Adaptations in the muscle-tendon unit with rehabilitative training following unilateral Achilles tendon injury

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Abstract

The Achilles tendon (AT) is connected in series to the triceps surae muscles to form a muscle-tendon unit (MTU), which is the primary actuator of foot plantarflexion during forward movement. The capability of humans to control and perform this movement is a significant indicator of independent mobility, due to its integral role during the stance phase of the gait cycle. The unique mechanical properties of the AT allow for the MTU to operate efficiently, since the AT can both store and release elastic energy during the gait cycle and allow for the triceps surae muscles to contract almost isometrically.

Achilles tendon rupture (ATR) and subsequent healing has been shown to lead to significant changes in tissue composition, suggesting inherent changes in mechanical properties and *in vivo* function. Two gaps of knowledge remain unaddressed in the literature. First, the biomechanical status and structure of the injured and contralateral MTU after ATR remains unclear. Second, the beneficial effect of more aggressive rehabilitative techniques, such as early weightbearing, remain unverified in their ability to enhance and accelerate the restoration of biomechanical function in post-ATR rehabilitation.

In order to address these gaps in knowledge, the biomechanical status of both the MTU and its function were assessed in long-term and short-term follow-up measurements in ATR patients. These investigations determined that injured MTUs continually exhibit significantly longer ATs compared to the contralateral side after ATR, in addition to continued deficits in single-limb strength. Bilateral gait analysis showed augmented ankle kinematics on the injured limb, but limited side-to-side differences in ankle moment production. Early weightbearing rehabilitation was found to allow for faster gains in single-limb strength between 8 and 12 weeks compared to standards. Furthermore, this early intervention also led to patients attaining symmetry in gait parameters at an earlier time point. No differences in absolute values of AT rest length and single-limb strength were found between rehabilitation groups.

Comparison of these patient data to a control cohort highlighted a significant deviation in MTU length changes and ankle kinematics during gait. The MTU appears to exhibit higher levels of lengthening and limited shortening that are concurrent with lower plantarflexion and higher dorsiflexion. Furthermore, the frontal plane displayed significantly higher mobility than in control subjects. A striking observation in many of these bipedal assessments was that not only did the injured limbs exhibit significant deviations from the controls, but the contralateral limbs did as well. This unexpected result suggests that contralateral limb function may adapt to the injured limb with time, though its MTU structure is unchanged and uninjured. The results from this dissertation suggest that contralateral limbs may not serve as a true comparative indicator of uninjured function. Furthermore, the knowledge of post-ATR changes in MTU function gained from this body of work offers a foundation for future investigations into concurrent muscle and tendon adaptations in the MTU after unilateral tendinous injury.

Zusammenfassung

Die Achillessehne (Achilles tendon = AT) bildet zusammen mit dem Trizeps Surae Muskel eine Muskel-Sehnen-Einheit (muscle-tendon unit = MTU), welche den primären Plantarflexor während der Vorwärtsbewegung bildet. Aufgrund dieser wichtigen Rolle in der Standphase des Gangzyklus ist die Fähigkeit des Menschen, diese Sprunggelenk-Bewegung zu kontrollieren und durchzuführen, ein wichtiger Indikator für unabhängige Mobilität. Eine besondere mechanische Eigenschaft der AT ist die Fähigkeit, elastische Energie während des Gangzyklus zu speichern und wieder freizugeben, wodurch eine effiziente Arbeitsfähigkeit der AT ermöglicht wird. Des Weiteren bewirkt die AT eine isometrische Kontraktion des Triceps Surae Muskels beim Gehen.

Achillessehnenrupturen (Achilles tendon rupture = ATR) und die anschließende Heilungsphase führen nachweislich zu wesentlichen Änderungen in der Gewebezusammensetzung, die wahrscheinlich mit Veränderungen der mechanischen Eigenschaften und der in vivo-Funktion einhergehen. Allerdings konnte bis heute nicht gezeigt werden, wie 1.) der biomechanische Status und die Struktur der verletzten und kontralateralen MTU nach dem ATR adaptiert und 2.) unterschiedliche Protokolle zur Rehabilitation sich auf die biomechanische Funktionsweise der ATR auswirken.

Um diese Wissenslücken zu füllen, wurden der biomechanische Status und die Funktion der MTU in lang- und kurzfristigen Messungen bei ATR-Patienten untersucht. In diesen Untersuchungen wurde festgestellt, dass nach der ATR die verletzte MTU eine deutliche längere AT im Vergleich zu der unverletzten aufweist. Außerdem konnten anhaltende Defizite in der einbeinigen Kraft detektiert werden. Eine bilaterale Ganganalyse zeigte eine vermehrte Kinematik im Sprunggelenk des verletzten Beins, wohingegen das Moment des Sprunggelenkes keinen Seitenunterschied aufgewiesen hat. Eine Rehabilitation unter frühzeitigem Einbezug des Körpergewichts ermöglicht einen schnelleren Anstieg an einseitiger Kraft zwischen 8 und 12 Wochen im Vergleich zu einer Standard-Rehabilitation. Darüber hinaus führte eine frühe Intervention auch zu einer früheren Symmetrie der Gangparameter. Zwischen den Rehabilitationsgruppen wurden keine Unterschiede hinsichtlich der absoluten Werte der Ruhelänge der AT und der einseitigen Kraft gefunden.

Der Vergleich zwischen Patientendaten mit einer gesunden Kontrollgruppe zeigte eine signifikante Abweichung in der MTU Längenänderung und der Sprunggelenks-Kinematik beim Gehen. Die MTU der Patienten wies eine vermehrte Verlängerung und begrenzte Verkürzung auf, die gleichzeitig mit einer überhöhten Dorsalflexion und begrenzten Plantarflexion übereinstimmt. Darüber hinaus zeigten die Patienten in der Frontalebene eine deutlich höhere Mobilität als die Kontrollgruppe. Hingegen der Erwartungen konnte gezeigt werden, dass nicht nur das verletzte Bein sich signifikant von der Kontrollgruppe unterscheidet, sondern auch das nicht-verletzte, kontralaterale Bein. Dieses Ergebnis lässt vermuten, dass sich die Funktion des gesunden kontralateralen Beins der des verletzten Beins anpasst, ohne jegliche Änderung der MTU-Struktur. Die Ergebnisse dieser Arbeit implizieren, dass die kontralaterale Extremität nicht ohne weiteres als Vergleichswert für eine unverletzte Funktion dient. Weiterhin bilden die aus dieser Arbeit gewonnenen Erkenntnisse über die Veränderungen der MTU-Funktion nach einer ATR eine wichtige Grundlage für zukünftige Untersuchungen zur gleichzeitigen Muskel- und Sehnen-Anpassungen in der MTU nach Sehnenverletzungen.

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1. Introduction

Humans have evolved specifically to move about with an upright stance on two limbs. Such upright bipedalism is one of the most prominent, defining characteristics of *Homo sapiens*. In fact, when considering all primates, humans are the only group of obligate primates [1]. Through millions of years of evolution, the primate hindlimbs—originally adapted for lumbering gait, tree climbing, and grasping branches—evolved into the arched foot and ankle complex found in *Homo sapiens*, acting as the only points of contact to the earth. At the end of this kinetic chain is the ankle, the articulation of which defines our ability to move forward efficiently, whether by walking or running. Though our top speed is fairly slow compared to potential predators, endurance running is uniquely human. It has been suggested that the ability of humans to undertake endurance running for long distances was evolved to run down and exhaust larger game animals, such as zebra and kangaroo, for hunting [2,3]. Complete hindlimb fossils of Dmanisi hominins (*Homo erectus georgicus*) dating from the early and middle Pleistocene eras also suggest that there was high selection pressure for enhanced efficiency in walking for hunting [4]. The lynchpin of the evolution of human physiology that allows this endurance predation, and the likely survival of our species, lies in the unique mechanical properties found in the calcaneal tendon, commonly referred to in humans as the Achilles tendon (AT) [5].

These mechanical properties allow the AT to perform a uniquely difficult task: transmit forces from skeletal muscle to bone while overcoming impedance mismatch between compliant and stiff tissues [6]. Once these properties are altered or compromised, drastic changes in locomotion can result. An extreme case is found in Ehlers Danlos Syndrome (EDS), a hereditary connective tissue disorder that negatively affects collagen production and leads to increased tendon laxity. These patients produce significantly lower power at the ankle joint compared to healthy controls, likely due to lowered force transmission efficiency at the AT [7]. The relationship between the AT and the triceps surae appears symbiotic in nature; yet the exact nature of this relationship, particularly in various types of adaptation, remains unclear. A further discussion of the structure and function of this muscle-tendon unit (MTU) in healthy patients is presented in Section 1.1 and Section 1.2.

Though the AT has incredible strength and enables powerful movement, like its namesake, it has an inherent vulnerability. The heel of Achilles was the one spot of weakness in an otherwise invincible warrior [8] that was brought down by an arrow piercing through the tissues. Modern-day warriors are similarly taken down in athletic activities by spontaneous rupture of the primary connective tissue exposed at that same spot: the AT. The Achilles tendon rupture (ATR) has become a more frequent problem in the modern age, though its etymological origins are ancient in nature. In particular, a curiosity is that this injury often affects otherwise athletic, very healthy people, that, in a moment of vulnerability to injury, become injured. As a result of ATR the overall function of the overall MTU is compromised compared to noninjured subjects, and the potential causes and mechanical repercussions are discussed in Section 1.3 and Section 1.4, respectively.

The consequent economic burden of ATR rehabilitation, in addition to the incomplete recovery of ankle function, frames the current need for a time-efficient and biomechanically effective clinical intervention. However, in order to develop ideal interventions, the biomechanical repercussions and adaptations in the MTU from such an injury must first be elucidated. The goal of this dissertation is to investigate how the muscle-tendon unit (MTU) adapts after injury of the tendinous component, using Achilles tendon rupture as a model. In order to achieve this, this work both (1) classifies resultant long-term adaptations in MTU structure and function after ATR and (2) investigates short-term adaptations in MTU structure and function with rehabilitation after ATR, as outlined in Section 1.5 and put forth in the main body of this dissertation.

1.1 The Muscle-Tendon Unit (MTU)

The mechanics of the ankle joint are primarily actuated by a muscle-tendon unit (MTU), in which two elements, namely a muscle and a tendon, work together as a three-component system in order to transmit forces and enable joint function. The basic structure of the MTU consists of a contractile element, which is the primary source of force, and two elastic components, one in series and one in parallel. In the MTU of interest for this work, the AT acts as the serial elastic component and the triceps surae muscles make up the contractile element and the parallel elastic component (**Figure 1**). The function and structure of the MTU constituents are described in the following sections.

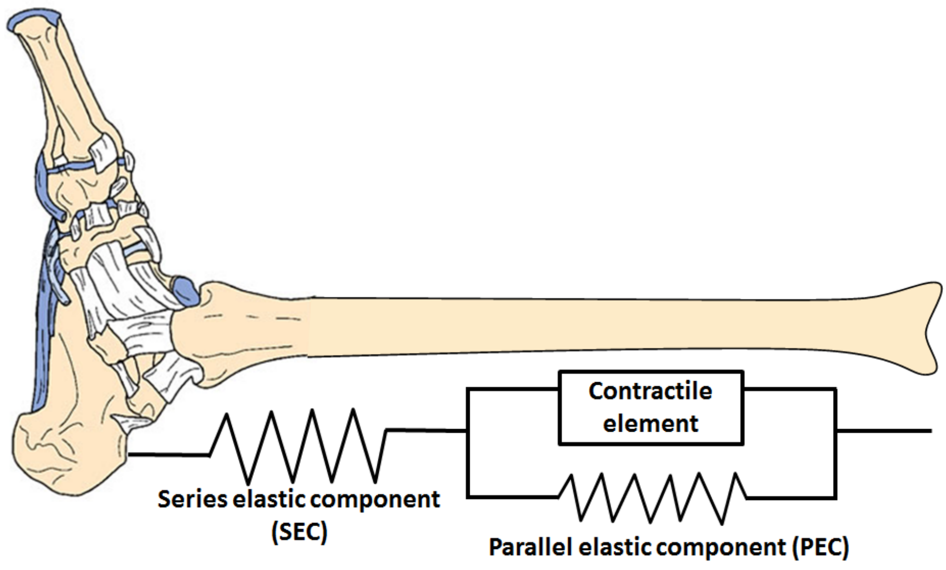

Figure 1. A schematic of the muscle-tendon unit that articulates the ankle joint.

1.1.1 The Achilles tendon

The healthy Achilles tendon (AT) successfully executes a demanding biomechanical task to enable locomotion: connection of a stiff, rigid body to a soft, compliant tissue. This is further complicated by the fact that the compliant tissue (in this case, skeletal muscle) can exert a large range of tensile forces on the AT. One of the most unique mechanical functions of the AT is its capability of overcoming and reducing this impedance mismatch, which can lead to high strain concentrations, and could ultimately lead to higher incidences of injury [6]. In order to better understand the post-rupture structure and function of the AT, this section will introduce the important physiological aspects of the healthy AT that contribute to its function in locomotion.

The AT is one of the largest, thickest, and strongest tendinous structures in the human body, connecting the double-headed gastrocnemius muscle, soleus, and plantaris muscles to the tuber calcanei (**Figure 2**). The AT can be further divided into different components: the gastrocnemius tendon component is measured from the calcaneal insertion to the end of the aponeurosis which inserts into the gastrocnemius muscle, and the free AT is defined as the distance between the calcaneus and the insertion into the soleus. Within this work, the term “Achilles tendon” (AT) will specifically refer to the length between the calcaneal insertion and the insertion of the aponeurosis into the gastrocnemius muscle.

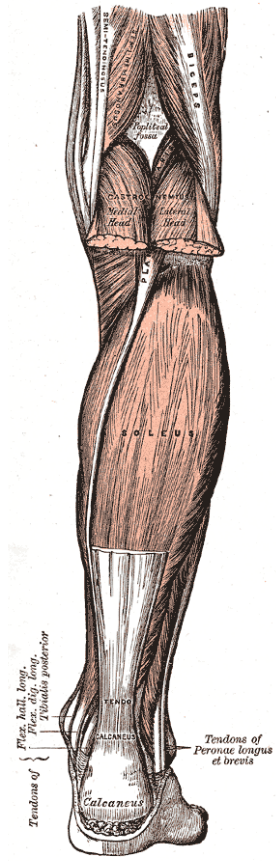

Figure 2: The musculo-tendinous anatomy of the posterior lower limb, showing the location of the Achilles tendon (referred to as the *tendo calcaneus*) in relation to the calcaneus and the triceps surae muscles (gastrocnemius and soleus) [9].

On average, the AT is 15cm in length, with a mean width of 6.8 cm at the gastrocnemius muscle insertion and 3.4 cm at the calcaneal attachment [10]. The narrowest portion of the tissue, often referred to as the “tendon waist”, is found at the midpoint of the free AT, found 20% proximal to the calcaneal attachment [10], and is the most common location in which spontaneous rupture can occur. Incidentally, microvascular anatomic studies of the AT found that this specific area is also considerably avascular compared to the rest of the tissue, in both blood vessel number and relative vessel area [11].

The AT tissue, like other tendons found in the human body, is a highly acellular tissue composed of a hierarchal collagen network that is interspersed with a system of noncollagenous molecules (**Figure 3**) [12]. However, unlike other tendons, the AT is not encapsulated by a tendon sheath, but rather surrounded by three layers of soft tissue that compose what is called the paratenon. This structure allows for free movement of the AT without impingement or friction on surrounding tissues [13]. The outermost paratenon layer is connected to the deep fascia, the middle layer composes the mesotenon, and the epitenon directly surrounds the tendon tissue. The fine collagen fibril network found in the epitenon is directly fused with superficial tendon fibrils [13].

The epitenon surrounds groups of organized collagen fibers (primarily Type I) that are arranged into parallel, rope-like tendon fascicles [14], each of which are surrounded by an endotenon. In the AT, both neural connections and the limited blood supply from the posterior tibial and peroneal arteries are found within the endotenon. The tendon fascicles consist of collagen fibers interspersed with tenocytes, elongated fibroblast-type cells that synthesize extracellular matrix (ECM) proteins. These 10-µm diameter tendon fibers [15] are composed of collagen fibrils, which are often in a crimped position at rest. These fibrils are composed of numerous microfibrils, which in turn are made up of five helical tropocollagen molecules, each of which are made up of three polypeptide chains of collagen [16]. This specific hierarchical structure allows for the AT to demonstrate unique macroscopic mechanical properties, as discussed in **Section 1.2**.

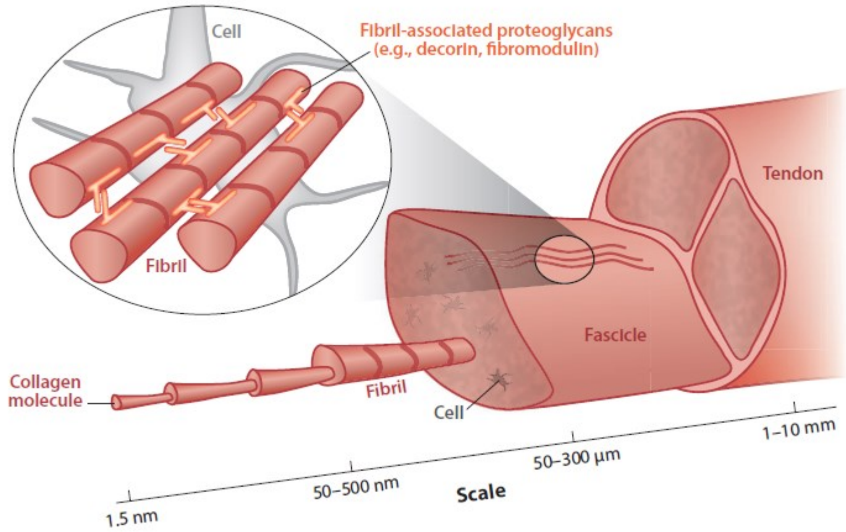

Figure 3: A scalar look at the hierarchical structure of tendons from the tissue to collagen fibril levels [12]

The AT is connected to the nervous system by proprioceptive sensory receptor organs, known as the Golgi tendon organs, which are primarily located at the musculo-tendinous junction (MTJ) location [17]. This sensor generates afferent information that allows for the central nervous system to process and determine the relative stretch in the tendon. Through the Ib afferent axon, this stretch sensor allows for the control and modulation of muscle contraction. Previous work comparing the effect of passive joint movement to active joint movement found that golgi tendon organs are completely unmodulated during passive movement compared to high modulation in active muscle contractions [18]. This highlights the importance of neuromechanical modulation from the central nervous system, and that active and passive movements, even in the same range of motion (ROM) are not comparable. Higher modulation of the golgi tendon body afferents yields muscle contraction, which induces tensile force on the tendon; low modulation in turn, relaxes the muscle and the tendon in turn remains fairly slack. This neuromechanical connection underscores the important relationship and dependence of the AT on the triceps surae muscle in series.

1.1.2 Triceps surae muscle

The AT is directly connected in series with the triceps surae muscle on its distal end, which acts as the contractile element of the MTU. The parallel elastic component is also located within this muscle group and consists of passive elastic elements found in the muscle fascia. Within the scope of this work, the primary focus will be on the contribution of the contractile element to the overall MTU. The triceps surae consists of two primary muscles, the gastrocnemius and the soleus, both of which are discussed below.

The gastrocnemius makes up the majority of the muscle volume in the lower limb, and is also the most superficial on the posterior calf. The muscle belly consists of two heads, medial and lateral, which are both connected to the calcaneus via the AT [9]. The medial head is the larger of the two and arises at the medial condyle of the femur; the lateral head originates at the lateral femoral condyle. Below the gastrocnemius is the soleus muscle, a long, thin muscle that originates at the fibula and the medial border of the tibia [9]. The gastrocnemius is composed of roughly 50% Type I muscle fibers and 50% Type IIa fibers, or slow oxidative and fast oxidative/glycolitic fibers, respectively. The soleus has a comparatively higher proportion of Type I (slow oxidative) muscle fibers. The local architecture of these fibers place an important role in force generation [19].

The triceps surae is primarily used in locomotion to power plantarflexion of the ankle joint in order to enable forward and upward vertical movement. The gastrocnemius muscle heads are often more involved in high-velocity movements and the soleus muscle plays an important role in supporting quiet upright stance.

The capability of the triceps surae muscle to produce force is dictated by its relative length; similarly to other skeletal muscles, a force-length relationship exists between the relative amount of force generated and the length of the overall muscle. During locomotion, the triceps surae muscles contract nearly isometrically within the ideal range of muscle length [20]. Furthermore, during stair navigation, the gastrocnemius medialis (GM) muscle fascicles contract nearly isometrically as well. During this movement, it was previously shown that the AT is the primary MTU component to undergo stretching in order to maintain an ideal muscle length for maximal force generation [21]. This further underscores the importance of the AT within the MTU during movement.

1.2 Function of the healthy MTU in locomotion

The triceps surae muscles and the Achilles tendon work in series as a muscle-tendon unit (MTU) to generate the necessary extrinsic torque for plantarflexion. Plantarflexion plays an integral role in ambulation, particularly in the propulsive period of the stance phase of gait [22], and the relative function and power of this movement dictates a person's gait efficiency and overall mobility [23,24].

The healthy AT plays a paramount role in efficient triceps surae function and joint movement, since they allow for a more compliant MTU [25]. This is critical during gait, as the AT slows muscle fascicle shortening velocity [26,27], which increases both muscle force potential and metabolic efficiency [28]. The Achilles tendon has a uniquely high capacity to store elastic energy during gait. As a result, the ankle is the most efficient of all joints in the lower limb [29]. It has been suggested that the unique elasticity and energy-storing capacity of the Achilles tendon plays a major role in determining ankle biomechanics [30–32] and allows for maximal efficiency and optimal power output of the muscle during forward movement [25,33–36]. During both walking and running, soleus muscles in healthy subjects tend to remain in the ascending portion of the force-length curve in order to resist perturbations in change of length [37]. The compliant AT is capable of efficiently transferring and storing energy during various speeds of locomotion [26]. This long tendon allows for energy savings of up to 50% during running [38,39] and storage during jumps.

The AT is a unique structure found in humans that enables upright bipedal gait, compared to apes, whose hindlimb muscles have little to no connecting tendinous structure for skeletal insertion [40]. The comparison of the calcaneal tendons in humans to chimpanzees (in the family *Hominidae*) show a limited tendon, and due to this, chimpanzees are unable to maintain bipedal locomotion (**Figure 4**).

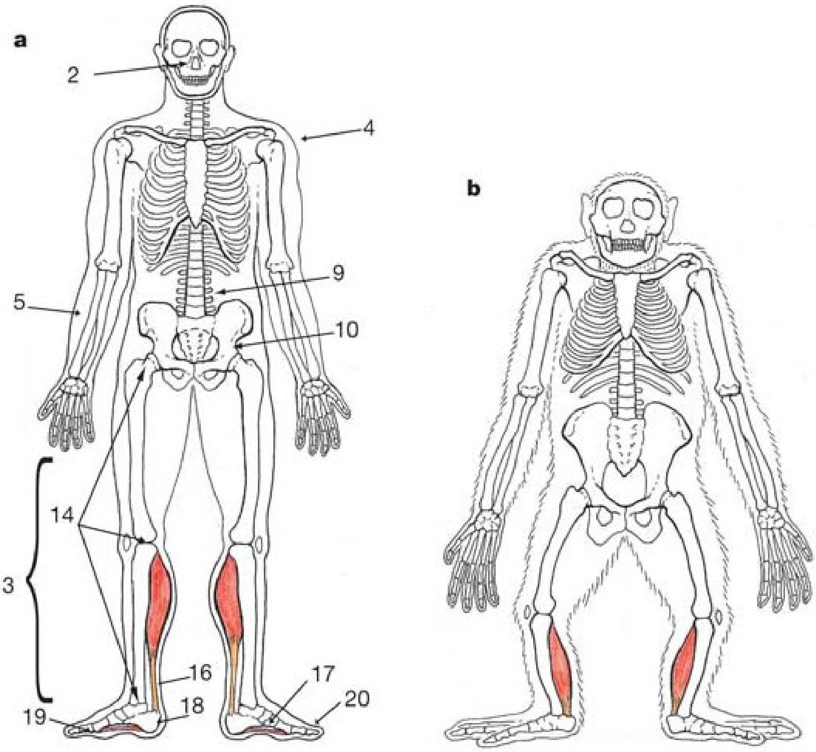

Figure 4: Comparative musculoskeletal anatomy of humans (a) to chimpanzees (b), which highlight the species-specificity in the tendinous component of the muscle-tendon unit [3].

Though the AT is spring-like in nature, the crimp-like architecture found at lower hierarchal levels allows for the tendon tissue to behave as a viscoelastic material. Thus simple spring-like approximations of its mechanical behavior during movement are inaccurate [41], complicating *in silico* representations of MTU behavior during different movements. One such model developed by Lichtwark and Wilson determined that in order to maximize energy output and muscle efficiency in the AT-MTU, optimal values of linear tendon stiffness should range from 108-144 N/mm during gait [35]. A later model developed by Arnold and co-workers examined muscle-tendon dynamics for eleven different components of the lower limb at a wide variety of speeds based on data from healthy subjects [25]. When the model's ATs were stiffer, the fibers of the plantarflexor muscles lengthened quickly during early stance and shortened quickly during late stance, resulting in excessive negative and insufficient positive ankle joint power, respectively. This model underscores the importance of AT mechanical properties, and that mechanical changes in the properties of a singular MTU component can have a dramatic effect on the function of the overall MTU.

1.3 Achilles tendon rupture (ATR)

1.3.1 Incidence and etiology of injury

Although the AT is one of the largest and strongest tendons in the human body, it is still the most prone to spontaneous rupture [42]. There is a limited record of Achilles tendon ruptures (ATRs) prior to 1929, and some of the earliest reports starting in the 1930's began to report upward trends in incidence through the middle of the twentieth century [43]. Numerous epidemiological studies undertaken in more recent decades have shown a general upward trend in the worldwide incidence rate of ATRs [44–49], specifically in developed countries [50], as illustrated in **Table 1**. A possible explanation for the increasing rate in recent decades may be due to increased continued participation in high-intensity recreational sports by adults after the third or fourth decade of life ([44,46,51]).

Authors	City or Country	Time period	Total patients	Initial incidence per 10^5 inhabitants	End incidence per 10^5 inhabitants	Male:female ratio
Leppilahti *et al.* [44]	Oulu, Finland	1979-1986	111	2	18	5.5:1
Maffuli *et al.*[45]	Scotland	1980-1995	4201	4.7	6.0	1.7:1
Levi [48]	Copenhagen, Denmark	1978-1995	213	~13.8	~13.4	2.8:1
Houshian *et al.*[49]	Ribe County, Denmark	1984-1996	718	18.2	37.2	3:1
Suchak *et al.*[52]	Edmonton, Canada	1998-2002	110	5.5	9.9	4:1
Tumility [47]	New Zealand	1998-2003	23	4.7	10.3	1.4:1

Table 1: A selection of reported incidences of Achilles tendon rupture (ATR) in the literature indicate an upward trend in developed countries.

The exact mechanism of how ATR occurs remains unclear, it appears to be a multifactorial in nature, stemming from both intrinsic and extrinsic factors [53]. Some of the intrinsic factors include the relative hypoxia found in the tissue due to the limited blood supply, the impaired metabolism found in the tissue, and the local inflammation within the tendon [53]. Additionally, repetitive training may cause microtrauma to the tissue that may aggregate over time and ultimately weaken the tissue, increasing the risk for rupture. Furthermore, degeneration and weakening of the tissue with age may also contribute to tendon weakening and increased ATR risk [54].

Extrinsic factors that contribute to ATR are often the external trauma and sudden impacts that lead to tendon failure [53]. The rupture usually occurs during an unexpected eccentric contraction when the muscle contracts while being stretched. The applied load from eccentric contractions is very high and the time over which it is applied is short; this can be enough to result in complete tissue failure [55]. Thus poor form, unexpected landings, and overexerted acceleration in active movement are often cited by patients as events leading up to a rupture.

Although the specific mechanism of the injury is unclear, epidemiological studies have elucidated characteristics of a typical patient that may have a higher risk for sustaining an ATR. Males have historically had a higher incidence of ATR compared to females, as seen in the literature reviewed in **Table 1**. Gender-based differences in foot skeleton anatomy may also predispose males to ATR, as males appear to have a more oblique subtalar axis than females, which may lead to the application of more asymmetric loads to the AT [37]. A higher incidence of ATR occurs in the third and fourth decades of life, and often occurs during participation in high-impact sports. One study found within their cohort that 88% of ATRs occurred during participation in ball games, particularly in volleyball, badminton, and soccer [44].

The economic burden of this injury is particularly significant, as this injury affects comparatively younger members of the workforce than invasive unilateral orthopaedic procedures such as total knee and hip replacement patients. One such economic analysis was performed recently in New Zealand. Tumilty found that within one year, the economic cost of a total of 412 ATRs in New

Zealand cost NZ$1.8 million (roughly €1.1 million), and rehabilitation of the injury adds extra burden on the health system [47]. These high rehabilitation costs on the workforce and the health system frame the current need to determine the best form of ATR treatment, as well as time-efficient and optimal rehabilitation protocols.

1.3.2 Current clinical ATR treatment

There are currently three different forms of available treatment for an Achilles tendon rupture: open surgery, percutaneous (minimally invasive) surgery, and conservative (non-surgical) treatment. Currently, there is no consensus on which approach is best. Conservative, nonsurgical methods are often suggested for patients where surgical intervention may pose a risk. In particular, older patients or patients with systemic disease with limited healing capacity are often referred to this particular mode. However, the incidence of rerupture may be higher with this particular mode. Open surgical techniques create one large cut into the lower leg, exposing the majority of the tendon. A major benefit of this method is that the surgeons visually ensure that the two tendon stumps are joined, further securing that the tissues will join during the healing process. This procedure has a higher infection risk than conservative handling, but the rerupture rate may be decreased. Percutaneous techniques have been recently used, offering the benefit of surgical handling with a lowered infection risk. As mentioned before, all of these different modes have their benefits and drawbacks, but there is currently no standard by which to compare the end-outcomes from each treatment.

Many studies that have endeavored to classify outcomes from different surgical interventions have primarily used clinical assessment scores in order to determine healed tendon function. The majority of these scores are in the forms of questionnaires to be answered by the patient, using numeric scales for the patient to self-assess levels of pain and function in day-to-day activities. Some of the scores also include parameters such as circumference of calf musculature and tactile assessment and ratings of the Achilles tendon itself. Some functional parameters are tested by seeing how well a patient can stand on the balls of their feet, or if they are able to perform a one-legged stand or hop. These highly subjective methods can vary by patient as well as by clinical practitioners, which is neither adequate nor precise enough to accurately determine the effectiveness of a particular surgical technique or a particular physical therapy intervention. There is also a lot of debate about the correct methods and the correct timing needed after surgical treatment. When patients were placed in casts and immobilized for longer periods, this period of disuse has led to significant atrophy of the affected side. Early mobilization and weight bearing have been suggested as potential improvements to current standards in physical therapy.

Some studies have also attempted to determine which of these interventions were most effective by focusing on laboratory-based functional tests. Many of these tests have focused on isolated plantarflexion strength as well as studying the relative range of motion in a dynamometer. Though these tests may give some idea of the relative strength and capability of the joint to move, it is not necessarily representative of the forces that come into play during forward ambulation, where the two sides work together to move the body forward. Another parameter used to determine function of the Achilles tendon post-injury has been vertical jumping tests, taking into account flight time, vertical ground reaction forces, and endurance. Though the Achilles tendon muscle-tendon unit is very involved in vertical propulsion, this movement is only one portion of its capability. Movement generated from the Achilles tendon is primarily across two axes: the vertical **and** the anterior-posterior (forward) axes. These jumping tests represent solely extreme loading conditions, isolated to a single axis and do not representative of efficiency of movement in daily activities.

According to the current clinical guidelines proposed by the American Academy of Orthopaedic Surgeons (AAOS), there is inconclusive evidence for them to recommend neither specific forms of postoperative physiotherapy, and only moderate support for restricted weight bearing immediately following operation. Additionally, with the current knowledge from the literature, the AAOS could not advocate a specific post-injury timepoint at which patients could return to activities of daily life and participate in athletic activities. This same report found that there was moderate evidence to suggest mobilization starting 2-4 weeks after injury, as well as moderate evidence to support early protected weight bearing [56].

This report from the AAOS identified some focal points in which they suggest future research should be conducted to improve treatment of Achilles tendon ruptures. They suggest investigations to determine the benefits of restricted weight bearing, as well as a justification for physiotherapy interventions. The biggest deficit in this area of research is that there is no particular standard to compare all of the end outcomes of the different surgical techniques, nor the effects of different types of physiotherapy [56].

1.4 Healing and regeneration of the Achilles tendon (AT) after rupture

1.4.1 Cellular changes in the AT after rupture

Unlike the regenerative processes that can occur in the two tissues found at opposite ends of the tendon (bone and muscle), an injured tendon has no capacity to recapitulate the exact structure, composition, and mechanics of the previously uninjured tissue. The highly organized hierarchal collagen network is often disturbed and disorganized as a result of the rupture [57], and reorganization of a collagen network improves with time but is not identical to non-ruptured tissue [58]. The attempted tendon healing occurs in three separate stages after injury: an initial inflammatory period, followed by proliferation, and ending with tendon tissue remodeling.

In the inflammatory healing period immediately following rupture, histopathological cell populations in the tendon change significantly [59], with an influx of cells recruited for both phagocytosis of necrotic tissue and angiogenesis initiation [60]. Additionally, the collagen fibers of the ruptured tendon show high irregularities in crimp angle along the length of the tendon and average collagen fiber diameter is reduced by 36% compared to healthy tendons [61].

During the proliferation phase one week post-injury, Type III Collagen production peaks. Injury sites have particularly increased levels of Type III Collagen and decreased levels of Type I Collagen, resulting in an overall reduction in tendon tensile strength [62,63].

About six weeks after injury, tendon remodeling begins and production of Type I Collagen increases. After about ten weeks for up to one year post-injury, the tissue begins to mature. In this phase the fibrous tissue slowly transforms into scar-like tissue while losing vascularity [60]. Though this entire process is sometimes incorrectly labeled as “regeneration” of the tendon, the resultant tendon tissue will ultimately remain deficient and not identical to the original, uninjured tendon [64].

1.4.2 *In vitro* and *in vivo* animal models of ATR

Existing studies in the literature have mostly investigated post-rupture tendon mechanics *in vitro* using animal models or excised human samples from cadavers. Both of these types of studies give a poor representation of the complex loads applied to the human Achilles tendon *in vivo*, since the attached triceps surae muscle consists of multiple muscles with different volumes [65]. However, these studies do give us insights into the load-dependent changes that occur in the tendon after rupture [12].

A benefit of animal models is the capacity to excise the entire AT tissue and to perform controlled *ex vivo* tests to determine mechanical properties across a large range of tensile loads, up to and including mechanical failure of the tissue. One such study in rats showed that there was a strong correlation between the function of the tendon and the failure load [66]. Fatigue properties were studied in mouse ATs following rupture and during the early stages of healing, which showed that compared to control ATs, the number of cycles to failure had dramatically decreased after injury but were recovered after 6 weeks [67].

Another such investigation in rat models found that short-term periods of loading after rupture increase the cross-sectional area of the tendon, nevertheless this had no effect on the mechanical properties of the tissue [68], but were improved when loading took place soon after injury [69]. These results may correlate to a clinical study that suggested improved healing and function with early weight-bearing, but these studies rely on solely on subjective clinical scores [70]. In order to determine rehabilitation procedures for optimal function, the mechanical properties of the healing tendon must first be determined *in vivo*.

1.4.3 Human studies after ATR

Early studies of post-rupture ATR tendon tissue have been primarily conducted by investigating AT samples from biopsies taken from the rupture site at the time of injury, often prior to surgical repair. At the rupture site, the original crimp angle that in the collagen fibers appears lost at the tendon stump ends, and the fibers themselves are also smaller in thickness [71]. Type I Collagen is the primary collagen produced by healthy ATs, but tenocyte cells recovered from the rupture site appears produce a comparatively higher amount of Type III Collagen [62]. Progressive passage of such cells in culture indicate a trend of increased Type III Collagen production compared with Type I production that increases with passage number [72]. It appears that this increased capacity for Type III Collagen production contributes to the subsequent production of scar tissue at the rupture site. The formed scar tissue often leads to an increased cross-sectional area of the tendon after ATR repair, as confirmed by magnetic resonance imaging [73].

On the opposite side of the scale spectrum, many studies have also been performed to determine *in vivo* function of the post-rupture AT using functional examinations. One gait analysis performed in ATR patients found that injured limbs exhibit higher maximum dorsiflexion than the contralateral limbs [74]. Another long-term follow-up assessment of post-ATR patients also found lower plantarflexion during one-legged heel raises (27), which was directly correlated to AT length. To date, it is still unclear how exactly the post-ATR tendon alters biomechanical function during movements.

Often investigations in lower limb strength have been used to determine functional recovery after ATR. This unilateral injury is thought to lead to asymmetry during high-impact exercises up to two years after surgery [75]. Loss of plantarflexor muscle strength after Achilles tendon rupture has already been well documented [76] Side-to-side imbalances in calf muscle strength can also persist after surgical repair. Plantar flexor strength in the affected side may be significantly weaker six months following post-operation [24], and eccentric muscle strength deficits can persist up to two years after surgery despite restoration of concentric strength, range of motion, and plantar flexor passive stiffness [25]. Persistent weakness on the affected side can contribute to the development of further tendinopathic conditions in the healing tissue [26]. To increase muscle strength and tendon elongation, and ultimately MTU functionality, rehabilitation of the post-operative joint includes active resistance training.

The capacity of the tendon to store energy *in vivo* has been primarily characterized by calculating the overall stiffness of the entire tissue during an isometric plantarflexion effort [77]. This estimation is adequate in healthy tendons, since the undisrupted collagen network deforms uniformly

[78]. Rupture destroys this network and subsequently stimulates the production of repair tissue, which is both hypercellular [79] and disorganized [61].

One group used roentgen-stereometric analysis (RSA) to measure tendon deformation over time after rupture with a system of implanted tantalum beads. They found a correlation between joint function and tendon deformation after one year [80], and that there was no difference in tendon mechanical properties between patients with operative and non-operative treatment [81]. This method has significant drawbacks, as the tantalum beads may loosen with time and embed in other tissues and patients may be adverse to implantation. An ideal method would be noninvasive and not directly disturb the healing tissues; our developed methods are completely noninvasive and will not interfere with the healing environment.

To date, there are significant deficits in the literature with regards to the numerous changes and adaptations that occur in the AT and the MTU after unilateral ATR. Current methods of assessing biomechanical status and function of the post-ATR MTUs are limited in scope and quantity. Functional assessments are limited to long-term follow-ups, at which point adaptive changes can no longer be observed, and have often only focused on single-limb function. Furthermore, structural changes in the MTU tissues following ATR have often been limited to only the injured limb, since the previously mentioned invasive methods require direct access to the injured AT and cannot be implemented in the uninjured contralateral side. Due to these gaps in knowledge, both the structural and functional adaptations in both the injured and contralateral limbs following ATR remain unclear. It is due to this lack of knowledge in both MTU structure and function that the mechanical deficits commonly found in ankle biomechanical function after unilateral ATR cannot currently be explained.

1.5 Thesis overview

This dissertation presents the motivation and methods used in order to characterize the post-ATR tendon *in vivo*. The introduction in Chapter 1 provides a historical and scientific background for the specific aims and goals of the research, highlighted in Chapter 2, which includes the primary study designs. Chapter 3 builds on this foundation by describing the technical methodologies used in this work, as well as the subjective clinical scores used for comparison. In Chapter 4, a retrospective cohort of ATR patients is assessed in order to determine both long-term function and structure of the AT after injury. This is followed by a short-term, prospective study of a separate ATR cohort in Chapter 5, in which the temporal effect of weightbearing during the initial rehabilitation period is examined. Chapter 6 examines the results from both the short-term and long-term results more closely, and suggests a new paradigm for functional changes after ATR injury and treatment. A concluding summary and an outlook for future research are presented in Chapter 7.

2 Goals & Study Design

2.1 Deficits in current knowledge

As the incidence of ATR has been steadily increasing in the past century, more and more methods have been suggested as valid treatment options, as outlined in Section 1.3.2. Yet it remains unclear what the biomechanical outcomes of such treatment options are on the *in vivo* AT, both immediately after and in the long-term after ATR injury. Long-term functional deficits found on the previously injured side during high-demand activities [75] and a loss of plantarflexor muscle strength after ATR [76].

Until now, the cause of these deficits has been suggested to be some form of a biomechanical deficit in the MTU tissues, but has yet to be investigated. It has also been similarly suggested in both animal models and in human studies that earlier mechanical loading and more aggressive weightbearing rehabilitation yield better results, but this also remains to be investigated in *vivo*.

Often in human studies of ATR, subjective clinical scores, such as the American Orthopedic Foot and Ankle Scores (AOFAS) or the Achilles Tendon Rupture Score (ATRS) have been used to determine both long-term and short-term outcomes. Such scores are mostly based on subjective patient responses to questions regarding the well-being of the AT and overall health. Such scores have not been shown to correlate to medium-term ankle function at 6 months after injury but not long-term function at 12 months, as measured by heel-rise height and work [82]. This underlines the need for objective methods of assessment to determine biomechanical function of the AT after ATR, as the primary methods of clinical scores are too unreliable and not reflective of *in vivo* AT status. Furthermore, these methods are not able to address two important gaps in knowledge about the healing ATR.

The first gap in knowledge is that the long-term biomechanical status of the injured and contralateral AT tissues years after ATR remains unclear, and if and how the contralateral tissue differs from the injured tissue. Any *in vitro* biomechanical tests on excised human AT tissues have been only gathered at the time of surgical repair. Due to ethical concerns, excision of human AT tissues from any other time point is impossible, and the availability of cadaver material with a healed ATR is limited to none. Some *in vivo* tests in humans have suggested that the stiffness increases with time, but have been limited to the injured side due to bead implantation [83]. Another *in vivo* test suggests that there are differences between injured and contralateral sides, but tests were done within one year of ATR [84]. The biomechanical status of the injured and contralateral ATs remains to be clarified in the years after ATR.

The second gap in knowledge is that it is unclear how biomechanical gains in the AT and MTU are made early in rehabilitation immediately following ATR, and if the specific timepoint for introduction of weightbearing plays a role in improving outcomes. Previous work has compared early weightbearing after surgical treatment to either immobilization or conservative, nonoperative treatment. However, a comparison has yet to be made between early and standard weightbearing protocols. Furthermore, as the literature appears to concur that weightbearing yields better biomechanical tissues, it has been often suggested that early interventions may also come with a higher risk of re-rupture or further injury. Multi-timepoint short-term studies within this initial weightbearing period of rehabilitation would allow for a better understanding of how biomechanical gains are made immediately ATR and what rehabilitation protocols would yield better patient outcomes.

2.2 Aims & Goals

In order to investigate the current gaps in knowledge outlined in the previous section, new information must be attained by assessing ATR patients at different stages of healing. There are two primary aims in this work: The first is to develop an understanding of the long-term *in vivo* biomechanical status and function of the post-rupture AT within the MTU. The second is to develop a similar understanding of the short-term biomechanical and functional changes *in vivo* that occur in the early stages of rehabilitation. The corresponding goals and primary hypotheses for the first and second aims are summarized below in Table 2 and Table 3, respectively.

First Aim - To better understand long-term AT function in the MTU		
Goal	Hypothesis Number	Hypothesis
To non-invasively characterize *in vivo* intra-patient differences in tendon structure and function between the previously ruptured AT and the uninjured contralateral AT 2-6 years after percutaneous repair in humans.	H1	The previously injured tendons (INJ) will exhibit significant differences in tendon stiffness and rest length compared to the non-injured contralateral (CON) side.
To assess and quantify long-term changes in ankle kinematics and moment production during gait.	H2	The INJ ankle will generate lower moments and forces and have limited mobility during gait compared to the CON ankle.
To assess the relationship between in vivo tendon stiffness and ankle function during gait.	H3	Increased intra-patient asymmetries in AT properties will correlate to asymmetries in ankle mobility and moment production during gait.

Table 2: Outlining the first aim of the thesis, and the associated goals and hypotheses

Second Aim – To better understand short-term AT function in the MTU		
Goal	Hypothesis Number	Hypothesis
To assess and quantify early functional gains to determine if early weightbearing (EWB) rehabilitation protocols enable faster recovery compared to standard weightbearing (SWB) protocols.	H4	Rehabilitation with EWB will lead to faster gains in ankle moment and strength in both single-limb and bipedal assessments on the INJ limb when compared to SWB patients.
To determine the temporal influence of WB on AT properties through *in vivo* assessment and quantification.	H5	EWB patients will demonstrate a longer AT rest length and increased stiffness on the INJ tendon compared to SWB patients.
To characterize and quantify ankle kinematics in the redevelopment of independent gait, one of the first activities of daily living mastered within the first few months post-ATR.	H6	EWB patients will exhibit higher ankle mobility and more symmetry in gait compared to SWB patients.

Table 3: Outlining the second aim of the thesis, and the associated goals and hypotheses

2.3 Study design

In order to assess the previously mentioned hypotheses, investigation of the AT properties needs to occur at relevant time points for tendon healing, which are summarized in **Figure 5**. A short introduction to the cellular changes that occur in the post-rupture AT was given in Section 1.4.1. In summary, tissue inflammation occurs within the first week post-ATR, followed by a proliferation phase between one and six to ten weeks after injury. The final tissue remodeling phase starts about ten weeks post-ATR and lasts up to a year after injury.

On a more macroscopic scale, most patients put limited, if any weight on the recently injured limb post-ATR. This is slowly increased in the first few weeks of rehabilitation, along with the gradual introduction of passive range of motion exercises performed with physiotherapists. Most patients are not capable of full weight bearing and walking without assistive devices until roughly 8 weeks after ATR, with most achieving full walking capacity by 16 weeks post-ATR. The suggested time for return to sports (if suggested by the clinician) is usually 6 months to 1 year after ATR.

In order to fully understand long-term changes in the AT, assessments of the AT tissues need to be made at least beyond one year of ATR injury. Furthermore, in order to properly assess short-term changes, patients need to be measured as early as possible after the proliferation stage of tendon healing.

The investigations conducted in this work have been split into two separate but related studies. The first retrospective study assessed patients 2-6 years following surgical repair of an ATR in order to assess long-term changes in AT biomechanics (**Chapter 4**). The second prospective study monitored ATR patients at 8, 12, and 16 weeks after ATR, and these patients were randomized to either early weightbearing or late weightbearing rehabilitation protocols (**Chapter 5**).

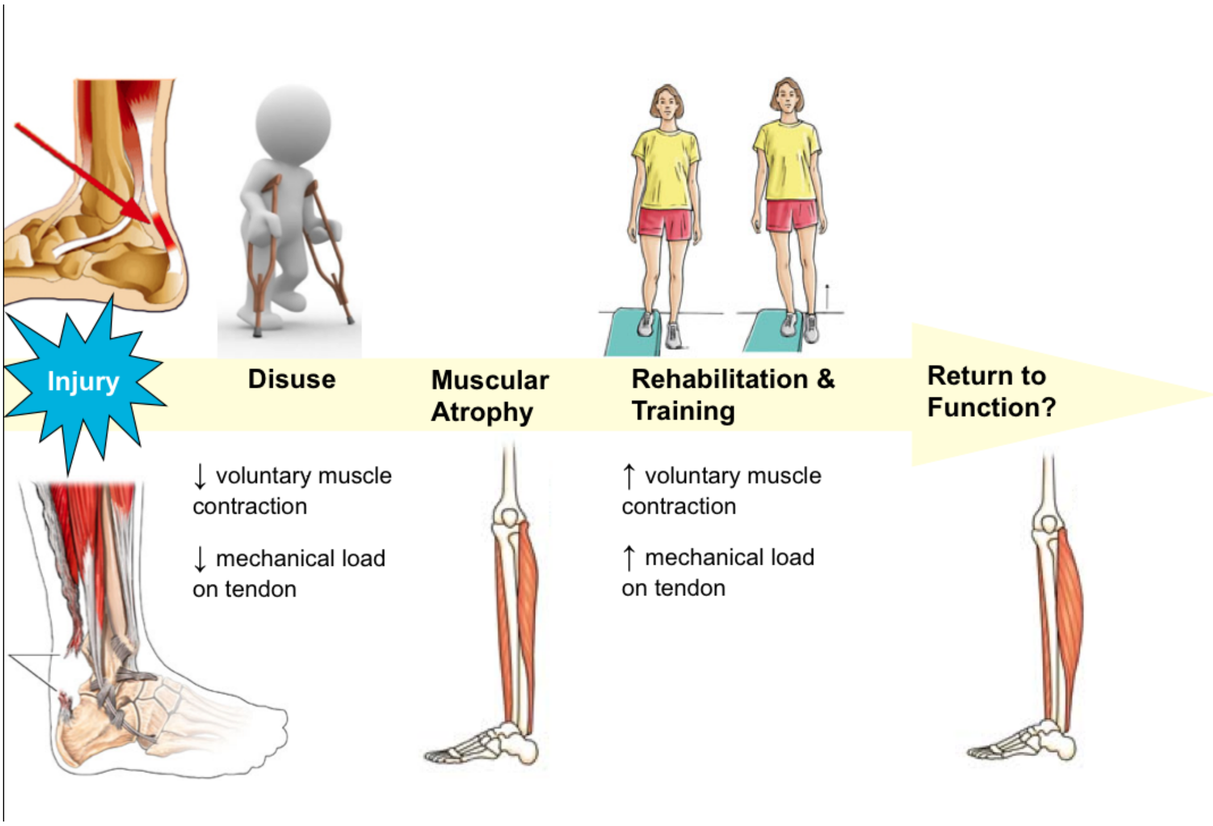

Figure 5: Timeline of tendon healing on the cellular level (upper) compared with the timeline of physiotherapy gains made after injury (lower).

3 *In vivo* assessment of AT and MTU function

Post-rupture changes in tendon tissue mechanics can have a profound effect on the overall function of the foot-ankle joint complex during forward motion. This work focuses on characterizing both the long-term and short-term adaptations that occur in the AT after rupture and assesses its relationship with end-outcome function *in vivo*. Thus it is critical to use noninvasive methods to characterize AT structure and function of the surrounding tissues, in order to not disturb the affected tissues during the healing and remodeling stages, and to avoid causing additional damage to the final healed tissue. This chapter introduces two methods of noninvasive assessment of AT *in vivo* function selected for use in this work, namely, a single-limb assessment using ultrasonography and dynamometry, and a bipedal assessment of AT function through gait analysis. Furthermore, the historical use and sensitivity of these functional methods are presented. Finally, clinical scores allow for determination of subjective outcomes as assessed by patient-reported questionnaires and subjective clinical examinations.

3.1 *In vivo* single-limb AT function - Ultrasonography

Since ATR greatly affects the composition and mechanics of the healed tissue, an ideal method would allow for elucidation of both characteristics. Methods commonly employed in biological assessment of the post ATR tendon in animal models involve excision or harvest of the target tissue, followed by histology and mechanical failure testing of the collected sample. Such techniques are not possible in human ATR subjects, as it is in the best interest of the patient not to remove tissue from the healed AT and thus would not be ethically allowed within the context of a scientific study. These constraints limit possible assessment techniques to functional, noninvasive imaging modalities.

This section introduces ultrasonographic methods used to noninvasively characterize the mechanical status of the healed AT tissue. Most importantly, this method can be used at various stages after ATR, including the early stages of the remodeling stage shortly after surgical repair. Its previous utility and sensitivity will be presented here, along with a detailed description of the method.

3.1.1 Background

B-mode (brightness mode) ultrasonography is an established diagnostic imaging modality used to noninvasively visualize the body's internal structures in real-time, particularly soft tissues and organs. One common example of clinical use includes ultrasounds of the abdomen, which can be used to diagnose inflamed appendixes or to monitor the development of a growing fetus. Similarly, the structure and movement of the triceps surae muscle and AT are also easily visualized in real-time with this method, since these tissues are superficial on the posterior lower limb.

An ultrasonography image is generated in three steps: (1) a sound wave is produced and focused through a transducer, (2) the echo returns to the transducer after reflecting against the targeted tissue, and (3) an image is formed from the strength of the returned signal and the time to return back to the transducer. The images produced from B-mode ultrasonography allow for a two-dimensional black and white picture of the target tissues in real-time. This allows for live monitoring of the AT and its connection to the triceps surae during plantarflexion moment generation.

Synchronous monitoring of AT movement and ankle moment generation allows for an estimation of tendon stiffness, which has been previously described in detail [85] and has been shown to be reliable when using a minimum of 5 tests [86,87]. This technique has been shown to be sensitive enough to determine differences in healthy subjects due to leg dominance, which leads to significant differences in mechanical properties and tendon stiffness [88]. This method has not yet been applied to monitor the time course of healing in a ruptured Achilles tendon, and there has been no particular study that shows how the mechanical properties of the tissue change, both noninvasively and *in vivo* following rupture. However, this particular technique has been used by a group to determine the biomechanical properties of the tendon in hemiparetic stroke survivors [89], finding significant differences in tissue properties between the affected and nonaffected sides. With these previous investigations in mind, this method was selected due to its sensitivity and previous application in clinical cohorts.

3.1.2 Detailed description

During each measurement session, the Achilles tendon stiffness was separately measured in both the previously injured and contralateral limbs. Prior to all measurements, all patients performed 10 minutes of exercise on a stationary bicycle in order to warm up the muscles and tendons prior to testing. While the patient was cycling, the testing procedure was explained in detail.

In order to determine the *in vivo* relationship of AT force to changes in AT length, all patients performed maximal voluntary isometric contractions (MVICs) on a dynamometer operating at 1000 Hz (Biodex System 3, Biodex Systems, Shirley, NY) while seated (115° hip angle) with the foot at a neutral angle (foot perpendicular to the tibia) and an extended knee over a 5-second ramped contraction, as depicted in **Figure 6**. A seven-camera motion capture system (VICON MX-F20, Oxford, UK, $f = 250$ Hz) monitored the actual motion of the limb as well as the dynamometer pedal to monitor small changes in ankle angle.

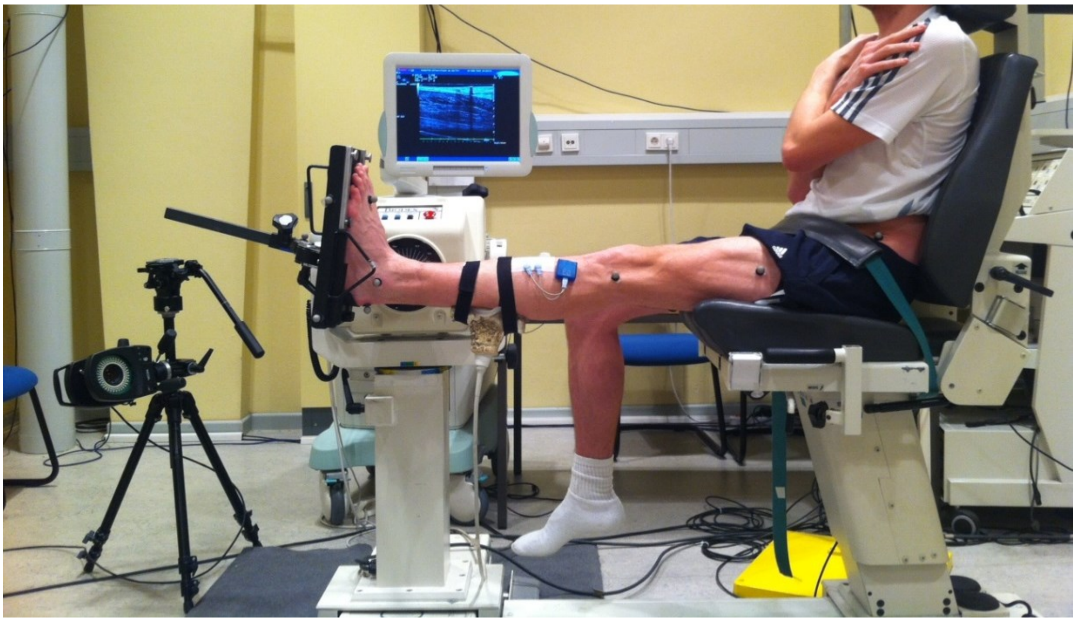

Figure 6. Photo of experimental setup for *in vivo* assessment of the MTU. The patient is seated with the foot in the dynamometer at a neutral position, and with the knee outstretched. The arms are crossed during each 5 second MVIC contraction.

Inverse dynamics calculations were performed to determine resultant joint movements from the collected kinematic data [90]. Since the tibialis anterior is an antagonist muscle that contributes a small but noticeable dorsiflexion moment during each plantarflexion contraction, EMG measurements of this muscle were taken at 1000 Hz (biovision, Wehrheim, Germany) during each MVIC. All dynamometric and EMG data were directly synchronized to the motion capture system (VICON Nexus 1.7.1, Oxford, UK) via analog channels. The resulting contribution of the tibialis anterior to the plantarflexion moment was estimated and corrected for using this EMG information, as described previously [91].

The AT force was calculated by dividing the measured MVIC plantarflexion moment (as measured by the dynamometer at a neutral angle of 90°) by the tendon moment arm using the tendon excursion method [92]. The alteration of the tendon lever arm due to the alignment of the tendon during the contraction was considered in the calculation of the lever arm values using the factor suggested by Maganaris and co-workers [93]. A schematic of these calculations and forces is depicted in Figure 7.

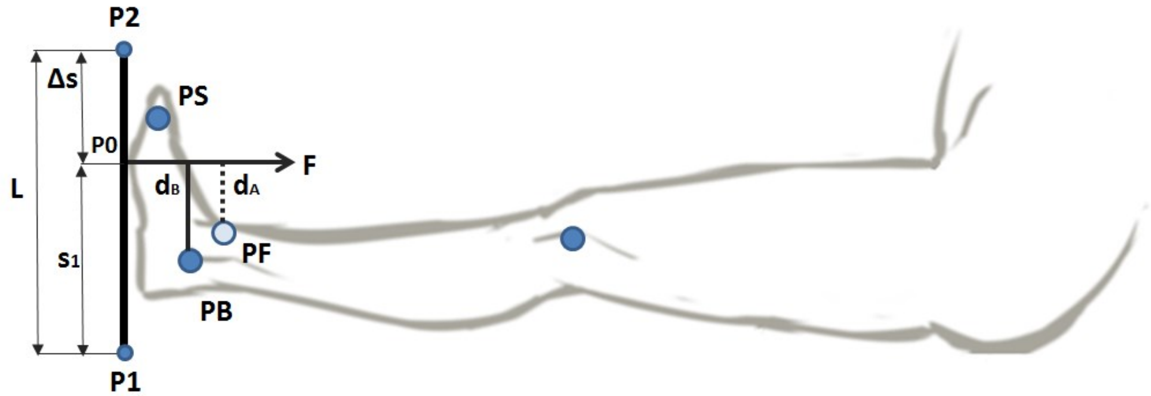

Figure 7. Diagram depicting the acting forces and points of interest during the MVIC from Arampatzis et al [85].
F denotes the force applied by the ball of the foot on the dynamometer footplate at P0, which is defined as perpendicular to the line between P1 and P2, which are located on the footplate. PB is the primary rotation axis of the dynamometer and PS is the location of a marker on the first metatarsal of the foot. PF is the midpoint of the line connecting the lateral and medial malleoli. dA is the lever arm of the force F to PF and dB is the lever arm of the force F to PB.

B-mode ultrasonography with a 10 cm, 7.5 MHz ultrasound probe (25 Hz, My Lab 60, Esaote S.p.A., Genoa, Italy) synchronously visualized displacement of the musculo-tendinous junction (MTJ), connecting the AT and the medial head of the gastrocnemius muscle (**Figure 8**). The probe was embedded in a custom-made form that was held in place on the limb with Velcro straps. The ultrasound transducer was placed longitudinally to the Achilles tendon during the MVICs, and an externally placed sound-absorbing marker was used as a reference point for MTJ movements) (**Figure 9**). An external analog trigger was activated immediately before and after each MVIC to synchronize ultrasound videos with all other data (dynamometry, EMG, kinematic data) collected in the motion capture system. The resulting ultrasound videos were analysed frame-by-frame using a customized graphical user interface developed in the MATLAB environment (Mathworks, Inc., Natick, MA).

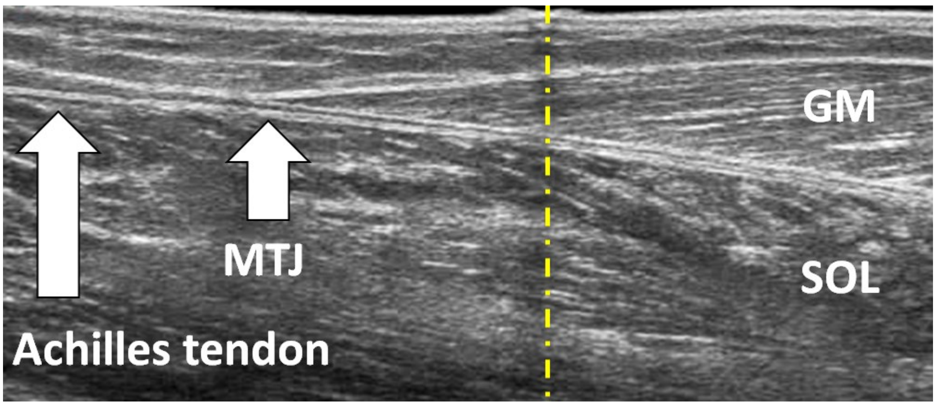

Figure 8. A sample ultrasonographic image of the visualized musculoskeletal structures used for measurements.
The musculoskeletal junction (MTJ) was identified as the intersecting point between the aponeurosis of the Achilles tendon, its insertion into the gastrocnemius medialis (GM) and the soleus (SOL) muscles. The yellow line emphasizes the ultrasound-absorbing skin marker used as a reference point to estimate overall changes in AT length during each MVIC.

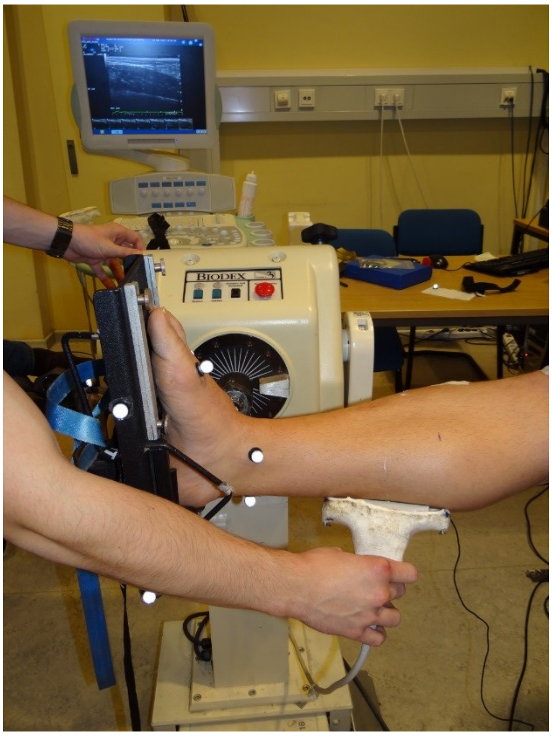

Figure 9. Placement of the linear ultrasound probe on the medial gastrocnemius-Achilles tendon junction on a patient. The ultrasound probe was held in place with Velcro straps once the MTJ was visualized.

A corrected value of tendon displacement was used, calculated as the difference between MTJ movement during an active plantarflexion effort and the MTJ displacement during passive joint rotation using the dynamometer [94]. To guarantee high reliability, the data of five MVIC trials were averaged, similar to the findings of Schulze and co-workers [87]. A customized data script was used to synchronize and merge all collected data in MATLAB (Mathworks, Inc., Natick, MA).

AT stiffness was calculated as the slope of the calculated tendon force versus the MTJ displacement, between 50-100% of the maximum tendon force, using linear regression. AT strains were calculated using the resting AT length, measured at an ankle angle of 110° with the knee at 180°, since the tendon complex begins to generate force at this position [95]. In order to measure the resting AT length, a flexible measuring tape was used to determine the distance from the tuberositas calcanei, which was found using manual palpation, to the sound-absorbing tape marker placed on the skin; the ultrasound probe was then used to determine the rest position of the MTJ [88]. The primary output parameters from each leg were the maximum plantarflexion moment during the MVIC, as well as AT stiffness, strain, and MTJ displacement (hereby referred to as AT elongation).

3.2 *In vivo* bipedal AT function – Gait analysis

3.2.1 Background

Functional analysis of the lower limb after ATR has historically focused on maximal and high-impact involvement of the ankle [75,76,82]. Single-leg heel rise tests have been used in long-term analyses of ankle function, to determine the full capacity of the healed AT [75,82]. Unfortunately, such analysis is not practical in early assessments after AT, as the patients' capacity and willingness to perform this high-demand task is limited. Furthermore, there is a potentially higher risk of re-rupture when such tests are performed soon after surgical repair.

For that reason, gait analysis was selected as an ideal method for assessing AT and MTU function in both short-term and long-term follow-up assessments. This technique allows for objective analysis of active ankle joint function with limited re-rupture risks to the patient. Furthermore, the bilateral nature of gait allows for synchronous assessment of both the injured and contralateral sides and is more reflective of ankle function on a day-to-day basis.

3.2.2 Detailed description

Ten infrared cameras (VICON MX-T20, Oxford, UK, **Figure 10**) collected kinematic data (*f*=120Hz) using twenty-two markers placed on the following landmarks: greater trochanter, lateral thigh, medial and lateral femoral condyles, tibia tuberositas, medial and lateral malleoli, heel, first/fifth distal metatarsal heads, second/third proximal metatarsal (**Figure 11)**. From these markers, segments were created for the left and right thighs, calves, and foot, visualized in **Figure 12**. Two embedded force plates (AMTI BP400600, Watertown, MA, USA, **Figure 10**) simultaneously recorded three-dimensional kinetic data (*f* = 960Hz) during all recorded tests.

Prior to functional analysis, two static trials were taken with the patient in a neutral standing position, in order to determine reference angles for kinematic calculations. One static trial was taken with the patient standing on a single force plate to determine the patient's body weight, and a second static trial was taken with the patient standing with one foot on each force plate, in order to determine a preference for weight bearing by each patient (**Figure 12**).

Kinematic and kinetic data were consequently measured during a total of three different activities: level walking, stair ascent, and stair descent. Gait analysis was performed on each patient while walking barefoot at a self-selected speed along a marked 10-meter pathway in the same laboratory (**Figure 12**). The placement of the force plates allowed for collection of both left and right foot ground reaction forces (GRFs) within a single walking trial when patients had an adequate stride length. To avoid any possible velocity bias, a minimum of five "clean" trials were accepted for analysis when both feet consecutively hit each force plate. In some cases, subjects were unable to hit both plates cleanly due to a short stride length. In these cases, a minimum of five clean trials on each foot was taken and the consequent ground reaction forces were controlled for velocity bias.

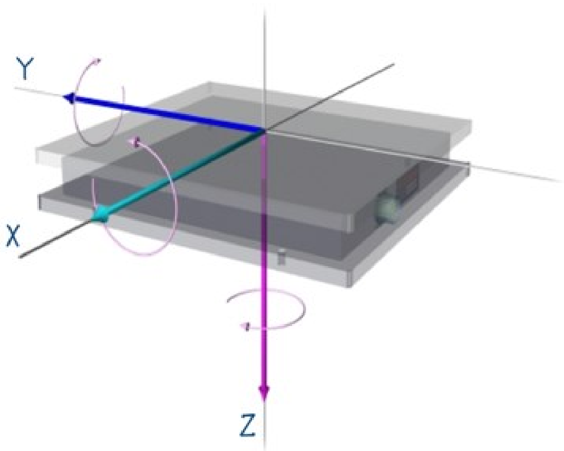

Figure 10. Measuring equipment used to capture data during gait analysis: Motion capture cameras (left) measured lower limb kinematics and force plates (right) measured ground reaction forces.

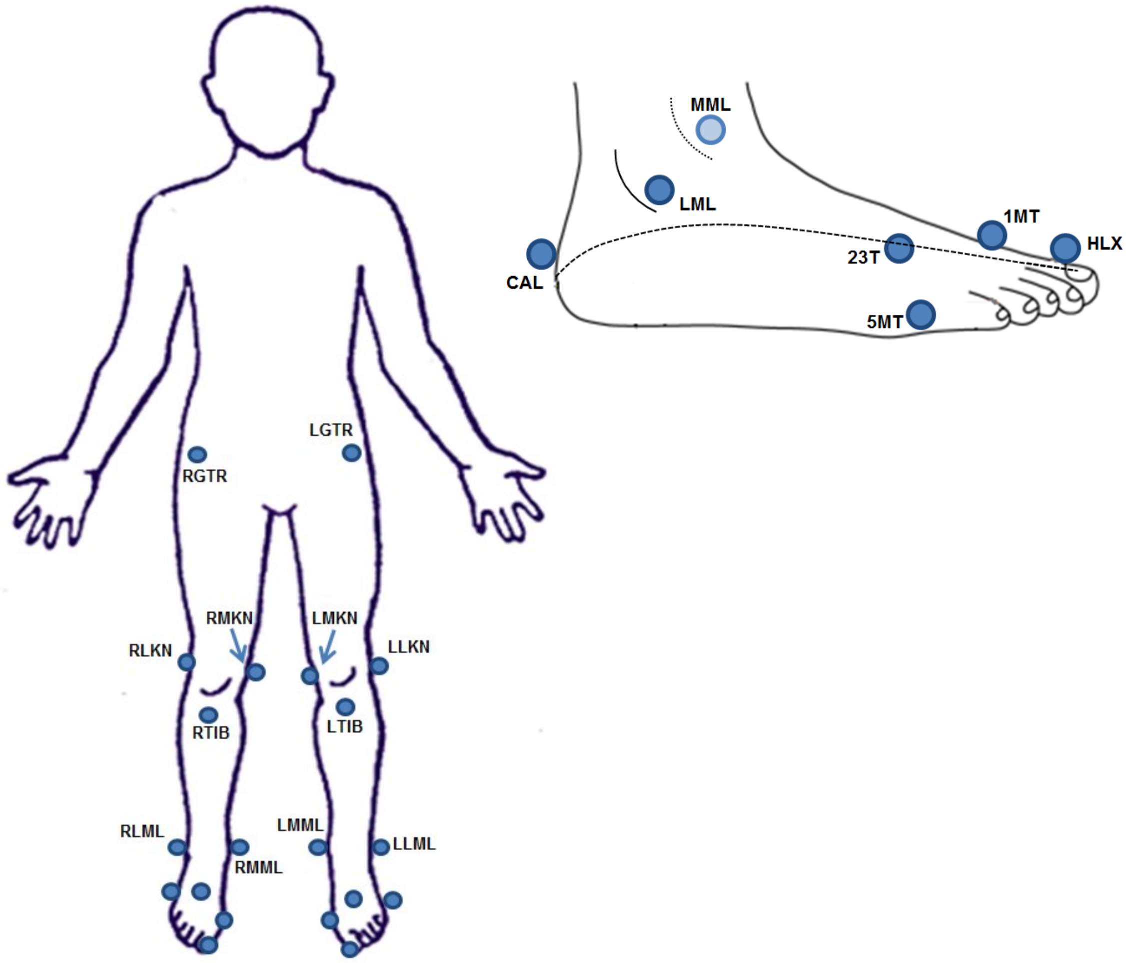

Figure 11. The minimal marker set used to capture lower limb kinematics on the body and on the foot (inset).

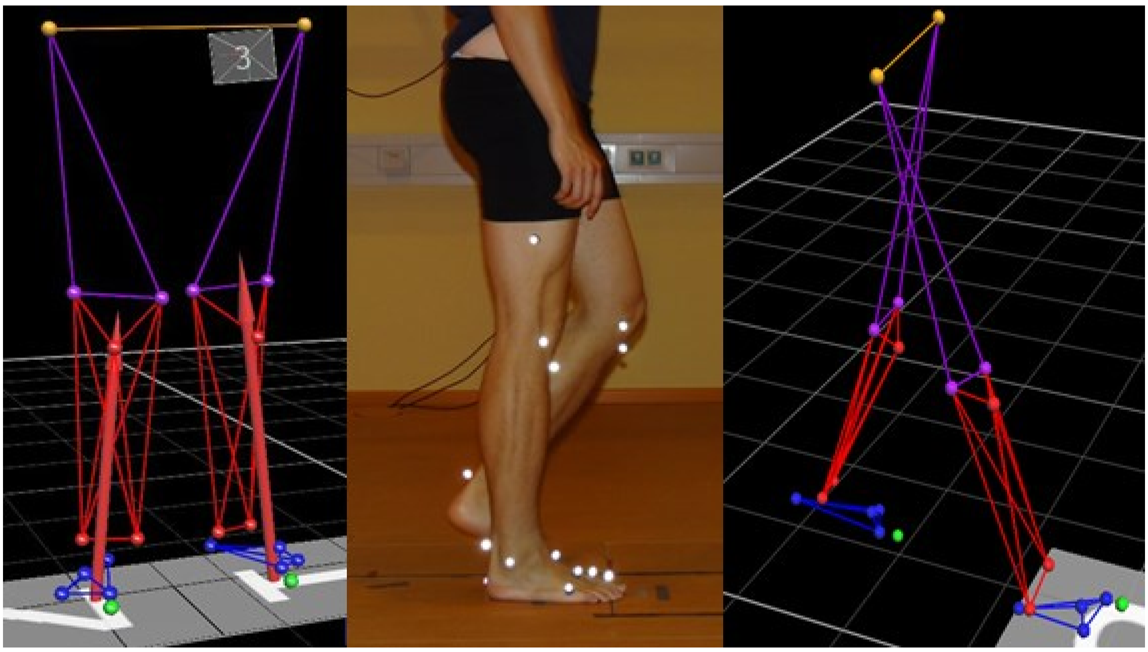

Figure 12. Motion capture data from a static test (left) and during gait analysis (right), captured from a patient (center). The red arrows in the static test show the direction and amplitude of the ground reaction force from each limb, indicating preferred the side-to-side difference in weight bearing. Views of a patient during gait analysis with reflective markers (center) and in the motion capture program (right).

All kinematic data from walking trials were separated into gait cycles using the foot velocity algorithm [96] for all retrospectively examined patients. Prospective patients measured soon after the incidence of ATR displayed more pathological gait patterns, and an algorithm based on the projected heel marker distance was developed and used to identify gait cycles in these cases [97]. Each gait cycle was separated into swing and stance phases by identifying the toe off event using the foot velocity algorithm [96].

Kinematic data using the same marker set was then collected during stair navigation on a custom-built, four step staircase. Similarly, the patients were asked to ascend and descend at a self-selected pace with a step over step pattern, without using the assistive handrail. Gait cycles were determined with the assistance of the built-in forceplates anchored below the staircase. The selected gait cycles for analysis during stair navigation are highlighted in **Figure 13**.

Ankle mobility during gait and stair navigation was assessed using ISB-recommended joint coordinate system conventions to monitor three-dimensional ankle angles [98] relative to the static trial. Inverse dynamics calculated three-dimensional reaction joint moments at the ankle during walking trials [99] using inertial parameters of the shank and foot segments were determined using anthropometric standards from de Leva [100]. All marker and GRF data were processed with customized scripts developed in MATLAB.

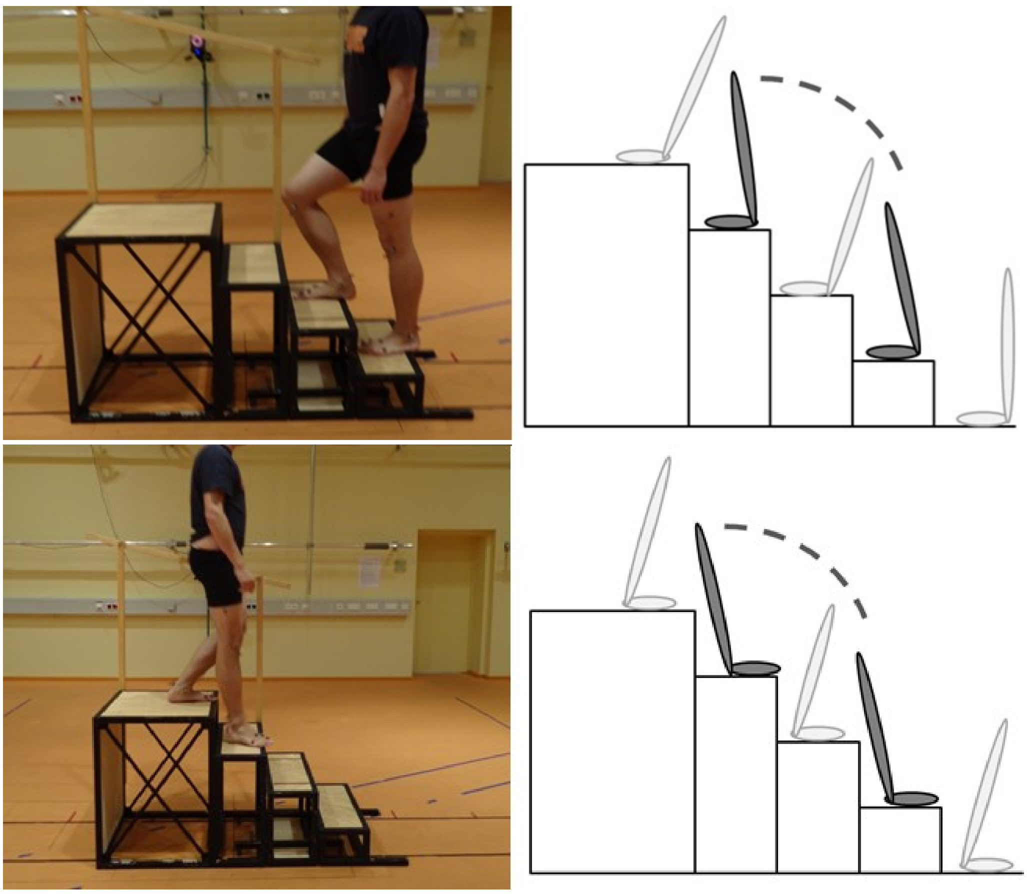

Figure 13. A patient performing stair ascent and descent on a custom-built staircase in the motion analysis laboratory. The corresponding diagrams on the right side depict the specific gait cycles that were selected for analysis, in which the darker limb is the gait cycle of interest.

The overall change in length of the entire AT-triceps surae MTU can also be estimated from the same kinematic data using equations previously derived in the work from Grieve et al [101]. In order to calculate this estimated MTU length, both the shank length and the sagittal ankle and knee ankles need to be determined. The shank length was calculated as the distance between the midpoint of the medial and lateral malleoli and the midpoint of the two markers on the knee joint space. The sagittal knee angles were calculated similarly as the ankle angles, using ISB recommendations relative to the static trial [98]. In order to adjust the length change for each patient, all absolute MTU length changes were normalized to the length of the shank segment, and the "rest length" of the MTU was set to 90° of plantarflexion and 90° of knee flexion [101].

3.3 Clinical measurements

3.3.1 Background

Currently, the majority of follow-up analyses use a combination of clinical measurements and patient-reported questionnaires as a primary outcome after ATR. These subjective metrics are susceptible to high variability and are subject and user-dependent. Some previous studies also using functional analysis have connected clinical scores to ankle function after ATR in short-term follow-ups, but the utility of such measures have yet to be compared in long-term follow-ups. Furthermore, it is unclear how these subjective scores reflect actual performance of the ankle joint during objective tests. The subjective measurements outlined in this section are reflective of common metrics used in clinical practice to determine patient recovery following ATR.

3.3.2 Calf circumference and ankle range of motion (ROM)

A number of passive tests were taken from each patient at the beginning of each measurement session, prior to gait analysis and ultrasonography. Circumferences of both limbs were recorded while the patient was standing. One measurement was taken on the calf located 15 cm distal to the knee space, and two measurements were taken on the thigh, at 10 and 20 cm proximal to the knee space. The circumferences found in the injured limb were compared to the contralateral limb, to allow for insights into relative muscle atrophy post-ATR.

While the patient was lying supine on an examination table, an experienced clinican passively moved each limb so the knee was at approximately a 90 degree angle. In this position, the ankle was passively moved to the maximal dorsiflexion and plantarflexion positions. A manual goniometer was used to record the angles, and the difference between these extreme positions was used as the passive range of motion (ROM).

Finally, in order to test the passive function of the AT, the clinician performed Thompson's test. At this point, the patient is prone with the feet hanging off the end of the examination table. The calf muscle is then squeezed slightly proximal to its widest portion, as the clinician simultaneously observes movement of the foot. A positive Thompson's test indicating ATR results in no dorsiflexion movement.

3.3.3 Patient-reported clinical scores

In order to determine subjective measures of AT function and overall well-being, patient-reported clinical scores were collected at each measurement session. Since there is currently no consensus in the literature as to which score is most adequate for assessment of the ankle post-ATR, a wide variety of scores were taken. These scores are subdivided into two groups: the first includes general scores that look at more systematic problems, whereas the second group of scores focuses locally on problems found directly on the AT and ankle joint.

The general scores are commonly used to determine how the patient feels on a day to day basis, with regards to pain, limitations, and activity. A visual analog scale (VAS) was used to determine (1) the average amount of pain that the patient felt on a daily basis and (2) how limited the patient felt with regards to activities of daily living. Furthermore, a Trillat score was taken, which is a determinant of activity level. For this the patient selects one of five options ranging from “Poor”, which signifies daily impaired function with severe pain and no athletic activities, to “Very good”, indicating unrestricted daily function and participation in athletic activities without pain.

Three scores specific to foot and ankle assessment were also included and the detailed questionnaire can be found in the Appendix. The Achilles Tendon Total Rupture Score (ATRS) is a ten-question survey in which limitations and difficulties related to the ATR are addressed. Each question has a value from 0-10, and the sum of all questions results in a score, with 100 points as the maximum. Both the American Orthopaedic Foot and Ankle Score (AOFAS) and Thermann-100-Point score require a combination of patient feedback and clinical observations, which similarly result in a score with 100 points as the maximum.

4 Long-term AT and MTU structure and function after ATR

Despite extensive research into different types of surgical treatment and rehabilitation [102], there is limited long-term biomechanical information about the healed AT tissue. Scar tissue is produced after Achilles tendon rupture in the final stage of tendon healing, which can last a year or more after injury [12,103]. Animal models show this healed tissue has weaker biomechanical properties compared to uninjured control ATs [58,104] and may never to pre-injury mechanical capacity [12], which may alter its overall function in force transmission.

Knowledge of the mechanical status and related function of the healed AT tissue in humans beyond this remodeling stage is limited. Considering the likely biomechanical changes that occur in the post-rupture AT, it is plausible that altered AT mechanical properties contribute to functional deficits on the injured side. However, the effect of unilateral changes in AT mechanics on bipedal movement remains unclear.

In silico models of human walking have emphasized the importance of optimal AT elastic properties for efficient gait [25,34], which allow the muscles in series to operate with minimal metabolic cost [36]. Once AT mechanics are altered drastically from their optimal range, functional deficits appear. One model found that increased tendon stiffness in the AT yielded deficits in positive ankle joint power in modeled gait [25]. To the best of our knowledge, there is currently a lack of *in vivo* knowledge connecting unilateral changes in AT tissue properties to function in bipedal gait.

This chapter addresses this deficit by working towards a better understanding of long-term AT function by assessing *in vivo* function in ATR patients beyond this remodeling stage. This retrospective study and its patient cohort are described in Sections 4.1 and 4.2, and the primary results are presented in Sections 4.3-4.6. Finally, a discussion of the results and their implications is outlined in Section 4.7.

4.1 Main goals and hypotheses

The overall aim of this retrospective study was to understand how the biomechanical properties and function of the *in vivo* AT change in the long-term after surgical repair of an ATR. In order to address this, the primary goals of this study (previously introduced in Section 2.2) were:

(G1) to non-invasively characterize *in vivo* intra-patient differences in tendon structure and function between the previously ruptured AT and the uninjured contralateral AT 2-6 years following percutaneous surgical repair in humans; and

(G2) to assess and quantify changes in ankle kinematics and moment production during gait.

(G3) to assess the relationship between in vivo tendon stiffness and ankle function during gait.

Based on knowledge from previous work, we set forth the corresponding hypotheses:

(H1) The previously injured tendons (INJ) will exhibit significant differences in tendon stiffness and rest length compared to the non-injured contralateral (CON) side.

(H2) The INJ ankle will generate lower moments and forces and have limited mobility during gait compared to the CON ankle.

(H3) Increased intra-patient asymmetries in AT properties will correlate to asymmetries in ankle mobility and moment production during gait.

4.2 Patient cohort

All included patients were operated in prone position under general anesthesia by a single surgeon in the Center for Musculoskeletal Surgery at the Charité-Universitätsmedizin Berlin within 10 days of acute ATR injury. Patients included in the study were sonographically classified with a type 2a or 3a Achilles tendon rupture at the time of initial consultation [105]. A percutaneous technique was employed, as its economic cost is more ideal compared to open and nonoperative methods [106], has been suggested to allow a prompt return to elite sports [107], and biomechanical results are similar to open surgery and superior to conservative treatment [108]. The Dresden instrument was used to perform percutaneous repair, which has been shown to be safe and effective in patients, limiting soft tissue and sural nerve damage [109].

The operation was conducted as described by Amlang et al. [110]. Postoperatively the foot was placed in a walker in a 30° equinus position for a period of 6 weeks. After the sixth week, heel height was reduced 10° per week and weight bearing was gradually increased. From the ninth postoperative week the patients were allowed to walk in a normal shoe. The physiotherapeutic regimens consisted of functional training of the muscles, proprioceptive training, stretching exercises and scar tissue massage. All patients were seen in the outpatient clinic at 6 and 12 weeks follow-up. Patients with postoperative complications like thrombosis, wound healing disturbance, sural nerve lesions or re-ruptures were not included for recruitment.

Twenty-three patients, consisting of 4 females and 16 males (body mass: 82.6 ± 13.4 kg; height: 175 ± 8 cm; BMI: 26.8 ± 3.6 kg/m^3; age: 45.0 ± 11.3 years), were recruited by telephone 2-6 years (43.5 ± 12.4 months) following percutaneous unilateral ATR surgical repair using the Dresden instrument as described above. All patients gave informed consent prior to participation. The local ethics committee approved this study (Charité, No EA/2/095/11) and all protocols were developed in accordance with the Declaration of Helsinki. Further exclusion criteria for this study included re-rupture of the affected AT, rupture of the contralateral AT, injury or operation on the lower extremities within 6 months prior to recruitment, or inability to walk without assistive devices.

On average, the patients received surgical treatment 4.1± 2.1 days after the occurrence of acute ATR and the surgical operation lasted for an average of 49.3 ± 27.7 minutes. In eight cases, the patients' dominant leg was the side of the ATR, and all but one case was a result of indirect trauma. 70% (16/23) of injuries were sustained during participation in sports and the remaining 30% (7/23) during minimal daily activities. The most common sports injury occurred during football (n=6), followed by racquet sports (n=4), martial arts (n=3), and handball, running, and hockey (all n=1). As a result of their injury, 26% of patients (6/23) were not able to resume participation in their preferred sport following ATR repair.

Seven patients reported having problems with their AT before sustaining a rupture. The most common pre-existing condition was achillodynia (n=5), and single cases of both burstitis and peritendinitis were found. At the time of biomechanical assessment, 57% of patients (13/23) reported current problems with their repaired AT, with primary complaints of discomfort during stair climbing (n=3), walking (n=2), while performing heel raises (n=1), or during sleep (n=1). Other patients reported swelling and pain during high-demand activities (n=2), feeling insecure with their AT (n=2), having a feeling of tension in the AT (n=1), or weather-dependent sensitivity (n=1).

Due to incomplete data sets stemming from technical problems, the final cohort included for this study consisted of twenty patients, consisting of 4 females and 16 males (body mass: 84.6 ± 14.4 kg; height: 175 ± 8 cm; BMI: 27.5 ± 3.9 kg/m^3; age: 45.6 ± 12.3 years).

4.3 *In vivo* tendon properties and MVICs

INJ tendons were significantly stiffer than CON counterparts (INJ: 335.7 ± 132.6 N/mm vs. CON: 198.6 ± 34.0 N/mm; $p < 0.001$; **Figure 14**). The INJ tendons displayed a lower AT elongation during MVICs (7.6 ± 2.4 mm vs. 10.8 ± 3.6 mm, $p = 0.002$) and lower tendon strain compared to CON (3.6 ± 1.2 mm vs. 5.4 ± 1.8 mm, $p < 0.001$) compared to the CON tendons. The measured rest length of the Achilles tendon was significantly longer on the INJ side (213.3 ± 29.4 mm) compared to CON (198.5 ± 21.8 mm, p = 0.009) at the time of assessment. The average maximum ankle plantarflexion moment during MVICs was significantly lower in INJ compared to CON (97.6 ± 32.1 Nm vs.108.0 ± 26.6 Nm, p =0.001).

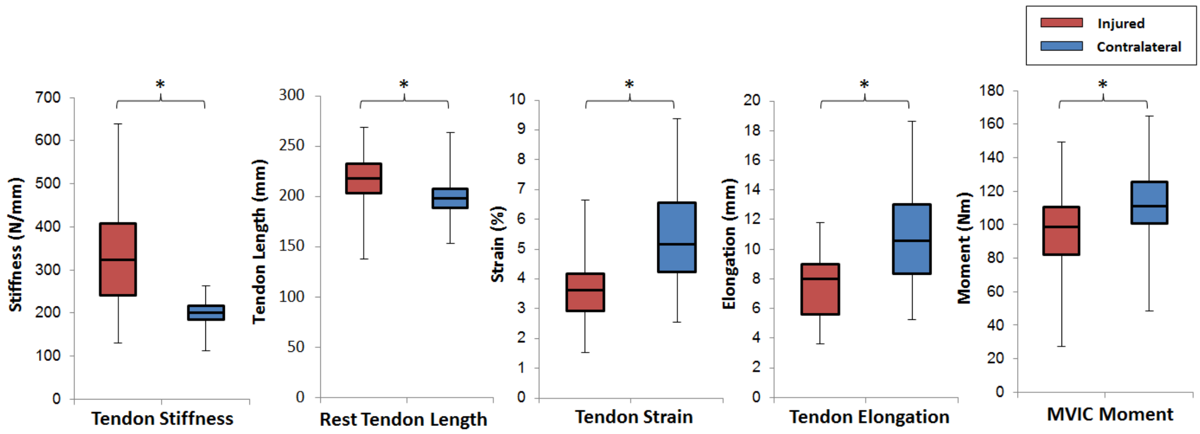

Figure 14. In vivo tendon parameters measured during MVICs and synchronous ultrasonography measurements. All box-and-whisker plots depict parameters for the injured (red) and contralateral (blue) sides. Significant differences between means with $p < 0.05$ are indicated with an asterisk.

4.4 Gait analysis

4.4.1 Kinematics during level walking

Upon comparison of the INJ to the CON angles over the entire gait cycle, differences were apparent in both the sagittal and frontal planes of movement (**Figure 15**). Analysis of the mean ankle angles in the sagittal plane yielded significantly lower plantarflexion in the INJ ankle during late stance and mid-swing ($p < 0.05$ between 65-86% of the gait cycle), with highly significant ($p < 0.01$) differences between 72-84% of the gait cycle. Similar assessment of the mean ankle angles in the frontal plane showed significantly higher eversion in the INJ ankle during late stance and mid-swing ($p < 0.05$ between 57-85% gait cycle), with highly significant ($p < 0.01$) differences found between 61-81% of the gait cycle.

Assessment of the maximal angles in the sagittal plane showed that INJ ankles had a significantly lower range of motion (ROM) during the gait cycle when compared to the CON ankles (30.2 ± 7.8° vs. 32.6 ± 5.8°, p = 0.011, **Table 4**). INJ ankles demonstrated lower plantarflexion (19.3 ± 7.0 ° vs. 22.9 ± 5.5°, p = 0.002) and higher dorsiflexion (10.9 ± 2.4° vs. 9.7 ± 3.2°, p = 0.015) than CON ankles during walking. In the frontal plane, ROM was similar in both the INJ and CON ankles (p = 0.541). Though pairwise comparison did not yield significant differences in frontal plane maximal angles, there was a tendency in the INJ ankles for higher eversion (8.6 ± 3.5° vs. 6.4 ± 3.1°, p = 0.087) and lower inversion (4.4 ± 3.0° vs. 5.9 ± 3.1°, p = 0.062). All ankle angle comparisons in the transverse plane revealed no significant differences.

4.4.2 Moments and ground reaction forces

When assessing the ankle moments throughout the stance phase at 1% intervals, no significant differences were found between INJ and CON in any of the measured planes (**Figure 15**). Pairwise comparison of the average three-dimensional maximum moments yielded only one significant difference, in which dorsiflexion moment was significantly lower in INJ compared to CON limbs (0.151 N·m/kg vs. 0.230 N·m/kg, p = 0.023). No significant differences were found between the INJ and CON limbs for the average maximum plantarflexion moment (p = 0.231), maximum inversion (p = 0.798) and eversion (p = 0.670) moments, or maximum internal (p = 0.082) and external rotation moments (p = 0.413).

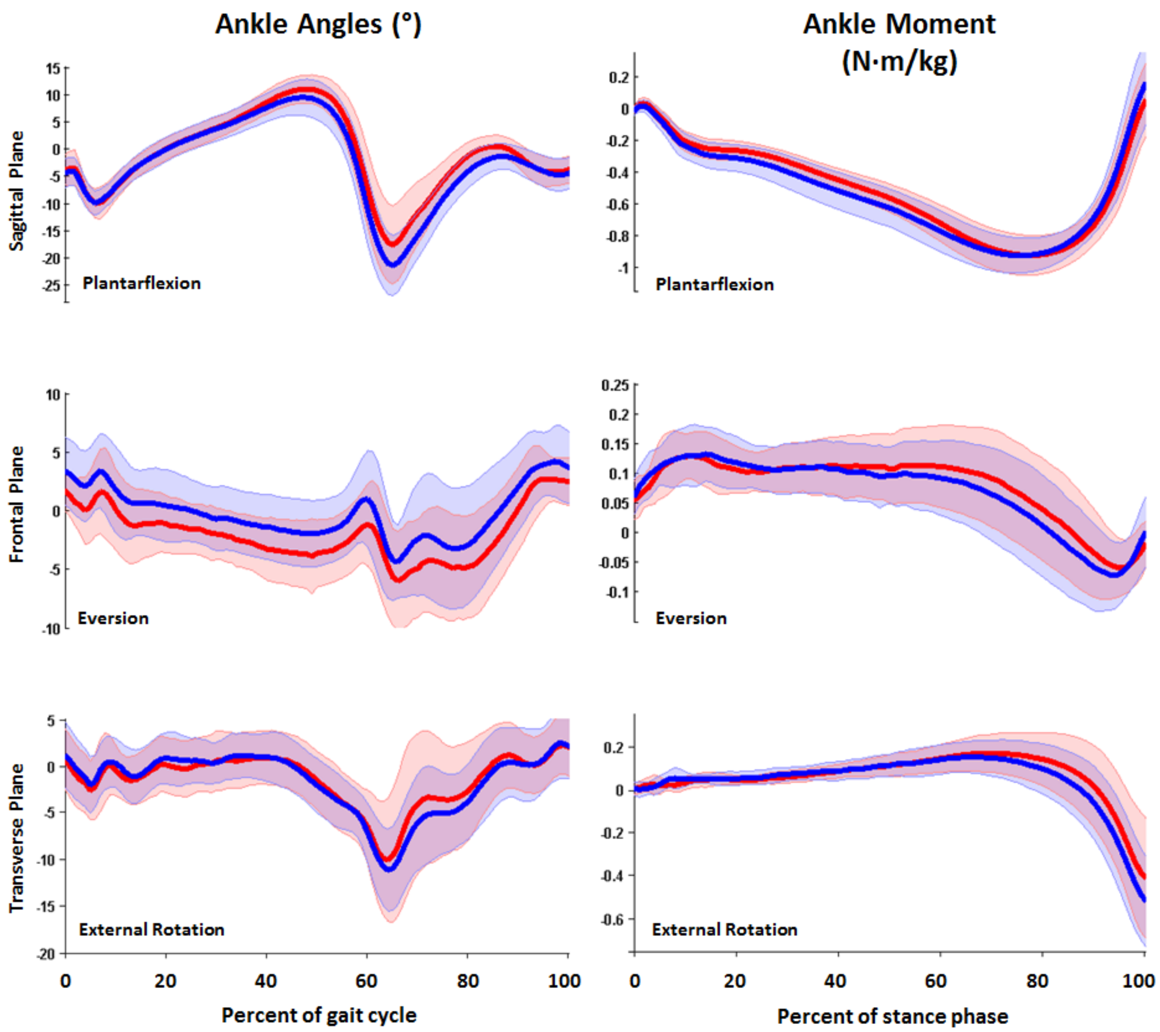

Figure 15. Three-dimensional ankle angles and moments during gait.

Left: Mean ankle angles as calculated in the sagittal, frontal, and transverse planes throughout the entire gait cycle in the injured (red lines) and contralateral (blue lines) limbs for all patients. Right: Mean ankle moment as calculated in the sagittal, frontal, and transverse planes during the stance phase of the gait cycle for both limbs.

Activity/Plane	Parameter	Injured	Contralateral	P-value
Walking				
Sagittal	Dorsiflexion	10.9 ± 2.4	9.7 ± 3.2	<0.001*
	Plantarflexion	19.3 ± 7.0	22.9 ± 5.5	<0.001*
	DF/PF- ROM	30.1 ± 7.8	32.5 ± 5.8	<0.001*
Frontal	Inversion	4.3 ± 3.0	5.9 ± 3.1	0.062
	Eversion	8.6 ± 3.5	6.4 ± 3.1	0.086
	Inv/Ev- ROM	13.0 ± 3.1	12.4 ± 2.6	0.328
Transverse	Internal Rotation	4.3 ± 2.5	4.8 ± 3.0	0.187
	External rotation	11.8 ± 5.9	12.3 ± 4.5	0.601
	Rotation ROM	16.1 ± 5.0	17.1 ± 4.8	0.332
Stair ascent	**Parameter**	**Injured**	**Contralateral**	**P-value**
Sagittal	Dorsiflexion	13.9 ± 3.5	12.2 ± 5.1	0.091
	Plantarflexion	19.6 ± 5.8	23.7 ± 4.6	0.006*
	DF/PF- ROM	33.5 ± 7.0	35.9 ± 5.5	0.167
Frontal	Inversion	2.1 ± 3.4	4.2 ± 6.9	0.145
	Eversion	6.3 ± 3.8	4.8 ± 7.7	0.575
	Inv/Ev- ROM	8.4 ± 2.9	9.0 ± 4.2	0.852
Transverse	Internal Rotation	4.2 ± 6.6	6.1 ± 7.7	0.433
	External rotation	7.2 ± 5.1	3.9 ± 6.4	0.091
	Rotation ROM	11.4 ± 5.0	10.0 ± 4.5	0.380
Stair descent	**Parameter**	**Injured**	**Contralateral**	**P-value**
Sagittal	Dorsiflexion	21.3 ± 5.1	22.3 ± 6.4	0.407
	Plantarflexion	27.8 ± 7.0	31.4 ± 5.2	0.029*
	DF/PF- ROM	49.1 ± 9.0	53.6 ± 6.6	0.025*
Frontal	Inversion	7.8 ± 3.5	6.9 ± 7.8	0.940
	Eversion	4.9 ± 4.8	6.4 ± 6.4	0.575
	Inv/Ev- ROM	12.6 ± 5.5	13.2 ± 5.1	0.709
Transverse	Internal Rotation	5.5 ± 5.1	6.2 ± 7.7	0.785
	External rotation	8.4 ± 5.0	7.3 ± 7.5	0.575
	Rotation ROM	13.9 ± 5.0	13.5 ± 5.6	0.737

Table 4. Mean (SD) of maximum three-dimensional ankle angles and ranges of motion (ROM) during the gait cycle across different activities.

Similar observation of the GRF at 1% intervals of the stance phase yielded no significant differences across all axes. Pairwise comparison of the peak propulsive force in the anterior-posterior axis was significantly lower in the INJ limbs (0.1839 ± 0.040 BW) than the CON peak propulsive force of 0.1940 ± 0.035 BW (p = 0.002). No significant differences were found between the INJ and CON limbs for peak forces in the vertical or mediolateral axes.

4.4.3 Kinematics during stair navigation

During stair ascent, plantarflexion was significantly lower in the INJ ankle compared to CON (p=0.006, **Table 4**). Although there were tendencies for increased dorsiflexion and external rotation (both p=0.091), no other significant differences were found in other planes. During stair descent, both plantarflexion (p=0.029) and sagittal ROM (p=0.025) were also significantly lower in the INJ ankle compared to CON. No significant differences were found in the frontal and transverse planes.

4.4.4 Changes in MTU length during gait

When comparing the estimated changes in overall MTU length between the injured and contralateral limbs, no significant differences were found at any point in the gait cycle (**Figure 16**).

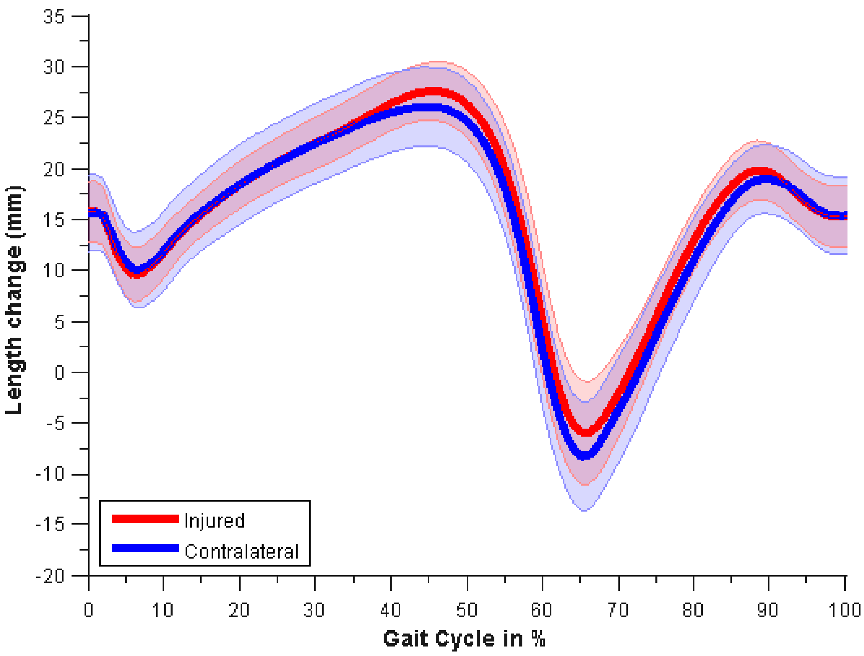

Figure 16. Depiction of the mean estimated changes, with standard deviations in the shared regions, in the overall MTU length during the entire gait cycle.

4.5 Clinical results

Calf circumference on the injured side was significantly lower on the injured side (36.5 ± 3.0 cm) compared to the contralateral side (38.3 ± 2.4 cm, $p < 0.001$). There was a tendency for a lower thigh circumference at 20 cm proximal to the knee space on the injured side (51.2 ± 4.0 cm) compared to the contralateral side (51.6 ± 3.7 cm, $p = 0.087$). No significant differences were found in the thigh circumference measured 10 cm proximal to the knee (injured: 43.0 ± 4.0 mm, contralateral: 43.0 ± 3.0 mm, $p = 0.968$).

Dorsiflexion was found to be significantly lower on INJ (15.3 ± 5.3°) compared to CON (16.9 ± 4.7° $p = 0.035$). Plantarflexion was also significantly lower on INJ (39.8 ± 7.1°) compared to CON (43.3 ± 7.8° $p = 0.022$). Overall ankle ROM was also found to be significantly lower on INJ (55.1 ± 9.1°) compared to CON (60.1 ± 10.0° $p = 0.001$).

The Trillat score for activity was 1.95 ± 0.7. The VAS scale for pain was 0.54 ± 0.89 and the VAS scale indicating limited function for 1.49 ± 1.63. For the foot and ankle-specific scores, the Thermann 100 Point score was 80.3 ± 9.9 and the ATRS score was 84.8 ± 12.6.

4.6 Statistical relationships among parameters

Intra-patient (INJ/CON) ratios of tendon stiffness negatively correlated to maximum plantarflexion moment during gait (r = -0.509, p = 0.011, **Figure 17**). Similar comparisons to dorsiflexion (p = 0.325), eversion (p = 0.344), inversion (p = 0.408), internal rotation (p = 0.318) and external rotation (p = 0.472) moments were not significant. No significant correlations were found between intra-patient ratios of tendon stiffness and kinematic ankle angle parameters.

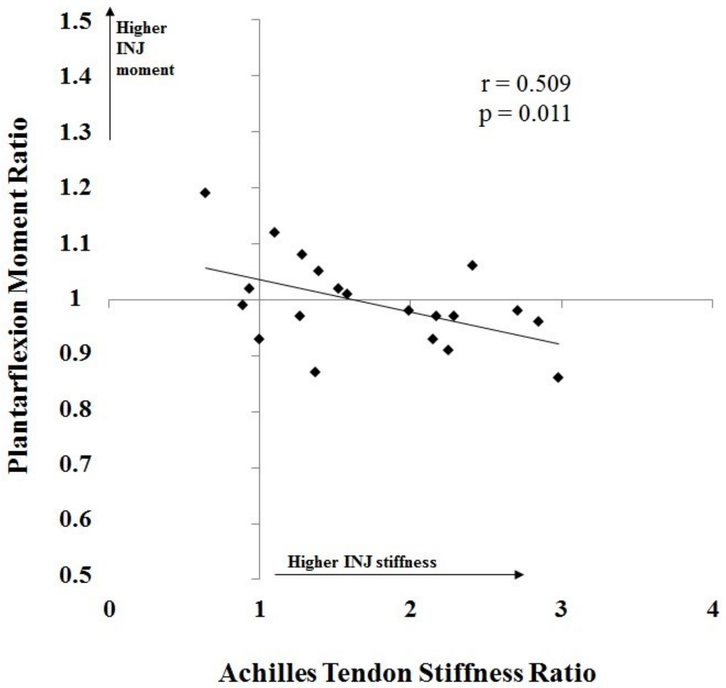

Figure 17. Linear correlation comparing intra-patient stiffness ratios to plantarflexion moments during gait.

Intra-patient ratios of resting AT length negatively correlated to maximum dorsiflexion angle (r = -0.514, p = 0.010, **Figure 18**) and positively correlated to maximum eversion angle (r = 0.386, p = 0.046) during gait. No significant correlations were found between intra-patient ratios of tendon stiffness and ankle moment parameters.

Correlation of tendon length differences with ankle angles during level walking yielded only one significant relationship: a positive correlation with intrapatient dorsiflexion (r = 0.393, p = 0.043). A tendency for a negative relationship with differences plantarflexion during walking was also found (r = -0.327, p = 0.08).

When relating tendon length with ankle angles during stair ascent, intrapatient differences in both eversion (r = 0.441, p = 0.026) and inversion (r = -0.385, p = 0.047) were found. There was also a tendency found for frontal plane ROM (r = -0.325, p = 0.081).

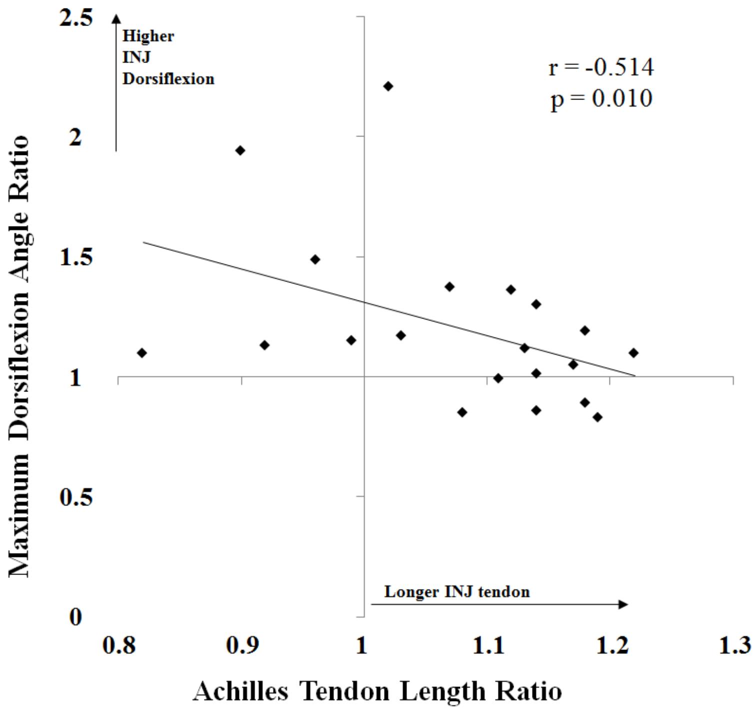

Figure 18. Linear correlation comparing intra-patient tendon length ratios to maximum dorsiflexion angle during gait.

4.7 Effects of age and time post-op

Since this patient cohort consisted of a wide spectrum of patients with regards to both time after surgery and age, a statistical analysis was performed to see if these factors had an influence on both clinical measures and intrapatient biomechanical asymmetries. Clinical measures taken into account included all patient-reported scores and calf circumference. Biomechanical asymmetries were calculated by dividing the INJ parameter by the correlating CON parameter, similar as the calculations performed previously in Section 4.6.

In order to determine if the post-op follow-up time affected outcomes, patients were separated into three groups: less than 3 years (n = 7), 3-4 years (n = 5), and more than 4 years post-op (n = 8). No significant differences were found between age groups with regards to both clinical measures as well as in biomechanical asymmetries.

Furthermore, the patient cohort was also analyzed with regards to age. Three groups were created, consisting of patients younger than 40 years old (n = 7), between 40-50 years old (n = 6), and older than 50 (n = 7). All clinical measures were found to be similar between the three age groups. With the exception of one parameter, biomechanical asymmetries were also found to be similar. The group of patients over 50 years old appeared to significantly higher asymmetries in plantarflexion moment (1.06 ± 0.08) during gait when compared to the group between 40-50 years of age (0.94 ± 0.05, $p = 0.012$) and a tendency for higher asymmetries compared to those younger than 40 years old (0.98 ± 0.06, $p = 0.081$). These results indicate that the oldest patients appear to exert a higher plantarflexion moment during gait on the injured limb.

4.8 Discussion

This work aimed to develop an understanding of the long-term changes in AT tissue following unilateral ATR by assessing *in vivo* tendon properties of the healed tissue at least two years after surgical repair, since AT remodeling can last for over a year.

The primary result found in this study showed that there are lasting asymmetries in AT stiffness 2-6 years after repair, due to significantly higher AT stiffness and AT length on the previously injured side, which supports the first hypothesis of this chapter. Previous work has assessed the healed AT tissue at a limit of one year post-op [84]. Furthermore, single-limb isometric dynamometric testing found that the INJ ankle was unable to produce a maximal plantarflexor moment comparable to that of CON, indicating long-lasting strength deficits.

Another goal of this work was to determine what long-term changes occur in ankle kinematics and moment production during bipedal gait as a result of ATR. The results here found that there were significant changes in ankle mobility in the sagittal plane on the INJ ankle when compared to the CON side. The INJ ankle did not only show altered sagittal kinematics during level walking, but also during stair ascent and descent. However, other than a significantly lower dorsiflexion moment on INJ compared to CON, the plantarflexion moment that is produced by the ATR during gait was found to be similar between the patients' two limbs. On the other hand, the maximal propulsive GRF in the anterior direction was found to be lower on INJ than in CON. With this in mind, the second hypothesis was only partially supported, as both ankle mobility and propulsive GRFs were found to be limited on INJ compared to CON, but the maximum plantarflexor moment produced on INJ during gait was similar between both limbs.

Furthermore, this study also aimed to determine if asymmetries in AT properties would relate to functional asymmetries in moment production by examining correlations between the two parameters. The results presented here found that intra-patient AT tendon stiffness asymmetries appear related to deficits in plantarflexion moment during gait, and that intra-patient changes in AT tendon length appear related to changes in ankle dorsiflexion, which supports our third hypothesis.

Our findings conflict with earlier work from Wang and colleagues, who reported significantly lower tendon stiffness in previously injured tendons as compared to their contralateral limbs [84] in patients assessed between 3-12 months after surgical ATR repair. This discrepancy in results could be attributed to the shorter follow-up time than in our study, as the patients' tendons in the previous work may still have been in the remodeling stage [12]. Considering that the patient cohort investigated in the current study was assessed at least two years post-ATR, it is probable that the patients' ATs were no longer in this remodeling stage. In their mice model, Palmes and colleagues (2002) showed that there was initially a drop in AT stiffness after ATR, which slowly increased with time until the end of the experiment after almost four months, at which point mobilized mice had AT stiffness' similar to controls. The combined information from these studies and these results suggest that post-ATR healing leads to an initial drop in AT stiffness, which increases to first match and then exceed AT stiffness on the contralateral side.

In addition to significant long-term changes in tendon tissue stiffness, sagittal kinematics were also significantly altered within each patient, with the INJ side exhibiting lower ROM, lower plantarflexion, and higher dorsiflexion during gait. This functional data corresponds to previous results from gait analysis performed on 2-year post-ATR patients, which also found increased peak dorsiflexion in the injured AT [74]. It should be noted that the differences between injured and contralateral are significant yet small, in the order of 2-4 degrees. Though the clinical significance of such small differences is unclear, such angle differences may contribute to changes in moment production. The results presented here found that within each patient, INJ ankles had a small but significant deficit in dorsiflexion moment, which may be due to altered kinematics.

In this work, intra-patient ratios of AT stiffness were primarily compared to intra-patient ratios of ankle angles and moments. The only such significant relationship was found between ratios of AT stiffness and maximum plantarflexion moment, which yielded a moderate negative correlation. In other words, patients with higher INJ-AT stiffness demonstrated lower INJ plantarflexion moment during gait compared to the CON limb. These results appear conflicting, as direct pairwise comparison of the stiffness yielded significantly different AT stiffness within each patient, yet similar comparisons of maximum plantarflexion moment during gait revealed no such differences. However, within-patient comparisons of maximum plantarflexion moment during single-sided MVICs yielded significant differences. One possible explanation for this is that the relative demand on the AT during gait is considerably lower than the high tension applied during MVIC plantarflexion efforts. Further long-term *in vivo* mechanical studies of the healed AT should investigate the tissue's capacity to perform under higher demands during high-impact activities like running or jumping, in which performance deficits would likely be more apparent. Such information could provide information as to why elite athletes often cannot return to pre-injury levels of athletic performance in the years after injury [111,112].

Another important result of this work is that AT rest length was found to be significantly longer in INJ limbs at the time of follow-up. The results from this cohort are similar to previously reported values in ATR patients by Silbernagel and colleagues [113], who found that AT elongation is related to deficits in single-side heel-rise performance. Within this study intra-patient ratios of AT length were compared to similar kinematic and kinetic ratios during gait, and patients with increased tendon elongation on the INJ side appeared to have more symmetrical dorsiflexion angles during gait. This suggested tendency is counterintuitive, as AT lengthening has been shown in cadavers to be linearly related to higher dorsiflexion [114]. It is possible that post-ATR changes in the physiology or activation of the surrounding muscles may contribute to this result during gait, which may be unique to bilateral movement compared to unilateral tasks.

There are some possible limitations in this study, including the nonsynchronous collection of AT stiffness and gait data. It is possible that AT stiffness values taken during MVIC testing may not necessarily be reflective of the exact AT stiffness during gait. Future studies may be able to simultaneously monitor gait and AT-dynamics in ATR patients, which would allow for more detailed information about the *in vivo* mechanical performance of the healed tissue. Another possible limitation is the variability in self-selected speed in each patient. Differences in gait velocity across the patients were fairly narrow with an average speed of 1.213 ± 0.139 m/s. Furthermore intra-patient ratios of gait parameters and AT stiffness were used in order to account for patient variability.

A clinically relevant finding was that patient-reported scores appeared to not be adequate in determining long-term outcomes after ATR, as most patients were fairly satisfied and on average, had very high scores. This is in further agreement with previous work, which found high ATRS scores at both 1- and 2-year follow-up examinations of ATR patients [115]. The utility of such scores may be more informative for clinicians in short-term follow-ups, but may not be relevant as an outcome parameter in long-term studies. Patients demonstrated limited pain and overall satisfaction with their AT and ankle. More useful clinical parameters were found in clinical examinations in both calf circumference and clinical ROM, which suggested that there were still lingering deficits in function. This conflict of subjective satisfaction and lasting deficits in function may potentially lead to further sports-related injuries, in which patients overestimate the capability of the AT to meet the mechanical demands of high-impact sports.

Recent work showed that leg dominance influences the symmetry of *in vivo* AT mechanical properties in healthy subjects [88]. It was suggested that contralateral AT properties might not be indicative of healthy AT behaviour, but that leg dominance could also play a role in modifying contralateral AT mechanics. Within this limited cohort, 35% of the patients (7 out of 20) sustained a rupture on the dominant leg. Covariate analysis showed no significant effect of leg dominance on the parameters presented here, and that the majority of patients had greater INJ AT stiffness. Further investigation in both ATR patients and uninjured subjects could elucidate the influence of leg dominance in healed AT mechanics and the effect of post-rupture ATR mechanics compared to healthy subjects.

Another important finding is that the AT appears to lengthen after ATR surgery when compared to CON, but functional intra-patient differences appear to be related to only kinematic changes and not to deficits in moment production during gait. This suggests that long after ATR surgery, ankle mobility in the previously injured AT is likely governed by this structural change. However, results from gait analysis indicate that this structural change does not have a negative impact on the post-ATR MTU's capability to generate a plantarflexor moment similar to the contralateral limb during walking. Though maximal strength produced by the previously injured limb is lower, there may be compensatory adaptations within the tendinous tissue itself to increase the efficiency of force transmission. Future work is clearly required in order to establish the link between long-term AT rest length, AT mechanical properties and athletic performance, which often declines after injury, and whether decline in performance is related to changes in AT structure or properties.

4.9 Conclusion

The results of this work show that in the years following ATR surgery, the resulting healed AT exhibits significantly higher stiffness and a longer rest length compared to the intact contralateral side. This contradicts shorter-term animal and human studies that purport that AT stiffness and mechanical properties on the previously injured side fall short of those found in non-injured, contralateral controls. This suggests that the adaptive process in the previously injured AT and the associated MTU continues long beyond the immediate post-injury period. Furthermore, comparison of biomechanical asymmetries suggest that increased AT rest length are related to ankle mobility deficits, and that AT stiffness changes are related to the capability to generate ankle plantarflexor moments. This result highlights that injury-related changes in not only AT structure but also and properties contribute to functional deficits on the injured limb.

5 The effect of weightbearing in rehabilitation on short-term AT and MTU structure and function after ATR: A prospective study

Restoration of pre-injury AT length and mechanical properties is the primary goal of ATR treatment, yet the capacity of current clinical and rehabilitation interventions to achieve this goal is still limited [116]. The results found in Chapter 4 of this work indicate that there are both structural and functional changes in the AT and the entire MTU that remain long after surgical treatment. It remains unclear how these changes develop, as well as how soon these changes occur after injury.

The post-surgery rehabilitation period is a critical time in ATR treatment, as it is during this time that external factors can exert positive or negative influences on tendon healing. To further complicate issues, the tissues involved in ATR healing are already mechanically disadvantaged and considerably weaker with lower collagen content [117]. Targeted rehabilitation protocols that could enhance the healing process may lead to improvements in functional post-ATR outcomes.

For instance, weightbearing (WB) in rehabilitation may allow for increased mechanical load on the healing AT, and WB's capacity to enhance tendon healing has been well documented in small animal models. An early mouse model showed that after surgically treated ATR, mobilized mouse ATs rapidly restored tensile strength compared to immobilized counterparts [104]. Histology of loaded ATs showed better structural outcomes, with more aligned collagen fibers and tenocyte deposition similar to those found in uninjured tissue [104]. More recent work has elucidated the temporal importance of WB, finding that short episodes of immediate WB through treadmill running enhanced AT healing compared to animals that began WB eight days after surgery [118]. The authors suggest that short periods of loading in the inflammatory stage, followed by more loading in the proliferative phase, could yield enhanced tendon healing in patients [118]. However, specific evidence that show both enhanced AT function through such rehabilitation in humans has yet to be presented.

As mentioned in Section 1.4.1, the inflammatory phase of tendon healing in human occurs immediately after the initial injury and can last until about 8 days. The subsequent proliferative phase lasts until about 6 weeks post-op. Often standard rehabilitation protocols suggest full WB to start roughly 8 weeks after surgery, beyond this proliferative phase. Considering the available non-invasive techniques to monitor *in vivo* AT function, studies in human subjects to date have been limited. To our knowledge, there is currently no work available in the literature that has been able to perform short-term (up to 4 months post-op) bipedal and single-limb functional assessments after ATR.

This chapter endeavors to address this gap in knowledge by assessing the early effects of differently timed WB rehabilitation protocols in ATR patients. In order to evaluate this, the current knowledge available from a literature search of ATR rehabilitation protocols is first summarized in Section 5.1. This background information emphasizes the goals and hypotheses of this prospective clinical study, as well as the patients and rehabilitation protocols used, which are described in Section 5.2 and Section 5.3, respectively. The biomechanical and clinical results of this prospective study are reported in Sections 5.4 to 5.5, respectively. Finally, a discussion of the primary results and their implications is presented in Section 5.6.

5.1 State of the art: post-ATR protocols and biomechanical basis

5.1.1 Meta-analyses of ATR rehabilitation protocols

As previously mentioned, there is no particular consensus among clinicians for the specific treatment of ATR. In addition there is also no particular consensus among physiotherapists for the best rehabilitation of the healing ATR. The possible combinations that result from various types of ankle mobilization, orthotic model, weight bearing, and temporal considerations are numerous. In the past decade, a number of systematic meta-analyses have attempted to determine the effectiveness of various ATR rehabilitation protocols.

One physiotherapeutic meta-analysis in 2012 by Kearney and colleagues aimed to find a consensus among all early methods of ATR rehabilitation, and included 424 patients in 9 separate studies [119]. An important note is that they included both conservative (n=188) and surgically treated (n=236) ATR patients. They determined that immediate weight bearing rehabilitation within an orthotic may be beneficial for patients in fighting muscular atrophy, but specific details such as orthotic type, degree of ankle PF, and timing of orthotic removal remain unclear [119]. An earlier meta-analysis included 6 surgical ATR studies (n=315), was the first to compare early functional rehabilitation to immobilization, and reported that patients with early function had better subjective outcomes, fewer surgical complications, and similar ankle ROM and re-rupture rates [120]. The specificity of WB in early functional rehabilitation was analyzed by Huang and colleagues in 2014, whose meta-analysis compared a combined rehabilitation approach utilizing both early ankle motion and early WB to a rehabilitation protocol that only included early ankle motion [121]. These results highlighted the importance of WB to early rehabilitation, as rehabilitation protocols that included only early ankle motion had limited improvements compared to immobilized patients. The combined approach was found to have a comparatively quicker recovery time and better functional recovery after ATR [121]. Overall, these three meta-analyses conclude that the implementation of a combined rehabilitation approach, including both WB and ankle mobilization, yield the best possible functional outcome for ATR patients compared to immobilization.

These previous suggestions for rehabilitation assist greatly in determining ideal outcomes, but the type of ATR treatment, whether surgical or conservative, can also influence rehabilitative preferences and biomechanical outcomes. Only one recent meta-analysis conducted a controlled literature search to only include open surgical methods, with the primary goal of comparing immobilization to combined functional treatment that incorporates immediate post-surgical WB [122]. They report that functional treatment leads to higher patient satisfaction and a quicker return to activity, along with no particular evidence for higher re-rupture or AT lengthening. Furthermore the authors suggest that immediate WB should take place with the ankle in 30° of plantarflexion within the first two weeks, which should be scaled to a free ROM at week 7. The authors additionally suggest that early mobilization, when introduced to the rehabilitation protocol at week 3, is most beneficial to the patient after surgical treatment [122].

Initially setting the ankle of the ATR patient in plantarflexion is crucial in the first stages of rehabilitation. This specific position allows for the two residual tendon ends to be closer together, ensuring that the newly formed tissue bonds the proximal and distal sides. Furthermore, the plantarflexed position allows for the attached triceps surae muscles to operate at a shorter overall length, which means that the muscle will not to generate high tension on the healing AT. An EMG investigation of healthy subjects walking in various lift heights in a walker boot showed that muscle activity in the triceps surae was lower when the lifts were higher [123]. As the patient becomes stronger with time, the lifts can gradually be removed from the walker boot, which will also slowly increase the applied tensile load on the tendon.

Though these suggested rehabilitative methods have been specified to create a more ideal healing environment for the post-ATR tendon, the problem of verification remains. Both excision and biopsy of the healed AT in humans are nearly impossible to perform due to ethical concerns for the patient, so histological examination of the healed tissue is impossible. The closest validation that can currently be obtained is through animal models, which allow for developing an understanding of how different WB interventions can affect tendon healing.

5.1.2 Animal models of ATR healing: The effects of weightbearing

As previously reviewed in Chapter 1, the inflammatory period of tendon healing occurs immediately after the incidence of ATR and results in significant changes in both the tendon tissue itself as well as its surrounding environment. During this time, the local cell population changes drastically with the introduction of cell types that will ultimately aid in the production of new tissues [55,124,125]. The collagen matrix makes up the structural backbone of tendon tissue, but at this time, collagen fiber diameter is reducedand crimp angles are significantly altered compared to uninjured tissue [71]. Disruption to the normally organized collagen structure likely contributes to deficits in mechanical strength, as many of the mechanical properties are highly dependent on collagen's hierarchical structure [13].

However, this disorganized tissue can be potentially be reorganized when exposed to tensile loads. Histological findings from animal models show that once specific tension is applied to tendons, the relative arrangement of the tissue is improved [126]. The same effects were found when animals had applied increased tension via mobilization in a separate study. The examined tissues were found to have better collagen arrangement in this ATR healing model after suture [104]. From these results, it is suggested that mobilization and WB during the healing phase after ATR in humans would similarly yield improved collagen arrangement and tissue structure [127].

Though such early tension and applied load on the healing tissue can yield great structural benefits for the tissue, there are unclear upper limits for magnitude and intensity, and a primary concern is re-rupture. Since the newly developed tissue is relatively weak and disorganized, the threshold for material failure is significantly lower than in intact tendon. Furthermore, mechanosensitive cells present in the tendon may trigger different processes depending on the relative intensity of the applied load. For instance, higher applied load in the form of uphill running showed improved expression of Type III Collagen, IGF-1, and lower expression of fibromodulin, biglycan, and TGF-B1 [128]. However, modification of load intensity by comparing different types of running shows that increased intensity can lead to the expression of non-tenocyte lineages by tendon stem cells. In fact, increased loading via intense bouts of running in mice leads to higher expression of tendon genes, but also bone and cartilage genes not found in moderate running episodes were present in the same tissue [129].The generation of these non-tendon precursors may lead to the generation of degenerative tendinopathic tissue, and result in continued functional deficits in the injured AT.

5.1.3 Previous studies in human ATR rehabilitation and the effect of loading

As previously mentioned in Section 5.1.1, current literature searches show that most existing studies of surgically treated ATR primarily compare early WB (EWB) rehabilitation protocols to immobilization of the ankle joint. Though these studies elucidate the influence of WB on the rehabilitation process, they do not specifically clarify the temporal effect of WB on healing. One of the earliest studies from Speck and Klaue investigated patients after open surgery, in which patients began full WB exercises altered with passive movements at 1 day post-OP [130]. Follow-up assessments were performed at 3, 6, and 12 months after surgery. Clinical evaluation with ultrasound, score collection, and isokinetic tests were performed at all timepoints. This initial study found no long-term within-patient differences in isokinetic strength and no heightened risk for re-rupture associated with EWB. This initial study gave the first suggestion that EWB is effective and suggested its use in practice, although no alternative rehabilitative group was included for comparison.

Further work investigating the effect of EWB in comparative studies has been able to provide functional information primarily at late timepoints after surgery. McNair and colleagues had compared immobilization and WB in ATR patients and found that WB patients had comparatively greater peak passive torque and energy storage in the ankle at a 6 month follow up; yet intrapatient deficits were still found in both rehabilitation groups [131]. Another study looked at the influence of EWB compared to non WB in conservatively managed ATR patients, and found similar functional deficits between the rehabilitation groups in a heel-rise test performed 1 year post-op [132]. Finally, Willits and colleagues looked at the effect of an operative versus a nonoperative ATR treatment in which both groups received accelerated rehabilitation procedures, consisting of both early WB and early ROM movement. Functional follow-up measurements of isokinetic plantarflexor and dorsiflexor strength performed at 1 and 2 years post-ATR found no differences between the treatment groups at these timepoints [133]. The primary drawback of these studies is that functional and biomechanical assessments were not performed at a relevant early rehabilitation timepoint, and information about early functional gains could not be determined.

Though information about AT function at an early timepoint is limited, there has been some information about the effect of EWB on AT structure in the short-term post-injury. Earlier work from Kangas et al used radiographs to monitor the lengthening of the AT at 1, 3, 6, 12, 24, and roughly 1 year after surgery when investigating the effect of either immobilization versus early movement after surgical repair of an ATR. All patients investigated were already at full WB by 3 weeks post-op. Tendon elongation was found in both intervention groups, with increased elongation in the immobilization group. Tendon elongation did not appear to correlate with age, BMI, or peak recorded isokinetic torques [134]. The primary drawback with this measurement is that monitoring tendon elongation only occurs on the injured side, as radiographic markers can only be inserted into the injured AT at the time of surgery once the injury site is opened. Monitoring of the contralateral side is not possible with this method.

Similar work performed by Schepull & Aspenberg investigated the effect of early controlled tension within walker boot in ATR patients. This study looked also at tendon lengthening, as well as material properties of the healing tendon, using implanted tantalum beads at the AT injury site and radiostereometric analysis to monitor their movement. The authors found that this early strength intervention appears to yield higher mechanical strength and properties in the long-term, with functional follow-up measurements occurring one year after surgery [135]. Similarly to the work performed by Kangas, which is described in the preceding paragraph, a limitation of this method is that only the injured AT can be monitored, and any investigation of the contralateral side is excluded. Furthermore, since the heel-raise test was used to determine AT function, this test could only be performed 1 year after ATR.

The works mentioned above have investigated surgical ATR treatment, but the aforementioned studies have only investigated open surgical methods. Comparatively few studies have looked at the effect of early WB specifically after percutaneous surgery, when compared to ankle immobilization. Calder and Saxby investigated a single patient group operated on with the Achillon minimally invasive instrument, and reported an excellent AOFAS score of 98 and a return to sports as soon as 6 months post-OP [136]. Metz and colleagues compared minimially invasive surgery to conservative, nonoperative treatment and found that surgery lead to lower (but non-significant) complications and risks. However, patients receiving surgery returned to work earlier than conservatively managed patients [137]. Another work from Majewski and colleagues investigated the effect of early functional therapy versus immobilization after percutaneous surgery, and found that immobilized patients returned to work significantly later than their early functional counterparts (67 versus 37 days post-op) [138]. Moreover, recent work comparing long-term biomechanical outcomes after different ATR treatments showed that surgical treatment yielded the best results, with no significant differences between percutaneous and open methods [108]. Thus it could be inferred that the specific type of surgery may not have an effect on the short-term biomechanical outcomes as well.

Regardless of surgical treatment, there has been to date no explicit comparison of EWB to standard WB (SWB) protocols. All studies mentioned here have primarily compared WB protocols to immobilization, but the temporal introduction of WB has yet to be investigated. Another major deficit is that all functional follow-up measurements have been exclusively performed at least 6 months to 1 year after injury. One of the most important benefits cited in EWB interventions is that early gains in strength and function occur; yet this explicit functional gain has yet to be elucidated. In fact, there are currently no studies in the literature that have monitored the ability of ATR patients to regain the ability to walk. Furthermore, short-term biomechanical properties and structure during the early stages of healing in the AT have yet to be investigated in both the injured and contralateral limb. It is highly likely that during these early stages, the relative compensatory actions that occur in the contralateral limb may also have play a great role in influencing the healing and development of the injured AT.

5.2 Main goals and hypotheses

The aim of this prospective study is to determine the temporal effect of weightbearing (WB) rehabilitation on *in vivo* MTU function after surgical treatment of an ATR. The results from this work could give unique insights in the types of short-term gains made in the early stages of rehabilitation, which may impact long-term outcomes. In order to address this, the primary goals of this study (previously introduced in Section 2.2) were:

(G4) to assess and quantify early functional gains to determine if early weightbearing (EWB) rehabilitation protocols enable faster recovery compared to standard weightbearing (SWB) protocols; and

(G5) to determine the temporal influence of WB on AT properties through *in vivo* assessment and quantification; and

(G6) to characterize and quantify ankle kinematics in the redevelopment of independent gait, one of the first activities of daily living mastered within the first few months post-ATR.

Based on knowledge from previous work, we set forth the corresponding hypotheses:

(H4) Rehabilitation with EWB will lead to faster gains in ankle moment and strength in both single-limb and bipedal assessments on the INJ limb when compared to SWB patients.

(H5) EWB patients will demonstrate a longer AT rest length and increased stiffness on the INJ tendon compared to SWB patients.

(H6) EWB patients will exhibit higher ankle mobility and more symmetry in gait compared to SWB patients.

5.3 Patient cohort & rehabilitation protocols

5.3.1 Recruitment and description of patient cohort

A total of fourteen patients, consisting of one female and thirteen males, were recruited for inclusion in the study at the time of ATR diagnosis in the clinic. All patients gave informed consent prior to participation. The local ethics committee approved this study (Charité, No EA/2/094/11) and all protocols were developed in accordance with the Declaration of Helsinki.

All patients included in the study received percutaneous surgery within 7 days of sustaining acute unilateral ATR. A single operator performed percutaneous surgical repair of the ATR at the Center for Musculoskeletal Surgery at the Charité-Universitätsmedizin, as described previously in Section 4.2.1. All patients were randomized to one of two different rehabilitation protocols at the time of surgery. In half of the cohort (7 out of 14) the patients' dominant leg was the side on which the ATR occurred, and all cases were due to indirect trauma.

5.3.2 Rehabilitation and assessment time points

Patients were prescribed a specific physiotherapy and rehabilitation protocol that commenced immediately after surgery. These protocols were specified based on recommendations from the operating orthopedic surgeon, clinicians, and physiotherapists. Up until 2 weeks after surgery, the two protocols are identical. A side-by-side comparison of the two rehabilitation protocols, with detailed information on the physiotherapy and specific exercises undertaken by the patients is found in the Appendix in **Section 9.5**.

Between the end of surgery and discharge from the hospital, patients received standard inpatient physiotherapy and cryotherapy. During this time, the ankle was immobilized in a walker boot (Vacoped, OPED GmbH, Oberlaindern, Germany) with the foot in 30° of plantarflexion. Furthermore, patients were guided through gait training and stair navigation with an estimated 15kg of partial weight bearing on under arm crutches. Pain management was limited to two anaglesics: paracetamol and tramadol. Administration of ibuprofen and Voltaren (diclofenac) for pain was excluded. Furthermore the anticoagulant and antithrombotic Fraxiparin (nadoparin) was also prescribed for use until patients could bear their full body weight on the injured limb.

All patients appeared at the clinic for a follow-up appointment with the operating surgeon seven weeks after surgery. During this clinical examination, the operational wound was manually and sonographically examined for adhesions, infection, and possible rerupture. The external sutures were also removed at the same appointment, and patients received prescriptions for physiotherapy and an appointment for biomechanical measurements within two weeks (corresponding to eight weeks after operation). Upon the first biomechanical measurement at 8 weeks post-op, the early weightbearing (EWB) group had already performed 6 weeks of full weight-bearing exercises. On the other hand, the standard weightbearing (SWB) group had just begun full weight-bearing exercises in the same week as the first biomechanical tests.

All recruited patients (n=14) appeared for the first biomechanical measurement session 8 weeks after surgery. One EWB patient dropped out of the study at 9 weeks, as an appendectomy was necessary and the additional rest period for post-surgical recovery interfered with the prescribed rehabilitation. Thus, a total of 13 patients were measured at 12 weeks post-op, with 5 EWB patients and 8 SWB patients.

A number of patients were unable to complete the third biomechanical measurement at 16 weeks for various reasons. In total, only two EWB patients were able to complete full biomechanical measurements at this time point. Another EWB patient was only able to complete gait analysis at 16 weeks, thus the gait analysis sample size for this group is slightly larger with n=3. Two other patients were unable to return due to one sustaining a myocardial infarction and another sustaining a re-rupture of the affected AT in. One SWB patient could not be reached for the third appointment, leaving the sample size for the 16-week follow-up at 7 for this group.

5.4 Results

5.4.1 Spatiotemporal gait parameters

The duration of the overall gait cycle and the stance phase were found to be similar between INJ and CON sides for both EWB and SWB patients for all time points (**Table 5**). The duration of the swing phase was similar for both WB groups at weeks 8 and 12, but was significantly lower on the INJ side at 16 weeks. Both the stride length, defined as the distance between two successive landings of the same foot, and the walking base, defined as the medio-lateral distance between the two feet, were similar between INJ and CON for both WB groups for all time points.

Stride height was significantly lower on INJ compared to CON at 8 weeks for both EWB and SWB groups. However, EWB patients continued to have a lower INJ stride height at 12 weeks whereas SWB patients had no significant difference at the same time point. Both WB groups showed no differences in stride height at 16 weeks. Minimum toe clearance during the gait cycle was symmetric in EWB for the entirety of the study. On the other hand, minimum toe clearance was significantly higher on INJ at 8 and 12 weeks, with a similar tendency at 16 weeks.

Step length, defined as the distance by which one foot moves forward in front of the other, was significantly higher on INJ compared to CON for both WB at 8 weeks. EWB patients recovered step length symmetry at 12 and 16 weeks, whereas SWB patients continued to have significantly higher step length on INJ for the remaining time points. The lower CON stride length is due to single leg support on INJ during this movement; the weaker INJ is, the shorter the CON stride length.

The foot progression angle (FPA), defined as the angle between the line of progression and the longitudinal axis of the foot, was measured both at heel strike and at midstance. FPA at midstance was significantly lower in INJ compared to CON for both WB for both WB at 8 and 12 weeks post-OP. EWB patients recovered midstance FPA symmetry at 16 weeks; whereas SWB patients continued to have significantly lower INJ midstance FPA at 16 weeks. FPA at heel strike was symmetric for all time points of EWB patients and for SWB at 8 weeks, but was significantly higher at 12 and 16 weeks.

5.4.2 *In vivo* AT structure and function

EWB patients did not appear to have the appearance of significant lengthening at 8 weeks, but a trend was seen towards apparent tendon lengthening at 12 and 16 weeks (**Table 6**). On the other hand, SWB patients constantly presented with significant INJ tendon lengthening. Significant asymmetries in both tendon strain and absolute tendon elongation were only present at 12 weeks post-op in both EWB and SWB patients. The estimated tendon force was found to be significantly lower at 8 weeks for both SWB and EWB groups. This asymmetry continued for SWB patients at 12 and 16 weeks post-op, but not for EWB patients. For all time points, there were no differences in rest tendon length, tendon strain, tendon elongation, and maximum tendon force between SWB and EWB.

Compared to SWB patients, EWB patients displayed more symmetry in tendon stiffness; however, on average, tendons appeared to demonstrate lower tendon stiffness on INJ. Upon comparison of the INJ tendon stiffness of both limbs, SWB patients were found to have significantly higher stiffness at 12 weeks post-op compared to EWB patients (p = 0.043), but no significant differences were found at both 8 and 16 weeks post-op between rehabilitation groups.

Early WB	**8 Weeks (n=6)**			**12 Weeks (n=5)**			**16 Weeks (n=3)**		
	INJ	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
Gait cycle time (s)	1.172 ± 0.10	1.174 ± 0.11	0.247	1.092 ± 0.08	1.089 ± 0.08	0.345	1.054 ± 0.09	1.056 ± 0.10	0.772
Stance phase time (s)	0.71 ± 0.07	0.74 ± 0.08	0.155	0.612 ± 0.19	0.604 ± 0.17	0.500	0.657 ± 0.06	0.629 ± 0.07	0.073 §
Swing phase time (s)	0.46 ± 0.07	0.43 ± 0.03	0.116	0.472 ± 0.09	0.484 ± 0.09	0.138	0.397 ± 0.03	0.427 ± 0.03	0.033*
Stride length (cm)	102.36 ± 15.74	102.39 ± 15.51	0.850	120.85 ± 11.34	121.20 ± 12.36	0.530	122.84 ± 8.19	122.60 ± 8.37	0.650
Stride height (cm)	20.39 ± 2.73	24.26 ± 1.41	0.005*	23.77 ± 1.45	25.76 ± 0.99	0.041*	24.58 ± 3.71	26.17 ± 2.52	0.246
Step length (cm)	60.27 ± 6.62	46.37 ± 7.27	<0.001*	64.49 ± 3.84	58.56 ± 7.88	0.066 §	63.37 ± 3.81	60.87 ± 5.25	0.279
Walking base (cm)	13.71 ± 4.25	13.60 ± 4.15	0.704	10.05 ± 4.30	10.20 ± 4.42	0.345	9.68 ± 3.65	9.70 ± 3.12	0.961
FPA at midstance (°)	11.14 ± 6.00	19.07 ± 9.67	0.006*	9.70 ± 7.15	18.34 ± 8.69	0.002*	8.48 ± 10.83	13.21 ± 12.04	0.113
FPA at heel strike (°)	12.88 ± 6.25	11.99 ± 6.80	0.535	13.06 ± 8.08	12.65 ± 7.68	0.878	13.60 ± 9.62	11.47 ± 11.23	0.385
Minimum toe clearance (cm)	2.13 ± 0.84	1.57 ± 0.47	0.080 §	2.23 ± 0.76	1.67 ± 0.46	0.066 §	2.06 ± 0.55	1.67 ± 0.46	0.735
Standard WB	**8 Weeks (n=8)**			**12 Weeks (n=8)**			**16 Weeks (n=7)**		
	INJ	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
Gait cycle time (s)	1.251 ± 0.18	1.251 ± 0.18	0.889	1.158 ± 0.14	1.153 ± 0.14	0.104	1.125 ± 0.07	1.130 ± 0.08	0.539
Stance phase time (s)	0.76 ± 0.13	0.79 ± 0.16	0.123	0.70 ± 0.09	0.71 ± 0.12	0.779	0.69 ± 0.04	0.68 ± 0.05	0.228
Swing phase time (s)	0.49 ± 0.06	0.46 ± 0.02	0.116	0.45 ± 0.05	0.45 ± 0.03	0.590	0.43 ± 0.04	0.45 ± 0.03	0.030*
Stride length (cm)	103.74 ± 15.83	103.89 ± 16.05	0.461	121.54 ± 15.89	121.33 ± 15.72	0.653	123.37 ± 7.77	123.39 ± 7.67	0.958
Stride height (cm)	22.50 ± 2.68	24.38 ± 2.16	0.001*	24.83 ± 2.35	25.37 ± 1.53	0.137	25.05 ± 1.34	25.49 ± 1.08	0.096
Step length (cm)	59.66 ± 5.81	47.06 ± 8.46	<0.001*	65.47 ± 5.33	57.47±10.04	0.010*	65.51 ± 2.47	58.77±6.10	0.016*
Walking base (cm)	11.17 ± 4.26	11.25 ± 4.16	0.298	9.17 ± 3.38	9.48 ± 3.23	0.167	8.67 ± 3.11	8.69 ± 3.20	0.921
FPA at midstance (°)	12.16 ± 7.08	18.09 ± 6.41	0.001*	13.43 ± 5.23	19.33 ± 4.70	<0.001*	11.33 ± 4.26	16.06 ± 5.21	0.005*
FPA at heel strike (°)	13.83 ± 6.36	11.85 ± 8.37	0.077 §	17.30 ± 6.15	14.22 ± 7.53	0.027*	15.40 ± 6.40	11.82 ± 5.51	0.018*
Minimum toe clearance (cm)	2.26 ± 0.58	1.66 ± 0.35	0.046*	2.53 ± 0.59	1.89 ± 0.32	0.025*	2.55 ± 0.66	1.99 ± 0.42	0.089 §

Table 5. Mean spatiotemporal gait parameters for all patient groups at all time points. All significant differences between injured (INJ) and contralateral (CON) ($p < 0.05$) are denoted with grey backgrounds and asterisks (*). All statistical tendencies ($0.05 < p < 0.10$) are denoted with section symbols (§).

5.4.3 Maximal Voluntary Isometric Contraction (MVIC)

Pairwise comparison of the average single-sided MVICs performed in the dynamometer yielded significantly lower values on INJ than on CON (51.5 N·m vs. 122.1 N·m, p = 0.001, **Table 6**) in the EWB patients at 8 weeks post-OP. At 12 weeks, the maximum MVIC values on INJ had increased to 83.4 N·m, but were still significantly lower than CON (120.0 N·m, p < 0.029). INJ values were improved to 90.8 N·m at 16 weeks, compared to CON values of 149.0 N·m. Due to a low sample size, no p-values are available. When these values are normalized to the patients' body weight, indications of significantly lower moment production at 8 weeks (0.635 BW·m vs. 1.516 BW·m, p = 0.002) and 12 weeks (1.014 BW·m vs. 1.463 BW·m, p = 0.030) were also present in EWB patients.

Similarly, SWB patients had significantly lower MVICs on the INJ side at 8 weeks (56.3 N·m vs. 137.6 N·m, p = 0.01). Though improvements on INJ were made at 12 weeks (72.6 N·m), they were still significantly lower than CON at the same time point (133.1 N·m, p = 0.001). At 16 weeks, there was a minor improvement in INJ (81.1 N·m) but was still significantly lower than CON (143.3 N·m, p = 0.001). When these values are normalized to the patients' body weight, significantly lower MVICs on INJ were seen at 8 weeks (0.655 BW·m vs. 1.630 BW·m, p < 0.001), 12 weeks (0.919 BW·m vs. 1.623 BW·m, p = 0.001), and 16 weeks post-OP (0.957 BW·m vs. 1.67 BW·m, p = 0.001).

Early WB	**8 Weeks (n=6)**			**12 Weeks (n=5)**			**16 Weeks (n=2)**		
	INJ	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
Rest Tendon Length (mm)	203.4 ± 20.0	197.3 ± 24.0	0.317	202.6 ± 12.8	182.7 ± 10.9	0.057 §	207.9 ± 17.1	177.2 ± 0.71	(n=2)
MVIC Moment (Nm)	51.5 ± 10.7	122.1 ± 17.8	0.001*	83.4 ± 7.8	120.0 ± 29.1	0.029*	90.8 ± 19.8	149.0 ± 8.4	(n=2)
MVIC Moment (BW-m)	0.635 ± 0.132	1.516 ± 0.268	0.002*	1.014 ± 0.111	1.463 ± 0.375	0.030*	1.1087 ± 0.200	1.825 ± 0.032	(n=2, p=0.109)
Max Tendon Force (N)	1439 ± 312	2387 ± 247	0.028*	1782 ± 271	2134 ± 657	0.500	2275 ± 400	2650 ± 377	(n=2, p=0.655)
Tendon Elongation (mm)	5.59 ± 3.11	10.92 ± 8.61	0.138	3.70 ± 2.54	7.85 ± 2.48	0.043*	5.43 ± 3.39	10.89 ± 5.09	(n=2, p=0.109)
Tendon Strain (%)	3.36 ± 1.28	5.54 ± 4.79	0.075 §	1.94 ± 1.36	4.21 ± 1.26	0.043*	2.85 ± 2.25	6.03 ± 2.67	(n=2, p=0.109)
Tendon Stiffness (N/mm)	113.9 ± 33	227.1 ± 133	0.197	100.3 ± 25	238.2 ± 90	0.166	94.0 ± 29	243.1 ± 78	0.125
Standard WB	**8 Weeks (n=8)**			**12 Weeks (n=7)**			**16 Weeks (n=7)**		
	INJ	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
Rest Tendon Length (mm)	200.3 ± 12.2	186.1 ± 14.5	0.037*	204.8 ± 10.0	183.1 ± 16.0	0.041*	204.8 ± 10.0	183.1 ± 16.0	0.035*
MVIC Moment (Nm)	56.3 ± 37.4	137.6 ± 63.3	0.01*	72.6 ± 37.6	133.1 ± 48.6	0.001*	81.1 ± 41.6	143.3 ± 52.2	0.001*
MVIC Moment (BW-m)	0.655 ± 0.328	1.630 ± 0.567	<0.001*	0.9185 ± 0.392	1.623 ± 0.498	0.001*	0.9573 ± 0.362	1.696 ± 0.411	0.001*
Max Tendon Force (N)	1626 ± 839	2642 ± 1178	0.017*	1730 ± 791	2776 ± 1038	0.050*	1796 ± 753	3211 ± 1358	0.043*
Tendon Elongation (mm)	6.87 ± 2.81	7.92 ± 8.61	0.398	4.92 ± 2.43	5.63 ± 2.71	0.249	6.88 ± 2.02	11.15 ± 7.56	0.091 §
Tendon Strain (%)	3.55 ± 1.34	4.30 ± 1.61	0.128	2.41 ± 1.24	3.05 ± 1.11	0.028*	3.35 ± 1.04	5.83 ± 4.02	0.091 §
Tendon Stiffness (N/mm)	132.6 ± 58	255.3 ± 57	0.020*	135.9 ± 32	183.4 ± 48	0.077	110.7 ± 48	216.9 ± 82	0.046*

Table 6. Mean parameters for *in vivo* tendon properties and dynamometric moments (MVICs) for all patient groups at all time points. All significant differences (p < 0.05) between injured (INJ) and contralateral (CON) limbs are denoted with asterisks (*). All statistical tendencies (0.05 < p < 0.10) are denoted with section symbols (§).

Upon comparison of the normalized values of INJ MVICs, statistical tests found no significant differences between the EWB and SWB patients at 8 weeks (EWB: 0.635 BW·m vs. SWB: 0.655 BW·m, p = 0.893), 12 weeks (1.014 BW·m vs. 0.919 BW·m, p = 0.610), and 16 weeks (1.109 BW·m vs. 0.957 BW·m, p = 0.600). Similarly, no differences were found on the CON side when comparing EWB to SWB patients at 8 weeks (p = 0.658), 12 weeks (p = 0.558), and 16 weeks (p = 0.684).

However, it was of note that EWB patients appeared to have a significant gain between the 8 and 12 week measurements in MVICs (0.635 to 1.014 BW·m, p = 0.039). On the other hand, SWB patients did not show a significant gain in strength between the 8 and 12 week measurements (0.655 to 0.919 BW·m, p = 0.130).

5.4.4 Moments during gait

All moments were calculated and divided by the patients' weight in kilograms. Pairwise comparison of the average maximum moments in the frontal and sagittal planes did not yield any significant differences in the EWB patients at 8 weeks post-OP. However, there was a tendency for lower maximum plantarflexion moments in EWB at 8 weeks on the INJ side (0.897 N·m/kg vs. 1.309 N·m/kg, p = 0.055, **Table 7**). At 12 weeks, the eversion moment was significantly higher on the INJ side in EWB patients (0.082 N·m/kg vs. 0.045 N·m/kg, p = 0.043); all other moments were not significantly different. At 16 weeks, all EWB moments were similar between INJ and CON.

At 8 weeks after surgery, the INJ ankle of SWB patients produced significantly lower plantarflexion moments (0.817 N·m/kg vs. 1.172 N·m/kg, p = 0.002) and inversion moments (0.184 N·m/kg vs. 0.250 N·m/kg, p = 0.018). The same dorsiflexion moment was significantly higher on INJ at 8 weeks (0.055 N·m/kg vs. 0.036 N·m/kg, p = 0.055). Eversion moments at 8 weeks were similar in SWB patients. All calculated moments for SWB patients at 12 and 16 weeks were found to be similar between the INJ and CON ankles.

Early WB	**8 Weeks (n=6)**			**12 Weeks (n=5)**			**16 Weeks (n=3)**		
(N-m/kg)	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
Max DF Moment	0.051 ± 0.031	0.040 ± 0.070	0.708	0.056 ± 0.010	0.127 ± 0.119	0.686	0.065 ± 0.010	0.200 ± 0.179	0.329
Max PF Moment	0.8971 ± 0.194	1.309 ± 0.234s	0.055 §	1.046 ± 0.104	1.109 ± 0.219	0.477	1.044 ± 0.193	0.972 ± 0.076	0.401
Inversion Moment	0.161 ± 0.085	0.203 ± 0.074	0.686	0.221 ± 0.051	0.198 ± 0.038	0.344	0.200 ± 0.014	0.226 ± 0.041	0.246
Eversion Moment	0.066 ± 0.072	0.082 ± 0.046	0.416	0.082 ± 0.037	0.045 ± 0.030	0.043*	0.070 ± 0.018	0.043 ± 0.027	0.218
Standard WB	**8 Weeks (n=8)**			**12 Weeks (n=7)**			**16 Weeks (n=7)**		
(N-m/kg)	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
Max DF Moment	0.055 ± 0.041	0.036 ± 0.037	0.019*	0.065 ± 0.055	0.094 ± 0.116	0.398	0.088 ± 0.092	0.100 ± 0.094	0.612
Max PF Moment	0.817 ± 0.151	1.172 ± 0.177	0.002*	1.034 ± 0.156	1.091 ± 0.170	0.674	0.946 ± 0.148	0.976 ± 0.159	0.644
Inversion Moment	0.184 ± 0.054	0.250 ± 0.103	0.018*	0.196 ± 0.028	0.224 ± 0.060	0.204	0.212 ± 0.070	0.187 ± 0.060	0.172
Eversion Moment	0.033 ± 0.044	0.066 ± 0.030	0.209	0.101 ± 0.047	0.060 ± 0.029	0.098	0.098 ± 0.071	0.074 ± 0.051	0.114

Table 7. Mean sagittal and frontal ankle moments during gait for all patient groups at all time points. All significant differences ($p < 0.05$) between injured (INJ) and contralateral (CON) are denoted with asterisks (*). All statistical tendencies ($0.05 < p < 0.10$) are denoted with section symbols (§).

One-way ANOVAS (normally distributed data) or Mann-Whitney Tests (not normally distributed data) were used to compare EWB moments to SWB moments. Across all time points, all calculated ankle moments were found to be similar between the two rehabilitation groups. When comparing gains in moments, EWB patients were found to exhibit similar moments across all time points for all four calculated moments. On the other hand, SWB patients were found to make a significant gain in plantarflexion moment during gait between 8 and 12 weeks post-op (p = 0.044), but no significant gains between 12 and 16 weeks post-op (p = 0.296).

5.4.5 Ground reaction force impulses during gait

All GRF calculations presented here are calculated as various integrals under the time curve, and all values were normalized to the patient's body weight (BW). The FZ integral refers to the total area under the curve in the vertical direction, and the FX integral refers to the total area under the curve in the medial direction of the foot. The FY1 integral refers to the entire area underneath the initial breaking curve (prior to crossing zero) and the FY2 integral refers to the entire area underneath the initial propulsion curve (after crossing zero).

Intra-patient comparison of EWB patient GRFs showed that significant differences were only found in the first measurement at 8 weeks. At this time point, both the vertical FZ integral (0.498 BW·s vs. 0.668 BW·s, p = 0.001, **Table 8**) and the propulsive FY2 integral (0.012 BW·s vs. 0.025 BW·s, p = 0.021) were significantly lower on the INJ side compared to CON. The breaking FY1 and the medial FX integral were similar within EWB patients at 8 weeks. All GRF integrals at 12 and 16 weeks post-OP were also found to be similar between INJ and CON in EWB patients.

Intra-patient pairwise comparison of SWB patient GRF integrals at 8 weeks also yielded significantly lower vertical FZ integrals (0.545 BW·s vs. 0.707 BW·s, p = 0.012, **Table 8**) and higher propulsive FY2 integrals (0.013 BW·s vs. 0.027 BW·s, p = 0.012) on the INJ side. Similar to EWB, the breaking FY1 and the medial FX integral were similar within SWB patients. At 12 weeks post-OP, only the vertical FZ (0.540 BW·s vs. 0.622 BW·s, p = 0.033) was still significantly lower on INJ in SWB patients. This vertical FZ integral asymmetry was improved but not yet resolved at 16 weeks post-OP (0.545 BW·s vs. 0.594 BW·s, p = 0.026).

Early WB	**8 Weeks (n=6)**			**12 Weeks (n=5)**			**16 Weeks (n=3)**		
	INJ	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
FZ integral (BW*s)	0.498 ± 0.054	0.668 ± 0.060	0.001*	0.522 ± 0.042	0.575 ± 0.060	0.091	0.515 ± 0.039	0.547 ± 0.059	0.170
FY1 integral (BW*s)	-0.024 ± 0.007	-0.014 ± 0.007	0.071	-0.029 ± 0.005	-0.026 ± 0.004	0.233	-0.028 ± 0.005	-0.026 ± 0.004	0.285
FY2 integral (BW*s)	0.012 ± 0.005	0.025 ± 0.009	0.021*	0.024 ± 0.005	0.023 ± 0.010	0.857	0.026 ± 0.002	0.028 ± 0.006	0.413
Standard WB	**8 Weeks (n=8)**			**12 Weeks (n=7)**			**16 Weeks (n=7)**		
	INJ	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
FZ integral (BW*s)	0.545 ± 0.049	0.707 ± 0.126	0.012*	0.540 ± 0.035	0.622 ± 0.107	0.033*	0.545 ± 0.024	0.594 ± 0.058	0.026*
FY1 integral (BW*s)	-0.024 ± 0.011	-0.018 ± 0.007	0.161	-0.027 ± 0.003	-0.023 ± 0.008	0.263	-0.029 ± 0.005	-0.027 ± 0.003	0.378
FY2 integral (BW*s)	0.013 ± 0.008	0.027 ± 0.007	0.012*	0.024 ± 0.006	0.032 ± 0.006	0.055 §	0.027 ± 0.004	0.031 ± 0.006	0.227

Table 8. Mean ground reaction force integrals during gait for all patient groups at all time points. All significant differences ($p < 0.05$) are denoted with asterisks (*). All statistical tendencies ($0.05 < p < 0.10$) are denoted with section symbols (§).

Interpatient one-way ANOVAS (normally distributed data) or Mann-Whitney Tests (not normally distributed data) were used to compare EWB moments to SWB moments. At 8 weeks, only the INJ vertical FZ integral was significantly lower in EWB compared to SWB (0.498 BW·s vs. 0.545 BW·s, p = 0.008). At 12 weeks, only the CON propulsive FY2 integral was significantly lower in EWB compared to SWB (0.023 BW·s vs. 0.032 BW·s, p = 0.030); no differences on the INJ limbs at the same time point were found. Furthermore, no differences were found between EWB and SWB at 16 weeks post-op on either leg.

5.4.6 Kinematics during walking

5.4.6.1 Comparison of sagittal angles at 1% intervals of the gait cycle

Further statistical comparison of the sagittal gait cycle angles was performed at 1% intervals of the gait cycle, as closer visual inspection revealed dramatically different curves between the injured and contralateral sides. In general, there was an overall trend of the INJ ankle presenting with lower dorsiflexion during early- and mid-stance (~5-45% of the gait cycle) and significantly lower plantarflexion during late stance and early swing (~45-80%) in the first two measurements. Comparison of the INJ sagittal angles between EWB and SWB patients showed no significant differences at all measured time points.

EWB patients demonstrated significant differences throughout the majority of the gait cycle (3-90%, 97-100%) between INJ and CON at 8 weeks, (**Figure 19**). Similarly at 12 weeks, EWB patients had significantly lower angles during early stance (3, 6-8, 12-13, and 15-46% of the gait cycle) and higher angles during late stance and early swing (47-74%) compared to CON. This trend continued at 16 weeks but significant differences were only found at the beginning (1%) and end of the gait cycle (98-100%).

A similar trend was found in SWB patients, with the majority of the gait cycle showing significant differences between INJ and CON (2-89, 93-100%) at 8 weeks post-op (**Figure 20**). At 12 weeks post-op, patients showed differences between INJ and CON at midstance and early swing (36-37, 39-79%) and at the end of the gait cycle (96-100%). Significant differences between the SWB patient limbs were lower in quantity at 16 weeks, limited to the beginning (2-3, 5-9%) and end (98-100%) of the gait cycle, as well as during late stance (53-68%).

5.4.6.2 Comparison of maximal angles

EWB patients showed minimal differences in maximal ankle angles at 8 weeks post-op. Except for the overall rotational ROM, which was significantly lower on INJ (7.95° vs. 12.46°, p = 0.046, **Table 9**), there were no significant differences found between INJ and CON. The rotational ROM continued to be significantly lower on INJ at 12 weeks (9.64° vs. 14.24°, p = 0.046). At 16 weeks, there were no more significant differences between INJ and CON in EWB patients. However, there was a tendency for increased dorsiflexion (9.88° vs. 14.47°, p = 0.091).

SWB patients also exhibited only one significant intra-patient difference with a lower rotational ROM on INJ at 8 weeks (6.90° vs. 12.44°, p = 0.003). At 12 weeks, the rotational ROM is still significantly lower on INJ compared to CON (10.95° vs. 14.05°, p = 0.043). Additionally there are changes in the sagittal plane, with significantly lower dorsiflexion (8.99° vs. 11.34°, p = 0.036), as well as changes in the frontal plane, with increased frontal ROM on INJ (8.16° vs. 6.38°, p = 0.027). At 16 weeks, the only remaining significant difference is a tendency for a lower rotational ROM on INJ (12.40° vs. 16.37°, p = 0.057).

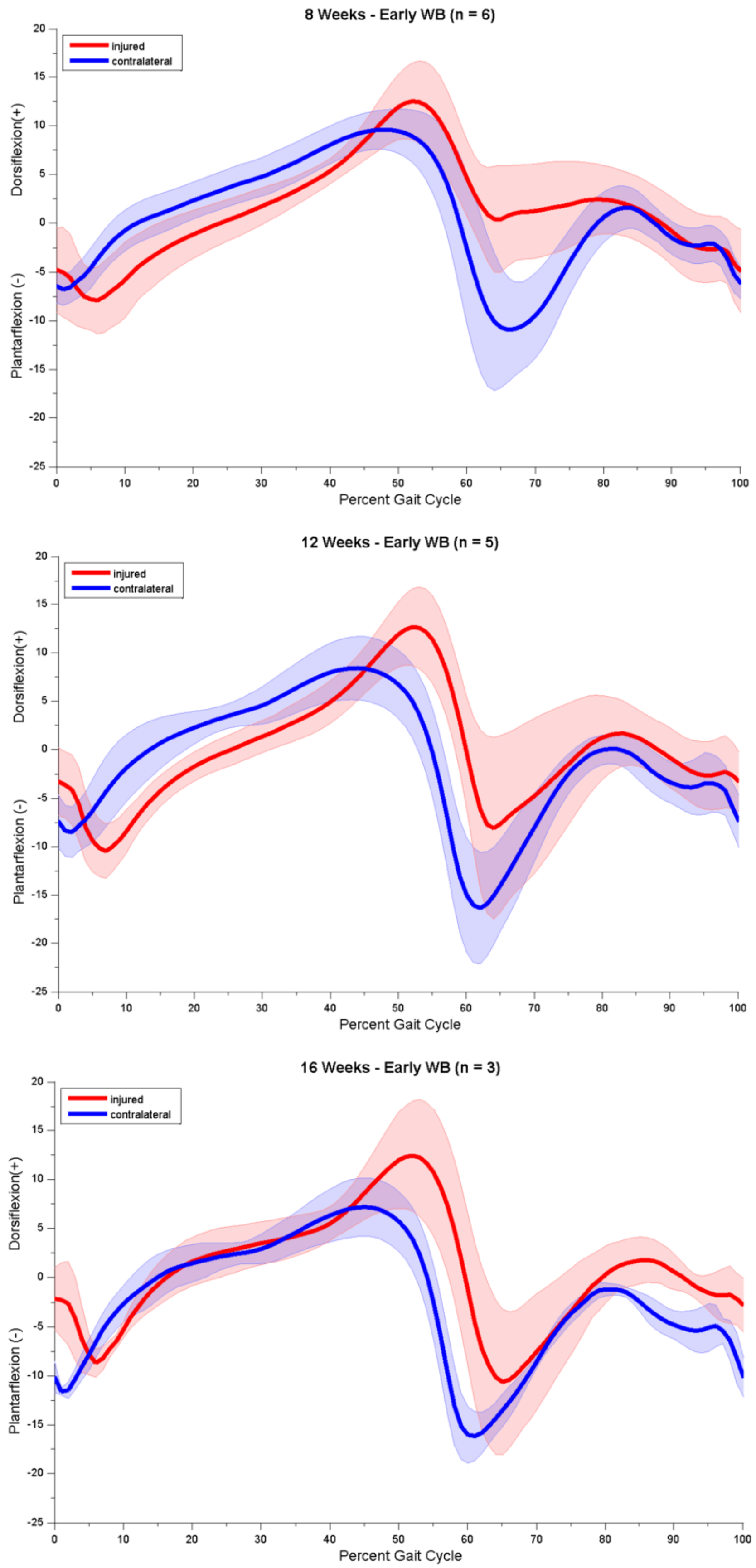

Figure 19. Mean sagittal angle curves in EWB patients, depicting the mean (solid line) and standard deviations (shaded area) at 1% intervals of the gait cycle for the injured (red) and contralateral (blue) limbs. Positive values indicate dorsiflexion.

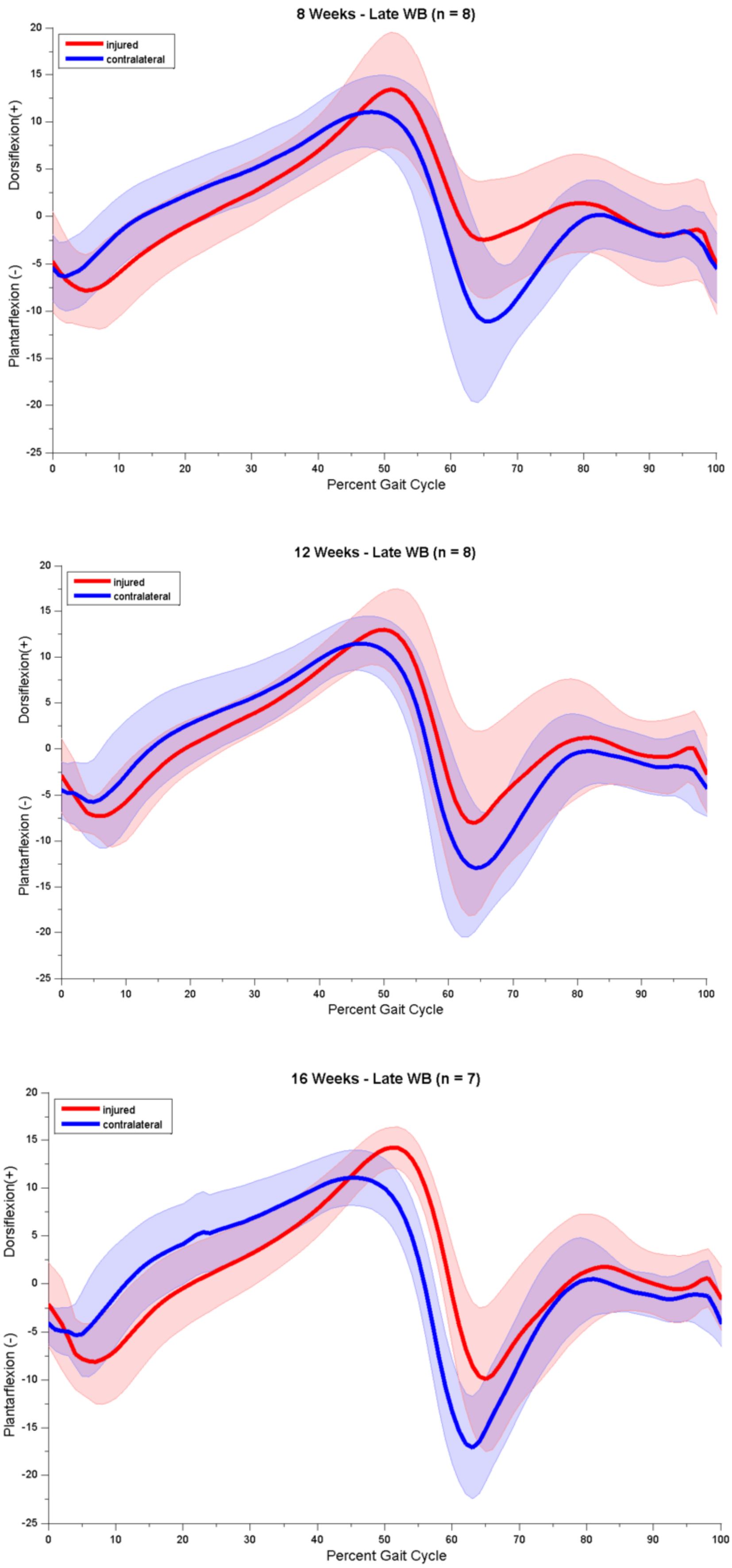

Figure 20. Mean sagittal angle curves in SWB patients, depicting the mean (solid line) and standard deviations (shaded area) at 1% intervals of the gait cycle for the injured (red) and contralateral (blue) limbs. Positive values indicate dorsiflexion.

At 8 weeks, there were no significant differences between EWB and SWB maximal angles, but there was a tendency for higher INJ internal rotation in SWB patients (8.91° vs. 2.31°, $p = 0.081$). At 12 weeks and 16 weeks, no significant differences between the rehabilitation groups on INJ were evident.

Early WB	**8 Weeks (n=6)**			**12 Weeks (n=5)**			**16 Weeks (n=3)**		
	INJ	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
Dorsiflexion	10.63 ± 2.65	12.31 ± 3.17	0.222	11.45 ± 2.58	13.72 ± 3.83	0.122	9.88 ± 1.59	14.47 ± 1.12	0.091 §
Early Stance: Plantarflexion	9.24 ± 3.51	7.26 ± 1.47	0.150	10.59 ± 2.81	9.05 ± 2.49	0.173	8.79 ± 1.45	11.93 ± 0.36	0.081 §
Late Stance: Plantarflexion	0.22 ± 5.60	12.31± 5.90	<0.001*	8.45 ± 9.30	16.68 ± 5.89	0.006*	11.07 ± 7.72	16.22 ± 2.62	0.157
Sag. ROM	23.51 ± 5.36	21.96 ± 2.54	0.363	24.51 ± 1.89	22.45 ± 3.12	0.294	22.72 ± 4.40	21.77 ± 3.49	0.484
Inversion	4.13 ± 1.97	2.94 ± 2.40	0.199	4.27 ± 1.77	3.85 ± 1.68	0.675	4.76 ± 2.22	4.82 ± 2.56	0.965
Eversion	2.05 ± 1.74	3.40 ± 1.26	0.236	3.06 ± 2.57	2.92 ± 0.62	0.905	2.73 ± 1.65	2.36 ± 0.95	0.615
Frontal ROM	6.18 ± 2.24	6.34 ± 1.97	0.900	7.33 ± 2.19	6.77 ± 1.22	0.572	7.49 ± 0.76	7.19 ± 2.60	0.875
Internal Rotation	2.31 ± 21.78	7.11 ± 9.42	0.638	12.01±12.05	6.86 ± 13.07	0.500	16.76±11.24	1.53 ± 3.68	0.154
External Rotation	5.63 ± 21.72	5.35 ± 12.27	0.753	-2.38 ± 13.10	7.37± 14.00	0.345	-5.50 ± 12.81	12.23 ± 4.16	0.165
Rot. ROM	7.95 ± 3.01	12.46 ± 4.37	0.046*	9.64 ± 2.07	14.24 ± 0.97	0.043*	11.27 ± 2.78	13.75± 1.72	0.378
Standard WB	**8 Weeks (n=8)**			**12 Weeks (n=7)**			**16 Weeks (n=7)**		
	INJ	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
Dorsiflexion	9.80 ± 5.17	11.23 ± 4.63	0.401	8.99 ±3.56	11.34 ±4.39	0.036*	10.41 ± 4.29	12.41 ± 4.97	0.177
Early Stance: Plantarflexion	8.97 ± 4.64	7.03 ± 3.22	0.278	8.86 ± 3.10	7.46 ± 4.20	0.173	9.44 ± 4.16	6.78 ± 3.68	0.072 §
Late Stance: Plantarflexion	3.45 ± 6.20	14.1± 6.26	0.001*	8.59 ± 9.84	15.55 ± 4.52	0.019*	10.22 ± 7.25	17.27 ± 5.40	0.008*
Sag. ROM	24.02 ± 3.29	22.84 ± 4.12	0.542	25.92 ±1.39	23.41 ±3.68	0.083 §	25.18 ± 2.80	23.92 ± 2.90	0.240
Inversion	4.00 ± 3.81	3.30 ± 2.79	0.575	4.05 ±2.12	2.75 ±1.30	0.162	3.85 ± 1.41	2.62 ± 2.04	0.129
Eversion	3.21 ± 4.02	3.44 ± 2.68	0.907	4.11 ±2.52	3.62 ±1.68	0.674	3.95 ± 2.68	3.90 ± 0.78	0.972
Frontal ROM	7.20 ± 2.17	6.75 ± 1.19	0.389	8.16 ±3.15	6.38 ±1.76	0.027*	7.80 ± 2.99	6.53 ± 1.43	0.151
Internal Rotation	8.91 ± 6.08	16.48 ± 12.96	0.327	15.28 ± 13.46	8.30 ± 13.17	0.401	9.21 ± 11.94	14.44 ± 15.94	0.612
External Rotation	2.01 ± 6.13	4.04 ± 11.03	0.734	-4.33 ± 15.69	5.75 ± 12.11	0.241	3.19 ± 13.39	1.93 ± 16.76	0.735
Rot. ROM	6.90 ± 1.37	12.44 ± 3.27	0.003*	10.95 ± 3.73	14.05 ± 3.75	0.043*	12.40 ± 1.96	16.37 ± 3.50	0.057 §

Table 9. Average maximum sagittal and frontal angles during gait for Early and Standard WB protocols. All significant differences ($p < 0.05$) are denoted with asterisks (*). All statistical tendencies ($0.05 < p < 0.10$) are denoted with section symbols (§).

Though maximal ankle angles in the sagittal plane appeared to have limited significant differences, visual inspection of the angle curves showed clear functional differences between the two limbs (**Figure 19 and Figure 20**). Overall maximal plantarflexion and dorsiflexion values were often found to be similar, but the time at which the maximal value occurred was very different in the injured and contralateral limbs. Maximal CON plantarflexion was often at the end of the stance phase or at early swing. However, maximal INJ plantarflexion occurred soon after initial contact at the beginning of the stance phase. For this reason, maximum plantarflexion angle was calculated at two points: early stance and late stance phases.

In the EWB patients, no differences were found in maximal plantarflexion in early stance between INJ and CON at all time points. However, EWB patients had significantly lower maximal plantarflexion at 8 (0.22° vs. 12.31°, $p < 0.001$) and 12 weeks (8.45° vs. 16.68°, $p = 0.006$) in late stance. At 16 weeks, only three EWB patients could be measured, but the mean late stance plantarflexion angle remained lower than the contralateral side, but without statistical significance (**Table 9**).

SWB patients similarly had no significant differences in maximal plantarflexion during early stance at 8 and 12 weeks post-op, but there was a tendency for increased initial stance plantarflexion in the INJ ankle at 16 weeks (9.44° vs. 6.78°, $p = 0.072$). During late stance, SWB patients were found to continuously display lower maximal plantarflexion angles on INJ compared to CON for all measured time points (**Table 9**). Upon comparison of both WB groups, no significant differences found between rehabilitation groups on the INJ limbs in maximal plantarflexion at all time points.

5.4.6.3 Rate of angular change

In order to further assess the functional capability of the MTU during bipedal gait, the rate of angular change during weight acceptance and propulsion was calculated. The rate of angular change during weight acceptance (Slope 1, $\Delta\theta_{Accept}$) was determined as the slope of the line connecting initial maximal plantarflexion to maximal dorsiflexion in mid-stance. The rate of angular change during push-off (Slope 2, $\Delta\theta_{Push}$) was calculated as the slope connecting maximal dorsiflexion to maximal plantarflexion in late stance (Figure 21).

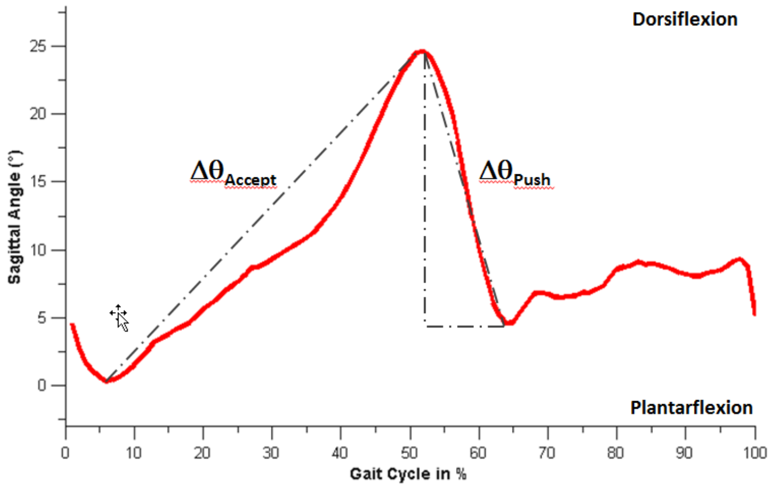

Figure 21. Illustration depicting a typical sagittal ankle angle curve for an injured limb during a single gait cycle and the two lines used to determine the rate of angular change during weight acceptance (Slope 1, $\Delta\theta_{Accept}$) and propulsive push-off (Slope 2, $\Delta\theta_{Push}$).

The rate of angular change during weight acceptance was significantly higher in INJ compared to CON limbs (Table 10) for SWB patients at all time points, but was not significantly different within the limbs of the EWB patients. The rate of angular change during push-off was not found to be different between the INJ and CON limbs as well as between the two rehabilitation groups for the first two time points. However, at 16 weeks post-op,

INJ angular rates were found to be similar between EWB and SWB for both time points.

Early WB	**8 Weeks (n=6)**			**12 Weeks (n=5)**			**16 Weeks (n=3)**		
	INJ	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
Slope 1 (°/% gait cycle)	0.47 ± 0.11	0.38 ± 0.04	0.057 §	0.52 ± 0.03	0.42 ± 0.08	0.08 §	0.47 ± 0.07	0.44 ± 0.06	0.098 §
Slope 2 (°/% gait cycle)	-1.12 ± 0.68	-1.18 ± 0.21	0.819	-1.68 ± 0.33	-1.44 ± 0.24	0.08 §	-1.73 ± 0.49	-1.46 ± 0.04	0.005*
Standard WB	**8 Weeks (n=8)**			**12 Weeks (n=7)**			**16 Weeks (n=7)**		
	INJ	**CON**	**P-value**	**INJ**	**CON**	**P-value**	**INJ**	**CON**	**P-value**
Slope 1 (°/% gait cycle)	0.49 ± 0.08	0.40 ± 0.08	0.008*	0.51 ± 0.05	0.45 ± 0.09	0.014*	0.53 ± 0.07	0.44 ± 0.09	0.005*
Slope 2 (°/% gait cycle)	-1.23 ± 0.58	-1.42 ± 0.28	0.252	-1.64 ± 0.44	-1.58 ± 0.27	0.654	-1.84 ± 0.36	-1.60 ± 0.23	0.056 §

Table 10. Summarized results showing the rates of angular change for each rehabilitation group with regards to weight acceptance (Slope 1) and during push-off phases (Slope 2).

5.5 Clinical Results

There was a tendency for a lower calf circumference in EWB patients on the INJ side at 8 weeks (36.7 ± 2.7 cm vs. 37.8 ± 1.8 cm, p = 0.052), and also at 12 weeks (36.8 ± 3.3 cm vs. 38.2 ± 2.7 cm, p = 0.066). The three measured EWB patients had lower INJ calf circumference that was not significant at 16 weeks (36.8 ± 3.3 cm vs. 38.2 ± 2.7 cm, p = 0.066, n=3). Significant differences in neither proximal nor distal thigh circumference were found at any time point for the EWB group.

In the SWB patients, no significant difference in calf circumference was found at 8 weeks post-op (37.8 ± 3.9 cm vs. 38.7 ± 4.0 cm, p = 0.167). However, the INJ calf was significantly smaller in circumference at 12 weeks (37.4 ± 3.3 cm vs. 38.7 ± 4.2 cm, p = 0.042) and at 16 weeks (36.9 ± 4.0 cm vs. 38.8 ± 4.4 cm, p = 0.017). Similar to the EWB patients, no significant differences in neither proximal nor distal thigh circumference were found at any time point in the SWB patients.

The AOFAS scores at 8 weeks post-OP were significantly lower in EWB patients (51.3 ± 12.3 points, out of 100) than in SWB patients (66.8 ± 11.4 points, p = 0.031). At 12 weeks, both the EWB (76.6 ± 11.2 points) and SWB patients (77.5 ± 17.7 points, p = 0.921) had improved to a similar level. Comparable improvements in AOFAS scores were also found at 16 weeks in EWB (86.7 ± 5.7 points) and SWB patients (88.1 ± 12.7 points, p = 0.856).

The Thermann scores at 8 weeks post-OP were similarly low in EWB (37.7 ± 8.3 points out of 100) and SWB patients (36.3 ± 12.4 points, p = 0.814). These scores were then improved at 12 weeks in both EWB (46.9 ± 10.5 points) and SWB patients (53.0 ± 16.7 points, p = 0.429). At 16 weeks, the scores were on average higher in EWB (72.7 ± 12.7 points) compared to SWB patients (56.4 ± 16.0 points, p = 0.160), but were not significantly different.

The ATRS scores at the 8 week time point were also similarly mediocre in EWB (49.7 ± 10.9 points out of 100) and SWB (44.6 ± 20.6 points, $p = 0.597$). These scores increased at 12 weeks post-op in both EWB (63.0 ± 16.0 points) and SWB (56.4 ± 23.2 points, $p = 0.59$) and progressed upwards at 16 weeks (EWB: 83.7 ± 10.4 points vs. SWB: 72.3 ± 19.9 points, $p = 0.386$).

The VAS scores for pain showed that patients presented at 8 weeks with some pain in both EWB (1.9 ± 0.6 points out of 10, with 10 as the worst pain) and SWB cohorts (1.7 ± 1.6 points, $p = 0.742$). Patients in the EWB group had on average less pain at 12 weeks (0.9 ± 0.7 points), whereas some patients in the SWB group had more pain at the same time (2.2 ± 2.5 points, $p = 0.524$). At 16 weeks, EWB patients continued to report lower pain (0.4 ± 0.4 points) as did SWB patients (0.9 ± 1.0 points, $p = 0.667$).

The VAS scores for injury-based restriction at 8 weeks were mediocre in both EWB (4.2 ± 1.5 points out of 10, with 10 as the most restriction) and SWB patients (4.3 ± 1.9 points, $p = 0.778$). At 12 weeks after surgery, both groups showed improvement, with similar results in the EWB (2.6 ± 1.6 points) and SWB patients (3.5 ± 2.4 points, $p = 0.496$). At 16 weeks, the VAS scores continued the trend for lower scores in both EWB (1.0 ± 1.0 points) and SWB patients (2.1 ± 1.6 points, $p = 0.304$).

5.6 Discussion

This aim of this study was to determine the temporal effect of WB rehabilitation on AT and MTU function after percutaneous ATR repair through early, objective assessment of both single limb and bipedal *in vivo* AT and ankle function. To our knowledge, this is the first multiple timepoint, short-term investigation of AT structure and function immediately after surgical repair of an ATR. The primary biomechanical results and their clinical implications are discussed below.

5.6.1 The effect of weightbearing on strength and moment production

Our first hypothesis in this study postulated that EWB would lead to improved strength on the INJ ankle in moment production and strength in both single-limb and bipedal assessments. The results presented here found that between 8 and 12 weeks, EWB patients were able to make significant gains in MVIC production during single-limb strength assessments. SWB patients did have strength gains, but this difference was not found to be significant. With this in mind, it EWB could potentially ensure earlier strength gains compared to SWB patients, thus supporting the first part of this hypothesis.

Furthermore, EWB patients appeared to achieve slightly more symmetric biplanar moments compared to SWB patients at 8 weeks. At this first measurement plantarflexion and inversion moments were significantly lower on the SWB patients' INJ limb compared to the CON. Furthermore, the SWB patients' maximal dorsiflexion moment was significantly higher on INJ. At the same time point, EWB patients had no significant differences, but rather a tendency for a lower INJ plantarflexion moment during gait. This suggests that at 8 weeks, EWB patients may be more slightly capable of generating more symmetrical forces during gait than SWB patients. However, this effect was quickly lost by the next measurement at 12 weeks, as the majority of moments in both rehabilitation groups were found to be similar on both INJ and CON.

Surprisingly, the absolute INJ moments from both single-limb and bipedal assessments yielded no significant differences upon comparison of EWB and SWB at all time points. It was expected that EWB patients would be able to generate an overall higher force on the INJ ankle, but this was not the case. In fact, absolute MVIC values showed that all patients able to achieve similar levels similar levels of INJ plantarflexor strength at 8, 12, and 16 weeks. For instance, EWB had a significant gain in single-limb strength between 8 and 12 weeks, whereas SWB did not. However, during gait, ALL patients were able to produce a symmetric bipedal moment at 12 weeks. This finding suggests that significant single-limb strength gains did not necessarily lead to more improvement in symmetric bipedal force production. It has been suggested that gains in early rehabilitation should target specific biomechanical gains in the weakness of the triceps surae [139], but a focus on only single-limb weakness may not necessarily correlate to improved symmetry during gait. Since all patients were able to achieve completely symmetric moment production during gait at 12 weeks, this questions the specific effectiveness of early strengthening and WB rehabilitation to facilitate faster functional gains on the injured limb.

An important factor that may influence these results during gait is the activation and recruitment of other neighboring muscle groups involved in walking. Unfortunately, it was not possible to measure EMG in these patients. Previous work suggests that there may be compensatory muscle activation that contributes to the overall plantarflexion moment. For instance, the flexor hallucus longis, which lies deeper in the shank, has been shown to increased EMG activation in ATR patients compared to healthy controls [140]. Other work shows that during walking, there were also different activation patterns in integrated EMG in ATR patients. These patterns appeared to have increased activation on the lateral gastrocnemius at 6 months, and of the medial gastrocnemius at 12 months post ATR, but no differences were found in the iEMG activation of the tibialis anterior [141]. It could be that these alternative activation patterns result in an overall symmetric reaction moment at the ankle, in order to compensate for muscle weakness at the triceps surae and a lengthened AT.

5.6.2 The effect of rehabilitation on the MTU and AT

The type of rehabilitation did not appear to make a difference with regards to AT structure within the MTU, rejecting our second hypothesis, which postulated that EWB patients would demonstrate a longer rest AT length compared to the SWB cohort. It was thought more aggressive WB rehabilitation would lead to higher strains *in vivo* during gait, thus leading to lengthening of the AT, as well as altered changes in AT properties. This did not seem to be the case, as both patient cohorts had similar changes over time.

It could be argued however, that since both cohorts presented with similar INJ ankle moments during bipedal gait, the day-to-day loads on the INJ AT between the two rehabilitation groups did not differ. The only difference was specifically in the rehabilitation treatment that occurred only for a few hours per week. This allows us to deduce that the excess loads on the AT brought on by EWB rehabilitation is not harmful to the patient by increasing the rest AT length compared to the more conservative loads applied during SWB.

A limitation of this work is that though the patients were prescribed a specific group of exercises (Appendix, **Section 9.5**); no specifications were made with regards to the intensity or duration of each exercise. Recent work in healthy subjects has shown that specific types of training intensity and volume can induce adaptations in the AT [142]. Since this was not controlled in the AT patients, this may lead to different adaptations in response to the rehabilitative training. Another further limitation is that though patients were encouraged to engage full WB, it was not possible to monitor the relative amount of WB that each patient actually applied during day-to-day activities. Though the amount of WB could be controlled in the physiotherapy sessions, it could not be controlled outside these appointments. Furthermore, patients were given the direction to apply “pain-adaptive” WB during the rehabilitative period. Pain thresholds can vary greatly from patient-to-patient, and those with a lower threshold will preferentially limit WB and activation of the INJ limb. To date, there are no subjective markers or standards for quantifying pain, thus any standardization made in the future is likely limited to the relative amount of WB.

Future work with a larger sample size could monitor day-to-day WB application, normalized to the patients' bodyweight. Another important aspect to investigate in subsequent studies should assess the effect of a standardized rehabilitation intensity and volume during the first few months post-operation, and compare this standard to the current "pain-adaptive" WB rehabilitation protocol presented here. These measures could allow for further investigation of the effect of WB on adaptations in the AT and MTU post-ATR.

5.6.3 Ankle mobility during gait

Our third hypothesis postulated that EWB patients will exhibit higher ankle mobility and more gait symmetry than SWB patients. The results in the sagittal plane found no significant differences between the EWB and SWB patients' INJ ankle ROM at any measured point. Furthermore, no differences between the maximal INJ ankle angles between the groups were found. This indicates that regardless of rehabilitation, all patients in this study were able to achieve the same amount of ankle mobility on the INJ ankle at all measurements, which rejects the first part of this hypothesis.

However, analysis of gait symmetry showed a few striking differences between the two rehabilitation groups. A quick overview of the spatiotemporal parameters from both patients shows that SWB patients demonstrate significantly more asymmetries when compared to the EWB patients. One of the most striking differences between the two rehabilitation groups is found step length. All patients present at 8 weeks with a significantly shorter CON step length. This occurs because in order to bring the CON limb forward, the INJ limb must bear the entire patient's BW during the CON swing phase. Since the INJ limbs are weaker, very often, the CON step length is shorter. EWB patients quickly corrected this asymmetry and no significant differences were found at 12 weeks. On the other hand, SWB patients continued to have a significantly lower CON step length at all measurements. With this in mind, EWB does appear to support more gait symmetry with regards to spatiotemporal gait parameters compared to SWB, supporting the second part of this hypothesis.

Gait symmetry was also taken into account with regards to ankle kinematics, in which no differences were found between the groups. All measured patients presented with lower end-stance plantarflexion on the INJ ankle compared to CON, which is likely due to a combination of weakness in the triceps surae muscles and the lowered capability of the AT to transfer force. All patients also demonstrated a lowered rotational ROM in the first two measurements, which is likely due to readjusting to walking with more degrees of freedom in the ankle joint. It is highly likely that patients are unused to walking with higher rotational mobility, as the walker boot limits movement within this plane. Considering that rehabilitation did not greatly affect the absolute kinematics during gait, these results do not support the second part of this hypothesis.

Further analysis of the rate of angular change during gait indicates that there is a significant difference between the two rehabilitation groups, particularly during weight acceptance early in the stance phase. INJ limbs in SWB patients consistently exhibited a significantly higher slope than their counterpart CON limbs. This indicates that during early stance, SWB patients reach maximal dorsiflexion much faster on INJ than on CON. This rapid angular change likely indicates eccentric weakness and lower motor control in the plantarflexor muscles, which control the advancement of the tibia over the static foot during midstance. These results indicate significant gait asymmetries, thus supporting the second part of this hypothesis.

In summary, the third hypothesis was not completely supported by these results. The first portion of the hypothesis was rejected, as ankle mobility on INJ was found to be similar between both rehabilitation groups. However, the second portion of the hypothesis was not fully supported. On one hand, SWB patients demonstrated more asymmetries in both spatiotemporal gait parameters and in the rate of angular change during weight acceptance in gait, yet both patient groups demonstrated similar asymmetries with regards to ankle angles. This indicates that EWB does not necessarily lead to complete symmetry compared to SWB, but may allow for comparably more gait symmetry.

5.6.4 Clinical implications

The results of this study have some important implications for clinical treatment of the post-ATR patient. First of all, since excessive tendon lengthening was not found in EWB patients, this protocol could be used without further exacerbating tendon lengthening found in SWB patients. EWB allows for patients to ensure faster strength gains between weeks 8 and 12 post-op. These EWB patients also have shown have a moderately faster return to symmetric moment production during gait. Thus there is some indication that EWB could lead to a faster recovery.

However, this could also lead to a sense of false security in the patients and lead to further injury by pushing their injured AT and affected MTU beyond their functional limitations. Clinicians and physiotherapists should motivate patients to engage in more activity but should minimize certain activities within 16 weeks, such as ball sports and sprinting.

On the other hand, patients treated EWB have poorer clinical outcomes at an earlier time point compared to SWB, mostly due to pain from the aggressive rehabilitation. This leads to a trade-off for the patient: a slightly faster return to function comes at the cost of more pain. Since these patients were only monitored up to 16 weeks post-op, it remains unclear if more painful rehabilitation leads to higher complications in the medium- and long-term after the surgery. However, the clinical scores were already quite similar between the two rehabilitation groups at 16 weeks, so this additional pain may be only limited to the initial few weeks of the protocol.

As mentioned earlier, future investigations should include monitoring patient compliance of WB during day-to-day activities. Ideally sensors would be placed into the walker boot that would be able to monitor in-shoe WB continuously during the rehabilitation period. Furthermore, it remains unclear if these early interventions also lead to long-term changes. Future studies could endeavor to assess patients at both short-term and long-term timespans to examine the direct effect of early interventions on long-term outcomes.

5.7 Conclusion

The primary aim of this work was to assess the temporal effect of weight bearing on short-term biomechanical and structural gains in the healing Achilles tendon following percutaneous repair. The results of this study indicate that EWB may ensure strength gains between the 8^{th} and 12^{th} weeks post-surgery compared to SWB. Furthermore, EWB patients exhibit an earlier reduction of gait asymmetries compared to SWB at 8 weeks post-op, and the more aggressive EWB treatment does not appear to have a negative effect on AT structure by increasing rest AT length. However, functional assessments lead to increasingly similar results between the two rehabilitation groups starting at 12 weeks post-op. The moderate functional improvements from EWB early in the rehabilitative period come at the cost of increased pain for the patient, as found in patient-reported clinical scores. EWB treatment is a safe and potentially more effective option for ATR treatment, if patients are willing to trade early pain for a faster recovery.

6 Adaptations in the Muscle-Tendon Unit with time after ATR

Current ATR treatments aim to recapitulate pre-injury AT structure and function, yet the results shown in Chapter 4 of this work indicate that patients continue to present with significant asymmetries. Some previous clinical studies report that ATR patients continue to report functional deficits, most dramatically in professional athletes [111,112]. However, it remains unclear how these deficits ultimately develop with time after ATR.

The results from the retrospective study in Chapter 4 indicate that after ATR, there are long-term changes in AT properties and structure, deficits in single-limb strength, along with limited ankle mobility in the sagittal plane during walking and stair navigation on the INJ ankle. Furthermore, the results from the prospective study in Chapter 5 gave insights into the early development of initial functional gains and structural changes in the AT soon after surgical ATR treatment.

The knowledge gathered from Chapters 4 and 5 of this work uniquely allow for a cumulative assessment of functional adaptations following ATR injury and surgical treatment. Since the same methods were employed to measure patients both in the short-term and long-term, it is possible to compare these groups of patients and to gain insights into the development of functional changes that occur after ATR. One of the primary assessments conducted in this chapter will compare short-term results from Chapter 5 to long-term assessments in Chapter 4.

Since it was not possible within this work to measure patients prior to ATR injury, a group of uninjured, young healthy control subjects (n= 8, Age: 27.3 ± 9.6 years old , BMI: 23.2 ± 2.7 kg/m^2,) were also measured in order to gain an insight of how both patient limbs differ from controls.

This central aim of this chapter is to develop an understanding of how post-ATR functional deficits develop with time. In order to accomplish this, results from both the retrospective (Chapter 4) and prospective (Chapter 5) studies are brought together for cumulative analysis. This chapter assesses the development of three different functional deficits from the collected data. First, changes in ankle kinematics and mobility during gait are examined in Section 6.1. Secondly, Section 6.2 includes a discussion of *in vivo* AT function and changes in strength at the different time points. Finally, structural assessments of both AT rest length and estimated MTU length during gait are examined in Section 6.3.

6.1 Changes in ankle mobility

In consideration of the results from Chapters 4 and 5, ankle mobility across the comparison groups was limited to two planes: the sagittal plane and the frontal plane. Since limited differences were found in transverse plane kinematics, this information is excluded. Furthermore, ankle angles in control subjects were not found to be significantly different between the dominant and non-dominant limbs. For clarity, all kinematic parameters from the controls were merged into a single group.

6.1.1 Sagittal plane

Comparison of the short-term measurements to the long-term measurements found that not only INJ but also CON limbs present with significantly lower maximum plantarflexion angles soon after injury **(Figure 22)**. Similarly, all short-term measurements were found to have significantly lower plantarflexion angles than control subjects. No significant differences were found between the control subjects and both limbs in long-term measurements.

Maximal dorsiflexion angles for all short-term and long-term INJ patient measurements were found to be significantly higher from the controls (**Figure 23**). The CON limb only demonstrated significantly higher dorsiflexion during gait at 8 weeks post-op, but afterwards was found to exhibit angles similar to the controls.

When assessing the overall changes in sagittal ROM, both INJ and CON limbs demonstrate lower ROM at 8 weeks post-op compared to controls (**Figure 24**). Furthermore, at 12 weeks post-op, the CON limbs of patients demonstrated a ROM lower than at 2-6 weeks. Though lower levels of significance were found, there appears to be a trend that patients initially have a limited ROM on both limbs but are able to improve this with time post-op, up to means that are similar to those found in control subjects.

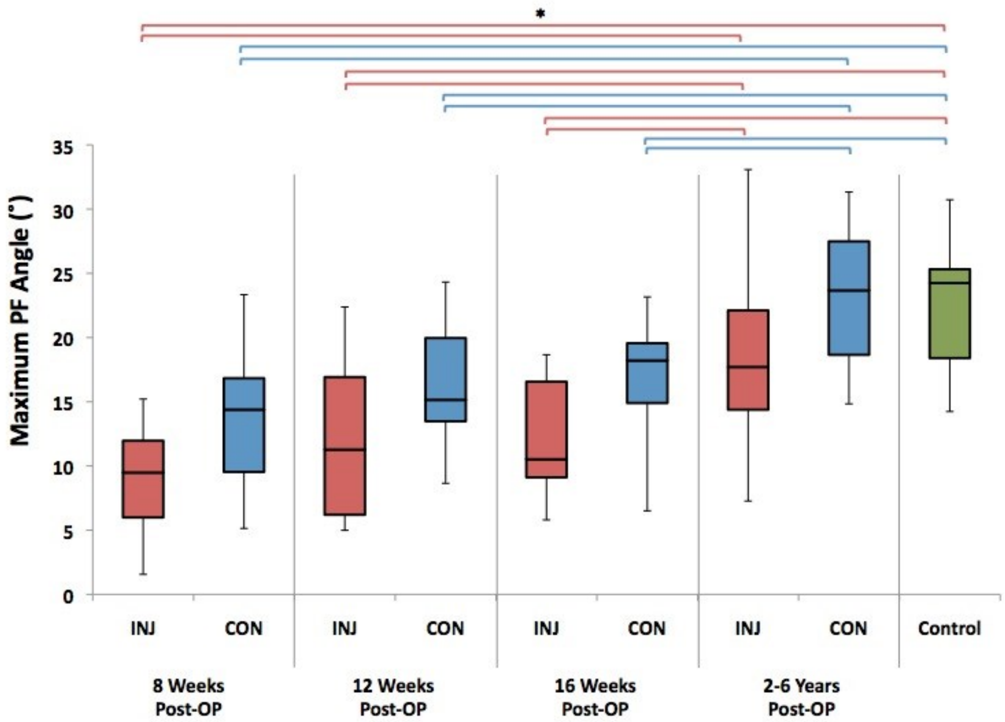

Figure 22. Summary of the maximal plantarflexion (PF) angles for all patient measurements and the control group. For all figures in this chapter, asterisks (*) indicate significant group differences with $p < 0.05$. Red brackets indicate significant differences involving INJ and/or the control values. Blue brackets involve CON and/or the control values.

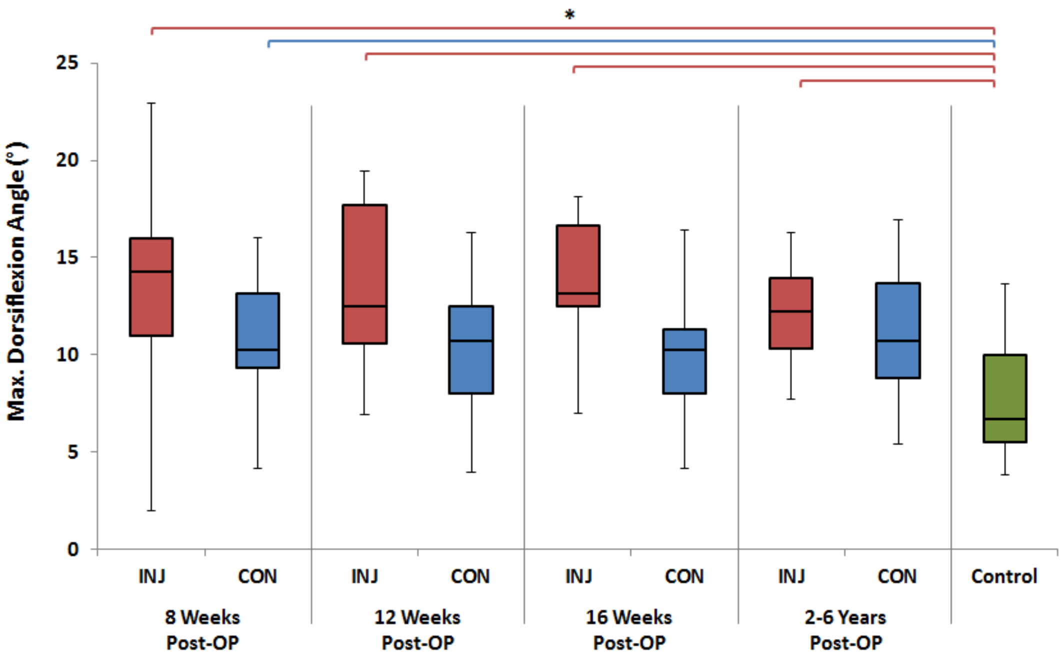

Figure 23. Summary of the maximal dorsiflexion angles for all patient measurements and controls.

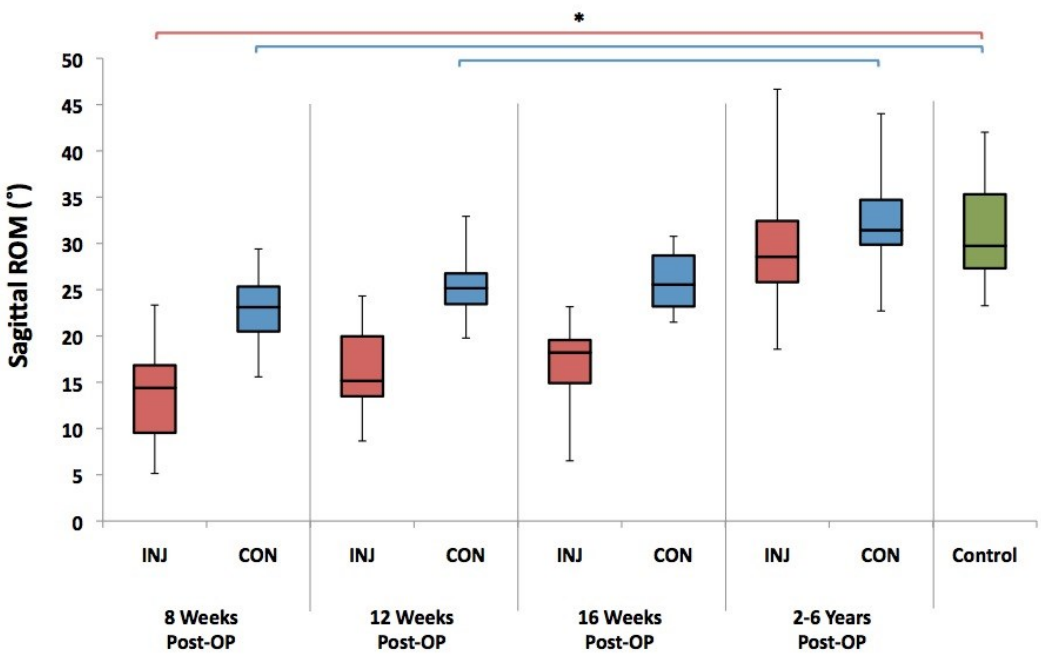

Figure 24. Summary of the sagittal range of motion (ROM) for all patient measurements and controls.

Within the sagittal plane measurements, it is likely that initial weakness in the INJ triceps surae muscles lead to a lower maximal plantarflexion angle and a lower ROM on the affected limb. The potential cause for consistently higher dorsiflexion values in the INJ limb may stem from a longer AT rest length in the MTU. What was most striking was that though the CON limb was not directly affected by the injury, there were significant differences between CON and control limbs in short-term measurements, particularly in maximal plantarflexion. This could be due to a mirroring effect soon after injury, in which CON kinematics are adapted to more closely match those on INJ.

6.1.2 Frontal plane

In this section, analysis of the frontal plane will be limited to the ROM, in which significant differences and trends were found across measurement points. All short-term INJ and CON patient limbs were also found to have significantly lower frontal plane ROMs than their long-term counterparts (**Figure 25**).

Both INJ and CON patient limbs were found to have a significantly lower frontal ROM than the controls at 8 weeks post-op, and this trend continued at 12 weeks post-op significant differences were only found between CON limbs and controls. Both INJ and CON patient limbs measured at 2-6 years post-op were also significantly different to control patients. Surprisingly, these patients had significantly higher frontal plane ROMs than controls, in contrast to the short-term patient limbs.

These results indicate a shift in frontal plane ankle mobility between the acute rehabilitation phase and long-term recovery. It was unexpected that patients would exhibit higher frontal plane mobility compared to controls. However, if other neighboring muscle groups adapt with time to compensate for a weaker, dysfunction AT-triceps surae MTU, this could lead to altered kinematics in the frontal plane. Muscles that make smaller contributions to ankle plantarflexion are also important in controlling inversion and eversion, particularly the tibials posterior and peroneus longus muscles.

The tibialis posterior is a deep muscle lies deep in the posterior compartment of the lower limb and is also activated during gait to contribute towards ankle plantarflexion, albeit with a smaller contribution compared to the AT-triceps surae MTU. The tibialis posterior also plays an important role in inversion of the foot; thus, increased activation of this muscle could both assist in plantarflexion and increase inversion. Another possiblity is the peroneus longus muscle, located in the lateral compartment of the lower limb. In addition to assisting with plantarflexion, this muscle is involved in ankle eversion; thus, increased activation could also lead to increased eversion.

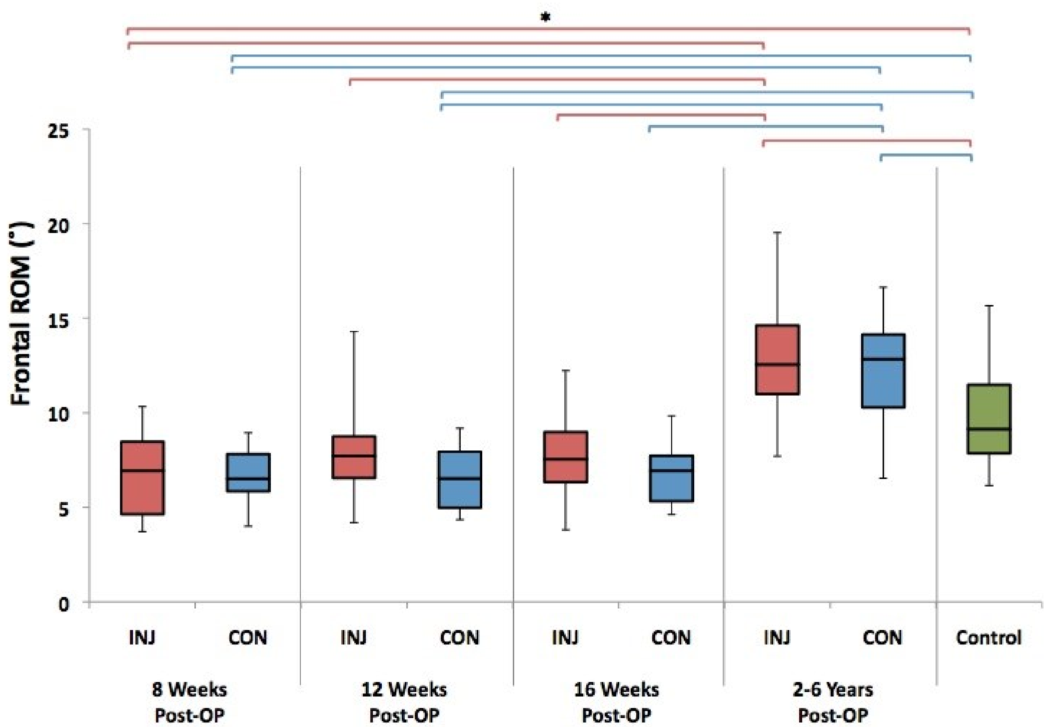

Figure 25. Summary of the maximal plantarflexion (PF) angles for all patient measurements and the control group.

6.2 Changes in strength and AT properties

6.2.1 Maximum voluntary isometric contractions (MVICs)

Comparison of all MVICs across all patient measurements to both long-term measurements and controls yielded limited differences among the INJ limbs (**Figure 26**). Maximal single-limb INJ strength at the initial 8-week time point was significantly lower than both the long-term INJ measurement and controls. For clarity, both non-dominant and dominant control limbs were combined for MVICs, ankle moments, and tendon stiffness, as no significant differences were found.

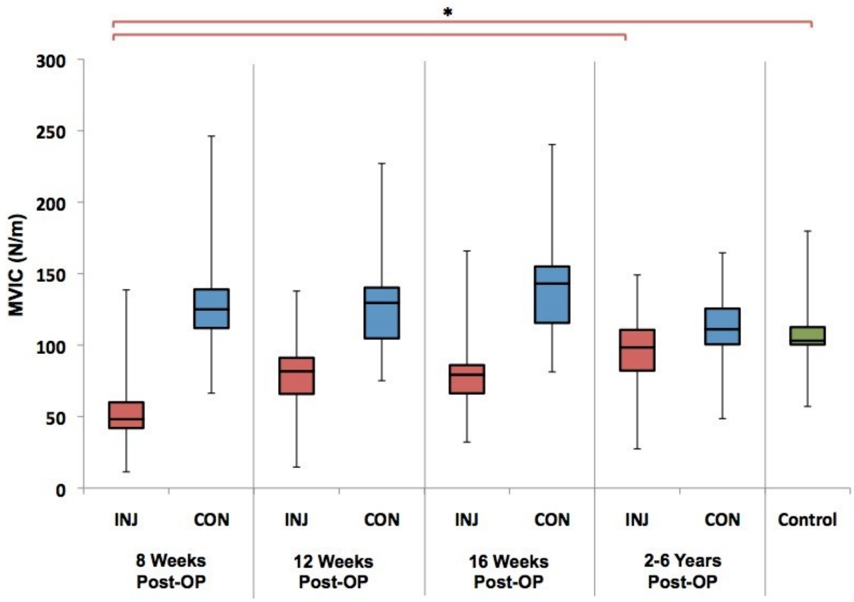

Figure 26. Summary of the maximal MVIC efforts for all patient measurements and the control group.

6.2.2 Ankle moments during gait

Upon comparison of plantarflexion moment during gait, no significant differences on the INJ limb were found, but significant differences were found with regards to CON (Figure 27). The CON limb demonstrated significantly higher moments at 8 weeks post-op compared to 16 weeks and 2-6 years post-op, as well as compared to controls. This may be due to the added dependence and burden on CON during gait in the early stages of rehabilitation, due to early weakness on INJ.

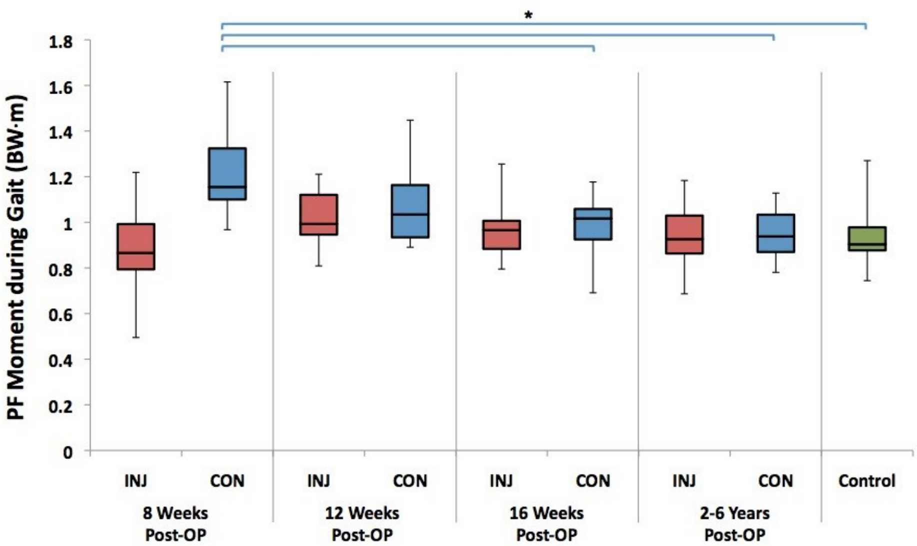

Figure 27. Summary of the maximal plantarflexion (PF) moments during gait for all patients and the control group.

6.2.3 Tendon stiffness

When comparing tendon stiffness across all groups, all INJ short-term measurements were found have significantly lower stiffness than both long-term INJ values and controls (**Figure 28**). No differences were found between the INJ long-term stiffness and the controls. Furthermore, all patient CON values were found to be similar to each other and to controls. Similar to frontal plane ROM, patients appear to have lower tendon stiffness closer to injury, but in the long-term, overshoot INJ values past the levels of control subjects.

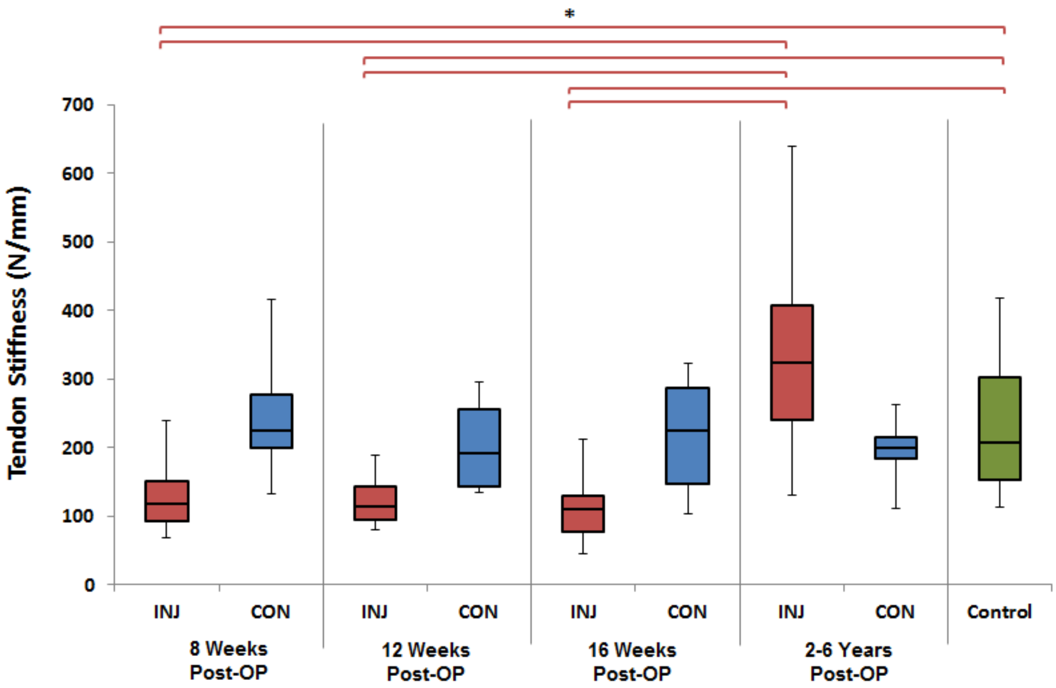

Figure 28. An overview of the mean estimated linear tendon stiffness from all patient and control subject measurements.

A possible explanation for this apparent change in tendon properties may be due to the method used to estimate tendon stiffness. The tracked MTJ movement, or tendon elongation during MVICs, was found to be similar on INJ for all patient groups at all time points. These values were comparatively very low to their noninjured counterparts, which displayed significantly more MTJ movement. But based on the data presented here, patients are likely able to make significant gains in maximal MVIC strength between 8 weeks post-op and in long-term follow-up measurements (Figure 26). Since tendon stiffness is calculated here as estimated tendon force over tendon elongation, the value appears much higher because a higher force is transmitted with minimal tendon elongation. However, since neither cross-sectional area nor volume of the AT could be measured within these studies, there is no information about the stress on the AT and its elastic modulus. Future work should include such measurements in order to gain more sight about the material changes in the healing AT.

6.3 Changes in AT and MTU structure

6.3.1 AT rest length

Comparison of the rest tendon length across all groups showed that all values of INJ and CON in patients are similar to that of controls (**Figure 29**). However, patients showed continued asymmetries at all measurements, with a significantly longer INJ rest AT length. Control AT lengths were separated by limb dominance, but no significant differences were found between these limbs.

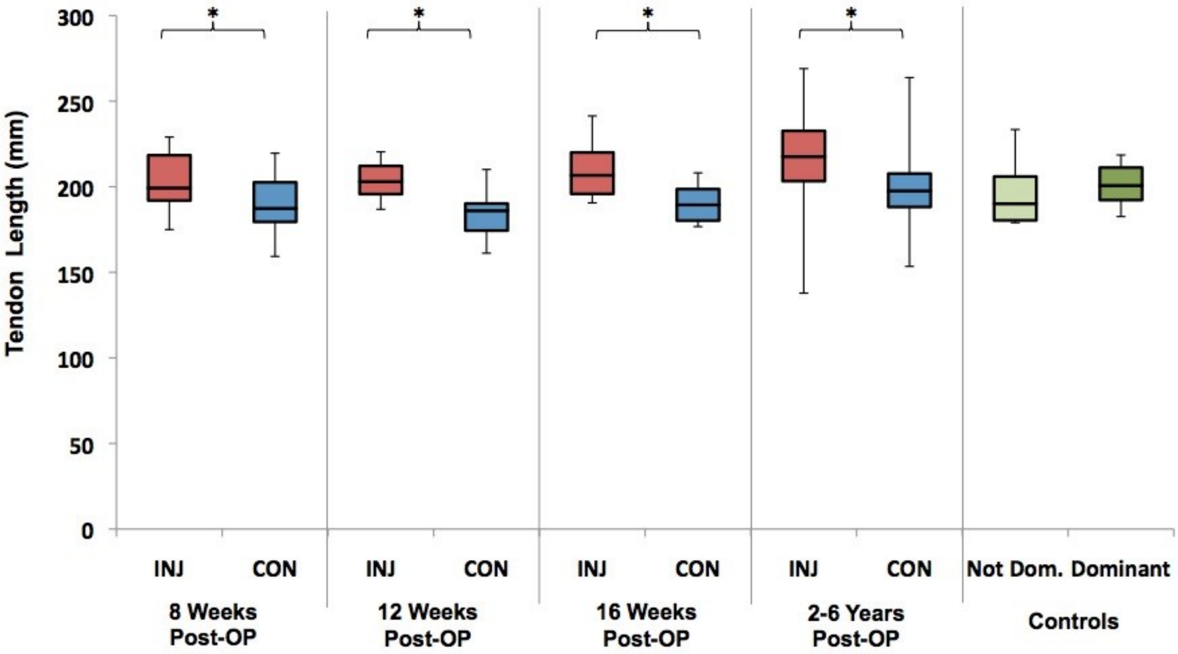

Figure 29. An overview of all rest tendon lengths in patients and controls. Control values are separated into the non-dominant (Not Dom.) and dominant limbs.

6.3.2 Estimated changes in MTU length during gait

The mean estimated MTU length changes on the INJ and CON limbs were calculated for all patients at all time points. For clarity, comparisons were limited to the sagittal plane and only conducted between the patients and the control angles. Since no significant differences were found between the dominant and non-dominant sagittal angles in the control subjects, these were combined into a single group. The overall curves showing the changes in MTU length, compared to a rest length assumed at 90˚ of knee flexion and a 90˚ ankle angle, are summarized in .

At 8 weeks post-op, INJ limbs have significantly higher angles at 4-10% and 45-78% of the gait cycle compared to controls. At the same time, CON values were also higher at 4-10%, 43-77% and 96-97% of the gait cycle. Compared to controls, INJ limbs had higher angles at 1-6%, 39-77%, and 94-100% and CON also had higher angles at 2-74% and 94-98% of the gait cycle at 12 weeks post-op. Furthermore INJ continued to have higher angles at 16 weeks post-op at 6%, 40-74%, and 93-99%, and CON similarly displayed higher angles at 6-78% and 93-99% of the gait cycle. Finally, in a comparison of the long-term patients to controls, both INJ and CON were found to have significantly higher angles than controls throughout the entire gait cycle. This result indicates that there is a significant shift in changes in MTU length developed over time post-injury. This shift affects both limbs and greatly differs from noninjured MTU dynamics.

When looking at the overall change in MTU length, both INJ and CON limbs display significantly lower values at 8 weeks post-op compared to both long-term patient measurements and control values (Figure 30). At 12 weeks post-op, only the MTU length change was still significantly lower on INJ compared to long-term MTU mobility on INJ.

Upon assessment overall MTU shortening during gait, all patient measurements were found to have a lower capacity for shortening compared to controls, except for the long-term CON limb (Figure 32). When short-term measurements were compared to the long-term measurements, both INJ and CON had significantly lower shortening capacities at 8 weeks post-op compared to their long-term counterparts. This was limited to only the INJ limb at 12 weeks post-op. The combination of a slightly longer, possibly more slack AT with triceps surae weakness likely contributes to this lowered capacity.

A striking finding was found in comparisons of maximum MTU lengthening during gait, which was found to be significantly higher in both INJ and CON limbs than in control limbs at all time points (Figure 33). This may be due in part to the increased rest AT length on INJ compared to CON in found in all patients. Though patients presented with significantly interpatient asymmetries on INJ, theses values were not significantly different from controls (**Figure 29**). Since knee flexion and extension is used to calculate these values, it is likely that there may also be increased knee flexion in patients during gait that may contribute to higher MTU lengthening.

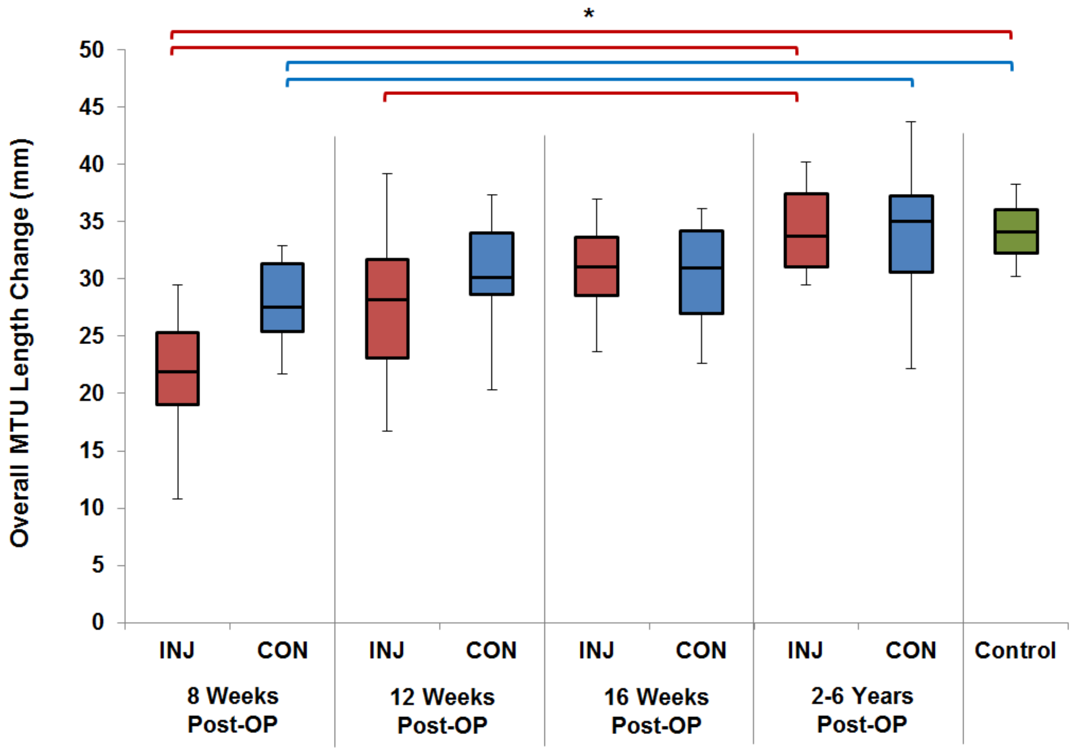

Figure 30. Summary of the overall estimated length change during gait, from maximum shortening to maximal lengthening.

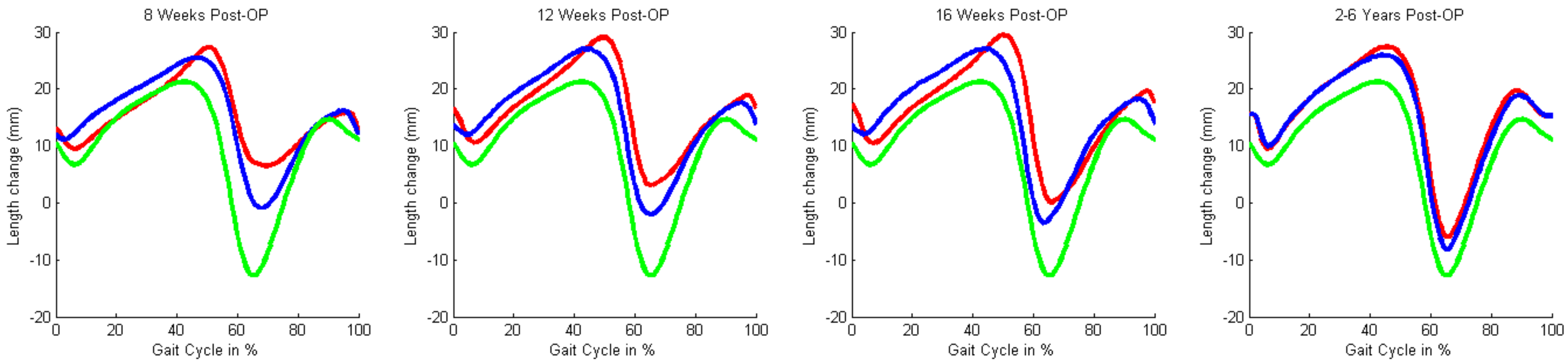

Figure 31. Traces of the mean estimated MTU length changes for INJ (red) and CON (blue) limbs over the gait cycle for each measurement point. Control (green) limbs displayed are identical in each graph. Positive values indicate MTU lengthening and negative values indicate overall MTU shortening.

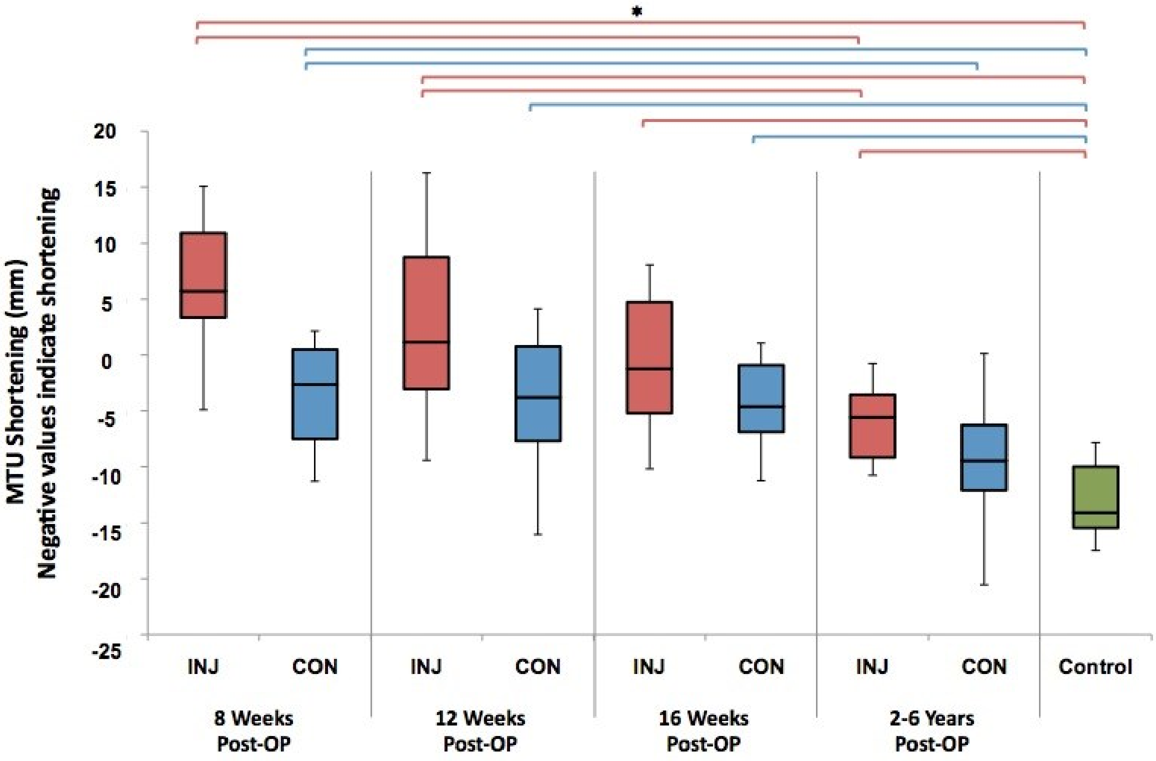

Figure 32. An overview of maximum estimated MTU shortening during gait in all subjects.

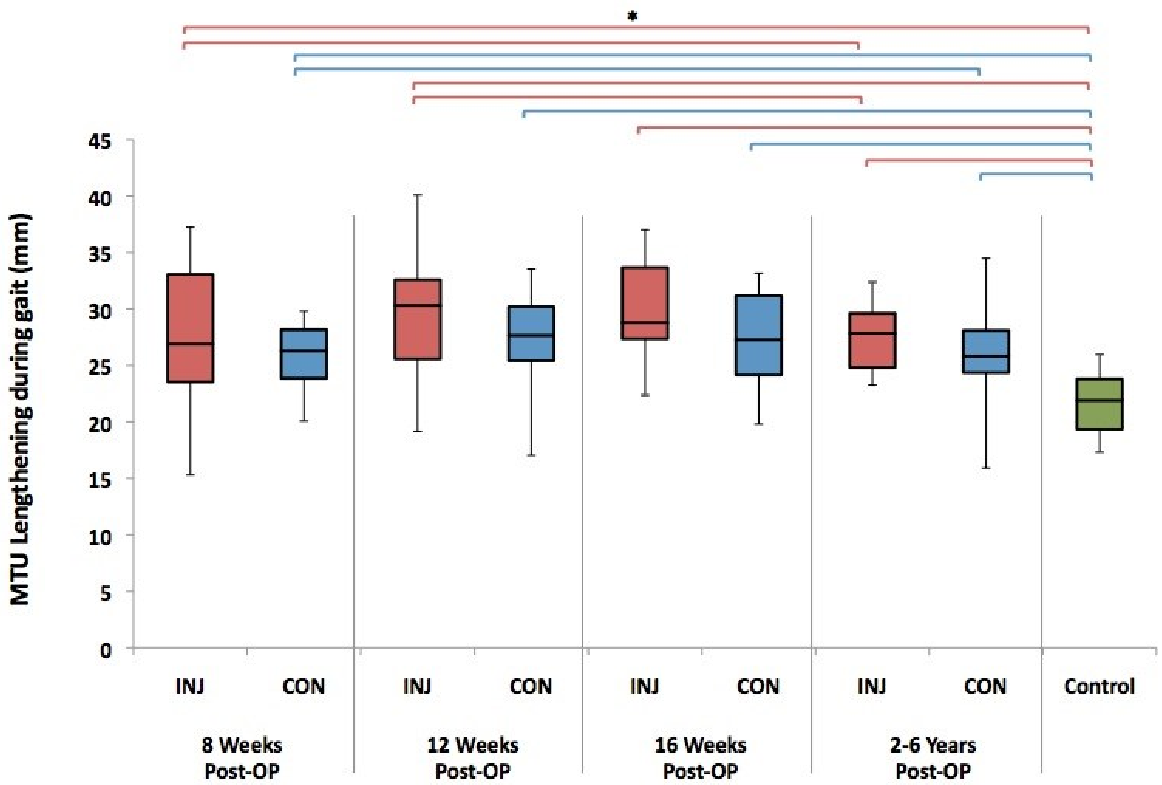

Figure 33. An overview of maximum estimated MTU shortening during gait in all subjects.

7 Conclusion

The AT plays a significant role in joint movement and muscle function within the MTU [25], and its unique, optimized mechanical properties allow for high efficiency during forward movement [25,33–36]. ATR injury introduces significant changes in AT tissue cellularity [79] and organization [61], suggesting that AT function and structure within the MTU are also significantly different on the affected limb.

Prior to this work, investigations on post-ATR adaptations in the AT and MTU were limited to medium and long-term measurements, and a specific timeline of functional adaptations after ATR was not established. Furthermore, previous studies often utilized the uninjured CON limb as a comparison group for a healthy control, but it remained unverified if CON limbs were truly indicative of noninjured function in bipedal assessments. Only by understanding of the adaptations that occur in both single-limb and bipedal MTU biomechanical function can an ideal rehabilitative intervention be developed in order to recapitulate pre-injury function as closely as possible.

This thesis addressed these deficits in knowledge directly through analysis of both single-limb and bipedal MTU and ankle function in ATR patients at multiple time points, as well as in a separate control cohort of uninjured subjects. The body of this work characterized the structural and biomechanical changes that occur in the AT after ATR, and the implications on overall MTU function in both the short-term and in the long-term. Furthermore, the effect of early WB, an often-suggested physiotherapeutic intervention, was assessed for its comparative efficacy in restoring post ATR-MTU function during the rehabilitative period.

As a conclusion to this dissertation, the major contributions and implications of this work are summarized in Sections 7.1 and 7.2, respectively. An outlook for future research based upon the results from this body of work is then presented in Section 7.3.

7.1 Contributions

The primary contributions of this dissertation to the existing body of knowledge on post-ATR adaptations in the MTU and ankle function are the following:

- *In vivo* measurement of the AT rest length at multiple time points demonstrated that the INJ AT is longer than CON at rest after surgery. This work confirms that post-ATR tendon lengthening occurs within 8 weeks post-op. This unilateral change in MTU structure remains present and unchanged in ATR patients for years after injury and surgical repair.

- ATR patients develop significant changes in sagittal plane kinematics after injury when compared to control subjects. The sagittal plane exhibits a shift to higher dorsiflexion and lower plantarflexion that develops with time after injury. This shift in ankle mobility begins as early as 8 weeks post-op, as excessive dorsiflexion already occurs at this time point.

- A concurrent investigation of frontal plane kinematics found that ATR patients exhibit a lower ROM in the short-term compared to control subjects. Patient frontal plane ROM increases with time, ultimately surpassing that ROM ranges found in controls.

- The MTJ movement monitored during MVICs was found to be lower on the INJ MTU compared to CON, and appears to remain lower than CON at most time points. This indicates that the maximal strain imposed on the INJ AT is considerably lower than on CON.

- ATR patients consistently exhibit lower MVIC strength on the INJ limb compared to CON, but these differences are more pronounced in the early stages post-op. MVIC strength appears to increase on INJ with time. Long-term measurements indicate that the INJ limb can produce similar MVICs to control subjects.

- Though ATR patients because stronger through rehabilitation, a higher force is transferred over the INJ AT but with limited changes in overall AT strain and MTJ movement. As a result, the estimated tendon stiffness in the INJ AT is initially lower than CON in the short-term, but ultimately surpasses both CON and controls in the long-term.

- To the best of our knowledge, this is the first work to successfully characterize early functional adaptations in bipedal gait in ATR patients. This investigation found that soon after injury, patients often reach maximal plantarflexion in the initial landing phase of gait but not during terminal stance. Furthermore, characterization of early gait using maximal plantarflexion angles would not reflect this changed dynamic.

- This work successfully employed motion analysis to estimate MTU length changes during gait at multiple time points. This assessment indicates that patients are unable to shorten the MTU early after gait, but are able to increase this capacity with time. There is also a trend towards higher MTU lengthening and lower MTU shortening after injury, while maintaining a similar ROM compared to controls.

- The implementation of EWB rehabilitation can ensure faster, significant gains in single-limb maximal strength compared to SWB between 8 and 12 weeks post-op. EWB patients also reach higher functional symmetry during gait at an earlier time point compared to SWB.

- The increased INJ AT rest length is an early adaptation in the MTU that occurs soon after surgery, and higher INJ AT stiffness develops in the long-term. INJ AT properties appear to adapt in response to the combination of a longer AT, low AT strain, and increased applied tension from the triceps surae muscles.

- Both changes in MTU structure and limitations on single-limb maximal function after ATR are unilateral and limited to the INJ side. Bipedal function, however, appears to be altered similarly in both the INJ and CON limbs. MTU length changes and ankle kinematics in ATR patients are nearly symmetric between the INJ and CON limbs in the long-term, but exhibit significant deviations from uninjured controls.

7.2 Implications

The results from this work have several important implications for future functional and biomechanical investigations of ATR patients. This dissertation implies that after ATR, functional adaptations are not only limited to the INJ limb, but are extended to the CON limb as well. This implies that there may be significant adaptations occurring in motor control, which depend on bilateral symmetry of the two limbs. There may be a mirror effect that occurs after ATR, in which the CON limb adapts and alters its overall ankle function to reflect the altered function in the INJ limb, even though the *in vivo* properties and structure of the MTU are significantly different.

An important implication of this work is that limiting bipedal assessments of post-ATR function to a comparison of INJ to CON limbs could lead to misinterpreted results. The comparisons in Chapter 6 signify that both INJ and CON show altered function compared to controls. If uninjured controls are excluded, it is likely that patients will appear to have nearly symmetric function during bipedal gait, as seen in Chapter 4.

Another implication of this work is that though some gains in single-limb INJ strength were made with time, this was often not reflected in plantarflexion moment during bipedal gait. This is likely due to the low relatively low demands placed on the MTU during this movement. In fact, this assessment of this task showed that on average, patients exhibited similar plantarflexion moments during gait on INJ compared to control patients. This implies that maximal single-limb plantarflexion efforts may not be an effective measure to determine the day-to-day loading of the MTU after surgery.

Since large long-term changes in the INJ linear AT stiffness were found in patients after ATR, it is highly likely that the inherent mechanical properties of the INJ tendon are also altered with time. Since the volume and elastic modulus of the AT could not be investigated within this work, the higher linear AT stiffness found here suggest that these properties are significantly different to both the CON limb and controls.

Finally, a long-term trend towards increased frontal plane ROM on both limbs in ATR patients compared to controls implies that other muscle groups have increased their contribution to ankle plantarflexion. Thus, with time, the affected limb must engage neighboring muscle groups to maintain function and articulation of the ankle joint. Though it remains unclear exactly how these activation patterns change with time, this result suggests that the triceps surae muscles in series appear incapable of recapitulating their full pre-injury function after ATR.

7.3 Outlook

Though this work was able to elucidate many of the adaptations that occur after ATR, the contributions and implications from these results provide a basis for future investigations of the MTU following ATR. Such future work could be categorized as either basic science investigations or clinical cohort studies.

Clinical studies are limited in their capability to histologically determine changes that occur in both the healed AT tissue and the connected triceps surae muscles in series, due to concerns from ethics committees. Thus future investigations of muscle-tendon dynamics after ATR could focus on how both muscle and tendon alter their tissue and cellular structure with time after repair and healing. Often such basic science studies have only focused on either the muscle or the tendon, but as these tissues are highly dependent on each other, theses tissues should be monitored together. The first strides have already been made in animal models that mimic tendon transfer or shoulder surgery. Rabbit experiments found asynchronous adaptations in muscle and tendon in models of tendon tensioning surgery [143]. If such models were performed in an ATR model with a longer time scale, this would help to further our understanding of what exactly occurs between the short-term and long-term results presented here.

With regards to clinical studies, the results from these smaller cohorts can offer a foundation for both larger cohorts of ATR patients to be recruited for both short-term and long-term assessments. This dissertation was able to analyze data from separate cohorts of ATR patients in the immediate period after injury and years afterwards. If the same patients could be measured in both the short-term and in the long-term, this would allow for more concrete evidence for the adaptive behavior suggested here.

Furthermore, large patient cohorts could allow for a more in-depth investigation of the effects of both age and sex on post-ATR changes in the MTU. Muscle structure [144], tendon adaptation [145], and triceps surae neuromechanical properties [146] have been found to be significantly different in men and women. Increased age also affects the mechanical properties of plantarflexor muscles [147] and AT compliance [148]. It remains unclear how these cofactors play a role in rehabilitation of the ATR, and information from such investigations could improve and personalize future interventions to enhance post-injury recovery.

Studies with larger patient cohorts could also elucidate the effect of WB more closely by monitoring patient compliance by measuring day-to-day WB using a sensor in the walker boot. Limiting measurements only to those gathered in a motion analysis laboratory may not necessarily reflect the daily demands and loads placed on the limb. Furthermore, usage of an in-boot sensor would allow for data collection of WB to begin at a much earlier time point that at 8 weeks post-op. Since animal studies suggest that higher WB within the first two weeks, correlating to the inflammatory phase of tendon healing, could lead to better outcomes, this method can compare levels of early WB to functional results. Future research will seek to further understand the effects of specific, controlled WB and strength interventions on bilateral MTU structure and function, building on this base of knowledge to continue optimization of the rehabilitation process for ATR patients.

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9 Appendix

9.1 List of abbreviations used

ANOVA	analysis of variance
AT	Achilles tendon
ATR	Achilles tendon rupture
BMI	body mass index
BW	body weight
CON	contralateral side
DF	dorsiflexion
EMG	electromyography
EWB	early weight bearing
FPA	foot progression angle
FWB	full weight bearing
GM	gastrocnemius medius muscle
GL	gastrocnemius lateralis muscle
INJ	injured side
MTU	muscle-tendon unit
MVIC	maximal voluntary isometric contraction
PF	plantarflexion
ROM	range of motion
SOL	soleus muscle
SWB	standard weight bearing
TA	tibialis anterior muscle
WB	weight bearing

9.2 Ethical approval

All patient protocols were approved by the local ethics committee (Ethikkomission der Charité-Universitätsmedizin Berlin) and were developed in accordance with the Declaration of Helsinki. The two approved studies are listed below, with original titles and an unofficial translation in English.

- **EA/2/094/11**: Eine prospective Studie zur Bestimmung der funktionellen Anpassung nach perkutaner Achillessehnnaht. [*A prospective study to determine the functional adaptation after percutaneous Achilles tendon suture.*]

- **EA/2/095/11**: Funktionelles Outcome nach perkutaner Achillessehnnaht. Eine retrospektive Studie. [*Functional outcome after percutaneous Achilles tendon suture. A retrospective study.*]

9.3 Associated peer-reviewed publications and presentations

9.3.1 Published in scientific journals

- **Agres AN**, Duda GN, Gehlen TJ, Arampatzis A, Taylor WR, Manegold S. “Increased unilateral tendon stiffness and its effect on gait 2-6 years after Achilles tendon rupture.” Scand J Med Sports. 2015. 25(6):860-867.

- Sharenkov A, **Agres AN**, Funk JF, Duda GN, Boeth H. “Automatic initial contact detection during overground walking for clinical use.” Gait Posture. 2014. 40(4):730-4.

9.3.2 Planned submissions

- Manegold S, Gehlen T, Tsitsilonis S, Knoechel J, Duda GN, **Agres AN**. "Tendon elongation and muscular atrophy after percutaneous Achilles tendon repair alter gait pattern." In preparation.

- **Agres AN**, Duda GN, Gehlen TJ, Arampatzis A, Taylor WR, Manegold S. "The temporal effect of full weight bearing on gait and tendon biomechanics at 8 and 12 weeks after Achilles tendon rupture." In preparation.

- Manegold S, Gehlen T, Tsitsilonis S, Duda GN, **Agres AN**. "Higher functional symmetry but lower subjective outcomes associated with early weightbearing after Achilles tendon rupture."

- **Agres AN**, Duda GN, Gehlen TJ, Arampatzis A, Taylor WR, Manegold S. "A comparison of short-term and long-term biomechanical deficits after Achilles tendon rupture."

9.3.3 Conference proceedings

"Rehabilitation nach perkutaner Achillessehnennaht: Welchen Einfluss hat die postoperative Vollbelastung?" Bartek B, Gehlen T, **Agres A**, Tsitsilonis S, Wichlas F, Kleber C, Manegold S. Oral presentation at the Deutsche Kongress für Orthopädie und Unfallchirugie (DKOU), October 20-23, 2015, Berlin, Germany.

"Early versus standard weightbearing in Achilles tendon ruptures: An assessment of tendon length and ankle function 8 weeks after percutaneous repair." **Agres AN**, Manegold S, Gehlen TJ, Taylor WR, Arampatzis A, Duda GN. Oral presentation in proceedings of the 61st Congress of the Orthopaedic Research Society (ORS), March 28-31, 2015, Las Vegas, USA.

"Langfristige Einschränkung der Sehnenelastizität und der Gelenkbeweglichkeit nach unilateraler Achillessehnenruptur" Manegold S, **Agres A**, Gehlen T, Tsitsilonis S, Wichlas F, Haas N, Duda G. Oral presentation at the Deutsche Kongress für Orthopädie und Unfallchirugie (DKOU), October 28-31, 2014, Berlin, Germany.

"The Effect of Early & Standard Weightbearing on Achilles Tendon Function 8 Weeks Postsurgery" **Agres AN,** Manegold S, Gehlen TJ, Arampatzis A, Taylor WR, Duda GN. Poster presented at the 3rd International Scientific Tendinopathy Symposium, September 5-6, 2014, Oxford, United Kingdom.

"Previous Achilles Tendon Rupture (ATR) Alters Both Ipsilateral and Contralateral Ankle Kinematics" **Agres AN**, Manegold S, Gehlen TJ, Arampatzis A, Taylor WR, Duda GN. Poster presented at the 7th World Congress of Biomechanics, July 7-11, 2014, Boston, USA.

"Long-term bilateral adaptations in ankle plantarflexion range of motion (ROM) after Achilles tendon rupture" **Agres AN**, Manegold S, Gehlen TJ, Arampatzis A, Taylor WR, Duda GN. Poster presented at the 60th Congress of the Orthopaedic Research Society (ORS), March 15-18, 2014, New Orleans, USA.

"Related deficits in tendon stiffness and ankle mobility after Achilles tendon rupture", **Agres A**, Manegold S, Gehlen T, Arampatzis A, Duda G. Oral presentation in proceedings of the 19th Congress of the European Society of Biomechanics (ESB), August 25-28, 2013, Patras, Greece.

"Related asymmetries in Achilles tendon stiffness and ankle mobility after rupture", **Agres A**, Manegold S, Gehlen T, Arampatzis A, Duda G. Oral presentation in proceedings of the 24th Congress of the International Society of Biomechanics (ISB), August 4-9, 2013, Natal, Brazil.

"Older patients exhibit increased tendon stiffness asymmetry after unilateral Achilles tendon rupture" **Agres AN**, Manegold S, Gehlen TJ, Taylor WR, Arampatzis A, Duda GN. Poster presented at the 59th Congress of the Orthopaedic Research Society (ORS), January 26-29, 2013, San Antonio, USA.

"Deficits in forward propulsion remain 2-5 years after unilateral Achilles tendon rupture", **Agres A**, Taylor WR, Gehlen T, Duda G, Manegold S. Oral presentation in proceedings of the Expert Science Meeting (ESM) August 1-4, 2012, Aalborg, Denmark.

9.4 Clinical score questionnaires

Midfoot Scale (100 Points Total)

Pain (40 points)	
None	40
Mild, occasional	30
Moderate, daily	20
Severe, almost always present	0
Function (45 points)	
Activity limitations, support	
No limitations, no support	10
No limitation of daily activities, limitation of recreational activities, no support	7
Limited daily and recreational activities, cane	4
Severe limitation of daily and recreational activities, walker, crutches, wheelchair	0
Maximum walking distance, blocks	
Greater than 6	5
4-6	4
1-3	2
Less than 1	0
Footwear requirements	
Fashionable, conventional shoes, no insert required	5
Comfort footwear, shoe insert	3
Modified shoes or brace	0
Walking surfaces	
No difficulty on any surface	10
Some difficulty on uneven terrain, stairs, inclines, ladders	5
Severe difficulty on uneven terrain, tairs,inclines,ladders	0
Gait abnormality	
None, slight	10
Obvious	5
Marked	0
Alignment (15 points)	
Good, plantigrade foot, midfoot well aligned	15
Fair, plantigrade foot, some degree of midfoot malalignment observed, no symptoms	8
Poor, nonplantigrade foot, severe malalignment, symptoms	0
Total=	100

American Orthopaedic Foot and Ankle Society
From: http://www.aofas.org/i4a/pages/index.cfm?pageid=3494

Outline of the point breakdown in the overall AOFAS score.

ATRS
(Achilles Tendon Total Rupture Score)

All questions refer to your limitations/difficulties related to your injured Achilles tendon.

Mark with an X in the box which matches your level of limitation!

1. Are you limited due to decreased strength in the calf/Achilles tendon/foot?

0 1 2 3 4 5 6 7 8 9 10

2. Are you limited due to fatigue in the calf/Achilles tendon/foot?

0 1 2 3 4 5 6 7 8 9 10

3. Are you limited due to stiffness in the calf/Achilles tendon/foot?

0 1 2 3 4 5 6 7 8 9 10

4. Are you limited due to pain in the calf/Achilles tendon/foot?

0 1 2 3 4 5 6 7 8 9 10

5. Are you limited during activities of daily living?

0 1 2 3 4 5 6 7 8 9 10

All questions refer to your limitations/difficulties related to your injured Achilles tendon

Mark with an X in the box which matches your level of limitation!

6. Are you limited when walking on uneven surfaces?

0 1 2 3 4 5 6 7 8 9 10

7. Are you limited when walking quickly up the stairs or up a hill?

0 1 2 3 4 5 6 7 8 9 10

8. Are you limited during activities that include running?

0 1 2 3 4 5 6 7 8 9 10

9. Are you limited during activities that include jumping?

0 1 2 3 4 5 6 7 8 9 10

10. Are you limited in performing hard physical labor?

0 1 2 3 4 5 6 7 8 9 10

Total Score:

The full questionnaire used to calculate the Achilles Tendon Rupture Score (ATRS).

9.5 Rehabilitation protocols in detail

<table>
<tr><th>Time</th><th>Early Weightbearing (EWB)</th><th>Standard Weightbearing (SWB)</th></tr>
<tr><td rowspan="2">Within the first week post op</td><td>- Rehabilitation protocols are identical</td><td>- Rehabilitation protocols are identical</td></tr>
<tr><td colspan="2">- All patients receive in-patient physiotherapy and cryotherapy
- Patients begin physiotherapist-assisted gait and stair training with partial weight bearing (WB)
on the injured limb (roughly 15 kg of load) with the assistance of underarm crutches.
- Ankle immobilized at 30° of plantarflexion in a walker boot (Vacoped)
</td></tr>
<tr><td>Week 2 (Two weeks Post-OP)</td><td>- Begin scar tissue massage to prevent adhesions from occurring

- Isometric tension exercises performed in the walker boot

- Therapeutic electric muscle stimulation of gastrocnemius & soleus

- Ergometer cycling, pushing flat-footed with the heel on the pedal

- Additionally prescribed from doctor if necessary:
o Manual therapy
o Phyisiotherapy on exercise/rehabilitation equipment
o Manual lymph drainage

- Exercise 1: Passive and active movement in both upper and lower ankle with a free range of motion with WB.
</td><td>- Begin scar tissue massage to prevent adhesions from occurring

- Isometric tension exercises, patient prone on examination table

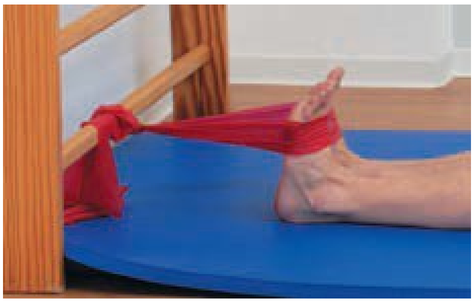
- Therapeutic electric muscle stimulation of gastrocnemius & soleus

- Ergometer cycling, pushing flat-footed with the heel on the pedal

- Additionally prescribed from doctor if necessary:
o Manual therapy
o Phyisiotherapy on exercise/rehabilitation equipment
o Manual lymph drainage

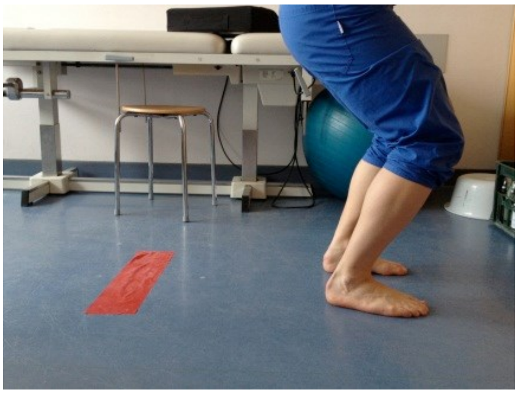
- Exercise 1: Passive and active movement in both upper and lower ankle with a free range of motion with patient lying prone on an examination table.</td></tr>
</table>

Week 2 (continued)	- Exercise 2: Stabilization exercises in the walker boot with WB. Once muscular control is regained, the exercise should be performed out of the walker boot - Exercise 3: Static and dynamic two-legged standing/forward lean exercises on foam mats or combined with other movements for a dual task (head movement, catching, throwing, etc.) with WB within pain tolerance. 	
Week 4	- Therapeutic electric muscle stimulation of gastrocnemius & soleus - Active movement exercises in the upper ankle with free ROM - Begin moderately active stretches of the gastrocnemius and soleus - Continued massage of the scar tissue and soft tissue techniques for adhesion prevention (deep transverse friction massage) should be performed in the tendon and muscle. - Supplementary training on a vibration platform (Galileo platform, Novotec Medical GmbH, Pforzheim, Germany) - All exercises should be performed within pain tolerance. Performing exercises beyond the pain threshold will not improve function and will extend rehabilitation time	- Therapeutic electric muscle stimulation of gastrocnemius & soleus - Active movement exercises in the upper ankle with free ROM - Begin moderately active stretches of the gastrocenmius and soleus - Continued massage of the scar tissue and soft tissue techniques for adhesion prevention (deep transverse friction massage) should be performed in the tendon and muscle. - Supplementary training on a vibration platform (Galileo platform, Novotec Medical GmbH, Pforzheim, Germany) - All exercises should be performed within pain tolerance. Performing exercises beyond the pain threshold will not improve function and will extend rehabilitation time

Week 4 (continued)	- Exercise 4: Strengthening of the plantarflexors and the lower limb with controlledWB:   - Exercise 4 (again – with increased intensity)   - Exercise 5: Static and dynamic two and one-legged stands on different support pads or combined with different movements (head movement, catching, throwing, etc.) 	- Exercise 4: Strengthening of the platnarflexors and the lower limb by providing resistance (manual or Theraband) with patient lying down on examination table – no WB on the injured limb:  

Week 6	- Free range of motion in the upper ankle joint - Further development of stabilization and proprioception through balance board training - Continue moderately active stretching of the gastrocenmius and soleus - All exercises should be performed within pain tolerance. Performing exercises beyond the pain threshold will not improve function and will extend rehabilitation time - Exercise 6: Two-legged and single-legged eccentric strengthening, with and without hanging the heel off a step  - 	- Free range of motion in the upper ankle joint - Active movement exercises in the upper ankle with free ROM - Continue moderately active stretching of the gastrocenmius and soleus - Continue similar exercises as above, which started at week 4. - All exercises should be performed within pain tolerance. Performing exercises beyond the pain threshold will not improve function and will extend rehabilitation time
Week 7	Second control appointment in the clinic - Clinical and sonographic control of the healing wound - Reduction of in-boot plantarflexion (weekly reduction of 10°) - Walker boot not needed to be worn at night	Second control appointment in the clinic - Clinical and sonographic control of the healing wound - Reduction of in-boot plantarflexion (weekly reduction of 10°) - Walker boot not needed to be worn at night - Pain adaptive transition to full weight bearing and weaning off of crutches

Week 7 (continued)	- Exercise 7: Gait training with the removal of the walker boot (start after sonographic examination and follow-up appointment with the operating surgeon at week 7) 	
Week 8	Continue similar exercises as above, which started at week 6. - Additionally prescribed from doctor if necessary: o Manual therapy o Phyisiotherapy on exercise/rehabilitation equipment o Manual lymph drainage	- **Target week of full weightbearing** : - Passive ankle movement exercises up to 0° of dorsiflexion - Exercise 2a: Stabilization exercises in the walker boot with WB. Once muscular control is regained, the exercise should be performed out of the walker boot. - Exercise 2b: o In walker boot: isometric and isokinetic exercises, knee flexion training with resistance o Without walker boot: start strength training of the calf muscles, slow and dynamic, with minimal resistance - Additionally prescribed from doctor if necessary: o Manual therapy o Phyisiotherapy on exercise/rehabilitation equipment o Manual lymph drainage
Week 9	Continue similar exercises as above, which started at week 6. - Additionally prescribed from doctor if necessary: o Manual therapy o Phyisiotherapy on exercise/rehabilitation equipment o Manual lymph drainage	- Once 0° dorsiflexion is achieved, patients can wear their own shoes and no longer need to wear the walker boot. - Patients should be bearing their full weight on the joint throughout the whole day, and the amount of load should be increasing with time. - Additionally prescribed from doctor if necessary: o Manual therapy o Phyisiotherapy on exercise/rehabilitation equipment o Manual lymph drainage

Week 12	– Third appointment at the clinic - If necessary, continuation of soft tissue therapy - Patients may start trying jump exercises at this time - Exercise 8: Two-legged forward hopping exercises 	– Third appointment at the clinic - If necessary, continuation of soft tissue therapy - Begin light jogging training - Begin sport-specific training
Long-term advisory for high-impact sports	- Contact and ball sports (at a competitive level) should not be undertaken until 6 months post-op	- Contact and ball sports (at a competitive level) should not be undertaken until 6 months post-op