*Specific Aims*

The lower leg is a complex structure with 26 bones, 33 joints, and more than 100 tendons, muscles and ligaments. With these many elements, it is not surprising that lower-leg injuries are very common. Approximately, 25,000 people sprain their ankle every day and more than one million people visit the emergency rooms every year in the United States with lower-leg injuries. Some pathologies such as Achilles tendon ruptures and chronic ankle instabilities often lead to deficit in functional performance and strength. To design effective treatments aimed to restore proper function of the lower leg, it is necessary to identify and understand the causes of deficit. However, experimental studies aimed to identify the underlying mechanisms of deficit are difficult to perform due to the large number of structural and functional parameters that may play a role in the deficit, and the difficulty of measuring those parameters non-invasively. As an alternative approach, we propose the use of a multiscale model of the lower-leg to identify possible causes of lower-leg function deficit after injury.

The objective of this study is to develop, validate and use a multiscale model to simulate passive and active function of the lower-leg. Specifically, this model will cover the region from the proximal tibia to the toes and will include tendons, ligaments and bones and muscle passive and active behavior. As an initial application, we will investigate the causes of functional deficit after an Achilles tendon rupture. To do this we will simulate the plantar flexion strength and heel-rise tests. Changes in tendon and muscle properties typically observed after an Achilles tendon rupture will be introduced in the model and their contribution to lower-leg deficit will be quantified. This analysis will identify which of altered parameters of the tendon-muscle unit will contribute the most to the functional deficit.

The lower-leg finite element model proposed in this study can be easily adapted to analyze a wide variety of pathologies and surgical procedures including (but not limited to) posterior tibial tendon dysfunction, foot drop, peroneal tendinosis, tendon lengthening, ankle arthrodesis and chronic ankle instability. Consequently, this model will become a powerful tool for the study of lower-leg pathologies.

Our team has extensive experience developing numerical models for variety of tissues and organs including orthopaedic tissues, measuring structure and mechanical properties of tissues, and quantifying lower-leg function. Therefore, we are ideally situated to perform the proposed study. To accomplish this objective, the study has been divided in the three aims:

**Aim 1: Implementing and validating a multiscale finite element model of the lower leg**. In this aim, we will build a finite element model by segmenting 3D magnetic resonance images of the lower leg, identifying individual tissues, and assigning structural and mechanical properties to each of the tissues. We will also validate the model by comparing numerical simulations of plantar flexion strength and heel-rise tests to experimental measurements.

**Aim 2: Finding relationships between abnormal properties of the tendon-muscle unit and lower leg deficit**. In this aim we will focus on elucidating the causes of functional deficit after an Achilles tendon rupture by quantifying changes in ankle torque and heel height caused by changes in tendon length, area and mechanical properties typically observed after a tendon injury. Additionally, the effect of muscle length, area and pennation angle on force production will be quantified. These simulations will identify the most likely cause of lower-leg functional deficit after a tendon injury.

**Aim 3: Predicting patient-specific lower-leg deficit based on morphological measurements of the muscle-tendon unit.** In this aim, the model will be modified to match patient-specific measurements of tendon length, area, and muscle size of patients who have had an Achilles tendon rupture and exhibit a functional deficit of the lower leg. The model will be used to simulate plantar-flexion strength and heel rise height and the results will be compared to those measured experimentally on the same patients.

This study will provide a power tool for the analysis of lower-leg injuries. Mechanical and morphological properties of tissues observed in specific pathologies or injuries can be incorporated into the model to identify their contribution to functional deficit. Therefore, this tool can be used to identify targets for optimized rehabilitation protocols and to predict the outcome of surgical interventions (virtual clinical trial).