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TITLE: Development of a Dynamic Compression Fusion Device for Lower Extremity Salvage of the Diabetic Foot

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14. ABSTRACT Significant research findings during the research period include: design and development of a dynamic compression device for use in challenging surgical foot procedures, such as fusion in the diabetic Veteran patient population. Initial testing results show superior mechanical performance in comparison to FDA-cleared competitor devices, including pull-out and bending performance, as well as the capacity for sustained compression in the face of simulated bone resorption. Additional project findings include introduction of large animal model for in vivo static and dynamic device evaluation featuring normal and low bone quality, as would be seen in more challenging patients. Implanted dynamic devices were observed to sustain compression over time, as assessed by serial radiograph examination. Microcomputed tomography was utilized to assess new bone formation at the joint fusion complex. Finally, mechanical testing of explanted joint complexes was demonstrated to assess integrity of joint fusion structures.						
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1. Introduction

This technology development research project is directly applicable to diabetes, specifically the research of interventions to treat diabetes complications, such as Charcot neuroarthropathy. Charcot neuroarthropathy, also known as Charcot Foot, is an often painless, progressive, inflammatory, destructive degenerative disease of the midfoot and ankle. It is characterized by joint dislocations and fractures that result in deformities of the foot. These deformities often lead to ulceration, infection, and lower limb amputation. The overarching challenge in correcting Charcot foot deformities involves addressing two clinical issues: poor bone quality and harsh loading conditions from neuropathic patients. With Charcot foot, enhanced osteoclastic activity drives bone resorption and osteolysis, which loosens current fusion devices. With loosening, the compressive forces of current devices are lost, thus bone-bone contact decreases and micromotion occurs, preventing fusion and leading to implant breakage. We present the use of the superelastic alloy nickel-titanium (NiTi), which has a large reversible strain recovery. This large strain recovery allows for a NiTi-based medical device to dynamically adapt to bone resorption by continuing to apply a compressive force to maintain bone-bone contact. This effectively creates a device that post-operatively responds automatically to changes in the bone healing environment during fusion. The objective of this technology development proposal is to develop a dynamic compression midfoot fusion device capable of enhanced bone fusion for salvage reconstruction of the diabetic Charcot foot. The central hypothesis is that a NiTi-based fusion device can enhance bone fusion by dynamically adapting to bone resorption to maintain bone-on-bone interfacial compression compared to a static competitor's device. Aim 1: Verify the prototype device's mechanical performance compared to an FDA-cleared competitor's device. Aim 2: Validate the prototype device's ability to apply dynamic compression in vivo using an ovine hindlimb fusion model. In Aim 1, the mechanical performance of the prototype fusion device will be compared against a competitor's device previously cleared by the FDA using relevant industry standards to ensure the safety of the device. These studies will generate the necessary mechanical data for FDA submission and further demonstrate the ability of dynamic sustained compression to adapt to bone resorption in small bones of the foot (Major Task 1). In Aim 2, the ability of the prototype device to enhance fusion via dynamic compression will be validated using an ovine hindlimb model. This study will ensure the efficacy of the device to enhance fusion in vivo compared to a static device. A control group of sheep with normal bone quality will undergo a multi-joint fusion of the hindlimb to simulate midfoot fusion. Radiographic and CT imaging, mechanical testing, and histological evaluation of the fusion site will be used to assess the efficacy of the prototype device to promote fusion under normal biological conditions (Major Task 2). To mimic Charcot foot, low bone quality will be induced in a separate group of sheep, followed by multi-joint fusion of the hindlimb. Radiographic and CT imaging, mechanical testing, and histological evaluation of the fusion site will be used to assess the efficacy of the dynamic prototype device to promote fusion under very challenging biological conditions (Major Task 3).

2. Keywords

Diabetic neuropathy, Charcot neuroarthropathy, arthrodesis, fusion, intramedullary, Nitinol, dynamic compression, biomechanics, midfoot, ovine model

3. Accomplishments

3.1 Specific Aim 1: *Verify the prototype device's mechanical performance compared to an FDA-cleared competitor's device.*

3.1.1 Major Task 1: *Verify the prototype device's mechanical performance compared to an FDA-cleared competitor's device.*

Subtask 1-Axial Pullout Test

Accomplishments: The prototype dynamic device went through multiple rounds of design iterations, especially in regards to its threaded end for fixation in cancellous bone and its overall diameter. Initially, the prototype device had a diameter close to 5 mm and transverse screws for fixation in bone; however, this would not have met the criteria for substantial equivalency for pull-out strength and bending strength. Thus, a second version of the dynamic prototype was developed with a threaded end for fixation in the proximal metatarsal and a slot for a transverse screw for fixation in the calcaneus to reconstruct the lateral column of the foot. The threaded end of the prototype device was designed with a taper to closely mimic the gradual taper of the proximal metatarsal intramedullary canal. The overall diameter was increased to 7mm to increase the bending strength and to be comparable to static predicate devices. A CAD model of the final dynamic prototype device and a manufactured prototype device is shown in Figure 1.

The first metric to examine was the pull-out force of the prototype device compared to a static predicate device (Synthes Midfoot Fusion Bolt, 140mm) (Figure 2). A finalized protocol has been developed and approved through the MedShape quality management system, ED-50388-00, DynaNail Mini Tapered Hybrid Pull-Out Testing Protocol, which follows ASTM F543 to determine the pull-out strength of medical bone screws. Briefly, the static predicate device or the dynamic prototype device is inserted into a synthetic bone block (Sawbones 20PCF), then a force is applied to the device via a pin to drive it in the opposite direction of its insertion (Figure 3). This allows for separation and independent examination of both fixation methods at each end of the devices. From the pictures, the left side of the device is noted as the cortical fixation as it fixates into cortical bone either with threads or a transverse screw. The right side of each device consists of thread length of 16 mm and is noted as the cancellous fixation. The pull-out force for each fixation method for each device is shown in Figure 4 (n=10/device). The cortical and cancellous pull-out force for the dynamic prototype device is greater than the static predicate device. While the static predicate device has fixed thread forms on each end of the device, the transverse screw tested for the cortical fixation of the dynamic prototype device was 14 mm in length. This represents the smallest transverse screw to be offered, thus the worst-case scenario. In practical application, the transverse screw will match the width of the calcaneus, thus it is expected that the pull-out force would be significantly higher.



Figure 1. (left) CAD model of final dynamic prototype device. (right) Manufactured dynamic prototype device.



Figure 2. Static predicate device for pull-out testing.



Figure 3. Test setup for determining pull-out force of each device.

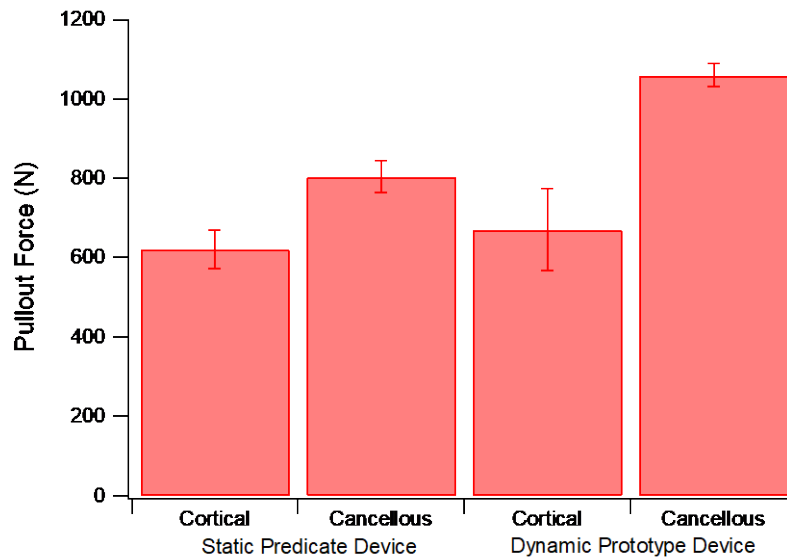


Figure 4. Pull-out force for static predicate device and dynamic prototype device.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Pull-out tests will be conducted in synthetic anatomically sized models of the metatarsal and calcaneus to produce more clinically relevant values of pull-out force. This testing is expected to conclude by the end of 2021.

Subtask 2-Static Bend Test

Accomplishments: A finalized protocol has been developed and approved through the MedShape quality management system, ED-50413-00, DynaNail Mini Tapered Hybrid and Predicate Static 4 Point Bend Testing Protocol, which follows ASTM F1264 to determine the static 4-point bending performance of intramedullary devices. The dynamic prototype device with an overall length of 140 mm was compared against a static predicate device (Wright Salvation Beam) with an overall length of 140 mm to represent the worst-case bending scenario. A picture of the 4-point setup is shown in Figure 5 on a MTS Mini Bionix load frame. Samples were tested past their yield point to permanently deform the specimens in bending (n=8/device). Exemplary bending curves are shown in Figure 6 for each device. Bending stiffness, yield moment and yield force were calculated for each test following ASTM F1264. The bending stiffness, yield moment, and yield force were greater for the dynamic device than the static predicate device (Figures 7,8,9).

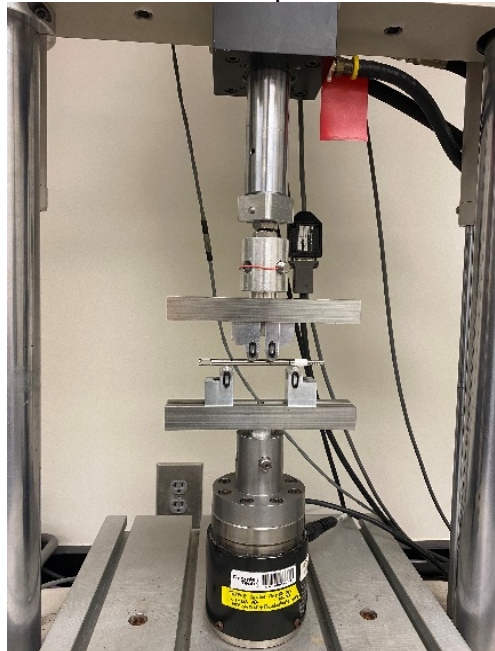


Figure 5. 4-point bending test setup.

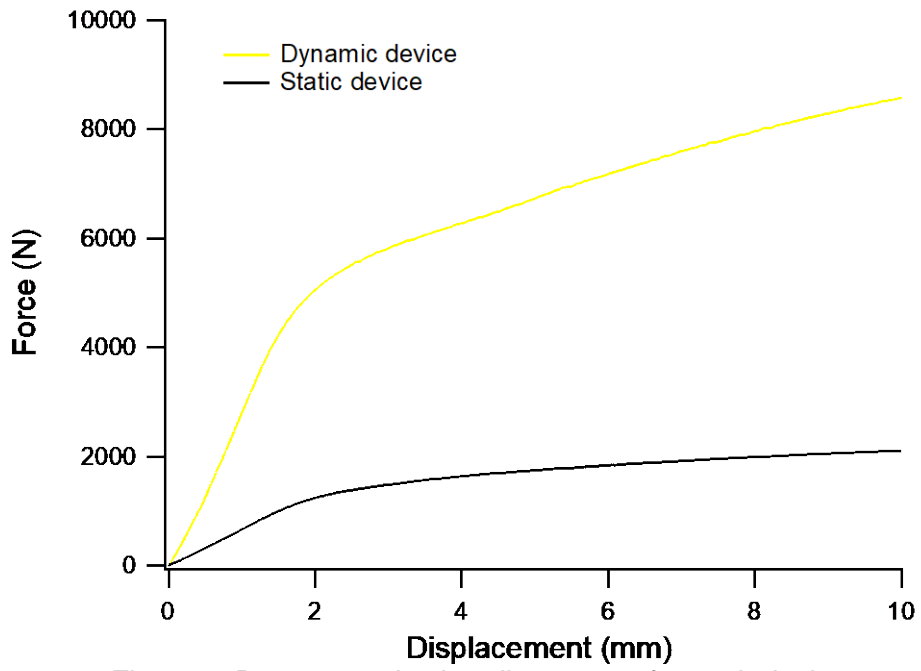


Figure 6. Representative bending curves for each device.

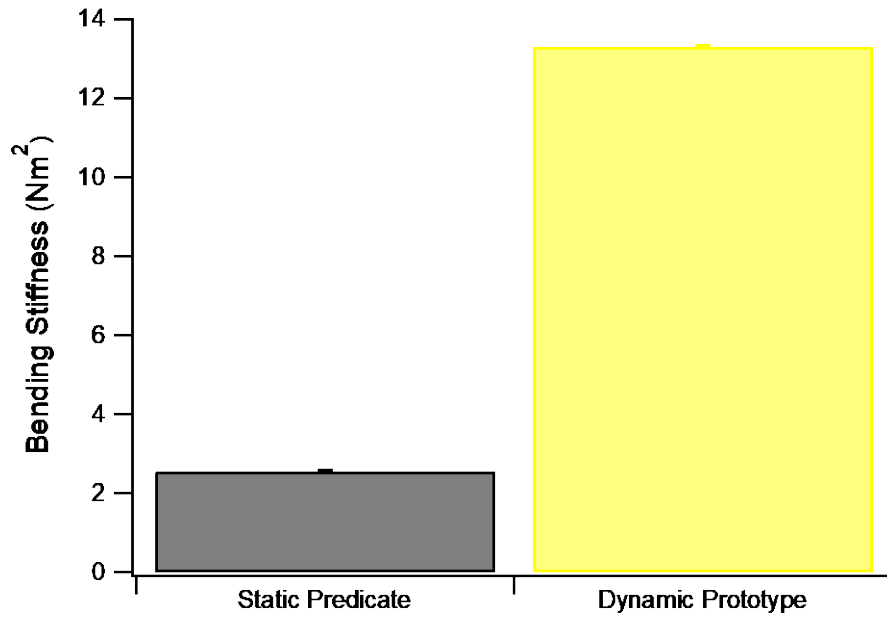


Figure 7. Bending stiffness for static predicate device and dynamic prototype device.

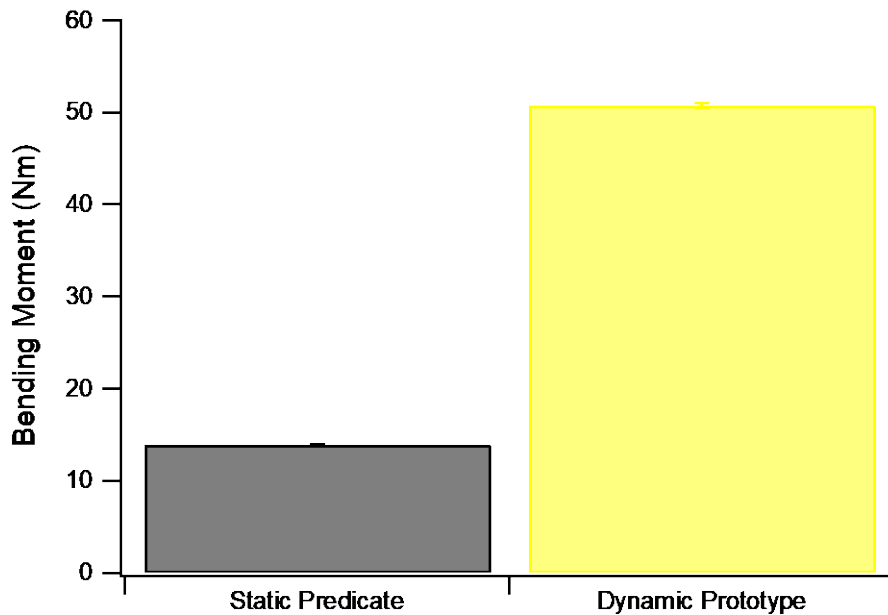


Figure 8. Bending moment for static predicate device and dynamic prototype device.

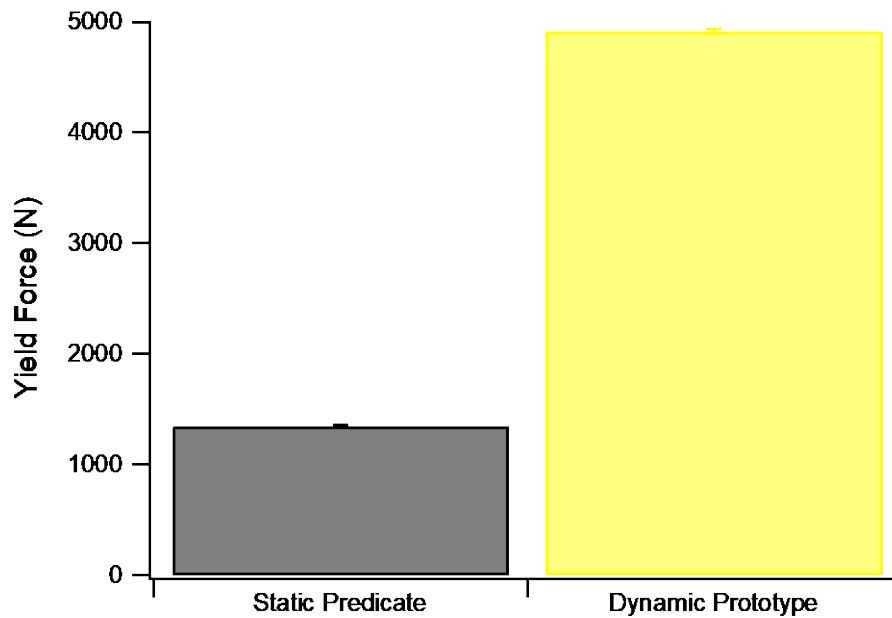


Figure 9. Yield force for static predicate device and dynamic prototype device.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Testing has been completed for this task.

Subtask 3-Static Torsion Test

Accomplishments: A draft protocol has been developed following ASTM F1264 to determine the torsional stiffness of intramedullary devices. A set of custom grips have been designed and machined (Figure 10, Figure 11) to grip the static predicate device and the dynamic prototype device for torsion testing at Colorado State University in a MTS Mini Bionix load frame. The MTS load frame at Georgia Tech does not have pneumatic grips, thus it is unable to apply the necessary forces for holding these custom grips.

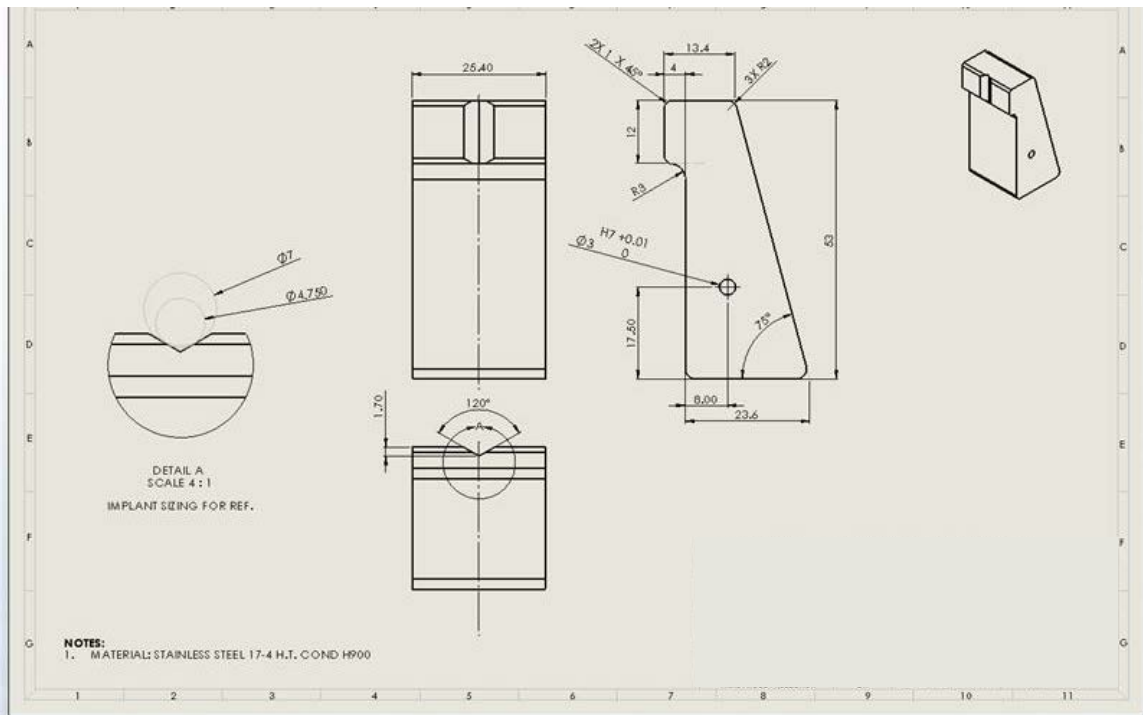


Figure 10. Drawing of grips for torsion testing.



Figure 11. Machined set of grips for torsion testing.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: A finalized testing protocol will be produced and routed through the MedShape quality management system by the end of October 2021. Following protocol approval, torsion testing will commence, and it is expected to finish with a final report by the end of November 2021.

Subtask 4-Cyclic Bend Test

Accomplishments: A finalized protocol has been developed and approved through the MedShape quality management system, ED-50411-00 DynaNail Mini Tapered Hybrid and Predicates Cyclic Bend Testing Protocol, which follows ASTM F1264. After determining the yield force from Subtask 3, the static predicate device and dynamic prototype device are loaded cyclically at 5 Hz at decreasing loads starting at 100% of the yield force to determine the run-out force. The test setup utilizes the same fixtures as Figure 5. Testing to date has shown that the static predicate device has a run-out of 1 million cycles near 75% of its yield force.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Further testing of the final dynamic prototype device will be concluded by the end of 2021. The run-out force for each device will be compared and a final report will be produced.

Subtask 5-Simulated Bone Resorption Test

Accomplishments: A finalized protocol has been developed and approved through the MedShape quality management system, ED-50403-00 DynaNail Mini Tapered Hybrid and Predicates Resorption Testing Protocol. The test setup consists of implanting the predicate device or the dynamic prototype device through a load cell, a custom stage to mimic bone resorption, and then fixated in two synthetic bone blocks (20 PCF) (Figure 12). The entire apparatus is placed inside a thermal chamber held at 37°C to mimic body temperature, as biological resorption would occur over weeks to months post-implantation following device temperature equilibration to body temperature. The stage is lowered to apply slack to the system and the change in compressive load is recorded (n=8/device). The compression load as a function of simulated resorption is shown in Figure 13. The static predicate device (Wright Beam 7x140 mm) loses all compression within 1 mm of simulated resorption, while the dynamic prototype device (7 x 140 mm) sustains compression for 7 mm of simulated bone resorption. Thus, the dynamic prototype device has greater capacity to adapt to bone resorption, which is critical in diabetic patients with Charcot.



Figure 12. Resorption assembly for the dynamic prototype device showing the upper synthetic bone block, load cell, custom resorption stage, and lower synthetic bone block.

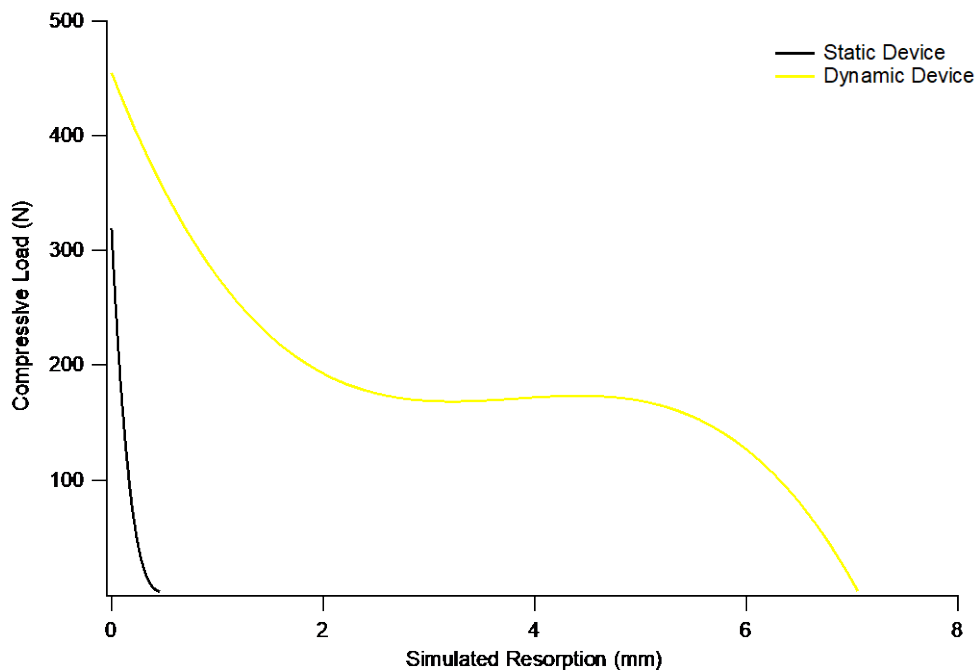


Figure 13. Compression profile during simulated resorption for the static predicate device and dynamic prototype device. Both devices have equivalent overall length of 140 mm.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Additional testing of the dynamic prototype device at lengths of 110 mm, 120 mm, and 130 mm will be performed by the end of 2021 to ensure that their ability to adapt to simulated bone resorption is equivalent to or greater than the static predicate device.

Subtask 6-Manufacture and Assembly

Accomplishments: Finalized manufacturing protocols have been developed and approved through the MedShape quality management system, ED-10928-00 Implant Assembly, DynaNail Mini Tapered Hybrid, which details assembly of the internal implant components for the dynamic prototype device (Figure 14), and ED-10929, Nail Assembly, DynaNail Mini Tapered Hybrid, which details assembly of the prototype device with its nail guide for surgical delivery (Figure 15). An exemplary fully assembled device is shown in Figure 16 with the device attached to its nail guide. All device components were manufactured, inspected, and assembled according to MedShape's quality management system. In order to keep Specific Aim 2 on schedule, the manufacture and assembly of devices for Specific Aim 2 were prioritized first. All devices for the animal study in Specific Aim 2 have been assembled and packaged.

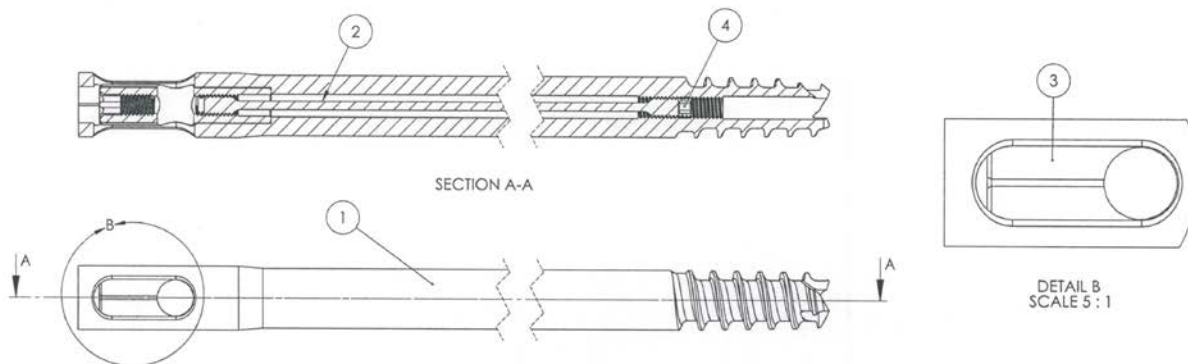


Figure 14. Manufacturing schematic for assembly of internal components of dynamic prototype device.

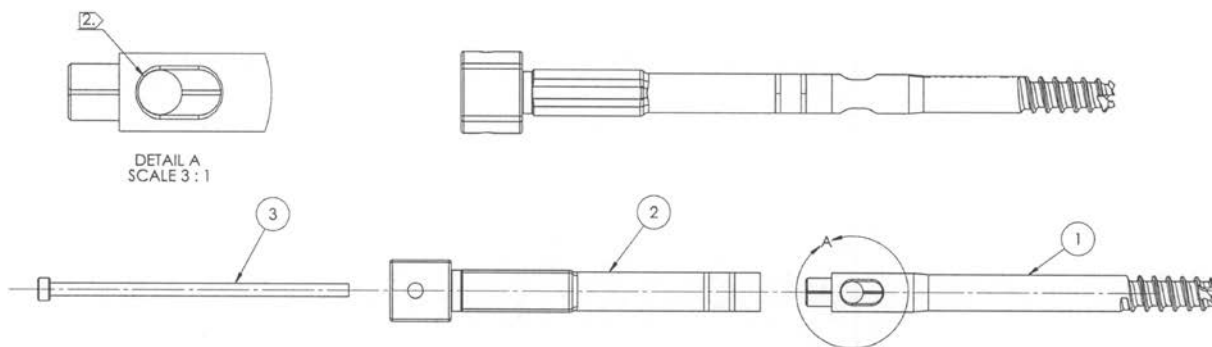


Figure 15. Manufacturing schematic for assembly of dynamic prototype device and nail guide.



Figure 16. Fully assembled device with nail guide on left side and dynamic prototype device on right side.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Dynamic prototype devices for packaging and sterilization testing will be assembled next due to prioritization of tasks. All device components have been received, inspected, and approved by the MedShape quality management system. These remaining devices will be assembled by November 2021.

Subtask 7-Packaging and Sterilization

Accomplishments: Packaging has been designed following, ED-10947 Item Master, DynaNail Mini Hybrid Tapered, and approved in MedShape's quality management system. Figure 17 and Figure 18 detail the packaging components for the dynamic prototype device. These have been adapted from prior MedShape products of similar size and weight.

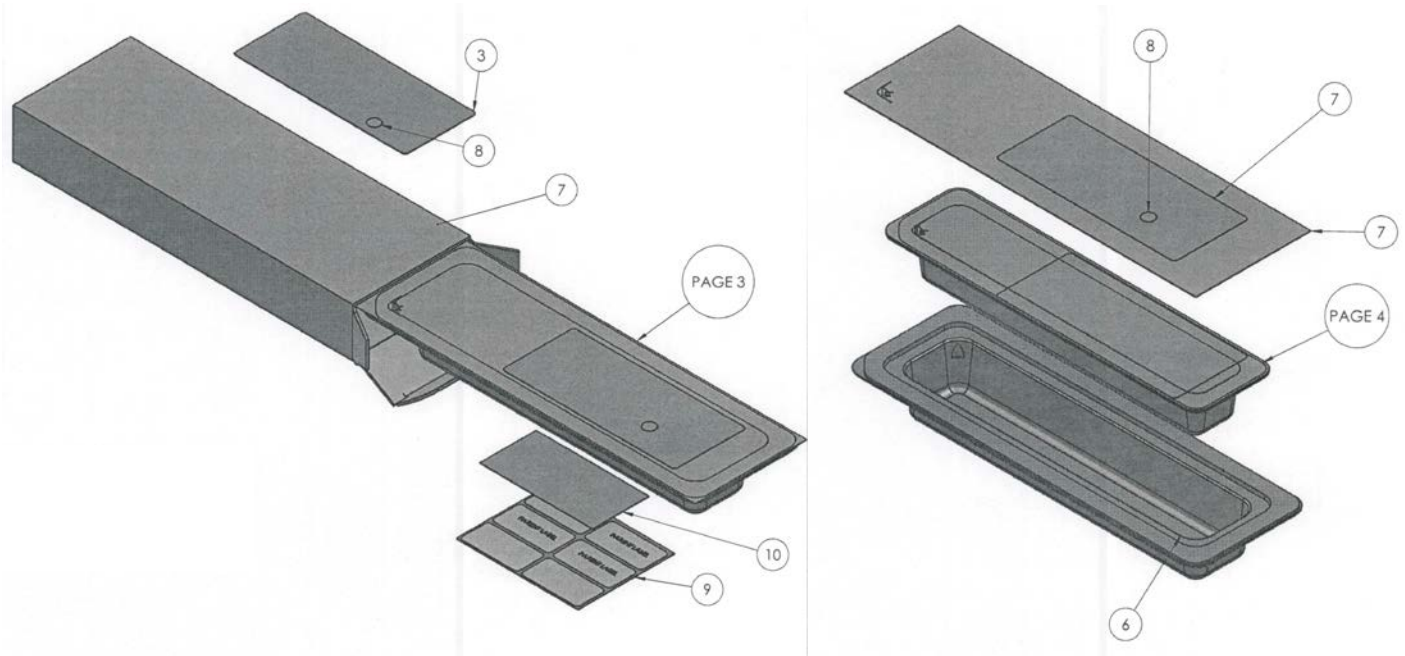


Figure 17. (left) Outer packaging components including label, carton, instructions for use, inner tray assembly. (right) Inner tray assembly components including sterilization indicator, label, outer lid, inner tray and outer tray.

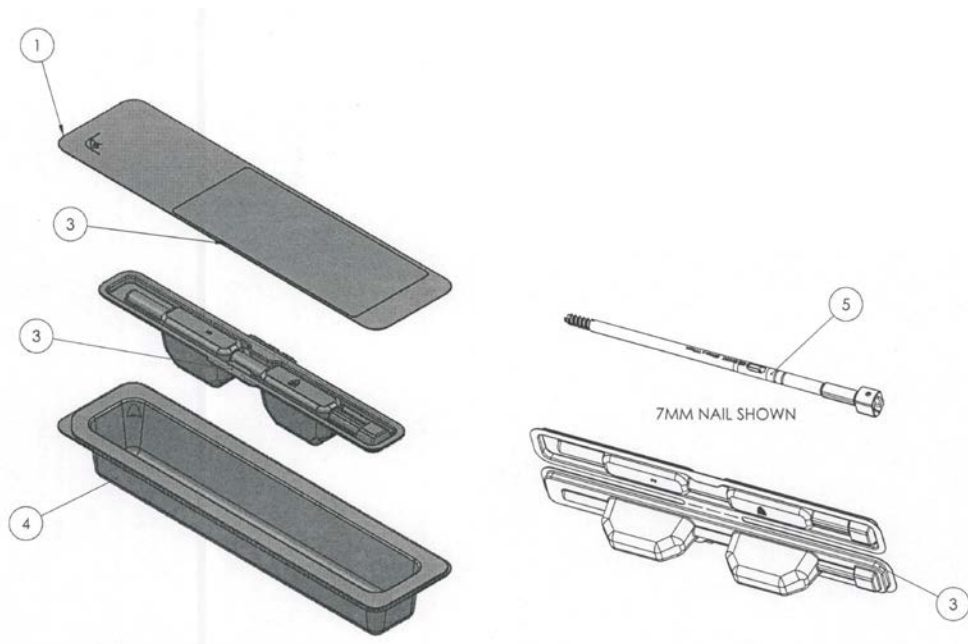


Figure 18. (left) Inner tray components including inner lid, clamshell, and inner tray. (right) Clamshell and assembled dynamic prototype device.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: There has been a vendor delay for producing the outer tray packaging, thus the package integrity testing and sterilization testing has been delayed. The anticipated reception date of the necessary packaging

components is November 2021. Packaging and sterilization testing will proceed immediately upon receipt. These tests will run in parallel with expected completion dates of February 2022.

Subtask 8-Regulatory Documentation

Accomplishments: Design documents have been developed and approved through the MedShape quality management system, ED-50377 Product development plan, DynaNail Mini Hybrid Tapered, and ED-50378 Design Record, DynaNail Mini Hybrid Tapered. These documents along with test reports from each of the above subtasks and data from Specific Aim 2 will be compiled for regulatory submission.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: A submission to the US FDA for a Class II device clearance is expected to occur in 2023.

3.2 Specific Aim 2: *Validate the prototype device's ability to apply dynamic compression in vivo using an ovine hindlimb fusion model.*

Subtask 1-Local IRB/IACUC Approval

Accomplishments: Protocol #1199-MedShape-Development of a dynamic compression fusion device for lower extremity salvage of the diabetic foot was approved September 1, 2020 by the Colorado State University IACUC. An amendment was approved on March 1, 2021, and another amendment was approved on July 30, 2021 for the same protocol.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: No further IACUC amendments are anticipated.

Subtask 2-ACURO Approval

Accomplishments: ACURO protocol PR191551 entitled, MedShape-Development of a dynamic compression fusion device for lower extremity salvage of the diabetic foot, was approved September 24, 2020. Additional ACURO approval was granted on April 14, 2021 and on August 6, 2021 for amendments to the original protocol for bone labels and additional imaging.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: No further ACURO approvals for amendments are anticipated.

3.2.1 Major Task 2: *Validate the prototype device's ability to apply dynamic compression in vivo using an ovine hindlimb fusion model with normal bone quality.*

Subtask 1-Fusion Surgery

Accomplishments: This study utilized a skeletally mature Rambouillet Cross ewe due to comparable anatomy and physiology of the ovine metatarsal and tarsal bones to those of humans. Approval for the surgeries performed on this animal was granted by the Colorado State University Animal Care and Use Committee (Approval No. #1199). Surgery was performed under general anesthesia and aseptic conditions. The device was inserted through the calcaneus and advanced to span the calcaneus-tarsus-metatarsus complex and fixed using transverse screws. For the normal bone quality model, the first two devices, one dynamic and one static, were implanted successfully without complication in early 2021. The first animal with a dynamic device was sacrificed at a 4 month timepoint and the hindlimb harvested for further analysis. Following the first two successful implantations, four more animals were enrolled, two with a dynamic device and two with a static device in August 2021. Figures 19, 20, 21 further detail the surgical implantation with guidewire placement, joint reaming, trial sizer placement to determine device length, and final placement of the device.

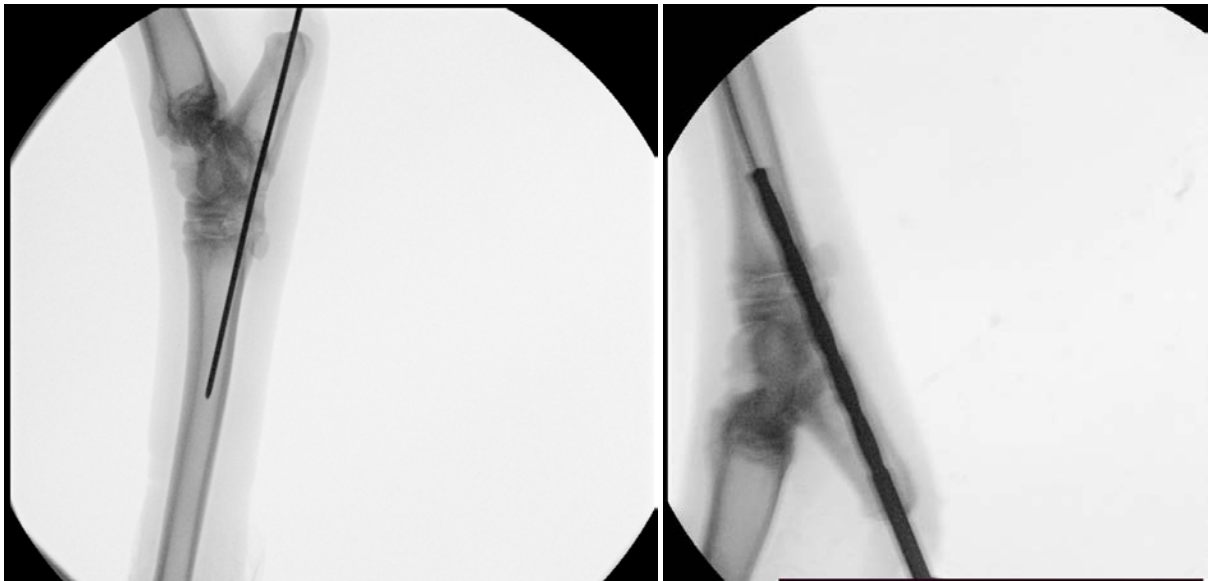


Figure 19. (left) Guidewire placement across the calcaneus-tarsal-metatarsal joint complex of the sheep hindlimb. (right) Reaming of joint prior to device placement.

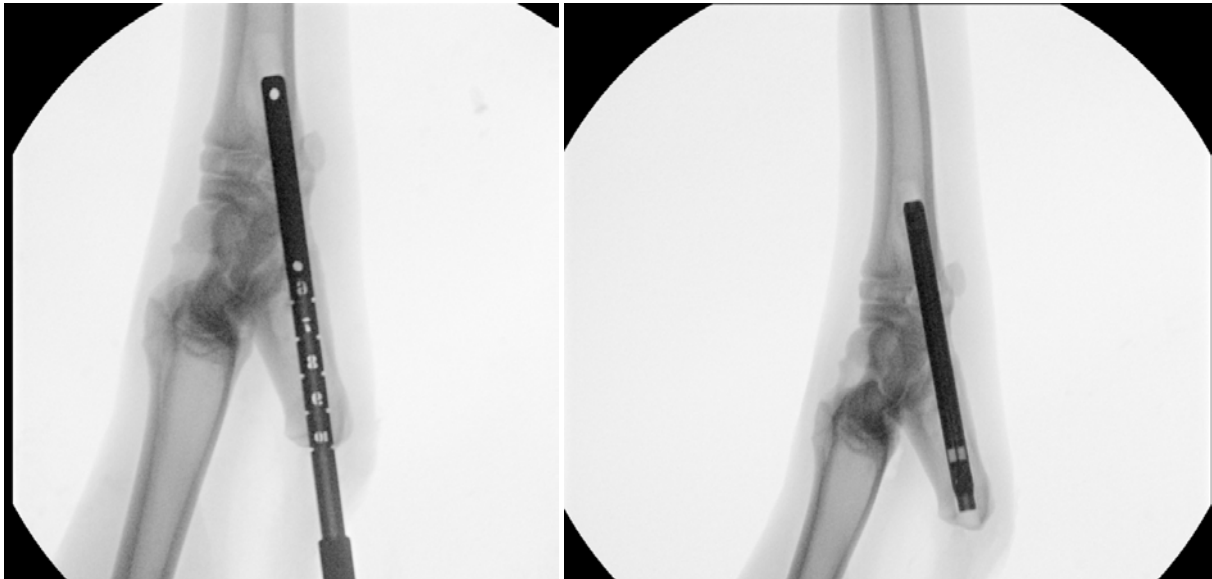


Figure 20. (left) Device length is determined by a trial sizer. (right) Placement of dynamic device.



Figure 21. (left) Radiograph of dynamic device post-operatively. (right) Radiograph of static device post-operatively.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: The remaining animals will be enrolled in the study throughout September 2021 through July 2022.

Subtask 2-Radiographs

Accomplishments: Serial radiographs are taken of each animal, in particular, the animals with dynamic devices because the decrease in the sliding element gap can be tracked to measure joint settling/bone resorption. Figure 22 shows the sequential movement of the sliding element within the outerbody over 4 months. Figure 23 shows a comparison of the post-operative distance, approximately 4 mm, to the 4-month distance, approximately 1 mm. Figure 24 shows the quantitative measurement of joint settling/bone resorption as determined by image analysis at each timepoint. Clinically, 3-5 mm of joint settling/bone resorption has been seen in patients with Charcot neuroarthropathy, thus 3 mm of joint settling/bone resorption in an ovine model represents the clinical scenario.



Figure 22. Serial radiographs for dynamic device.

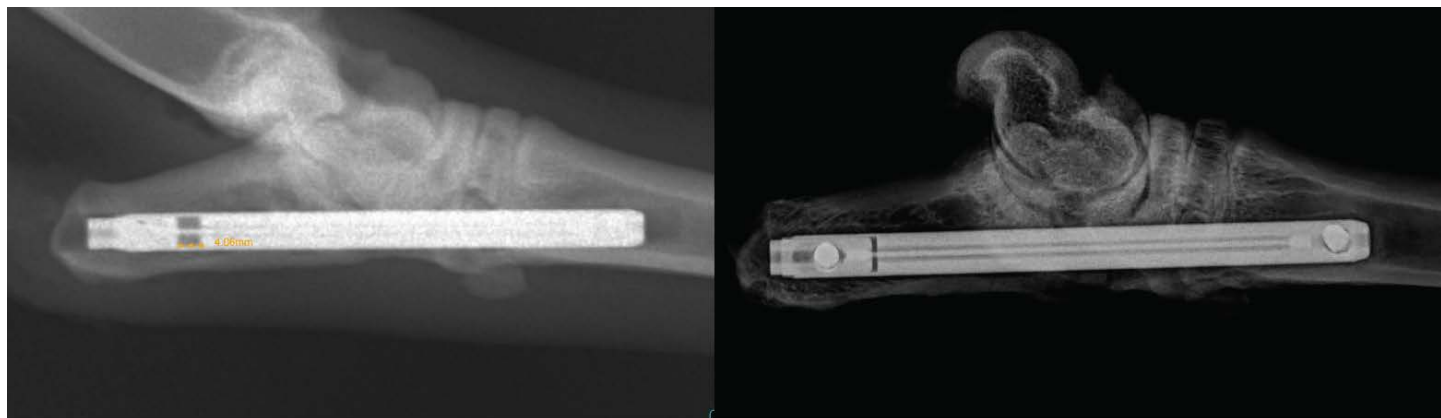


Figure 23. (left) Radiograph at post-op. (right) Radiograph after 4 months.

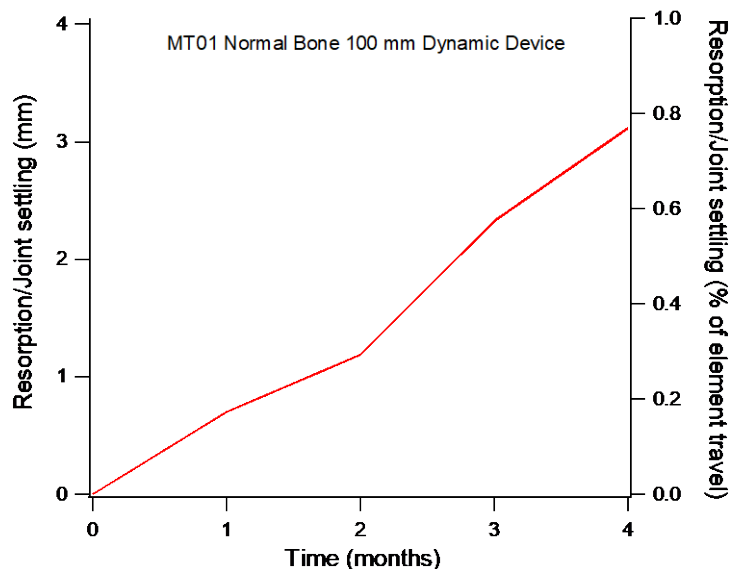


Figure 24. Quantitative evaluation of joint settling/bone resorption during post-operative healing.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Radiographs will continue to be taken for all remaining animals during the study period.

Subtask 3-Mechanical Evaluation

Accomplishments: Mechanical testing from the first animal has been completed by using a nondestructive 4-point bending test (Figure 25). Five conditioning cycles were used to load the construct to 1000 N at a rate of 1 mm/s. The data was taken from the last loading cycle. The stiffness was determined to be 1459 N/mm.

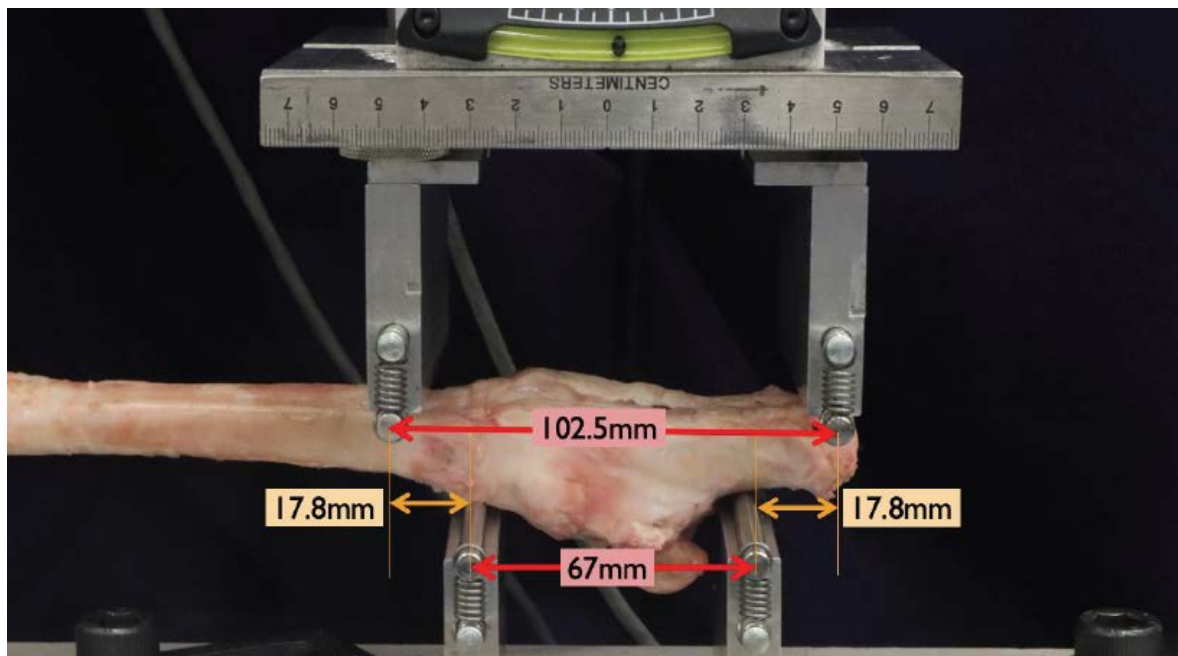


Figure 25. 4-point bend test setup for ovine hindlimbs.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Mechanical analysis will occur for all remaining animals during the study period.

Subtask 4-Micro-CT

Accomplishments: Micro-computed tomography (MicroCT) scans were performed on both the treated and contralateral hock joints at a resolution of 37 μm (Scanco μCT 80, Scanco Medical AG, Bruttisellen,

Switzerland). The device was carefully removed from the treated joint before scanning to eliminate inaccuracies attributable to radiographic artifact. The region of interest of each specimen was centered over the interfaces of the tarsal bones (Figure 26) and each region was evaluated for bone volume (BV) and mean density of the bone volume (MDBV) using automatic segmentation techniques with thresholds to a range of 250 and 450 mgHA/ccm. To further minimize error due to automatic segmentation practices, the contralateral limb was evaluated using the same parameters to establish a baseline. New bone formation of the treated limb was calculated by the difference in bone volume of the treated and contralateral limbs. The volume of immature bone was 26.3% higher within the defined ROI in the treated limb than in the untreated limb. Bone formation was observed primarily around the outside of the joint with visible evidence of preliminary bridging across some of the intertarsal joint capsules (Figure 26). The volume of bone reported between the threshold limits was measured as 5,740 mm³ in the treated joint complex compared to 4,545 mm³ in the contralateral. The mean density of regions of immature bone was 328 mgHA/ccm and 301 mgHA/ccm in the treated and contralateral limbs, respectively.

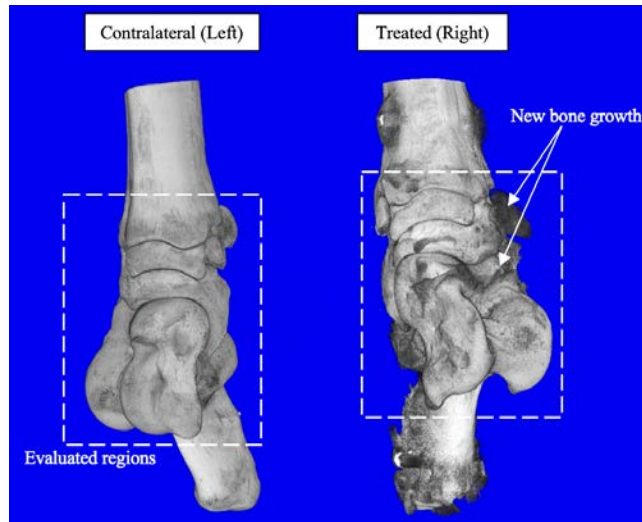


Figure 26. Micro-CT of ovine hock joints.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Micro-computed tomography analysis will occur for all remaining animals during the study period.

Subtask 5-Histological Evaluation

Accomplishments: Nothing to Report.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Histological analysis will occur for all specimens collected during the study period.

3.2.2 Major Task 3: *Validate the prototype device's ability to apply dynamic compression in vivo using an ovine hindlimb fusion model with low bone quality.*

Subtask 1-Partial Unload Surgery

Accomplishments: The first partial unload surgery took place in the second quarter of 2021 following CSU IACUC 1199 to attach an external fixator across the hock joint of the ovine hindlimb for a period of 4 weeks to decrease the bone quality. A representative image of the external fixator is shown in Figure 27. Additional animals were enrolled at the beginning of August 2021 with external fixators for 4 weeks.

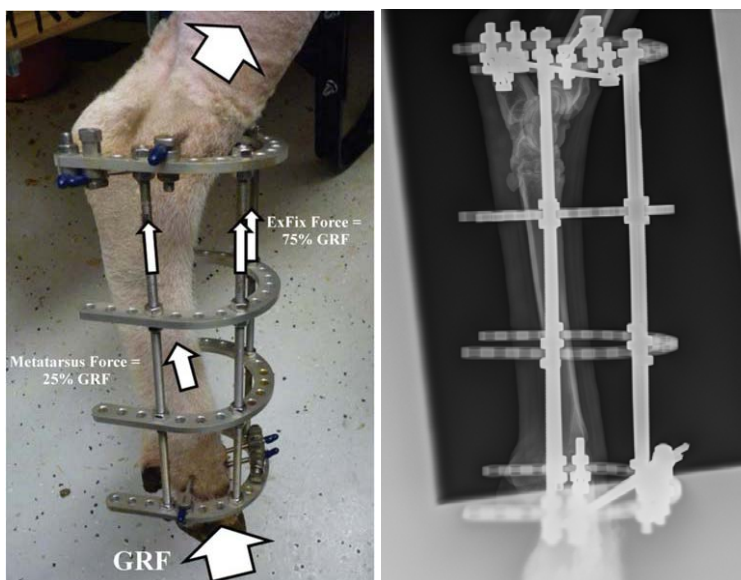


Figure 27. External fixator placement on ovine hindlimb.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: The remaining animals will be enrolled in the study throughout September 2021 through July 2022.

Subtask 2-Fusion Surgery

Accomplishments: The first animal with lower bone quality successfully underwent device implantation following CSU IACUC 1199. The same procedures and protocols were followed for device implantation as Major Task 2 Subtask 1. A dynamic device was implanted in the first animal and post-op radiograph is shown in Figure 28.



Figure 28. Radiograph post-op of dynamic device in ovine hindlimb after removal of external fixator.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: The remaining animals will be enrolled in the study from September 2021 through July 2022.

Subtask 3-Radiographs

Accomplishments: As in Major Task 2 Subtask 2, serial radiographs are taken of each animal, especially, the animals with dynamic devices because the decrease in the sliding element gap can be tracked to measure joint settling/bone resorption. The two-month timepoint radiograph is shown in Figure 29 for the first animal with low bone quality.



Figure 29. Two-month radiograph for animal with low bone quality and dynamic device.

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Radiographs will continue to be taken for all remaining animals during the study period.

Subtask 4-Mechanical Evaluation

Accomplishments: Nothing to Report

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Mechanical analysis will occur for all remaining animals during the study period.

Subtask 5-Micro-CT

Accomplishments: Nothing to Report

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Micro-computed tomography analysis will occur for all remaining animals during the study period.

Subtask 6-Histological Evaluation

Accomplishments: Nothing to Report

Training and Professional Development Opportunities: Nothing to Report

Dissemination of Results: Nothing to Report

Future Plan: Histological analysis will occur for all specimens collected during the study period.

4. Impact

4.1 Impact on the development of the principal discipline

Project results to date present evidence of an orthopedic medical device with mechanical properties superior to current competitor devices that is also capable of sustaining compressive loads in the face of bone resorption or other factors that would be associated with gapping between fusing bones. This gapping often occurs in at-risk patient populations such as diabetics with Charcot neuroarthropathy. The sustained compression demonstrated by the project device in both mechanical testing and large animal model will add to the existing list of clinical and pre-clinical evidence supporting a shift in the orthopedic foot and ankle surgery discipline from static devices incapable of post-day surgery change to dynamic adaptive compression devices that can contribute to fusion throughout the extended healing process.

4.2 Impact on other disciplines

The fundamental mechanobiological principles of joint fusion via sustained dynamic compression hold across multiple joints, whether in the foot and ankle or beyond, such as upper extremities. As such, other orthopedic

surgical disciplines could show improved clinical outcomes via adoption of sustained dynamic compression devices similar to that developed in this project.

4.3 Impact on technology transfer

While no official transfer has occurred to date in the project, a portion of the study results to date were submitted and accepted for presentation at the 2021 Military Health System Research Symposium (MHSRS), such that the study results to date would be shared with the military medical community.

Future project activities include regulatory submission to the FDA so that the device can be used clinically, and in particular used in at-risk patients, especially the Veteran population, who are not being adequately treated using existing static internal fixation technology. Project results to date suggest that the prototype device will be found to be substantially equivalent to competitor devices already cleared by the FDA.

4.4 Impact on society beyond science and technology

While there is nothing to report for the current period, there is a likely future impact due to the project and its results. Current product biomechanical testing data indicate that the study device is capable of sustaining compression in simulated joint fusion. Other MedShape joint fusion internal fixation devices providing sustained compression have already been granted their own unique ICD-10-PCS code by the Centers for Medicare and Medicaid Services (DynaNail and DynaNail Mini). It is likely that the subject prototype device will also be eligible for addition in this unique coding set. CMS granted the code based upon data showing novelty and clinical superiority of sustained compression devices. This superiority has led to improved human health and capabilities in recipient patients, thus allowing them earlier and greater potential return to work where they can contribute to the workforce and help to drive the US economy, as well as engage in social activities requiring mobility and activity.

5. Changes/Problems

5.1 Changes in approach and reasons for change

Nothing to Report

5.2 Actual or anticipated problems or delays and actions or plans to resolve them

The initial prototype device design had a diameter of 5.25 mm to allow for an anterior surgical approach through the lateral column of the midfoot; however, such a small diameter device necessitated even smaller diameter transverse screws to lock into cortical bone. These 2.25 mm transverse screws were not mechanically robust enough compared to predicate device. Thus, the prototype device had to be redesigned. By using a posterior surgical approach, a larger diameter device can be used, 7 mm, which allows for increased bending strength and a larger diameter transverse screw to lock into the cortical bone. Now, the pull-out strength is greater than the predicate device.

The manufacturing vendor that produces the production grade outerbodies for the dynamic devices for both the animal study and benchtop device testing experienced a 10-week delay during 2021, which pushed back many of the testing activities on the production grade devices and assembly activities. The decision was made to prioritize the vendor to produce the devices necessary for the animal study first as delays to the tasks in Major Task 2 and Major Task 3 could delay the overall project timeline. A delay to activities for Major Task 1 can be accommodated as these activities can be run in parallel during Major Task 2. These testing activities are expected to be completed by the first quarter of 2022.

The packaging vendor that produces the outer trays (Figure 17) is experiencing at least a 4-month delay in their manufacturing timelines due to raw material supply delays, labor shortages, and capacity constraints related to covid-19. The packaging is expected to arrive in November 2021, and the testing activities for Major Task 1 Subtask 7 will commence immediately upon receipt. The tasks will be completed in parallel with Major Task 2 activities and not affect the overall project timeline.

5.3 Changes that had a significant impact on expenditures

Nothing to Report

5.4 Significant changes in use or care of vertebrate animals

Nothing to Report

6. Products

6.1 Publications, conference papers, and presentations

An abstract was submitted to the Military Health System Research Symposium, "Biomechanical Comparison in Simulated Bone of Dynamic versus Static Intramedullary Fixation Devices for Foot and Ankle Arthrodesis". The abstract was accepted for a poster presentation; however, the meeting was cancelled due to covid-19.

6.2 Website(s) or other Internet site(s)

Nothing to Report

6.3 Technologies or techniques

From this research, a new animal model of arthrodesis has been developed, specifically calcaneal-tarsal-metatarsal fusion in an ovine model. A device is placed antegrade through the calcaneus into the metatarsal, then fixated in both the metatarsal and the calcaneus with transverse screws. The surgical technique itself follows that used clinically in humans for hindfoot and midfoot fusion. The technique has been successfully adapted to an ovine model, which allows for further biomechanical and bone biology research to be conducted. This technique and animal model will be shared at future Orthopaedic Research Society meetings.

6.4 Inventions, patent applications, and/or licenses

Nothing to Report

6.5 Other Products

Medical Device:

The outerbodies of the dynamic prototype device went through multiple design iterations. Ultimately, a design with a tapered threaded end for bone fixation that matched closely to the size of the proximal intramedullary canal of the 4th metatarsal was chosen as the final design. The other end of the device utilizes a transverse screw like other intramedullary devices. Overall lengths were chosen to range from 110 mm to 140 mm to span the length of the lateral column using a posterior surgical approach. Future project activities include regulatory submission to the FDA so that the prototype device can be used clinically, especially in at-risk patients, especially the Veteran population, who are not being adequately treated using existing static internal fixation technology. Project results to date suggest that the prototype device will be found to be substantially equivalent to competitor devices already cleared by the US FDA.

7. Participants & Other Collaborating Organizations

7.1 Individuals on Project

Name:	David Safranski
Project Role:	PI
Research Identifier:	0000-0001-5722-5831
Nearest Person Month:	2
Contribution to Project:	Dr. Safranski has managed overall project, device design, protocol development, quality monitor of testing, data management, and management of subawardee.
Funding Support:	N/A

Name:	Jack Griffis
Project Role:	Senior Personnel
Research Identifier:	
Nearest Person Month:	1
Contribution to Project:	Mr. Griffis has worked on the CAD drawings and drafting of project documents for future regulatory clearance.
Funding Support:	N/A

Name:	Ilya Dolgopyat
Project Role:	Machinist

Research Identifier:	
Nearest Person Month:	1
Contribution to Project:	Mr. Dolgopyat has worked on machining of prototype devices.
Funding Support:	N/A

Name:	Rachel Grosswald
Project Role:	Co-operative student/Intern
Research Identifier:	
Nearest Person Month:	2
Contribution to Project:	Ms. Grosswald has worked on protocol development and biomechanical testing of devices, and data processing.
Funding Support:	N/A

7.2 Active Support of PI and Key Personnel

Nothing to Report.

7.3 Subawardee Organization

The Presurgical Research Laboratory and the Orthopaedic Bioengineering Research Laboratory at Colorado State University are serving as the subawardee for this research grant, where they will perform the *in vivo* animal model and subsequent analysis.

Organization: Colorado State University

Location: Fort Collins, Colorado

Contribution: Research facilities and research collaboration as a subawardee to perform the animal model

8. Special Reporting Requirements

Nothing to Report

9. Appendices

9.1 List of Abbreviations and Acronyms

ACURO – Animal Care and Use Review Office

ASTM – American Society for Testing and Materials

BV – Bone Volume

CAD – Computer Aided Drafting/Design

CSU – Colorado State University

CT – Computed Tomography

FDA – (United States) Food and Drug Administration

HA – hydroxyapatite

IACUC – Institutional Animal Care and Use Committee

ICD-10-PCS – International Classification of Diseases, 10th Edition, Procedure Codes

IRB – Institute Review Board

MDBV – Mean Density of the Bone Volume

MTS – Materials Test Systems

NiTi – Nickel Titanium (alloy)

PCF – Pounds per Cubic Foot (density)