt Initials: ___ ___ ___

**Foot and Ankle Disability Index (FADI) Score and Sports Module**

Visit Date: _____/_____/_____ □ **6 week** □ **3 month** □ **6 month** □ **12 month**

**Please answer every question with one response that most closely describes your condition within the past week. If the activity in question is limited by something other than your foot or ankle, mark N/A.**

| **ACTIVITY** | **No difficulty** | **Slight difficulty** | **Moderate difficulty** | **Extreme difficulty** | **Unable to do** |
|---|---|---|---|---|---|
| Standing | | | | | |
| Walking on even ground | | | | | |
| Walking on even ground without shoes | | | | | |
| Walking up hills | | | | | |
| Walking down hills | | | | | |
| Going up stairs | | | | | |
| Going down stairs | | | | | |
| Walking on uneven ground | | | | | |
| Stepping up and down curves | | | | | |
| Squatting | | | | | |
| Sleeping | | | | | |
| Coming up to your toes | | | | | |
| Walking initially | | | | | |
| Walking 5 minutes or less | | | | | |
| Walking approximately 10 minutes | | | | | |
| Walking 15 minutes or greater | | | | | |
| Home responsibilities | | | | | |
| Activities of daily living | | | | | |
| Personal care | | | | | |
| Light to moderate work (standing, walking) | | | | | |
| Heavy work (push/pulling, climbing, carrying) | | | | | |
| Recreational activities | | | | | |
| | | | | | |
| **PAIN** | **No Pain** | **Mild** | **Moderate** | **Severe** | **Unbearable** |
| General level of pain | | | | | |
| Pain at rest | | | | | |
| Pain during your normal activity | | | | | |
| Pain first thing in the morning | | | | | |

| SPORT ACTIVITY | No difficulty | Slight difficulty | Moderate difficulty | Extreme difficulty | Unable to do |
|---|---|---|---|---|---|
| Running | | | | | |
| Jumping | | | | | |
| Landing | | | | | |
| Squatting and stopping quickly | | | | | |
| Cutting, lateral movements | | | | | |
| Low-impact activities | | | | | |
| Ability to perform activity with your normal technique | | | | | |
| Ability to participate in your desired sport as long as you would like | | | | | |

**Foot and Ankle Disability Index (FADI) Score: _____**

**Foot and Ankle Disability Index (FADI) Score SPORT: _____**

## General Info

FileNo: -1
Title: A Prospective Randomized Multi Center Study to Compare Open Reduction, TightRope Fixation and Ligament Repair (ART) versus Open Screw Fixation (OS) of the Tibio - Fibular Syndesmosis.
Start Date: 01/08/2014
End Date: 01/08/2016
Keywords: screw fixation versus Tightrope and ligament repair of unstable syyndesmosis injuries

## Project Members

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Country:
Comments:

**Others**

| Rank | Last Name | First Name | Affiliation | Role In Project |
|---|---|---|---|---|
| Research Staff | Tieszer | Christina | Schulich School of Medicine and Dentistry\Orthopaedic Surgery | Research Support Staff |
| | Lawendy | Abdel | Schulich School of Medicine and Dentistry\Surgery | Co-Investigator |

## Common Questions

**1. 1. Registration Information**

| # | Question | Answer |
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| | | |
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| 1.1 | Please confirm that you have reviewed the eligibility requirements for the Health Sciences Full Board application form. | Yes |
| 1.2 | Indicate the funding source for this study. | Granting Agency |
| 1.3 | Please specify the name of the funding source selected above. | Arthrex -unrestricted educational grant administered through the Orthopedic Trauma Association |
| 1.4 | Is this a student project? | No |
| 1.5 | Is this a multi-site study? | Yes |
| 1.6 | If YES has been selected in question 1.5 above, name the lead site and project leader for the study. If the study is administered by a Coordinating or Contract Research Organization (CRO) provide the name and contact information. | LHSC, Victoria Hospital/ Western University, London , On Dr. David Sanders 800 Commsissioners Rd London, On N6A4G5 |
| 1.7 | Are the investigator(s) based at any of the sites below or will the study utilize any patient data, staff resources or facilities within any of these sites? (Please indicate all applicable sites and read the associated notes found in the blue information icon above) | LHSC - Victoria Hospital |
| 1.8 | Lay Summary of the study (typically less than 5 lines). | This prospective study evaluates anatomic reduction and function in patients who have undergone surgical repair of their unstable fracture of the ankle. We will compare radiographic, economic and functional outcomes measures from patients who have had repair of their unstable syndesmosis by open reduction and internal fixation (ORIF) and anatomic repair with TightRope stabilization of the syndesmosis coupled with anterior ligament (AiTFL) augmentation repair (ART) to those who have received open reduction and syndesmosis stabilization by screw only (OS). |

**2. 2. Background, Methodology and Analysis**

| # | Question | Answer |
|---|---|---|
| 2.1 | Has the study undergone a formal scientific or peer review (i.e. CIHR, NSERC, NIH)? If yes, please attach the approval letter (or relevant correspondence). | No |
| 2.2 | Outline the study rationale including relevant background information and | The syndesmosis is the space between the two bones (tibia and fibula) in the lower leg above |

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| | justification. Cite references where appropriate. | the ankle joint. It functions to provide stability and give flexibility to the ankle joint. It also provides a site of attachment of a set of ligaments which control ankle motion. Syndesmosis injury can occur in isolation or in association with ankle fractures (16 to 45 % of all ankle fractures patterns) (2). The method of injury is assumed to disrupt the syndesmotic ligaments, leading to instability of the ankle mortise (1). For an unstable syndesmosis, surgery is the standard of care. The goal of operative treatment is to anatomically reduce (realign) the ankle mortise (joint) to permit ligament healing and restoration of the normal tibiofibular joint kinematics in order to lessen the risk of posttraumatic arthritis (10, 11, 12, 13, 21-23). Even 1 mm of displacement or lateral shift of the talus will affect ankle joint loading and lead to dysfunction and potentially degenerative joint changes (8). Syndesmosis repair can be performed using either open or closed reduction, combined with fixation between the distal tibia and fibula. For open reduction, an incision is made over the ankle in order to visibly see the joint and ligaments. Closed percutaneous reduction relies on the use of intraoperative xrays to manipulate the ankle joint before it is fixed in position with screws. While closed screw fixation provides stability, concerns exist regarding excessive rigidity and high rates of non anatomic reductions greater than 40% (11). More recently, flexible fixation techniques combined with anatomic (open) syndesmosis reduction has demonstrated substantial improvements in both functional outcomes and rates of anatomic reduction. Both open reduction and flexible TightRope fixation have considerable support in the literature (14, 21, 22). Clinical studies have shown that anatomic (open) reduction of the posterior ligament (PiTFL) provides a more accurate reduction of the ankle mortise than percutaneous (closed) reduction (21), while fixation of the PiTFL has been shown on both biomechanical (17) and clinical studies to provide greater stability than with syndesmotic screws alone |

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| | | (20). However, due to the mechanism of injury, the anterior ligament (AiTFL) is the first lateral ligamentous stabilizing structure compromised in syndesmotic injury. Kinematically, this ligament provides roughly half of the strength of the syndesmosis (20). Current syndesmosis repair techniques traverse the tibia and fibula (trans syndesmotic repair), but do not anatomically reconstruct the AiTFL. Biomechanical and clinical studies have demonstrated that a flexible trans-bone fixation technique may be viable and may improve ligamentous healing (14-22). We recently conducted biomechanical studies in our lab using cadaveric ankles. We compared whether a technique of syndesmosis repair concentrating on restoration of the AiTFL ligament (Anatomic repair technique or ART) provides a more anatomic reconstruction of the syndesmosis joint than rigid screw or posterior malleolus fixation. Our findings have demonstrated that anatomic repair technique (ART) offers a repair which is sufficiently stable compared to screw fixation, with a lower incidence of malreduction as visualized on CT scan. Our research suggests that ORIF repair of the AiTFL in addition to the stability provided by syndesmotic screw repair enhances syndesmosis stability substantially, as the AiTFL is a primary stabilizer to external rotation forces. In other words, fixing the anterior ligament may provide a better outcome and faster return to functioning. Recently, we have added direct repair of the AiTFL to open anatomic syndesmosis reduction. We have noted that restoration of the AiTFL combined with open reduction provides an anatomic repair and a trend towards better functional outcome in a cohort study (26, 27). We believe that this study will enhance excellence in patient care. In light of the existing models of syndesmosis injury, and our understanding of the importance of syndesmosis reduction, this study aims to provide clinical evidence that open reduction and repair of the AiTFL may potentially unlock a higher rate of anatomic reductions and positive outcomes for patients, enhancing their |

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| | | return to functioning. REFERENCES 1. Harris I.A and Jones H.P. The fate of the syndesmosis in Type C ankle fractures: a cadaveric study. Injury. 28(4), 275-277. 1997. 2. Leeds H.C, Ehrlich M.G. Instability of the distal tibiofibular syndesmosis after bimalleolar and trimalleolar ankle fracture. J Bone Joint Surg (Am). 66(4) :490-503, 1984. 3. Ebraheim, N.A.; Mekhail, A.O.; Gargasz, S.S.: Ankle fractures involving the fibula proximal to the distal tibiofibular syndesmosis. Foot Ankle Int. 18(8):513-21, 1997. 4. Boden SD, Labropoulos PA, McCowin P, et al.: Mechanical considerations for the syndesmosis screw, a cadaver study. J Bone Joint Surg, Am. 71A:1548-1555, 1989. 5. Michelson J.D. Current concepts review: Fractures about the ankle. J Bone Joint Surg. 77A, 142-152, 1995. 6. Solari J., Benjamin J., Wilson J. Lee R., Pitt, M. Ankle mortise stability in Weber C fractures: indications for syndesmotic fixation. J Orthop Trauma 5(20, 190-5, 1991. 7. Yamaguchi, K.; Martin, C.H.; Boden, S.D.; Labropoulos, P.A.: Operative treatment of syndesmotic disruptions without use of a syndesmotic screw: a prospective clinical study. Foot Ankle Int. 15(8):407-14, 1994. 8. Ramsey P.L. and Hamilton W. Changes in tibiotalar area of contact caused by lateral talar shift. J Bone Joint Surg. 58A. 356-357, April 1976 9. Parfenchuck, T.A.; Frix, J.M.; Bertrand, S.L.; Corpe, R.S.: Clinical use of a syndesmosis screw in stage IV pronation-external rotation ankle fractures. Orthopaedic Review. Suppl:23-8, 1994. 10. . Bauer M, Jonsson K, Nilsson B: Thirty-year follow-up of ankle fractures. Acta Orthop. Scand. 56:103-106, 1985. 11. Gardner MJ, Demetrakopouls D, Briggs SM, et al.: Malreduction of the tibiofibular syndesmosis in ankle fractures. Foot Ankle Int. 27:788-792, 2006. 12. Phillips WA, Schwartz HS, Keller CS, et al.: A prospective randomized study of the management of severe ankle fractures. J Bone Joint Surg. 67A:67-78, 1985. 13. Ramsey PL, Hamilton W: Changes in tibiotalar area of contact caused by lateral talar shift. J Bone Joint Surg Am. 58:356-357, 1976. |

14. Coetzee JC, Ebeling P. Treatment of syndesmosis disruptions with TightRope Fixation. Tech Foot Ankle Surg. 7(3):196-202, 2008. 15. Forsythe K, Freedman KB, Stover MD, et al.: Comparison of a novel fiberwire-button construct versus metallic screw fixation in a syndesmosis injury model. Foot Ankle Int. 29(1):51-54, 2008. 16. Soin S, Knight T, Dinah F, et al.: Suture button versus screw fixation in a syndesmosis rupture model: A biomechanical comparison. Foot Ankle Int. 30(4):346-352, 2009. 17. Gardner MJ, Brodsky A, Briggs SM, et al.: Fixation of posterior malleolar fractures provides greater syndesmotic stability. Clin Orthop Rel Res. 447:165-171, 2006. 18. Klitzman R, Zhao H, Zhang LQ, et al.: Suture button versus screw fixation of the syndesmosis: A biomechanical analysis. Foot Ankle Int. 31(1):69-75, 2010. 19. Miller RS, Weinhold PS, Dahners LE. Comparison of tricortical screw fixation versus a modified suture construct for fixation of ankle syndesmosis injury: A biomechanical study. J Orthop Trauma. 13(1):39-42, 1999. 20. Ogilvie-Harris DJ, Reed SM, Hedman TP: Disruption of the ankle syndesmosis: Biomechanical study of the ligamentous restraints. Arthroscopy. 10(5):558-560. 21. Miller, A., Carroll, E et al. Direct visualization for syndesmotic stabilization of ankle fractures. Foot & Ankle Int. Vol 30. No. 5/May 2009: 419-426. 22. . Pelton, k, Thordarson, d , Barnwell, j. Open versus closed Treatment of the Fibula in Maissoneuve Injuries. Foot & Ankle Int. Vol 31. No. 7/July2012604-608. 23. Miller, A., Carroll, E et al. Posterior Malleolar Stabilization of Syndesmotic Injuries is Equivalent to Screw Fixation. Clin. Orthop Rel Res. 2010, 468: 1129-1135. 24. David Sanders, MD, A. Walid Hamam, MD, Christina Tieszer, CCRP, Abdel Lawendy, MD. A Prospective Study to Compare Open Reduction and Ligament Repair Versus Percutaneous Screw Fixation of the Tibia Fibular Syndesmosis.. Abstract # 138. COA Meeting Montreal June 2014. 25. David Sanders, MD, A. Walid Hamam, MD, Christina

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| | | Tieszer, CCRP, Abdel Lawendy, MD. A Prospective Study to Compare Open Reduction and Ligament Repair Versus Percutaneous Screw Fixation of the Tibia Fibular Syndesmosis. Abstract # 6588. OTA Meeting Tampa October 2014. |
| 2.3 | Study Objectives. | This multi centre randomized study evaluates accuracy of the reduction and function in patients who have undergone surgical repair of their unstable fracture of the ankle. We will compare radiographic, economic and functional outcomes measures from patients who have had repair of their unstable syndesmosis by open reduction and internal fixation (ORIF) and anatomic repair with TightRope stabilization of the syndesmosis coupled with anterior ligament (AiTFL) augmentation repair (AR) to those who have received open reduction and syndesmosis stabilization by screw only (OS). The research questions that this study will answer include the following: 1. Does anatomic reduction, AiTFL repair with TightRope syndesmosis stabilization (AR) provide better reduction compared to open reduction and syndesmosis screw only stabilization (OS)? 2. Which surgical technique provides better functional outcomes? 3. Are complications and costs associated with repair comparable between surgical techniques? We hypothesize that AR will provide better reduction and functional outcomes compared to OS. The result of this study will be important to define the future state of AR in syndesmosis surgery. The scientific aims of this study are to compare: 1. anatomic reduction between the two groups using CT scan and plain radiographs. 2. post-operative pain and functional performance in each group. 3. rates of complication for each method of fixation. |
| 2.4 | Describe the study design and methodology. Please be specific (e.g. Randomized, cohort, double blind). | This study is a multi centre randomized controlled trial comparing clinical, economic and functional outcomes between open reduction, flexible Tightrope syndesmosis fixation coupled with anterior ligament (AiTFL) repair (AR) to open reduction screw fixation (OS) for syndesmotic injuries in high ankle fractures, involving the fibula 1 cm above the |

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| | | level of the syndesmosis (Weber-C (OTA 44.C)). We anticipate recruiting 60 patients (30 in each arm) from 3 clinical sites across North America. Post operative follow up will occur at 2 and 6 weeks, 3, 6, and 12 months. At each follow up, radiographic and functional outcomes will be assessed as well as documentation of costs associated with treatment and rehab. Patient recruitment At time of fracture diagnosis and prior to surgery, patients meeting the study eligibility above will be approached by a member of their health care team for study participation. The study will be explained to the patient in detail and any questions answered. The patient will be given sufficient time to consider the study until time of surgery. If the patient agrees to participate, the study consent will be signed. A copy will be given to the patient. Randomization Determination of whether syndesmosis repair is needed, may at times only be made during surgery. Therefore, patients will be consented to the study and randomized to a treatment group prior to surgery (i.e randomize with presumed injury, exclude if stress test indicates syndesmosis is stable (< 5mm diastasis). Surgical Procedure Perform fibular/malleolar fixation as required using standard "AO" techniques. Following fibular and/or malleolar fixation, syndesmosis reduction is performed as per randomization procedure below. For both operative groups, the following will be performed as necessary: 1) ORIF of the fibular, medial or posterior malleolar fracture using standard "AO" techniques. 2) Fluoroscopic stress test of the syndesmosis to determine stability (talar shift of >1 mm or diastasis of > = 5 mm). Those patients that do not demonstrate instability will be withdrawn from the study. 3) If the syndesmosis is unstable, reduction and fixation according to randomization. Group 1 (Control- OS group): Syndesmosis reduction will be by open reduction followed by stabilization with at least two 3.5 mm cortical screws in tricortical fixation. Group 2 (Study: AR Group): Syndesmosis reduction will be performed under |

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| | | direct visualization allowing for anatomic reduction, AiTFL repair and TightRope stabilization of the syndesmosis. i) If the AiTFL is repairable, use swivel lock suture anchor (1.5 mm lateral; 3.5 mm swivel lock anchor) ii) If AiTFL unrepairable, use Lateral Brace (Arthrex): 5 mm tibia; 3.5 mm swivel lock anchor, 5 mm lateral tape.) iii) Tightrope transyndesmotic repair (knot or knotless as available). Post op rehab: Following surgery, both groups will be treated the same: 1) non weight bearing in plaster slab for 2 weeks. 2) After 2 weeks, non weight bearing in removable boot cast. Non impact range of motion exercises are encouraged. 3) At 6 weeks, weight bearing as tolerated (WBAT) in boot cast. Continue range of motion. Start physio and/or continue with exercises. 4) At 3 months, discontinue boot cast, WBAT, strengthening and range of motion with physiotherapy. Assessment of AIM 1 of Study: Does anatomic reduction, AiTFL repair with TightRope syndesmosis stabilization (AR) provide better reduction compared to open reduction and syndesmosis screw only stabilization (OS)? Clinical outcomes: At 6 weeks, 3, 6 and 12 months, surgeons will perform a radiographic assessment of fracture reduction. Accuracy of reduction between the two treatment groups will be assessed using bilateral ankle CT scans at 3 months. Axial CT images measured 1 cm above the tibial plafond will be used to compare to contralateral side for each treatment. Statistical Analysis Two sided T test comparisons will be made between the injured and non injured ankle in both groups. 1 mm of anterior or posterior translation or increase of diastasis of 1 mm will be considered a malreduction. Assessment of AIM 2 Study: Which surgical technique permits better functional outcomes? Functional outcomes: All patients will complete validated self administered functional outcome, pain and quality of life questionnaires at the time of study enrolment and at 6 weeks, 3, 6 and 12 months following enrolment. Questionnaires will include a generic health status measurement |

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| | | instrument (EQ-5D) and a disease specific outcome measure (Foot and Ankle Disability Index (FADI)). The EQ5D is widely used to describe the extent to which patients are having a problem in each of 5 dimensions of health (mobility, ability to self care, usual activities, pain, and anxiety/depression). The FADI is designed to assess functional limitations related to foot and ankle conditions. It captures activities of daily living and more difficult tasks essential to sport activity (FADI Sport). In addition, the AAOS Hindfoot Score will be completed by the surgeon. This score assesses pain, function, alignment, stability and motion. Patients will be asked if they have returned to work with modified duties. Statistical Analysis Secondary endpoints include the validated patient completed, EQ5D, FADI and the surgeon completed AOFAS Hindfoot Score. Differences in secondary outcome measures will be compared by ANOVA ($P<0.05$) between the two treatment groups. Assessment of AIM 3 of Study: Are complications and costs associated with repair comparable between surgical techniques? Cost comparison, Work Productivity and Complications At each follow up visit (2, 6 weeks, 3, 6 and 12 months), the patient will complete 1) the Work Productivity Impairment Questionnaire: specific Health Problem (WPAI:SHP). This questionnaire captures the patient's ability to perform work duties and activities of daily living. 2) a Cost Diary in which information about costs associated with their treatment/injury( e.g. time off work, medications, equipment, physical therapy) will be recorded. Complications are secondary outcomes in this study and will be included in the secondary analyses. Deep infection, superficial wound infection, skin ulceration or breakdown, reflex sympathetic dystrophy or complex regional pain syndromes, cast or brace failure requiring change, loss of reduction not felt to require operative intervention, delayed union (failure of progression of the fracture to heal at 3 months), prominent hardware not requiring removal, and |

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| | | ankle stiffness. The need for reoperation will also be assessed at each visit. QALY / Cost utility ratio The QALY is a standard measure of health related quality of life in medical cost effectiveness research. The cost of a QALY may be used to compare the cost effectiveness of value of diverse medical treatments. Cost effective treatments have lower costs per QALY. When combined with the cost of providing the intervention, a cost utility ratio can be determined. Costs will be defined as the sum of facility costs (hospital) plus the surgical professional fee as determined by Ontario Ministry of Health billing guidelines. QALYs will be determined by multiplying the difference in health related quality of life scores (EQ5D), before and after treatment by life expectancy . |
| 2.5 | Indicate the inclusion criteria. | 1. male or female 18 years of age or greater with a diagnosis of a closed Weber C ankle (OTA 44C) fracture or isolated syndesmotic injury. 2. demonstrates lateral subluxation of the talus on x-ray or stress views (instability) 3. no history of previous severe ankle injury or pathologic fracture, metabolic bone disease or ligamentous laxity . 4. no ipsilateral lower extremity injury. 6. no neuromuscular or sensory deficiency. |
| 2.6 | Indicate the exclusion criteria. | 1. pathologic fracture 2. history of previous severe ankle injury and/or retained hardware. 3. ipsilateral lower extremity injury that would impede results. 4. neuromuscular or neurosensory deficiency that would limit the ability to assess the operative procedure. |
| 2.7 | Document the usual standard of care at the trial site(s) for this population (including diagnostic testing, frequency of follow up visits). | Standard of care includes xrays and an external rotation stress test to assess stability of the fracture. Unstable syndesmosis injuries can be treated by using a long lateral incision with anatomic reduction of the fibula fracture with osteosynthesis using a plate and several screws for the fixation (open reduction and internal fixation) if required. Syndesmosis stabilization can be done using one or two rigid syndesmosis screws inserted to maintain the relationship of the fibula to the tibia or through the use of a flexible syndesmosis stabilization system, using fiber wire (ARTHREX Tightrope) .<br>Ligamentous repair may be carried out if badly |

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| | | ruptured. Follow up visits are scheduled to occur at 2 and 6 weeks, 3, 6 and 12 months depending on the progress of fracture healing and complications. These visits include xrays and a physical assessment of range of motion, stability and pain. |
| 2.8 | Document the study procedures and any study specific testing that will be done. | Undergoing the consent process, randomization to study treatment and completion of quality of life questionnaires are not part of routine care. Study specific assessment includes the completion of questionnaires on return to functioning and pain as well as completion of a Cost/Expense Diary . Study visits are designed to coincide with routine care for this type of fracture. No extra visits are necessary. In the event that a patient misses a clinic visit, the questionnaire will be mailed. Patients do not have to answer any questions or complete any assessments that they find disturbing. |
| 2.9 | Will any participant(s) be withdrawn from or denied usual therapy, or be subjected to other restrictions for any condition in order to participate in the study? | No |
| 2.10 | If YES has been selected in question 2.9 above, please explain. | |
| 2.11 | Describe the primary and secondary outcomes of this study and how they will be measured. | Assessment of AIM 1 of Study: 1. Does the anatomic repair technique (AR) provide better reduction compared to closed syndesmosis stabilzation (CR) only in unstable syndesmosis injuries?. Clinical outcomes: At each follow up visit (6 weeks, 3, 6 and 12 months), surgeons will perform a radiographic assessment of fracture reduction maintenance, degree of cortical bridging, measurement of medial and tibiofibular clear space and a clinical assessment for pain, weight bearing, gait examination, range of motion, complications and union. Union in this study is defined as radiographic appearance of bridging callus on 3 of 4 cortices. Accuracy of reduction between the two groups will be assessed using bilateral ankle CT scans taken prior to mobilization/weight bearing (2-6 weeks) and after fracture healing and mobilization (3 months). Assessment of AIM 2 Study: 2. Which surgical technique permits better functional outcomes, lower rates of |

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| | | complications and faster return of patients to work and activities? Functional outcomes: All patients will complete validated self administered functional outcome, pain and quality of life questionnaires at the time of study enrolment and at 6 weeks, 3, 6 and 12 months following enrolment. Questionnaires will include a generic health status measurement instrument (EQ-5D) and a disease specific outcome measure (Foot and Ankle disability Index (FADI)). The EQ5D is widely used to describe the extent to which patients are having a problem in each of 5 dimensions of health (mobility, ability to self care, usual activities, pain, and anxiety/depression). The FADI is designed to assess functional limitations related to foot and ankle conditions. It assesses activities of daily living and more difficult tasks essential to sport activity (FADI Sport). In addition, the AAOS Hindfoot Score will be completed by the surgeon. This Score assesses pain, function, alignment, stability and motion. Complications and events are secondary outcomes in this study and will be included in the secondary analyses. Re-operations will be assessed at each follow-up visit. Surgical procedures that will be documented include surgery to treat deep infection, improve a failed reduction or malunion, bone grafting, implant removal to treat infection or irritation, ankle arthroscopy, ankle debridement, ankle manipulation, tendon lengthening and releases, ankle arthrodesis or replacement. Complications that do not require reoperation, will also be documented. These include superficial wound infection, skin ulceration or breakdown, reflex sympathetic dystrophy or complex regional pain syndromes, cast or brace failure requiring change, loss of reduction not felt to require operative intervention, delayed union (failure of progression of the fracture to heal at 3 months), prominent hardware not requiring removal, and ankle stiffness. Assessment of AIM 3 of Study: 3. Are costs associated with repair and return to functioning comparable between surgical techniques? Cost comparison, and Work |

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| | | Productivity At each follow up visit (2, 6 weeks, 3, 6 and 12 months), the patient will complete 1) the Work Productivity Impairment Questionnaire: specific Health Problem (WPAI:SHP). This questionnaire captures the patient's ability to perform work duties and activities of daily living. 2) a Cost Diary in which information about costs associated with their treatment/injury( e.g. time off work, medications, equipment, physical therapy) will be recorded. QALY / Cost utility ratio The QALY is a standard measure of health related quality of life in medical cost effectiveness research. The cost of a QALY may be used to compare the cost effectiveness of value of diverse medical treatments. Cost effective treatments have lower costs per QALY. When combined with the cost of providing the intervention, a cost utility ratio can be determined. Costs will be defined as the sum of facility costs (hospital) plus the surgical professional fee as determined by MOH billing guidelines. QALYs will be determined by multiplying the difference in health related quality of life scores (EQ5D), before and after treatment by life expectancy. |
| 2.12 | What is the local sample size? | up to 60 |
| 2.13 | What is the total sample size? | 60 |
| 2.14 | Is the sample size justified in the sponsor or other study protocol? | No |
| 2.15 | If YES in question 2.14 above, indicate the protocol page number. If NO, provide sample size justification. | Sample Size: Estimated total sample size/number of patients is 40 (20 in each treatment arm) to reach statistical significance. Sample size was determined from literature based on estimated clinical syndesmosis malreduction rates for open reductions as follows: 1) Open reduction (device group): 0-15% clinical malreduction rate was found (Sagi et al.2012) Even with an estimated standard deviation of 20 to 25%, the level of confidence ranges from 97 to 100% with the numbers (DSS Research Statistical Power Calculator). However, with an estimated loss to follow up of 20% (common amongst orthopedic patients with ankle fractures) and estimated 20 % that do not qualify for the study during operative |

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|---|---|---|
| | | assessment, we will need to enroll and treat up to 60 patients ( 30 per treatment group). Gardner MJ, Brodsky A, Briggs SM, et al.: Fixation of posterior malleolar fractures provides greater syndesmotic stability. Clin Orthop Rel Res. 447:165-171, 2006. Sagi, H. Claude MD; Shah, Anjan R. MD; Sanders, Roy W. MD. The Functional Consequence of Syndesmotic Joint Malreduction at a Minimum 2-Year Follow-Up. J. Ortho Trauma: 26(7): 439–443. July 2012. |
| 2.16 | Describe the method(s) for data analysis. | The primary endpoint is the radiographic measurement of syndesmosis reduction based on CT scans at 3 months postop. Two sided T test comparisons will be made between the injured and non injured ankle in both groups. 1 mm of anterior or posterior translation or increase of diastasis of 1 mm will be considered a malreduction. Secondary endpoints include the validated patient completed, EQ5D, FADI and the surgeon completed AOFAS Hindfoot Score. Differences in secondary outcome measures will be compared by ANOVA ($P<0.05$) between the two treatment groups. The QALY is a standard measure of health related quality of life in medical cost effectiveness research. The cost of a QALY may be used to compare the cost effectiveness of value of diverse medical treatments. Cost effective treatments have lower costs per QALY. When combined with the cost of providing the intervention, a cost utility ratio can be determined. Costs will be defined as the sum of facility costs (hospital) plus the surgical professional fee as determined by Ontario Ministry of Health billing guidelines. QALYs will be determined by multiplying the difference in health related quality of life scores (EQ5D), before and after treatment by life expectancy |
| 2.17 | Is an interim analysis planned? | No |
| 2.18 | If YES to question 2.17 above, please describe. | No official interim analysis is planned. However, if it is noted during data review that one group appears to have better outcomes or if there a more or fewer adverse events, the data will be reviewed. An interim statistical analysis from the functional outcome questionnaires and radiology results will be made. |
| 2.19 | How will the results of this study be made | Peer reviewed publication\|Presentation |

| | | |
|---|---|---|
| | public? | |
| 2.20 | If report to participants or other is selected above, please explain. | |
| 2.21 | Does this study include any use of deliberate deception or withholding of key information that may influence a participant's performance or response? | No |
| 2.22 | If YES in question 2.21 above, describe this process and provide justification for the planned deception or partial disclosure. Also describe how and when the participants will be debriefed. Please include the debriefing letter of information and consent. | |
| 2.23 | Are biological specimens to be taken or analyzed for the purposes of this research protocol? | No |
| 2.24 | Are any biological specimens being taken for future genetic testing or other unspecified testing or studies? | No |
| 2.25 | The subsequent use of tissue or biomaterials (except blood) originally collected for diagnostic purposes must be approved by the Department of Pathology Tissue Use Committee prior to submission to the HSREB and a copy of their approval appended to this form. If the Tissue Committee approval is not available at the time of submission to the HSREB, ethics approval will be withheld until a copy of Tissue Committee approval is received. | Not applicable |

**3. 3. Drugs and Natural Products**

| # | Question | Answer |
|---|---|---|
| 3.1 | Does the study involve drugs or natural products? If NO, please proceed to the Clinic Trials tab. | No |
| 3.2 | Is Drug 1 an investigational drug? | |
| 3.3 | Drug 1 - Generic Name | |
| 3.4 | Drug 1 - Brand Name | |
| 3.5 | Drug 1 - Dose | |
| 3.6 | Drug 1 - Frequency | |
| 3.7 | Drug 1 - Route | |

| | | |
|---|---|---|
| 3.8 | Drug 1 - Duration | |
| 3.9 | Is Drug 2 an investigational drug? | |
| 3.10 | Drug 2 - Generic Name | |
| 3.11 | Drug 2 - Brand Name | |
| 3.12 | Drug 2 - Dose | |
| 3.13 | Drug 2 - Frequency | |
| 3.14 | Dose 2 - Route | |
| 3.15 | Drug 2 - Duration | |
| 3.16 | Is Drug 3 an investigational drug? | |
| 3.17 | Drug 3 - Generic Name | |
| 3.18 | Drug 3 - Brand Name | |
| 3.19 | Drug 3 - Dose | |
| 3.20 | Drug 3 - Frequency | |
| 3.21 | Drug 3 - Route | |
| 3.22 | Drug 3 - Duration | |
| 3.23 | Is Drug 4 an investigational drug? | |
| 3.24 | Drug 4 - Generic Name | |
| 3.25 | Drug 4 - Brand Name | |
| 3.26 | Drug 4 - Dose | |
| 3.27 | Drug 4 - Frequency | |
| 3.28 | Drug 4 - Route | |
| 3.29 | Drug 4 - Duration | |
| 3.30 | Is Drug 5 an investigational drug? | |
| 3.31 | Drug 5 - Generic Name | |
| 3.32 | Drug 5 - Brand Name | |
| 3.33 | Drug 5 - Dose | |
| 3.34 | Drug 5 - Frequency | |
| 3.35 | Drug 5 - Route | |
| 3.36 | Drug 5 - Duration | |
| 3.37 | Is Drug 6 an investigational drug? | |
| 3.38 | Drug 6 - Generic Name | |
| 3.39 | Drug 6 - Brand Name | |
| 3.40 | Drug 6 - Dose | |
| 3.41 | Drug 6 - Frequency | |
| 3.42 | Drug 6 - Route | |
| 3.43 | Drug 6 - Duration | |
| 3.44 | Is Drug 7 an investigational drug? | |
| 3.45 | Drug 7 - Generic Name | |
| 3.46 | Drug 7 - Brand Name | |
| 3.47 | Drug 7 - Dose | |

| | | |
|---|---|---|
| 3.48 | Drug 7 - Frequency | |
| 3.49 | Drug 7 - Route | |
| 3.50 | Drug 7 - Duration | |
| 3.51 | Is Drug 8 an investigational drug? | |
| 3.52 | Drug 8 - Generic Name | |
| 3.53 | Drug 8 - Brand Name | |
| 3.54 | Drug 8 - Dose | |
| 3.55 | Drug 8 - Frequency | |
| 3.56 | Drug 8 - Route | |
| 3.57 | Drug 8 - Duration | |
| 3.58 | Is Drug 9 an investigational drug? | |
| 3.59 | Drug 9 - Generic Name | |
| 3.60 | Drug 9 - Brand Name | |
| 3.61 | Drug 9 - Dose | |
| 3.62 | Drug 9 - Frequency | |
| 3.63 | Drug 9 - Frequency | |
| 3.64 | Drug 9 - Route | |
| 3.65 | Drug 9 - Duration | |
| 3.66 | Is Drug 10 an investigational drug? | |
| 3.67 | Drug 10 - Generic Name | |
| 3.68 | Drug 10 - Brand Name | |
| 3.69 | Drug 10 - Dose | |
| 3.70 | Drug 10 - Frequency | |
| 3.71 | Drug 10 - Route | |
| 3.72 | Drug 10 - Duration | |

**4. 4. Clinical Trials**

| # | Question | Answer |
|---|---|---|
| 4.1 | Is this a clinical trial? If this is NOT a clinical trial, please select NO and proceed to the Risks and Benefits section. | Yes |
| 4.2 | Proposed type of clinical trial: | Phase 4 |
| 4.3 | Does this trial involve a drug, device or natural health product used for an indication outside the Health Canada Notice of Compliance (NOC) or Drug Identification Number (DIN) application or Medical Device License? | No |
| 4.4 | If YES to question 4.3 above, have you received a No Objection Letter (NOL) or comparable document from Health | |

| | | |
|---|---|---|
| | Canada? | |
| 4.5 | Is this a US Food and Drug Administration monitored study? | No |
| 4.6 | Has this study been or will this study be registered on a publicly accessible clinical trial registry? | Yes |
| 4.7 | If YES is specified in question 4.6 above, please indicate the registry name and registration number. | clinical trial.gov |
| 4.8 | Is there a data safety monitoring board (DSMB)? If YES, please note that you must submit the Data Safety Monitoring Committee report(s) to the Office of Research Ethics using Form 2-F-014. | No |
| 4.9 | If there is a DSMB, is it independent of the sponsor? | |
| 4.10 | If NO in question 4.9 above, please provide justification. | |
| 4.11 | Has the drug or other therapy been evaluated in previous human trials? | Not applicable |
| 4.12 | If NO in question 4.11 above, please describe any animal studies that have led to this study. (Cite references where applicable) | |
| 4.13 | Will this trial use a placebo or active comparator? | No |
| 4.14 | If YES in question 4.13 above, please describe the placebo or active comparator and justify its inclusion. Also, please describe how the risks to participants will be minimized. | |

**5. 5. Risks and Benefits**

| # | Question | Answer |
|---|---|---|
| 5.1 | Describe any direct benefits to the study participants. | No direct benefits can be guaranteed. However, patients are given extra attention and closer monitoring than standard of care with additional self assessments as to performance and pain. Patients also are provided extra information on outcomes and what to expect which may alleviate any anxiety. |
| 5.2 | Describe the potential benefits to society. | There are no immediate benefits to society as a result of participating in this study, but this |

| | | |
|---|---|---|
| | | research may provide information for future treatment of people with this specific type of ankle fracture. |
| 5.3 | List and describe the potential risks/harms/inconveniences of the study, including risks from radiation exposure. This information must be included in the informed consent documentation. | Radiographs will be performed according to standard care procedures, therefore, no additional risk related to x-ray exposure is associated due to study participation. A CT scan will be conducted after 3 months to assess alignment and stability as per standard of care. There are general risks related to having surgery, which are not changed or increased by participation in this study. Some of these risks are: infection; problems with wound healing; the plate used to hold the pieces of the bone together could break or loosen; and sometimes the bone does not heal and further surgeries are needed. These risks are discussed with patients in detail when the standard consent for the surgery is being obtained. The construct used to repair the ligaments may fail. The interviews and questionnaires received during the course of the study may be upsetting or distressing. Patients are not required to answer those questions found to be distressing. |
| 5.4 | For the study risks listed above, describe the monitoring to be undertaken during and following the study conclusion. | Clinical follow up will occur at 2 and 6 weeks, 3, 6 and 12 months following surgery. At each clinic visit , xrays will be conducted as well as a clinical exam to assess fracture healing, range of motion, and stability of the repair. Patients will be asked about their return to activities of daily living, recreational/sport activities and work duties. Any concerns/problems will be documented and followed up with at the next clinic visit. If the pateint is no longer equired to come to clinic (e.g. fracture has healed and pateint has returned to activities), a follow up telephone call will be made. Any questionnaires will be mailed or completed over the phone as time permits. |
| 5.5 | If a research participant is/or becomes pregnant, breastfeeds a child or fathers a child while in the study, does their participation in the study pose a possible risk to the fetus or child? | No |
| 5.6 | If YES is selected in question 5.5 above, please discuss these risks and indicate what | |

| | | |
|---|---|---|
| | monitoring will be undertaken during the study and following the study conclusion? | |
| 5.7 | If a research participant fathers a child while in the study, will access to the health records of the "pregnant" partner and/or her child be required and/or will the woman or child be monitored by this study during and/or after the pregnancy? | No |

**6. 6. Recruitment and Informed Consent**

| # | Question | Answer |
|---|---|---|
| 6.1 | Describe the method(s) for recruiting participants. | Investigators will approach their own patients/students |
| 6.2 | If OTHER or DATABASE OF PEOPLE is selected in question 6.1 above, please specify here. | |
| 6.3 | Will personal health information (PHI) be used to identify potential participants? | Yes |
| 6.4 | If PHI will be used, please describe the screening and consent process regarding PHI. | Personal health information such as PIN, full name, will be used to identify patients as per standard hospital procedure. Lists are kept of patients requiring treatment in order to book the operating room time. Patient lists and information will be kept confidential as per hospital policy and is only accessible to members of the health care team. Consenting for surigcal procedure and study inclusion will be done in as confidential an environment as possible. This may include an examining room. The subject will be informed that his/her medical records may be reviewed by members of the study team or representatives of the Health Sciences Ethics Board for study auditing purposes or as required by law. The subject will be told that confidentiality of his/her medical information will be maintained at all times. Publications will not identify subjects; case report forms do not contain their names and conditions under which records will be made available (under federal requirements) to the sponsoring company and regulatory authorities are disclosed in the Letter of Information. |
| 6.5 | How will potential participants be contacted? Please provide a copy of all | In Person |

| | | |
|---|---|---|
| | telephone scripts and correspondence documents in the attachments tab. | |
| 6.6 | If OTHER is selected in question 6.5 above, please specify in this box. | |
| 6.7 | Describe the process for obtaining informed consent. Please attach a copy of the Information Letter/Consent Form, Audio/Video Recording Consent Form, and the content of any telephone script and/or any other material that will be used in the informed consent process. | The PI, and orthopaedic residents are involved in identifying these potential subjects as members of the patient's health care team. The inclusion /exclusion criteria will be reviewed by the PI or designee. He or she will decide if the patient is appropriate for the study. If the patient meets all the inclusion criteria and does not meet any exclusion criteria, then the study protocol is reviewed in detail in a face-to-face meeting between the PI or designee and patient/individual responsible for care. 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. The patient will receive a copy of the letter of information. |
| 6.8 | Indicate if the research will involve any of the following: | Patients |
| 6.9 | Will minors or persons not able to consent for themselves be included in the study? | No |
| 6.10 | If YES is selected in question 6.9 above, describe the consent process and indicate who will be asked to consent on their behalf and discuss what safeguards will be employed to ensure the rights of the research participant are protected. | not applicable |
| 6.11 | When the inability to provide an informed consent is expected to be temporary, describe what procedures will be used to regularly assess capacity and to obtain consent if the individual later becomes capable of providing consent. Alternatively, if diminished capacity is anticipated for the study population, describe the procedure used to assess capacity and obtain ongoing consent. | not applicable |
| 6.12 | List any anticipated communication difficulties: | None |
| 6.13 | Describe the procedures to address any communication difficulties (if applicable): | not applicable |

| | | |
|---|---|---|
| 6.14 | Indicate what compensation, if any, will be provided to participants and include a justification for compensation. | not applicable |

**7. 7. Confidentiality and Data Security**

| # | Question | Answer |
|---|---|---|
| 7.1 | Are you collecting personal identifiers for this study? | Yes |
| 7.2 | Identify any personal identifiers collected for this study. Select all that apply. | Full name\|Initials\|Address\|Full postal code\|Telephone number\|Hospital number |
| 7.3 | Explain and justify the use of this identifier - Full name: | Patient identifiers such as full name and address will be collected and retained at the local site only to assist in contacting the patient for appointment changes, reminder calls, or the completion of follow up data collection |
| 7.4 | Explain and justify the use of this identifier - Initials: | patient initials in addition to a unique study number are used on data collection forms in order to provide an extra level of data tracking and cross reference. |
| 7.5 | Explain and justify the use of this identifier - Health card number: | |
| 7.6 | Explain and justify the use of this identifier - Address: | Patient identifiers such as full name and address will be collected and retained at the local site only to assist in contacting the patient for appointment changes, reminder calls, or the completion of follow up data collection. |
| 7.7 | Explain and justify the use of this identifier - Full postal code: | Patient identifiers such as full name and address will be collected and retained at the local site only to assist in contacting the patient for appointment changes, reminder calls, or the completion of follow up data collection. |
| 7.8 | Explain and justify the use of this identifier - Partial postal code: | |
| 7.9 | Explain and justify the use of this identifier - Telephone number: | Patient identifiers such as full name and address will be collected and retained at the local site only to assist in contacting the patient for appointment changes, reminder calls, or the completion of follow up data collection. |
| 7.10 | Explain and justify the use of this identifier - Email: | |
| 7.11 | Explain and justify the use of this identifier - Family Physician: | |
| 7.12 | Explain and justify the use of this identifier | This is necessary to ensure the only patients 18 |

| | | |
|---|---|---|
| | - Date of birth: | years of age and over are approached for the study |
| 7.13 | Explain and justify the use of this identifier - Partial date of birth: | |
| 7.14 | Explain and justify the use of this identifier - Hospital number: | Collection of hospital number is necessary to confirm appointments, surgery dates, radiographic data assessment etc |
| 7.15 | Explain and justify the use of this identifier - Other: | |
| 7.16 | Where will information collected as part of this study be stored? (select all that apply) | University or Hospital network drive (specify below) |
| 7.17 | If required, please specify further information below. | The original hard copies of the data at London Health Sciences will be kept in a locked secure area as in keeping with the hospital's customary practice for protecting patient information. This includes a locked filing cabinet, in a locked office in a locked corridor. Access is by authorized personnel only such as the study coordinator or site investigator. Data is entered in a password protected database accessible only to the PI and study coordinator. This is on a firewall [protected hospital server that is backed up daily. The PI and research coordinator will have access to identifying information described previously, including the hospital PIN within the master list for linkage purposes. This master list will be located on the password protected LHSC server in a restricted document available only to the PI and research coordinator. The system is backed up daily |
| 7.18 | If identifiable participant information is stored on a hard drive or portable device, the device must be encrypted. Describe the encryption being used. | not applicable |
| 7.19 | How will you record study data? | Data will initially be collected on hard copy forms. Stored Data is entered in a password protected spreadsheet accessible only to the PI and study coordinator. This is on a firewall protected hospital server that is backed up daily. |
| 7.20 | Describe the coding system to protect identifiable information or explain why the data must remain identifiable. | Each patient is assigned a unique study number in addition to their initials. Patients initials are used on data collection forms in order to provide an extra level of data tracking and cross reference. No other identifiable information is stored with the study data . Data is entered in a |

| | | |
|---|---|---|
| | | password protected database accessible only to the PI and study coordinator. This is on a firewall [protected hospital server that is backed up daily. |
| 7.21 | How will you store and protect the master list, signed original letters of information and consent documents or other data with identifiers? | Paper file (Required Protection: Locked cabinet in locked institutional office)\|Electronic file (local) (Required Protection: Password protected computer on a secure network behind institutional firewalls - specify location) |
| 7.22 | If any options are selected above, please provide the specific details here. | The original hard copies of the data at London Health Sciences will be kept in a locked secure area as in keeping with the hospital's customary practice for protecting patient information. This includes a locked filing cabinet, in a locked office in a locked corridor. Access is by authorized personnel only such as the study coordinator or site investigator. The PI and research coordinator will have access to identifying information described previously, including the hospital PIN within the master list for linkage purposes. This master list will be located on the password protected LHSC server in a restricted document available only to the PI and research coordinator. The system is backed up daily. |
| 7.23 | How will you store and protect data without identifiers? | The original hard copies of the data at London Health Sciences will be kept in a locked secure area as in keeping with the hospital's customary practice for protecting patient information. This includes a locked filing cabinet, in a locked office in a locked corridor. Access is by authorized personnel only such as the study coordinator or site investigator. Data is entered in a password protected database accessible only to the PI and study coordinator. The PI and research coordinator will have access to identifying information described previously, including the hospital PIN within the master list for linkage purposes. This master list will be located on the password protected LHSC server in a restricted document available only to the PI and research coordinator. The system is backed up daily. |
| 7.24 | If you plan to de-identify the study data, please describe the method of de-identification. | All data will be identified by study number and patient initials. Xray or CT scan data will be deannotated by use of computer software |

| | | |
|---|---|---|
| | | function inherent in the Xray program |
| 7.25 | How long will you keep the study data? | Electronic data will be kept indefinitely on a password protected hospital server. Hardcopy data will be kept for 5 years after study end and data analysis is complete. |
| 7.26 | How will you destroy the study data after this period? (If applicable) | Hardcopy files will be shredded as confidential waste as per hospital policy |
| 7.27 | Does this study require you to send data outside of the institution where it is collected? This includes data taken off-site for analysis. Please note that Western/Robarts are considered off-site locations for hospital/Lawson based studies, and vice-versa. | No |
| 7.28 | Where will the data be sent? | |
| 7.29 | Does the data to be transferred include personal identifiers? If yes, a data transfer agreement may be necessary. | No |
| 7.30 | List the personal identifiers that will be included with the data sent off-site. | |
| 7.31 | How will the data be transmitted? | |
| 7.32 | Please specify any additional details on data transmission below. | not applicable |
| 7.33 | Will you link the locally collected data with any other data sets? | No |
| 7.34 | If YES is selected in question 7.33 above, identify the dataset | |
| 7.35 | If YES is selected in question 7.33 above, explain how the linkage will occur. | |
| 7.36 | If YES is selected in question 7.33 above, provide a list of data items contained in the dataset. | |
| 7.37 | Will the study data be entered into a database for future use? | No |
| 7.38 | If YES is selected in question 7.37 above, please specify where it will be stored, who the custodian will be, who will have access to the database and what security measures will be in place. | |
| 7.39 | Please list agencies/groups/persons outside of your local research team who will have access to the identifiable data and indicate why access is required. | Representatives of Western University Health Sciences Research Ethics Board or members of the Lawson Quality Control team may require access to study-related records to monitor the conduct of the research. |

**8. 8. Conflict of Interest**

| # | Question | Answer |
|---|---|---|
| 8.1 | Will any investigators, members of the research teams, and/or their partners or immediate family members function as advisors, employees, officers, directors or consultants for a study-related sponsor or funding source? | No |
| 8.2 | Will any investigators, members of the research team, and/or their partners or immediate family members have a direct or indirect financial interest (including patents or stocks) in the drug, device or technology employed in this research study? | No |
| 8.3 | Will any investigators, members of the research team, and/or their partners or immediate family members receive any personal benefit (apart from fees for service) as a result of, or connects to this study? | No |
| 8.4 | If YES is selected in any of the above, please describe the nature of the conflict of interest and how all conflict(s) of interest will be managed. | |

**9. 9. Industry Sponsored Protocols**

| # | Question | Answer |
|---|---|---|
| 9.1 | Is this an industry sponsored protocol? | No |
| 9.2 | Billing Information - Company Institution: | |
| 9.3 | Contact Person: | |
| 9.4 | Email of Contact Person: | |
| 9.5 | Street Address: | |
| 9.6 | City: | |
| 9.7 | Country: | |
| 9.8 | Province/State: | |
| 9.9 | Phone Number: | |
| 9.10 | Fax: | |
| 9.11 | Contract and/or protocol reference number required: | |
| 9.12 | Additional Sponsor Reference or contact information: | |

| | | |
|---|---|---|
| 9.13 | Do you wish to apply for a REB Administration Fee Adjustment/Waiver? | Yes |
| 9.14 | Do you agree to the Conditions for Industry Funded Research Investigators? | Yes |
| 9.15 | Do you agree to provide supporting documents? (These can be added in the attachments section) | Yes |

**10. 10. Confirmation of Responsibility**

| # | Question | Answer |
|---|---|---|
| 10.1 | I assume full responsibility for the scientific and ethical conduct of the study as described in this REB application and submitted protocol. | Yes |
| 10.2 | I agree to conduct this study in compliance with the Tri-Council Policy Statement (TCPS2), Ethical Conduct in Research Involving Humans and any other relevant regulations and guidelines. | Yes |
| 10.3 | I certify that all researchers and other personnel involved in this project at this institution are appropriately qualified and experienced or will undergo appropriate training to fulfill their role in this project. | Yes |
| 10.4 | I certify that any and all conflicts of interest have been declared. | Yes |
| 10.5 | I have obtained all necessary resource utilization signatures, and all costs associated with the use of these resources have been declared. | Yes |
| 10.6 | On behalf of my research team, I recognize the importance of maintaining the confidentiality of all personal information, including personal health information, and the privacy of individuals with respect to that information. I will ensure that the personal information is used only as necessary, to fulfill the specific research objectives and related research questions described in this application and approved by the REB. This includes all conditions and restrictions imposed by the REB govern | Yes |
| 10.7 | I will adhere to the Protocol and Informed | Yes |

| | | |
|---|---|---|
| | Consent document as approved by the Health Sciences REB. | |
| 10.8 | Have you exported a copy of this submission to Word using the "Export to Word" button? Note that you will be unable to submit future revisions if this is not done. | Yes |

**OTA Directed Topic Research Grant Application**
**"Prospective Randomized Controlled Trial To Investigate Treatment Of Ankle Syndesmotic Injuries"**

**Deadline: July14, 2014**



| SALARIES AND WAGES<br>(List all personnel for whom money is requested) | % Of Time on this project | Requested from OTA Funds (Omit Cents) |
|---|---|---|
| Lead site Research Coordinator ($40000 x .25 FTE x 1.5 years or 18 months): study administration/contact for all sites, site set up, patient follow up, data collection and organization from all sites, database entry, preparation of presentation material, protocol data evaluation. | 25% | $15000 |
| Local Site Study Coordinators: patient recruitment, follow up, data collection and submission:<br><br>We are requesting funding to cover coordinator time for study preparation, patient recruitment and follow up as below at 3 participating sites:<br><br>Ethics/Study Set up at all participating sites to cover coordinator time: $1500 x 3 sites = $4500<br><br>Per patient cost - $1200 x 60 patients = $72000<br>Breakdown as follows: $300 payable for 2-6 week follow up; $300 payable for 3 and 6 month follow up; $300 payable for 12 month follow up. CT scan at 3 month = $300<br><br>Statistical analysis: $1000 study statistical plan; $500 for ongoing interim analysis; $1500 for final analysis and publication = $3000 | | $4500<br><br>$72000<br><br>$3000 |
| | % | |
| | % | |
| | TOTAL | $94500 |

| PERMANENT EQUIPMENT (Justification to be appended) | |
|---|---|
| Not applicable | |
| | |
| | |
| | |
| Subtotal | 0 |