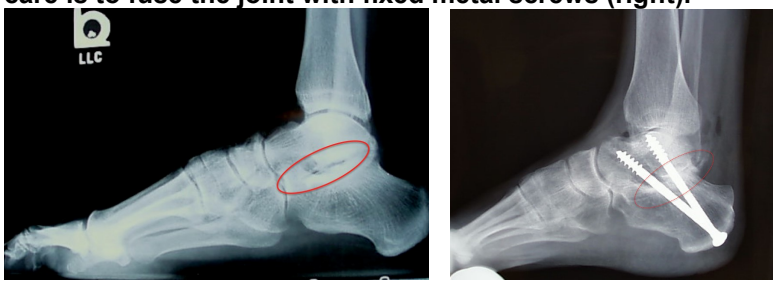
RESEARCH STRATEGY

A. SIGNIFICANCE

Subtalar joint damage due to degenerative joint disease (arthritis), traumatic injury, or other problems affects more than 15,000 Americans annually. The subtalar joint is a complex joint located in the hind foot just below the ankle joint. It is composed of the calcaneus (heel) bone on the bottom and talus bone on the top (**Figure 1**). This joint adapts to changes in terrain while walking, pivots the body on the feet and acts as a shock absorber as the feet hit the ground. It inverts and everts to allow ambulation over uneven terrain. Subtalar arthritis can result from trauma (fracture), primary (idiopathic) talocalcaneal arthritis (instability/deformity) (1), posterior tibial tendon dysfunction, or autoimmune disorders (**Figure 1**, left). In 2004, musculoskeletal diseases accounted for approximately $510 billion in direct costs, or $849 billion including lost wages (2-5).

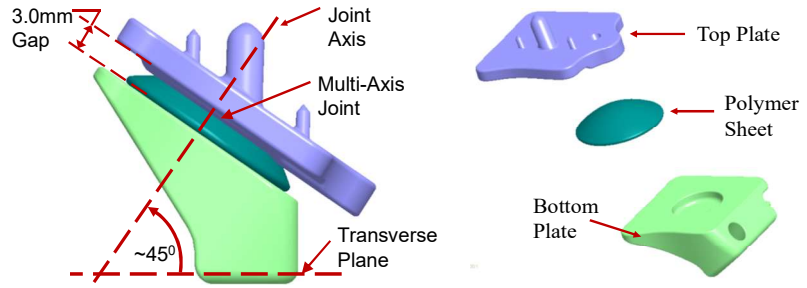
Figure 1. The subtalar joint, just below the ankle joint, frequently sustains damage (left). The current standard of care is to fuse the joint with fixed metal screws (right).



The current standard of care for treating subtalar joint damage (arthritis) is joint fusion using solid fixed screws, which eliminates joint range of motion (**Figure 1**, right) (3, 4). Joint dysfunction usually fails to respond to injections and arthroscopy. There are no other joint-preserving options, due to the difficulty of prosthesis insertion within the complex subtalar joint anatomy and the high weight to surface area ratio of this joint. However, joint fusion degrades human gait, quality of life, and requires that other adjacent joints be over extended and/or stressed to compensate for the lost range of motion. Over time, these effects accelerate wear and increase joint damage on the ankle and other neighboring joints thus increasing the risk of developing arthritis at those sites as well (4). More than other joints affected by arthritis or injury, incurable subtalar joint damage has a profound effect on patient care and quality of life.

Four total ankle replacement devices are approved by the US Food and Drug Administration (FDA) and on the market (one mobile bearing and 3 fixed bearing). The most popular product is the Scandinavian Total Ankle Replacement (STAR) (Small Bone Innovations Inc.). The STAR has been used successfully for more than 10 years in the US and nearly 30 years in Europe to replace the ankle joint while maintaining full range of motion (6). The implants are well tolerated and have survivability rates of up to 91% after 5 years and up to 86% after 10 years (7). However, the STAR approach addresses only the tibiotalar joint and cannot be used for subtalar joints. This is due to differences in size, geometry, and joint kinematics, dynamics, and loading characteristics. To our knowledge, the IBIS subtalar joint replacement device is the first device to address a critical unmet need with a novel approach to repair damage to the hind foot while restoring near-normal gait by preserving joint range of motion.

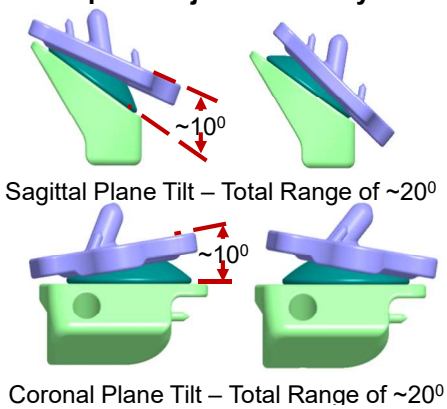
Figure 2. Schematic diagram of IBIS subtalar joint replacement device. Left: side view; right: exploded view.



The innovative IBIS subtalar joint replacement device is designed for surgical joint replacement that preserves range of motion. The device consists of: 1) a top plate that will be surgically anchored to the talar bone; 2) a bottom plate that will be surgically anchored to the calcaneal bone; and 3) a polymer sheet that will provide a smooth curvilinear dome-shaped surface enabling the two plates to rotate, translate (for the mobile bearing design only), and move up and down relative to one other **(Figure 2)** similar to the native subtalar joint**.** In the final product, the talar and calcaneal plates will be produced from medical grade titanium (Ti-6Al-4V) alloy or cobalt chrome, depending on factors such as device wear rates, manufacturing cost, and device peak operating stresses. The curvilinear disk will be produced from an FDA approved Ultra High Molecular Weight Polyethylene (UHMWPE) similar to what is used in the STAR total ankle replacement. This assembly will restore (nearly) full range of motion in all anatomic planes to the subtalar joint and support a normal walking

gait **(Figure 3).** IBIS has developed and tested several initial designs. The next technological challenge is to refine the designs such that the device properly conforms to the anatomic geometry of the talus and calcaneus bones while restoring native subtalar joint range of motion, which is quite complex, and adequately withstands the necessary loading conditions imparted during normal activities of living. The device designs also must meet necessary survivability rates for component wear as determined by the FDA for installation in the body.

Figure 3. Schematic design of the subtalar joint replacement device showing the tilt that will provide joint flexibility.



The STAR mobile ankle device was the first joint replacement device approved by the FDA to use a mobile bearing polyethylene (floating poly) 3-piece design. It was developed to facilitate ankle axial rotation, potential joint axis misalignments during surgical insertion, and reduce wear on the mobile bearing polyethylene component. IBIS will use a similar approach with a "floating poly" disk design as one option enabling the joint axis to move through range of motion of the subtalar joint. The axis of the subtalar joint is positioned at approximately 45° from the transverse plane when the patient is at plantagrade neutral. When the subtalar joint articulates through its entire range of motion, the joint axis can move between 5 and 10 mm. However, this joint axis movement is not well understood and will be better characterized during Phase I.

To facilitate ease of surgical implantation, IBIS designed three cutting jigs to precisely remove the ends of the damaged bones and prepare the joint for insertion of the prosthetic device, which conforms to the cut bone surfaces. A distractor device has been designed to open the subtalar joint enough to provide adequate working space and line of sight for insertion. These devices will be prototyped and characterized for ease of use, form, fit, and function during Phase I. However further testing, optimization, and designing of the surgical devices is beyond the scope of this Phase I project and will be performed in the anticipated future Phase II project.

Joint replacement devices are a $30 billion market in the US alone (2), with ankle joint replacement devices representing approximately 5% of the total market share. About 12,000 subtalar joint fusions are performed each year in the US, of which 80% might qualify for a subtalar joint replacement device implantation due to such factors as age, weight, health and activity levels. Therefore, availability of the novel subtalar prosthesis is expected to increase this market by another $10 million annually once it is fully integrated as the standard of care in orthopedic medicine.

IBIS' commercial strategy is to market the novel subtalar joint replacement device to orthopedic surgeons specializing in foot and ankle surgery. The product will be commercialized in partnership with an established orthopedic device design company such as Innovative Medical Device Solutions (IMDS). Preliminary discussions with this company piqued great interest in our technology and IMDS will consult on this project. For the anticipated Phase II proposal, we will explore a strategic alliance that will provide expertise and potential future support for commercialization.

Regulatory pathway. The STAR total ankle joint replacement device was regulated by the FDA as a Class III device that required Pre-Market Approval (PMA). Based on initial discussions with the FDA, we expect that our mobile-bearing subtalar joint replacement device design will be classified as a Class III device that will require PMA as well. Therefore, we will consider reducing regulatory approval stringency by using a fixed or semi-fixed bearing design, which should allow for a Class II 510K device classification and yet substantially restore joint kinematics and range of motion. We will select the top 2 designs, one mobile-bearing and one fixed or semi-fixed. This will be determined in collaboration with IMDS, which has extensive expertise in medical device design and FDA regulatory strategies. Also, it is unknown whether a mobile bearing design will have substantially longer survivability (wear) rates compared to a fixed or semi-fixed design, which will be determined in the Phase II project. If the wear rates are similar, IBIS will likely only pursue a fixed or semi-fixed design for further development and FDA approval, as developing a mobile bearing design would take longer and cost more with little to no performance benefits (wear rates or joint kinematics).

IBIS plans to use materials similar to those in the STAR since the loading conditions and anatomic position of the ankle vs. subtalar joints are very similar. We will approach the FDA for regulatory guidance and device classification during the anticipated Phase II project period collaborating with IMDS and Exponent Inc., which have extensive expertise with the FDA regulatory process. Exponent also will aid in the cadaver installation

and testing, including wear and fatigue analysis and characterization during Phase II.

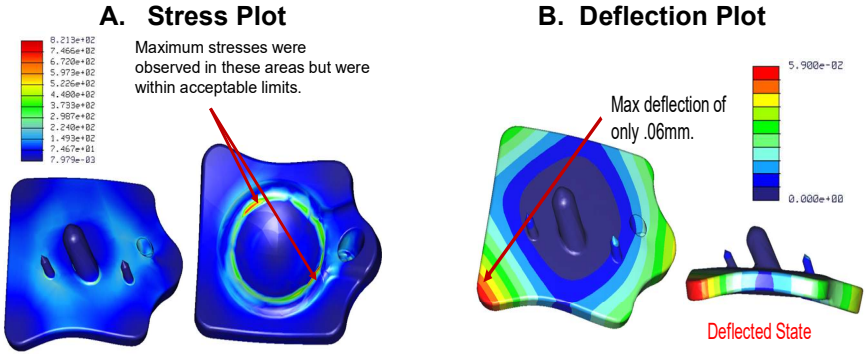
B. INNOVATION

Introducing a subtalar joint replacement device into the field of orthopedic surgery would represent a novel and important technological advancement over joint fusion, the current standard of care. There is no product on the market today that enables mobile subtalar joint replacement and repair. The IBIS design is innovative in that it is based on a unique geometry that is designed specifically for replacement of the subtalar joint and accommodates the unique loading conditions and restores the complex and unique joint kinematics, dynamics, and range of motion of the subtalar joint. Similar to the STAR prosthesis, the IBIS prosthesis has a mobile bearing polyethylene component that enables planar slide and accommodates a variable joint axis, for the mobile bearing design only, as the subtalar joint axis moves approximately 5-10mm through its range of motion. As a result, the replaced joint should provide full or nearly full range of motion and normal patient gait perseveration. The subtalar joint replacement device also accommodates a unique 45° lateral approach for surgical installation, which is important due to extreme line-of-site and access constraints imposed during the surgical procedure.

C. APPROACH

PRELIMINARY STUDIES

Figure 4. Initial stress and deflection FEA contour plots of the top (talar) plate show that it can withstand large static loads (3000 pound force) while having small deflections (0.06 mm).



Preliminary Fine Element Analysis (FEA) of stress and deflection using CAD models showed that the IBIS subtalar joint replacement design will be strong enough to withstand typical loading in the human body. A static 3000 pound force was applied to the top surface of the talar plate and stresses and deflections were evaluated (**Figure 4).** The observed deflections were less than 0.07 mm, which is quite small and considered adequate to enable boney in-growth of the top plate to the talus bone. Furthermore, the top plate was within yield strength of titanium (Ti-6Al-4V) alloy. Once boney in-growth of the top and bottom plates is achieved, much of the loads imparted will be transmitted from the device to the bones, which should extend the device life to an estimated 20 to 30 years or longer. Preliminary computer animations showed that the initial design had approximately 20° total of both sagittal and coronal plane tilt (**Figure 3**). While subtalar joint kinematics, dynamics, and range of motion need to be better characterized during the Phase I project period, preliminary research showed that 20° is a reasonable benchmark to prove initial feasibility.

Overview. The objectives of this Phase 1 project are to refine the CAD models, perform detailed FEA, and produce working prototypes of the device to characterize range of motion, kinematics, and dynamics as well as overall form, fit, and function. Work will focus primarily on the joint replacement device but will include characterization of the surgical installation tools (distractor and 3 cutting jigs). The objective of Aim 1 is to improve the CAD models so that they conform to the anatomy of the talus and calcaneus bones. We will use 3-D CAD bone models developed using CT Scans of a 50 percentile male subject. The objective of Aim 2 is to optimize the device using detailed FEA of the CAD design to ensure device integrity once installed in the body. Failure stresses, component deflections, dynamic shock limits, and fatigue strength will be characterized to ensure it can withstand the necessary loading conditions encountered during activities of daily living.

There are no predicate medical devices on the market. No one to our knowledge has ever developed or attempted to develop a subtalar joint replacement device, and there is little published data about operating loads and other physical characteristics of the subtalar joint. Therefore, there are no defined success criteria provided by the American Society for Testing and Materials (ASTM) or the FDA for such a device, and no defined FDA regulatory success criteria. The most similar device in the market today is the STAR device. Since the ankle joint is close anatomically (although not geometrically) to the subtalar joint, we will use the STAR as a benchmark for durability (5 and 10 yr survivability) and performance under similar loading

conditions, as determined by wear analysis characterizations that will be performed during the Phase II project.

Characterization of the device will be based on the STAR total ankle replacement to define loading conditions and device survivability rates, and on knee replacement devices to define kinematics and range of motion for wear testing setups. STAR wear analysis was performed while aligned in 5° of plantar flexion and loaded statically to 3000 N (~674.4 pound force) of joint compression. Under displacement control, it was articulated through 15° of fully reversing flexion, 2.0° of fully reversing axial rotation, and 2.5 mm of fully reversing anterior translation with sinusoidal 1 Hz motions. Five specimens were tested in custom, single-station motion simulators for 10 million motion cycles. We will use this information about the STAR to develop minimum success criteria, and will provide this as rationale to the FDA during the Phase II project. However, range of motion, kinematics, and dynamics of the subtalar joint resemble the knee more than they resemble the ankle, and FDA regulatory criteria for knee replacement devices are well established. Therefore, we will use the knee as a benchmark for joint kinematic characterization and wear testing setups. In the anticipated Phase II project, we will use an AMT1 six-station knee wear simulator and the loads, cycle count, frequency, interval inspection points, etc as defined by the STAR to perform wear analysis for the subtalar joint replacement device aided by Exponent and IMDS. This data is also planned to be published and used for the standard of subtalar joint characterizations for future medical device development of similar products, which is considered a substantial contribution to the medical device design space.

Aim 1. To use CAD to refine the models of the subtalar joint replacement device to conform to typical human subtalar joint anatomy.

Overview. Prior studies used conceptual architectural models to produce a preliminary CAD design for a subtalar joint replacement device. Initial modeling, FEA, and animations confirmed that the device would fit within the provided space of the subtalar joint, withstand large static loads (3000 pound force), and have good initial range of motion (approximately 20° total of both sagittal and coronal plane tilt) and joint kinematics and dynamics. However, bearing surface areas must be increased to improve wear rates and device survivability, and the device must be modified to conform better to the anatomy of the interacting bones. Therefore, we will purchase a detailed three-dimensional (3D) bone model assembly of the foot, and use it to test and refine the CAD design to optimize bearing surface areas and ensure that the device conforms to the interacting bone geometry. We will select the top 3 designs (2 mobile and 1 fixed) for further development. Collaborator **Joe Ferguson** (IMDS) will review design test results and advise on all design selections.

Task 1.1: Characterize the anatomic joint kinematics, dynamics, and angular range of motion of the native subtalar joint.

Currently our device has a 20° total range of motion in both the sagittal and coronal planes. The joint axis can shift up to 5 mm and the axial rotation range of motion is not limited by the device architecture. We will use published data (9) to help characterize joint range of motion, kinematics and dynamics. Joint kinematics for the subtalar joint were calculated in three anatomical planes using coordinate transformations into the principal axes of the calcaneus and talus. Data were normalized to percent of the stance phase. Subtalar joint range of motion in the sagittal, frontal, and transverse planes was 5.0°, 2.5°, and 12.3° during shod running, and 5.5°, 2.0°, and 15.4° during barefoot running, respectively (9). These data will be analyzed and applied to our device to ensure that it has the proper kinematics and range of motion to accommodate the native subtalar joint.

Task 1.2. Select the top 3 designs for further analysis.

Based on data from Task 1.1, the top-performing 3 designs will be evaluated through a series of in-depth design reviews. The best 2 designs (1 mobile and 1 fixed) will be selected for further analysis based on sagittal, frontal, and transverse plane total angular motion restoration. Success criteria: The device must have at least 5.5°, 2.5°, and 15.4° of sagittal, frontal, and transverse plane range of motion, respectively, and be able to have a joint axis shift of at least 10 mm for the mobile bearing design only.

Task 1.3: Use anatomically correct 3D solid modeled bones to optimize the design.

We will purchase 3D solid bone models of the entire foot that were created by high-definition CT scans of a 50 percentile male subject (Zygote Media Group, Inc., American Fork, UT). We will overlay this model with our subtalar joint replacement device via CAD and modify the device design to achieve the most accurate anatomic geometry that best conforms to human anatomy. Specifically, we will use Pro Engineer, a commonly used CAD modeling program, to adjust the design of the talar and calcaneal plates to the models of their respective bones and make any compensating changes to the polymer sheet between them. Our objective is

to maximize the device size within anatomical constraints, preferably an increase of at least 25% over the size of the current prototype, in order to increase the overall bearing surface areas and ultimately to reduce wear rates and increase device survivability. Success criteria: The device design will conform to the geometry of the interacting bones, as seen visually when overlaying the device on top of the bones using CAD, and the bearing surface areas will be maximized and increased by at least 25% from their current state.

- ***Milestone 1: Optimize the design so that it conforms to the geometrical anatomy of the human foot and compensates for the native subtalar joint range of motion.***

Pitfalls and Alternatives. Successful completion of these tasks will result in: 1) a refined design for the subtalar joint replacement device that better conforms to standard models of the anatomic bone structure of the human foot; and 2) a device that can properly compensate for the full range of motion of the native subtalar joint. The IBIS team has extensive experience in design engineering and medical and surgical best practices, and with the acquisition of the 3-D solid bone models we expect to successfully improve the CAD design. If the device cannot compensate for native range of motion, we will increase the height of the polyethylene joint component, which will increase the distance between the plates and increase the range of motion. However, the overall stack height of the device must be small enough to fit within the space of the joint anatomy. Making the top and bottom plates thinner would allow an increase in poly height, but this must be balanced by the device failure strength as thinner components may weaken the device. Furthermore, IMDS has advised that based on their experiences and discussions with the FDA, the plate thicknesses must be at least 2.0mm.

Aim 2. To optimize the subtalar joint replacement design through detailed FEA of the CAD design.

Overview. FEA based on 3D models will be used to test the optimized designs from Aim 1 and characterize their projected strength under the typical stresses imparted during normal activities of daily living. We will test specifically for stress and strain, deflection, fatigue, and dynamic shock to simulate the loading conditions once installed in the human foot. Due to the complexity and specific requirements of this step, FEA analysis will be performed by **Ming Wu, Ph.D.,** (Exponent, Inc.), who has extensive experience with FEA, and reviewed by collaborating senior engineer **Shivakumar Raman, Ph.D.** (University of OK).

Task 2.1: Define all boundary conditions including materials, loads, and constraints.

The top and bottom plates will be produced from either titanium (Ti-6Al-4V) alloy or cobalt chrome alloy. The bearing joint surface component will be produced from UHMWPE. These materials are commonly used in current joint replacement devices, are biocompatible, and were used in the STAR total ankle replacement device. In the STAR device, the tibial and talar plates are made from cobalt chrome and coated with pure titanium in the places where they touch the bone surfaces. IBIS will test both cobalt chrome and titanium metal alloys and compare their wear rates during the Phase II project period. Based on testing criteria of the STAR total ankle, we will statically load the design to 3000 N (~674.4 pound force) and measure stress/strain, dynamic shock, fatigue strength, and maximum deflection. We also will define the maximum static and dynamic shock loads that our device can withstand in simulations that mimic *in vivo* conditions. Success criteria: Ensure that the proper materials (titanium alloy and cobalt chrome alloy), loads (3000 N (~674.4 pound force), and constraints are applied in the FEA models created by Exponent.

Task 2.2: Analyze the results and refine the models as necessary

Stress and deflection plots (similar to **Figure 4**) will be constructed to determine whether the device exceeds the targeted yield strength of 880 MPa and has < 0.10 inch of deflection under the specified boundary conditions defined by Task 2.1. If these criteria are not met, then we will refine the models to correct for stiffness, increase radius values to redistribute stress, and/or modify the materials or add post- processing heat treatments to strengthen the material properties as required. The models will be retested until the success metrics are achieved. Two designs (one mobile bearing and one fixed or semi-fixed) will be selected for prototype analysis in Aim 3 based on the following success criteria: deflection $\leq$ 0.10 inch and an 880 MPa yield strength not exceeded under a static and dynamic shock load of 3000 N (~674.4 pound force).

- ***Milestone 2: Complete FEA to prove analytically that the device can withstand the expected loads during normal gait and select the top 2 designs for prototype analysis.***

Pitfalls and Alternatives. Successful completion of these tasks will result in a device that analytically will not exceed material yield strength or maximum deflection as defined in task 2.2. This will establish feasibility of the design by confirming that the device will not fail under *in vivo* conditions. It also will show that the device

will permit minimal deflections to enable boney in-growth into the top and bottom plates, which is critical for long-term survivability. If the device does not meet these criteria, we will refine the models to correct for stiffness, increase radius values to redistribute stress, and/or modify the materials or add post-processing heat treatments to strengthen the material properties, then retest the models until the success metrics are achieved.

Aim 3. To develop and test working prototypes of the implant device and surgical tools.

Overview. The final test of design feasibility will be to produce to-scale prototypes of the subtalar joint replacement device, then test joint kinematics, dynamics and range of motion, and evaluate feature size and overall form, fit, and function. Prototypes also will be made of the distractor and 3 cutter jigs to test size, function, and surgical usability. The device top and bottom plates will be produced from titanium (Ti-6Al-4V) alloy and made by Direct Metal Laser Sintering (DMLS); the joint component, distractor and cutter jigs will be made from liquid ultraviolet curable photopolymer resin by stereolithography (SLA). This effort will be facilitated by consultant **Curtis Sauer,** who has extensive demonstrated expertise in manufacturing technologies and prototype creation and analysis. Collaborating senior engineer **Shivakumar Raman, Ph.D.** (University of OK) will review the prototypes to ensure that they will meet regulatory and manufacturing requirements.

Task 3.1: Produce prototypes for testing.

Titanium alloy (Ti-6Al-4V) and SLA prototypes will be produced from our final CAD design by Harbec Inc. (Ontario, NY). Parts will be produced using DMLS, a commercial rapid prototyping method to produce metal parts in a single process. DMLS produces a dense part with high detail resolution that is well suited for medical device implants. We will produce 2 prototypes for each design selected in Aim 2. The polymer sheet will be produced from liquid ultraviolet curable photopolymer via SLA. We also will produce 1 distractor prototype and 1 prototype for each of the 3 cutter jigs. These surgical tools will be tested for form, fit, and surgeon usability to ensure that they accurately meet the needs of joint distraction and bone removal.

Task 3.2: Use the device prototypes to characterize range of motion, joint kinematics and dynamics.

By articulating the device through its range of motion, we will assess how it moves in 3D space and measure angular ranges of motion to ensure it meets the requirements as defined in Task 1.1. Success criteria: Ensure the device has the range of motion in the sagittal, frontal, and transverse planes of at least 5.5°, 2.5°, and 15.4°, respectively; for the mobile bearing design, ensure that the joint axis can vary by as much as 10 mm as defined by Task 1.1. Orthopedic surgeon **Vytas Ringus, MD** will test the tools with current usability standards.

The top-performing designs will be evaluated by strength, maximum deflection, total range of motion, and ability to properly restore the native subtalar joint kinematics. They will be selected for further analysis based on the following criteria: Maximum yield strength during static and dynamic shock loading, maximum deflection under maximum specified loading conditions, ensure maximum range of motion in the sagittal, frontal, and transverse planes, and maximum joint axis shift for the mobile bearing design.

Task 3.3: Refine the models and re-run FEA as necessary.

If the device is modified due to lack of range of motion based on prototype analysis, it may be necessary to re-run FEA based upon the criteria as defined by Tasks 2.2 and 2.3. Success criteria: as defined in Aim 2.

- ***Milestone 3: Successfully build prototypes for the device and surgical tools and that meet success criteria for form, fit, function, range of motion and joint kinematics and dynamics.***

Pitfalls and Alternatives. Successful completion of these tasks will result in a working prototype of the device and installation tools. This will establish final proof of concept for the subtalar joint replacement device and position us for the studies anticipated for Phase II (described below). If the prototypes do not meet the success criteria defined, we will refine the designs as necessary to address any issues that may arise.

Conclusion. Successful completion of this Phase 1 project will result in an optimized design for the IBIS subtalar joint replacement device and establish its feasibility based on modeling and prototype testing *in vivo*. We expect to apply for a Phase II SBIR grant to: 1) test device prototypes in human cadavers to evaluate feasibility, reproducibility and ease of use; 2) test range of motion, joint kinematics and dynamics and device wear rates *in vivo*; and 3) prepare and submit regulatory documentation to obtain FDA approval for clinical trials.

Timetable	Month					
Specific Aim	**1**	**2**	**3**	**4**	**5**	**6**
1. To refine CAD models to confirm to human ankle anatomy	■	■				
2. To optimize the prosthesis design through FEA			■	■	■	
3. To produce and test working prototypes						■